

Industria y Comercio  
SUPERINTENDENCIA



Organizacion y  
Digitalizacion CSA Ltda

DELEGATURA DE PROPIEDAD INDUSTRIAL  
DIVISION DE NUEVAS CREACIONES

01-137086

SOLICITUD DE PATENTE DE  
INVENCION

21/37

TITULO: MODULADORES DE LA GAMMA SECRETASA

SOLICITANTE: SCHERING CORPORATION

DIRECCIÓN: 2000 Galloping Hill Road, Kenilworth, NJ 07033-0530 E.U.A.

APODERADO: CARLOS R. OLARTE

BOGOTÁ 01 de Diciembre de 2009

# OLARTE RAISBECK

OLARTE RAISBECK MOURE & CASTRO LTDA.



SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 09-137086- -00000-0000

Fecha: 2009-12-01 16:37:09 Dep. 2020 DIR.NUEVASCR  
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI  
Act. 411 PRESENTACION Folios: 674

## PETITORIO - FORMULARIO

### PATENTE PCT

### ENTRADA EN FASE NACIONAL

P2009/000198

### SOLICITUD DE:

☒

Patente de Invención.

☐

Patente de Modelo de Utilidad.

☒

Capítulo I.

☐

Capítulo II.



**SOLICITANTE**  
(71)

Nombre: SCHERING CORPORATION

Dirección: 2000 Galloping Hill Road, Kenilworth,  
NJ 07033-0530 E.U.A.

Nacionalidad o Domicilio: Estadounidense

Lugar de Constitución: Estados Unidos

Teléfono: \_\_\_\_\_

Fax: \_\_\_\_\_

E-mail: \_\_\_\_\_

### IDENTIFICACIÓN

C.C. ☐

NIT ☐

C.E. ☐

Otro ☐

Cual \_\_\_\_\_

Número \_\_\_\_\_

**REPRESENTANTE**  
**O APODERADO**

Nombre: CARLOS R. OLARTE

Dirección: World Trade Center, Torre A, Calle  
100 No. 8A-37 Piso 10.

Teléfono: 601-7700 Fax: 601-7799

E-mail: office@olarteraisbeck.com

### IDENTIFICACIÓN

C.C. ☒

NIT ☐

C.E. ☐

Otro ☐

Cual \_\_\_\_\_

Número 79.782.747 Btá  
TP 74.295



**INVENTOR (ES)**  
(72)

Nombre: VER PAGINA ADJUNTA

Dirección: VER PAGINA ADJUNTA

Nacionalidad o Domicilio: VER PAGINA ADJUNTA



### PCT (86)

Solicitud Internacional No. PCT/US2008/006734

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Publicación Internacional No. WO 2008/153793

Fecha

Diciembre 18, 2008



### Título (54) MODULADORES DE LA GAMMA SECRETASA

**Clasificación Internacional (51)** C07D 403/10, C07D 471/04, C07D 487/04, C07D  
498/04, A61K 31/4166, A61K 31/517, A61K 31/519, A61K 31/5365, A61P 25/28

### Prioridad

SI

☒

NO

☐

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US

US

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Junio 1, 2007

Noviembre 1, 2007

(31) Número de Solicitud

60/941,405

60/984,484



Comprobante de pago No. 09-

Fecha Diciembre 1 de 2009

10

**ANEXOS**

☒

Comprobante de pago de la tasa de presentación de la solicitud.

☒

Documento que acredita la existencia y representación legal cuando el solicitante sea persona jurídica.

☒

Poderes, si fuere el caso. Adjunto copia simple ver expediente No. 07-132.393

☐

Documento de cesión del inventor al solicitante o a su causante.

☐

Declaraciones.

☒

Copia de la solicitud internacional. (Resumen, descripción, reivindicaciones, dibujos).

☒

Traducción de la solicitud internacional al castellano. (Resumen, descripción, reivindicaciones, dibujos).

☐

Copia del examen preliminar internacional efectuado por la Autoridad Internacional de Examen Preliminar (IPEA).

☐

Traducción del examen preliminar internacional efectuado por la IPEA.

☐

De ser el caso, copia del contrato de acceso.

☐

De ser el caso, documento que acredite la licencia o autorización de uso de conocimientos tradicionales de las comunidades indígenas.

☐

De ser el caso, certificado de depósito del material biológico.

☐

Arte final 12 x 12.

☐

De ser el caso, información sobre otras solicitudes de patente o títulos obtenidos en el extranjero por el mismo titular o su causante, relacionadas parcial o totalmente con la invención de esta solicitud.

☐

De ser el caso, modificaciones efectuadas a la solicitud internacional.

☒

Otros. Búsqueda Internacional.

11

**FIGURA CARACTERÍSTICA:**

12

Solicito la concesión de la patente,

NOMBRE: CARLOS R. OLARTE

FIRMA: 

C.C. 79.782.747 Btā T.P. 74.295

LISTA DE INVENTORES

PCT/US2008/006734

3

1. **Zhaoning ZHU**,  
6 Cypress Court,  
Plainsboro,  
New Jersey 08536  
Estados Unidos  
Nacionalidad: Estadounidense
2. **William J. GREENLEE**,  
115 Herrick Avenue,  
Teaneck,  
New Jersey 07666  
Estados Unidos  
Nacionalidad: Estadounidense
3. **Xianhai HUANG**,  
16 Hemlock Circle,  
Warren,  
New Jersey 07059  
Estados Unidos  
Nacionalidad: China
4. **Brian A. MCKITTRICK**,  
14 Millbrook Road,  
New Vernon,  
New Jersey 07976  
Estados Unidos  
Nacionalidad: Estadounidense
5. **John W. CLADER**,  
428 North Union Avenue,  
Cranford,  
New Jersey 07016  
Estados Unidos  
Nacionalidad: Estadounidense
6. **Mark D. MCBRIAR**,  
14 Crestview Drive,  
Clinton,  
New Jersey 08809  
Estados Unidos  
Nacionalidad: Estadounidense
7. **Anandan PALANI**,  
25 Reinhart Way,  
Bridgewater,  
New Jersey 08807  
Estados Unidos  
Nacionalidad: Estadounidense



## SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176009-2

RECIBO OFICIAL DE CAJA : 09 - 90,209  
FECHA : DICIEMBRE 1 DE 2009

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 09-137086- -00000-0000

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Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI  
Act. 411 PRESENTACION Folios: 674

## \*\*\*\*\* CONSIGNACION \*\*\*\*\*

| DEPOSITANTE    | TIPO PAGO    | BANCO           | CUENTA    | Nº. PAGO  | FECHA PGO  | Vr. PAGO   |
|----------------|--------------|-----------------|-----------|-----------|------------|------------|
| CLARTE RAISBEK | CONSIGNACION | BANCO DE BOGOTA | 062754387 | 130524623 | 01/12/2009 | 540,000.00 |

## \*\*\*\*\* C O N C E P T O \*\*\*\*\*

| CANT. | RENTISTICO  | CONCEPTO                          | TOTAL CONCEPTO |
|-------|-------------|-----------------------------------|----------------|
| 1     | 50005-01-01 | SOLICITUDES                       |                |
| 1     |             | TRAMITES DE SOL. DE PATENTE DE IN | 540,000.00     |
|       |             | TOTAL :                           | \$ 540,000.00  |

SON: QUINIENTOS CUARENTA MIL PESOS

RESPONSABLE :

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. \_\_\_\_\_

**APOSTILLA EN PODER DE REPRESENTACIÓN DE  
SCHERING CORPORATION**

**APOSTILLA**

(Convención de la Haya del 5 de octubre de 1961)

1. País: Estados Unidos de América  
- Este documento Público
2. ha sido firmado por Marguerite La Corte
3. Quien ejerce funciones de Notario público de Nueva Jersey
4. Lleva el sello de Marguertie La Corte Notario

**CERTIFICADO**

5. En Trenton, Nueva Jersey
6. El 29 de agosto 2003
7. Por John E. McCormac Contador Publico- Tesorero de Nueva Jersey
8. No. A 180345
9. Gran Sello del Estado de Nueva Jersey
10. Firma legible de John M.

**PODER DE REPRESENTACIÓN**

Bilingüe inglés- español otorgado en Kenilworth, Nueva Jersey, Estados Unidos, el 7 de agosto de 2003 y firmado por Edward H. Mazer - Director Juridico senior.

**CERTIFICADO NOTARIAL**

Bilingüe inglés- español, fechado el 7 de agosto, 2003 certificando las funciones de Edward H. Mazer - Director Juridico senior, de Schering Corporation.

Las certificaciones anteriores se basan en el Poder de representación fechado el 4 noviembre de 2002.

Sello: Marguerite La Corte- Notario público,  
Estado de Nueva Jersey  
Su comisión vence el 7 de octubre de 2003.  
Sello en alto relieve del Notario Público

---  
Es traducción fiel del inglés, con  
confrontación. Bogotá 5 septiembre, 2003.

copia archivo, para  
*Marlén Neira*  
MARLEN NEIRA CASTRO  
Traductor e Intérprete Oficial  
Inglés - Español - Inglés  
Resolución No. 2117 del 7 Oct 1987

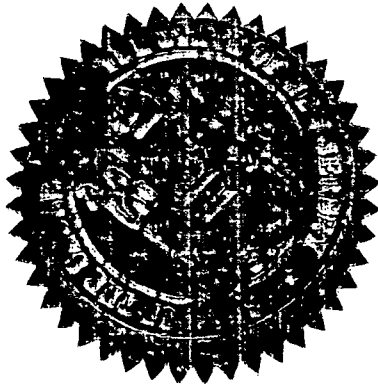
APOSTILLE

(CONVENTION DE LA HAYE DU 5 OCTOBRE 1961)

1. COUNTRY: UNITED STATES OF AMERICA
2. THIS PUBLIC DOCUMENT HAS BEEN SIGNED BY:  
MARGUERITE LA CORTE
3. ACTING IN THE CAPACITY OF:  
NOTARY PUBLIC OF NEW JERSEY
4. BEARS THE SEAL/STAMP OF:  
MARGUERITE LA CORTE, NOTARY

CERTIFIED

5. AT TRENTON, NEW JERSEY
6. THE 29TH DAY OF AUGUST 2003
7. BY: John E McCormac, CPA, NEW JERSEY TREASURER
8. NO. A180345
9. SEAL/STAMP:
10. SIGNATURE



*John E McCormac*

# OLARTE RAISBECK

OLARTE RAISBECK & FRIERI, LTDA.  
LEGAL & PROFESSIONAL SERVICES

WORLD TRADE CENTER - TORRE C  
CALLE 100 No. 8A-55 Piso 10  
BOGOTA, COLOMBIA  
TELEPHONE: +57-1 638-6200  
Fax: +57-1 638-6201

www.olarteraisbeck.com

## Power of Attorney

The undersigned,  
**SCHERING CORPORATION**

domiciled in  
**2000 Galloping Hill Road, Kenilworth, New Jersey 07033-0532, U.S.A.**

by means of these presents hereby grants to **Carlos R. Olarte and/or Ana María Frieri** full and sufficient Power of Attorney to file, prosecute, obtain, defend and enforce any and all of the company's Patents, Utility Models and Industrial Designs in the Republic of Colombia, to which end it empowers them to take all steps necessary before any administrative or judicial authority of any class for the objects stated, to file petitions, appeals, replies and oppositions, pay taxes and annuities, request testimonies, receive documents and securities, abandon applications and collect refunds. Sufficient power is hereby granted to receive notifications on behalf of the Company, to confer powers on those who are to represent the company judicially and extrajudicially, to answer in court in the matter of all claims and demands that may be presented in connection with the objects stated, giving them likewise power to substitute these presents and revoke such substitutions.

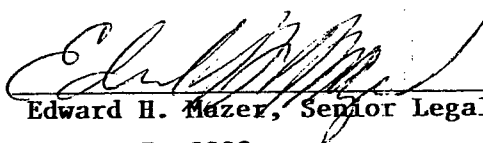
## Poder

El suscrito,

domiciliado en

por medio del presente otorga a **Carlos R. Olarte y/o Ana María Frieri** poder especial, amplio y suficiente para presentar, tramitar, obtener, defender y hacer respetar todas y cualquiera de Patentes, Modelos de Utilidad y Diseños Industriales de la compañía en la República de Colombia, a cuyo efecto los faculta para dar todos los pasos necesarios ante cualquier autoridad administrativa o judicial de cualquier jerarquía para cumplir con lo encomendado, elevar solicitudes, apelaciones, respuestas y oposiciones, pagar impuestos y anualidades, solicitar testimonios, recibir documentos y valores, desistir y percibir. Se concede poder bastante para recibir notificaciones a nombre de la compañía, otorgar poderes a quienes vayan a representar a la compañía judicial y extrajudicialmente, responder en juicio a todas las reclamaciones o demandas que por motivo de lo encomendado se presentaren, dándoles asimismo facultad para sustituir el presente y revocar dichas sustituciones.

Signature/Firma:



**Edward H. Mazer, Senior Legal Director**

Date/Fecha:

**August 7, 2003**

City/Country/Ciudad/Pais: **Kenilworth, New Jersey, U.S.A.**

# OLARTE RAISBECK

OLARTE RAISBECK & FRIERI, LTDA.  
LEGAL & PROFESSIONAL SERVICES

WORLD TRADE CENTER - TORRE C  
CALLE 100 No. 8A-55 Piso 10  
BOGOTA, COLOMBIA  
TELEPHONE: +57-1 638-6200  
Fax: +57-1 638-6201

www.olarteraisbeck.com

## Notarial Certification

On this date, **August 7, 2003**

The undersigned Notary Public certifies:

1. That **Edward H. Mazer**

of legal age and domiciled in

**119 Greenwood Drive, Millburn, New Jersey 07041, U.S.A.**

signed the foregoing document.

2. That the grantor has executed the foregoing document as **Senior Legal Director of SCHERING CORPORATION**

3. That **SCHERING CORPORATION**

having its principal place of business located in

**2000 Galloping Hill Road, Kenilworth, New Jersey 07033-0530, U.S.A.**

is duly incorporated, is currently in existence, and that the purposes for which the Power of Attorney is granted are within the scope of its corporate purposes.

4. That the grantor has the authority to execute the Power of Attorney and that his/her representation is legal.

5. The foundation for my certifications contained in points 2, 3 and 4 was the exhibition of the following authentic document(s):

**Power of Attorney, dated November 4, 2002.**

## Certificación Notarial

En esta fecha,

el Notario Público suscrito certifica:

1. Que

mayor de edad y domiciliado

suscribió el documento que antecede.

2. Que el otorgante ha suscrito el referido documento en su carácter de de

4. Que

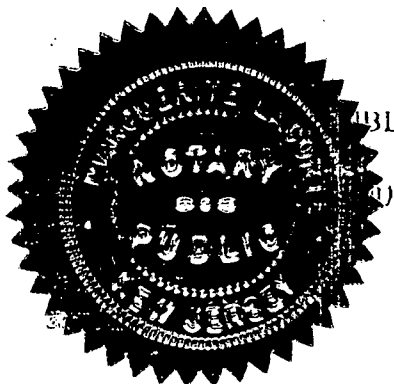
con sede principal ubicada en

**2000 Galloping Hill Road, Kenilworth, New Jersey 07033-0530, U.S.A.**

está legalmente constituida, que tiene existencia legal vigente y que los propósitos para los cuales se otorga el poder se encuentra dentro de los que comprenden su objeto social.

4. Que el otorgante tiene la representación para suscribir el poder, y que ésta es legítima.

5. El fundamento de mis certificaciones contenidas en los puntos 2, 3 y 4 fue la exhibición de los (del) siguiente(s) documento(s) auténtico(s):



PUBLIC (Signature):

*Marguerite La Corte*

Marguerite La Corte

Notary Public of New Jersey

My Commission Expires October 7, 2003

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A61K 31/4166 (2006.01)

(US). PALANI, Anandan [US/US]; 25 Reinhart Way,  
Bridgewater, New Jersey 08807 (US).

(74) Agent: JEANETTE, Henry, C.; Schering Corporation,  
2000 Galloping Hill Road, Patent Dept. K-6-1 1990, Ke-  
nilworth, New Jersey 07033 (US).

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60/984,484 1 November 2007 (01.11.2007) US

(71) Applicant (for all designated States except US): SCHER-  
ING CORPORATION [US/US]; 2000 Galloping Hill  
Road, Kenilworth, New Jersey 07033 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): ZHU, Zhaoning  
[US/US]; 6 Cypress Court, Plainsboro, New Jersey 08536  
(US). GREENLEE, William, J. [US/US]; 115 Herrick  
Avenue, Teaneck, New Jersey 07666 (US). HUANG,  
Xianhai [CN/US]; 16 Hemlock Circle, Warren, New  
Jersey 07059 (US). MCKITTRICK, Brian, A. [US/US];  
14 Millbrook Road, New Vernon, New Jersey 07976 (US).  
CLADER, John, W. [US/US]; 428 North Union Avenue,  
Cranford, New Jersey 07016 (US). MCBRIAR, Mark, D.  
[US/US]; 14 Crestview Drive, Clinton, New Jersey 08809

(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,  
CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE,  
EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID,  
IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC,  
LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN,  
MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,  
PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV,  
SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,  
ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every  
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GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL,  
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CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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(54) Title: GAMMA SECRETASE MODULATORS

(57) Abstract: In its many embodiments, the present invention provides a novel class of heterocyclic compounds of the formula: as  
modulators of gamma secretase, methods of preparing such compounds, pharmaceutical compositions containing one or more such  
compounds, methods of preparing pharmaceutical formulations comprising one or more such compounds, and methods of treatment,  
prevention, inhibition, or amelioration of one or more diseases associated with the central nervous system using such compounds or  
pharmaceutical compositions.

WO 2008/153793 A3

**GAMMA SECRETASE MODULATORS**

5

**Reference to Related Application**

This application claims the benefit of U.S. Provisional Application No. 60/941405 filed June 1, 2007, and of U.S. Provisional Application No. 60/984484 filed November 1, 2007.

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**Field of the Invention**

The present invention relates to certain heterocyclic compounds useful as gamma secretase modulators (including inhibitors, antagonists and the like), pharmaceutical compositions containing the compounds, and methods of treatment using the compounds and compositions to treat various diseases including central nervous system disorders such as, for example, neurodegenerative diseases such as Alzheimer's disease and other diseases relating to the deposition of amyloid protein. They are especially useful for reducing Amyloid beta (hereinafter referred to as A $\beta$ ) production which is effective in the treatment of diseases caused by A $\beta$  such as, for example, Alzheimers and Down Syndrome.

**Background of the Invention**

Alzheimer's disease is a disease characterized by degeneration and loss of neurons and also by the formation of senile plaques and neurofibrillary change. Presently, treatment of Alzheimer's disease is limited to symptomatic therapies with a symptom-improving agent represented by an acetylcholinesterase inhibitor, and the basic remedy which prevents progress of the disease has not been developed. A method of controlling the cause of onset of pathologic conditions needs to be developed for creation of the basic remedy of Alzheimer's disease.

A $\beta$  protein, which is a metabolite of amyloid precursor protein (hereinafter referred to as APP), is considered to be greatly involved in degeneration and loss of neurons as well as onset of demential conditions (for example, see Klein W L, et al *Proceeding National Academy of Science USA*,

Sep. 2, 2003, 100(18), p. 10417-22, suggest a molecular basis for reversible memory loss.

Nitsch R M, and 16 others, *Antibodies against  $\beta$ -amyloid slow cognitive decline in Alzheimer's disease*, Neuron, May 22, 2003, 38(4), p. 547-554)  
5 suggest that the main components of A $\beta$  protein are A $\beta$ 40 consisting of 40 amino acids and A $\beta$ 42 having two additional amino acids at the C-terminal. The A $\beta$ 40 and A $\beta$ 42 tend to aggregate (for example, see Jarrell J T et al, *The carboxy terminus of the  $\beta$  amyloid protein is critical for the seeding of amyloid formation: implications for the pathogenesis of Alzheimer's disease*, Biochemistry, May  
10 11, 1993, 32(18), p. 4693-4697) and constitute main components of senile plaques (for example, (Glenner GG, et al, *Alzheimer's disease: initial report of the purification and characterization of a novel cerebrovascular amyloid protein*, Biochemical and Biophysical Research Communications, May 16, 1984, 120(3), p. 885-90. See also Masters C L, et al, *Amyloid plaque core protein in Alzheimer*  
15 *disease and Down syndrome*, Proceeding National Academy of Science USA, June 1985, 82(12), p. 4245-4249.).

Furthermore, it is known that mutations of APP and presenelin genes, which is observed in familial Alzheimer's disease, increase production of A $\beta$ 40 and A $\beta$ 42 (for example, see Gouras G K, et al, *Intraneuronal A $\beta$ 142 accumulation in human brain*, American Journal of Pathology, January 2000,  
20 156(1), p. 15-20. Also, see Scheuner D, et al, *Nature Medicine*, August 1996, 2(8), p. 864-870; and Forman M S, et al, *Differential effects of the Swedish mutant amyloid precursor protein on  $\beta$ -amyloid accumulation and secretion in neurons and nonneuronal cells*, Journal of Biological Chemistry, Dec. 19, 1997,  
25 272(51), p. 32247-32253.). Therefore, compounds which reduce production of A $\beta$ 40 and A $\beta$ 42 are expected as an agent for controlling progress of Alzheimer's disease or for preventing the disease.

These A $\beta$ s are produced when APP is cleaved by beta secretase and subsequently clipped by gamma secretase. In consideration of this, creation of  
30 inhibitors of  $\gamma$  secretase and  $\beta$  secretase has been attempted for the purpose of



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reducing production of  $A\beta$ s. Many of these secretase inhibitors already known are peptides or peptidomimetics such as L-685,458. L-685,458, an aspartyl protease transition state mimic, is a potent inhibitor of amyloid  $\beta$ -protein precursor  $\gamma$ -secretase activity, *Biochemistry*, Aug. 1, 2000, 39(30), p. 8698-8704).

Also of interest in connection with the present invention are: US 2007/0117798 (Eisai, published May 24, 2007); US 2007/0117839 (Eisai, published May 24, 2007); US 2006/0004013 (Eisai, published January 5, 2006); WO 2005/110422 (Boehringer Ingelheim, published November 24, 2005); WO 2006/045554 (Cellzone AG, published may 4, 2006); WO 2004/110350 (Neurogenetics, published December 23, 2004); WO 2004/071431 (Myriad Genetics, published August 26, 2004); US 2005/0042284 (Myriad Genetics, published February 23, 2005) and WO 2006/001877 (Myriad Genetics, published January 5, 2006).

There is a need for new compounds, formulations, treatments and therapies to treat diseases and disorders associated with  $A\beta$ . It is, therefore, an object of this invention to provide compounds useful in the treatment or prevention or amelioration of such diseases and disorders.

## Summary of the Invention

In its many embodiments, the present invention provides a novel class of heterocyclic compounds as gamma secretase modulators (including inhibitors, antagonists and the like), methods of preparing such compounds, pharmaceutical compositions comprising one or more such compounds, methods of preparing pharmaceutical formulations comprising one or more such compounds, and methods of treatment, prevention, inhibition or amelioration of one or more diseases associated with the  $A\beta$  using such compounds or pharmaceutical compositions.

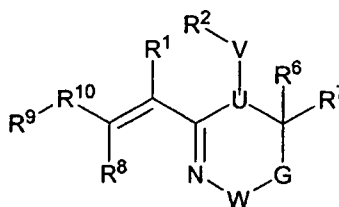
The compounds of this invention (Formula I) can be useful as gamma secretase modulators and can be useful in the treatment and prevention of

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diseases such as, for example, Alzheimers disease, mild cognitive impairment (MCI), Downs Syndrome, Glaucoma (Guo et.al., Proc. Natl. Acad. Sci. USA 104, 13444-13449 (2007)), Cerebral amyloid angiopathy, stroke or dementia (Frangione et al., Amyloid: J. Protein folding Disord. 8, suppl. 1, 36-42 (2001),

5 Microgliosis and brain inflammation (M P Lamber, Proc. Natl. Acad. Sci. USA 95, 6448-53 (1998)), Olfactory function loss (Getchell, et.al. Neurobiology of Aging, 663-673, 24, 2003).

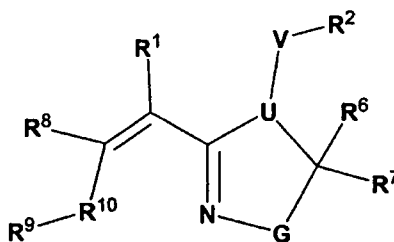
This invention provides compounds of formula I:



Formula I

wherein  $R^1$ ,  $R^2$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ , G, U and W are as defined below.

In one embodiment, the present application discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in Formula IA:



Formula IA

wherein  $R^1$ ,  $R^2$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ , G, U and V are as defined below.

The compounds of Formula I can be useful as gamma secretase modulators and can be useful in the treatment and prevention of diseases such as,

20 for example, central nervous system disorders such as Alzheimers disease and Downs Syndrome.

This invention also provides compounds of formula I.

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This invention also provides pharmaceutically acceptable salts of the compounds of formula I.

This invention also provides pharmaceutically acceptable esters of the compounds of formula I.

5 This invention also provides pharmaceutically solvates of the compounds of formula I.

This invention also provides compounds of formula I in pure and isolated form.

This invention also provides compounds of formula I in pure form.

10 This invention also provides compounds of formula I in isolated form.

This invention also provides compounds 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1..

15 This invention also provides compounds 1 to 20 (i.e., the compounds in Table 1).

This invention also provides compounds 1 to 20, and 23.

This invention also provides compounds 21, 22, and 24.

20 This invention also provides pharmaceutical compositions comprising an effective amount of one or more (e.g., one) compounds of formula I, or a pharmaceutically acceptable salt, ester or solvate thereof, and a pharmaceutically acceptable carrier.

25 This invention also provides pharmaceutical compositions comprising an effective amount of one or more (e.g., one) compounds of formula I, or a pharmaceutically acceptable salt, ester or solvate thereof, and an effective amount of one or more (e.g., one) other pharmaceutically active ingredients (e.g., drugs), and a pharmaceutically acceptable carrier.

30 This invention also provides a method for modulating (including inhibiting, antagonizing and the like) gamma-secretase, comprising administering an effective (i.e., therapeutically effective) amount of one or more compounds of formula I to a patient in need of treatment.

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This invention also provides a method for modulating (including inhibiting, antagonizing and the like) gamma-secretase, comprising administering an effective (i.e., therapeutically effective) amount of a compound of formula I to a patient in need of treatment.

- 5        This invention also provides a method of treating one or more neurodegenerative diseases, comprising administering an effective (i.e., therapeutically effective) amount of one or more compounds of formula I to a patient in need of treatment.

- 10       This invention also provides a method of treating one or more neurodegenerative diseases, comprising administering an effective (i.e., therapeutically effective) amount of a compound of formula I to a patient in need of treatment.

- 15       This invention also provides a method of inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), comprising administering an effective (i.e., therapeutically effective) amount of one or more compounds of formula I to a patient in need of treatment.

- 20       This invention also provides a method of inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), comprising administering an effective (i.e., therapeutically effective) amount of a compound of formula I to a patient in need of treatment.

This invention also provides a method of treating Alzheimer's disease, comprising administering an effective (i.e., therapeutically effective) amount of one or more compounds of formula I to a patient in need of treatment.

- 25       This invention also provides a method of treating Alzheimer's disease, comprising administering an effective (i.e., therapeutically effective) amount of a compound of formula I to a patient in need of treatment.

- 30       This invention also provides a method of treating Alzheimer's disease, comprising administering an effective (i.e., therapeutically effective) amount of one or more compounds of formula I, in combination with an effective (i.e.,

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therapeutically effective) amount of one or more cholinesterase inhibitors (such as, for example, ( $\pm$ )-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1 *H*-inden-1-one hydrochloride, i.e., donepezil hydrochloride, available as the Aricept<sup>®</sup> brand of donepezil hydrochloride), to a patient in need of  
5 treatment.

This invention also provides a method of treating Alzheimer's disease, comprising administering an effective (i.e., therapeutically effective) amount of one or more compounds of formula I, in combination with an effective (i.e., therapeutically effective) amount of one or more compounds selected from the  
10 group consisting of A $\beta$  antibody inhibitors, gamma secretase inhibitors and beta secretase inhibitors.

This invention also provides combinations comprising an effective (i.e., therapeutically effective) amount of one or more compounds of formula I, in combination with an effective (i.e., therapeutically effective) amount of one or  
15 more compounds selected from the group consisting of cholinesterase inhibitors (such as, for example, ( $\pm$ )-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1 *H*-inden-1-one hydrochloride, i.e., donepezil hydrochloride, available as the Aricept<sup>®</sup> brand of donepezil hydrochloride), A $\beta$  antibody inhibitors, gamma secretase inhibitors and beta secretase inhibitors.

This invention also provides a method of treating Alzheimer's disease, comprising administering an effective (i.e., therapeutically effective) amount of a compound of formula I, in combination with an effective (i.e., therapeutically effective) amount of one or more (e.g., one) cholinesterase inhibitors (such as, for  
20 example, ( $\pm$ )-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1 *H*-inden-1-one hydrochloride, i.e., donepezil hydrochloride, available as the Aricept<sup>®</sup> brand of donepezil hydrochloride), to a patient in need of treatment.  
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This invention also provides a method of treating Downs syndrome, comprising administering an effective (i.e., therapeutically effective) amount of one or more compounds of formula I to a patient in need of treatment.

This invention also provides a method of treating Downs syndrome, comprising administering an effective (i.e., therapeutically effective) amount of a compound of formula I to a patient in need of treatment.

This invention also provides a method of treating Downs syndrome,  
5 comprising administering an effective (i.e., therapeutically effective) amount of one or more compounds of formula I, in combination with an effective (i.e., therapeutically effective) amount of one or more cholinesterase inhibitors (such as, for example, (±)-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1 *H*-inden-1-one hydrochloride, i.e., donepezil hydrochloride,  
10 available as the Aricept® brand of donepezil hydrochloride), to a patient in need of treatment.

This invention also provides a method of treating Downs syndrome, comprising administering an effective (i.e., therapeutically effective) amount of a compound of formula I, in combination with an effective (i.e., therapeutically  
15 effective) amount of one or more (e.g., one) cholinesterase inhibitors (such as, for example, (±)-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1 *H*-inden-1-one hydrochloride, i.e., donepezil hydrochloride, available as the Aricept® brand of donepezil hydrochloride), to a patient in need of treatment.

This invention also provides combination therapies for (1) modulating  
20 gamma-secretase, or (2) treating one or more neurodegenerative diseases, or (3) inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), or (4) treating Alzheimer's disease. The combination therapies are directed to methods comprising the administration of an effective amount of one or more (e.g. one) compounds of formula I and the  
25 administration of an effective amount of one or more (e.g., one) other pharmaceutical active ingredients (e.g., drugs).

This invention also provides a method of treating mild cognitive impairment, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

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This invention also provides a method of treating glaucoma, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

5 This invention also provides a method of treating cerebral amyloid angiopathy, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

This invention also provides a method of treating stroke, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

10 This invention also provides a method of treating dementia, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

This invention also provides a method of treating microgliosis, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

15 This invention also provides a method of treating brain inflammation, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

This invention also provides a method of treating olfactory function loss, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

20 This invention also provides pharmaceutical compositions comprising a combination of an effective amount of one or more (e.g., one) compounds of formula I, in combination with an effective amount of one or more compounds selected from the group consisting of cholinesterase inhibitors, A $\beta$  antibody inhibitors, gamma secretase inhibitors and beta secretase inhibitors. The pharmaceutical compositions also comprise a pharmaceutically acceptable carrier.

25 This invention also provides a kit comprising, in separate containers, in a single package, pharmaceutical compositions for use in combination, wherein one

A

container comprises an effective amount of a compound of formula I in a pharmaceutically acceptable carrier, and another container (i.e., a second container) comprises an effective amount of another pharmaceutically active ingredient, the combined quantities of the compound of formula I and the other

5 pharmaceutically active ingredient being effective to: (a) treat Alzheimer's disease, or (b) inhibit the deposition of amyloid protein in, on or around neurological tissue (e.g., the brain), or (c) treat neurodegenerative diseases, or (d) modulate the activity of gamma-secretase.

This invention also provides a kit comprising, in separate containers, in a

10 single package, pharmaceutical compositions for use in combination, wherein one container comprises an effective amount of a compound of formula I in a pharmaceutically acceptable carrier, and another container (i.e., a second container) comprises an effective amount of another pharmaceutically active ingredient (as described below), the combined quantities of the compound of

15 formula I and the other pharmaceutically active ingredient being effective to: (a) treat Alzheimer's disease, or (b) inhibit the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), or (c) treat neurodegenerative diseases, or (d) modulate the activity of gamma-secretase.

20 This invention also provides any one of the methods disclosed above and below wherein the compound is selected from the group consisting of the compounds 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

This invention also provides any one of the methods disclosed above and

25 below wherein the compound of formula I is selected from the group consisting of the compounds 1 to 20, and 23.

This invention also provides any one of the methods disclosed above and below wherein the compound of formula I is selected from the group consisting of the compounds 21, 22 and 24.



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This invention also provides any one of the methods disclosed above and below wherein the compound of formula I is selected from the group consisting of the compounds 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

5        This invention also provides any one of the pharmaceutical compositions disclosed above and below wherein the compound is selected from the group consisting of the compounds 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

10        This invention also provides any one of the pharmaceutical compositions disclosed above and below wherein the compound is any one of the compounds 1 to 20, and 23.

      This invention also provides any one of the pharmaceutical compositions disclosed above and below wherein the compound is any one of the compounds 21, 22 and 24.

15        This invention also provides any one of the pharmaceutical compositions disclosed above and below wherein the compound is any one of the compounds 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

20        Other embodiments of this invention are directed to any one of the embodiments above or below that are directed to formula I, or the use of formula I (e.g. the embodiments directed to methods of treatment, pharmaceutical compositions and kits), wherein the compound is a compound of formula IA instead of formula I. Those skilled in the art will appreciate that the compounds of formula I and formula IA are isomers of each other.

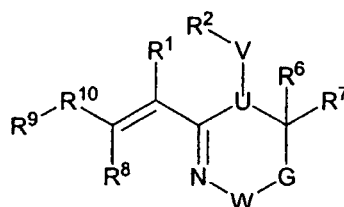
25        This invention also provides any one of the above mentioned methods of treatment wherein the compound of formula I is selected from the group consisting of the compounds in **Table 1**.

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### Detailed Description

In one embodiment, the present invention discloses compounds which are represented by structural Formula I, or a pharmaceutically acceptable salt, solvate, ester or prodrug thereof, wherein the various moieties are described below.

In one embodiment, the present application discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in Formula I:



Formula I

wherein:

either (i) R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or (ii) R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or (iii) R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5

substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; and  $R^2$  and  $R^6$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or (iv)  $R^6$  and either  $R^3$  or  $R^4$  of the  $-C(R^3)(R^4)-$  G moiety, are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or (v)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with said heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; and

U is  $\begin{matrix} \diagup \\ \diagdown \end{matrix} -C(R^5)$  or N;

W is selected from the group consisting of a bond; -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, and -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G is selected from the group consisting of  $-C(R^3)(R^4)-$ , -C(O)- and  $-N(R^{13})-$ , with the proviso that when W is -O- or -S-, G is not  $-N(R^{13})-$  or -C(O)-;

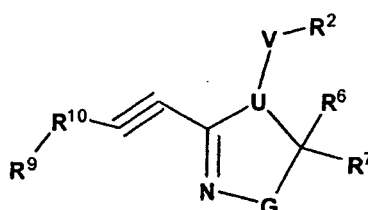
V is selected from the group consisting of a bond, -O-, -C(O)-, and  $-N(R^{14})-$ ;

$R^1$  (when  $R^1$  is not joined to  $R^2$ ),  $R^2$  (when  $R^2$  is not joined to  $R^1$  or  $R^6$ ),  $R^5$ ,  $R^6$  (when  $R^6$  is not joined to  $R^2$ ), and  $R^7$  can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-,



aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or  
 5 optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

or, alternatively,  $R^1$  (when  $R^1$  is not joined to  $R^2$ ) and  $R^8$  are taken together to form a bond (i.e., there is a triple bond between the carbon atom to which  $R^1$   
 10 was bonded to and the carbon to which  $R^8$  was bonded to, i.e., the compound of formula I is a compound of formula II:



formula II

and  $R^2$ ,  $R^5$ ,  $R^6$ , and  $R^7$  are as defined above, and  $R^3$ ,  $R^4$ ,  $R^{11}$  and  $R^{12}$  are as defined below);

15  $R^3$  is selected from the group consisting of H, halo (and in one example, F), -OR<sup>15</sup> (and in one example  $R^{15}$  is H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>),  
 20 S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-  
 25 can be unsubstituted or optionally independently substituted with 1-5 substituents

which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or

$R^3$  and  $R^6$  taken together form a bond (i.e.,  $R^3$  and  $R^6$  form a bond between G and the carbon to which  $R^6$  is bound), provided that when  $R^3$  and  $R^6$  form a bond: (1) W is not a bond, (2)  $R^2$  and  $R^6$  are not joined together to form a cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety (as described in (ii) and (iii) above) (3)  $R^6$  and either  $R^3$  or  $R^4$  of the  $-C(R^3)(R^4)-$  G moiety are not joined together to form a cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety (as described in (iv) above), and (4)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety are not joined together to form a heterocyclyl or heterocyclenyl moiety (as described in (v) above);

$R^4$ ,  $R^{11}$  and  $R^{12}$  can be the same or different, each being independently selected from the group consisting of H, halo (and in one example, F),  $-OR^{15}$  (and in one example  $R^{15}$  is H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

provided that when one of  $R^3$  or  $R^4$  is selected from the group consisting of:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , and  $-N_3$ , then the other is not selected from the

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- group consisting of:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , and  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , and  $-N_3$  (i.e., if one of  $R^3$  or  $R^4$  is  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , or  $-N_3$ , then the other one is not  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , and  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , or  $-N_3$ );
- provided that when one of  $R^{11}$  or  $R^{12}$  is selected from the group consisting of:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , and  $-N_3$ , then the other is not selected from the group consisting of:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , and  $-N_3$  (i.e., if one of  $R^{11}$  or  $R^{12}$  is  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , or  $-N_3$ , then the other is not  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,

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$-\text{S}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})\text{R}^{15}$ ,  $-\text{S}(\text{O})_2\text{R}^{15}$ ,  $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ,  $=\text{NOR}^{15}$ , or  $-\text{N}_3$ ;

- $\text{R}^{13}$  is independently selected from the group consisting of H, alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-,
- 5 arylcycloalkylalkyl-, heteroarylalkylalkyl-, arylheterocycloalkylalkyl-, heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylalkyl-, heterocycloalkyl-, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl, arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylalkyl-, heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-,
- 10 alkynyl, arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-, heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylaryl-, heterocycloalkenylaryl-,  $-\text{OR}^{15}$ ,  $-\text{CN}$ ,  $-\text{C}(\text{O})\text{R}^8$ ,  $-\text{C}(\text{O})\text{OR}^9$ ,  $-\text{S}(\text{O})\text{R}^{10}$ ,  $-\text{S}(\text{O})_2\text{R}^{10}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{11})(\text{R}^{12})$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{11})(\text{R}^{12})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{11})(\text{R}^{12})$ ,  $-\text{NO}_2$ ,  $-\text{N}=\text{C}(\text{R}^8)_2$  and  $-\text{N}(\text{R}^8)_2$ ; and wherein
- 15 said  $\text{R}^{13}$  alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-, arylcycloalkylalkyl-, heteroarylalkylalkyl-, arylheterocycloalkylalkyl-, heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylalkyl-, heterocycloalkyl, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl, arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylalkyl-, heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-,
- 20 alkynyl, arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-, heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylaryl-, and heterocycloalkenylaryl- groups are optionally substituted with 1 to 5 groups independently selected from the
- 25 group consisting of: alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo,  $-\text{CN}$ ,  $-\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{R}^{15}$ ,  $-\text{C}(\text{O})\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{SR}^{15}$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{CH}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{C}(=\text{NOR}^{15})\text{R}^{16}$ ,  $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ,  $-\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{alkyl}-\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,
- 30  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{CH}_2-\text{R}^{15}$ ,  $-\text{CH}_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,

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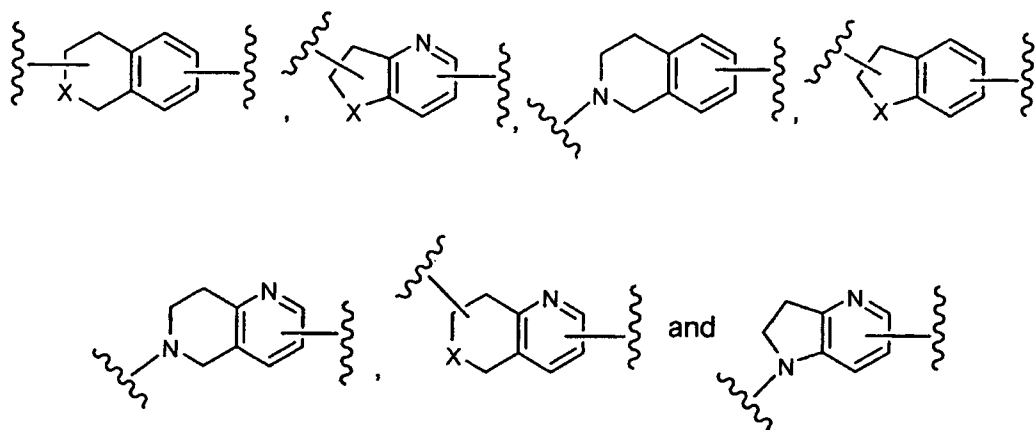
-N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and  
 -S(O)<sub>2</sub>R<sup>15</sup>;

5 R<sup>14</sup> is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, and -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);

10 R<sup>8</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, with each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- being  
 15 unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

R<sup>10</sup> is selected from the group consisting of a bond, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,

20 heteroarylalkyl-, heterocyclyl-, heterocyclalkyl- and the moieties:



where X is O, N(R<sup>14</sup>) or S;



wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl-, heterocyclylalkyl- for  $R^{10}$  as well as the above-noted moieties for  $R^{10}$  can be unsubstituted or optionally independently substituted with 1-3 substituents which

5 can be the same or different, each being independently selected from the group consisting of the moieties shown below; and

$R^9$  is selected from the group consisting of alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-,

10 alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

15  $R^{15}$ ,  $R^{16}$  and  $R^{17}$  are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, arylcycloalkyl-, arylheterocyclyl-,  $R^{18}$ -alkyl,  $R^{18}$ -cycloalkyl,  $R^{18}$ -cycloalkylalkyl-,  $R^{18}$ -heterocyclyl,  $R^{18}$ -heterocyclylalkyl-,  $R^{18}$ -aryl,  $R^{18}$ -arylalkyl-,  $R^{18}$ -heteroaryl and  $R^{18}$ -heteroarylalkyl-;

20  $R^{18}$  is 1-5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl-, arylalkenyl-, arylalkynyl-,  $-NO_2$ , halo, heteroaryl, HO-alkoxyalkyl-,  $-CF_3$ ,  $-CN$ , alkyl-CN,  $-C(O)R^{19}$ ,  $-C(O)OH$ ,  $-C(O)OR^{19}$ ,  $-C(O)NHR^{20}$ ,  $-C(O)NH_2$ ,  $-C(O)NH_2-C(O)N(alkyl)_2$ ,  $-C(O)N(alkyl)(aryl)$ ,  $-C(O)N(alkyl)(heteroaryl)$ ,  $-SR^{19}$ ,  $-S(O)_2R^{20}$ ,  $-S(O)NH_2$ ,  $-S(O)NH(alkyl)$ ,

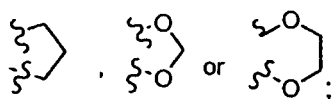
25  $-S(O)N(alkyl)(alkyl)$ ,  $-S(O)NH(aryl)$ ,  $-S(O)_2NH_2$ ,  $-S(O)_2NHR^{19}$ ,  $-S(O)_2NH(heterocyclyl)$ ,  $-S(O)_2N(alkyl)_2$ ,  $-S(O)_2N(alkyl)(aryl)$ ,  $-OCF_3$ ,  $-OH$ ,  $-OR^{20}$ ,  $-O-heterocyclyl$ ,  $-O-cycloalkylalkyl$ ,  $-O-heterocyclylalkyl$ ,  $-NH_2$ ,  $-NHR^{20}$ ,  $-N(alkyl)_2$ ,  $-N(arylalkyl)_2$ ,  $-N(arylalkyl)-(heteroarylalkyl)$ ,  $-NHC(O)R^{20}$ ,  $-NHC(O)NH_2$ ,  $-NHC(O)NH(alkyl)$ ,  $-NHC(O)N(alkyl)(alkyl)$ ,  $-N(alkyl)C(O)NH(alkyl)$ ,

30  $-N(alkyl)C(O)N(alkyl)(alkyl)$ ,  $-NHS(O)_2R^{20}$ ,  $-NHS(O)_2NH(alkyl)$ ,

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-NHS(O)<sub>2</sub>N(alkyl)(alkyl), -N(alkyl)S(O)<sub>2</sub>NH(alkyl) and  
-N(alkyl)S(O)<sub>2</sub>N(alkyl)(alkyl);

or, alternately, two R<sup>18</sup> moieties on adjacent carbons can be linked together

to form: ;

5 R<sup>19</sup> is alkyl, cycloalkyl, aryl, arylalkyl- or heteroarylalkyl-;

R<sup>20</sup> is alkyl, cycloalkyl, aryl, halo substituted aryl, arylalkyl-, heteroaryl or heteroarylalkyl-;

wherein each of the alkyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, alkylaryl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in R<sup>1</sup>, R<sup>2</sup>, R<sup>1</sup>-R<sup>2</sup>, R<sup>2</sup>-R<sup>6</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>14</sup> is independently unsubstituted or optionally substituted by 1 to 5 R<sup>21</sup> groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>,  
10 -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
15 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and -S(O)<sub>2</sub>R<sup>15</sup>;

wherein each of the alkyl, cycloalkenyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in R<sup>21</sup> is independently unsubstituted or substituted by 1 to 5 R<sup>22</sup> groups independently selected from the group consisting of alkyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>),  
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- alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and  
5 -S(O)<sub>2</sub>R<sup>15</sup>.

The statement above: "either (i) R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents  
10 which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or (ii) R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being  
15 substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or (iii) R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or  
20 optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; and R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl  
25 moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or  
(iv) R<sup>6</sup> and either R<sup>3</sup> or R<sup>4</sup> of the -C(R<sup>3</sup>)(R<sup>4</sup>)- G moiety, are joined together to form  
30 a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl

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moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or (v)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; " means that the occurrences of (i), (ii), (iii), (iv) and (v) are mutually exclusive and that only one of (i), (ii), (iii), (iv) and (v) can be present at any given time.

It should be understood that when  $R^1$  and  $R^2$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, each of said cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety independently may optionally additionally be fused with an aryl or heteroaryl ring, wherein the ring moiety resulting from the fusion may be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown above (i.e., each substituent is independently selected from the group consisting of the  $R^{21}$  substituents).

It should also be understood that when  $R^2$  and  $R^6$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, each of said cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety independently may optionally additionally be fused with an aryl or heteroaryl ring, wherein the ring moiety resulting from the fusion may be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown above

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(i.e., each substituent is independently selected from the group consisting of the  $R^{21}$  substituents).

It should be understood that when  $R^6$  and either  $R^3$  or  $R^4$  of the  $-C(R^3)(R^4)-$  G moiety, are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, each of said cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety independently may optionally additionally be fused with an aryl or heteroaryl ring, wherein the ring moiety resulting from the fusion may be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown above (i.e., each substituent is independently selected from the group consisting of the  $R^{21}$  substituents).

It should be understood that when  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, each of said cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety independently may optionally additionally be fused with an aryl or heteroaryl ring, wherein the ring moiety resulting from the fusion may be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown above (i.e., each substituent is independently selected from the group consisting of the  $R^{21}$  substituents).

In one embodiment, either:

(i)  $R^1$  and  $R^2$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown above (i.e., each substituent is independently selected from the group consisting of the  $R^{21}$  substituents); or

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(ii)  $R^2$  and  $R^6$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown above (i.e., each substituent is independently selected from the group consisting of the  $R^{21}$  substituents); or

(iii)  $R^1$  and  $R^2$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; and  $R^2$  and  $R^6$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown above (i.e., each substituent is independently selected from the group consisting of the  $R^{21}$  substituents).

In one embodiment,  $R^1$  (when  $R^1$  is not joined to  $R^2$ ),  $R^2$  (when  $R^2$  is not joined to  $R^1$  or  $R^6$ ),  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$  (when  $R^6$  is not joined to  $R^2$ ),  $R^7$ ,  $R^{11}$  and  $R^{12}$  can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown above

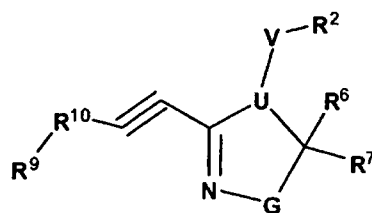
(i.e., each substituent is independently selected from the group consisting of the  $R^{21}$  substituents).

In one embodiment, each of the alkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkenyl and alkynyl groups in  $R^1$ ,  $R^2$ ,  $R^1$ - $R^2$ ,  $R^2$ - $R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{14}$  is independently unsubstituted or optionally substituted by 1 to 5  $R^{21}$  groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, heterocyclyl, heterocyclylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and -S(O)<sub>2</sub>R<sup>15</sup>; and each of the alkyl, cycloalkenyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkenyl and alkynyl groups in  $R^{21}$  is independently unsubstituted or substituted by 1 to 5  $R^{22}$  groups independently selected from the group consisting of alkyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and -S(O)<sub>2</sub>R<sup>15</sup>.

In another embodiment,  $R^1$  (when  $R^1$  is not joined to  $R^2$ ) and  $R^8$  are taken together to form a bond (i.e., there is a triple bond between the carbon atom to

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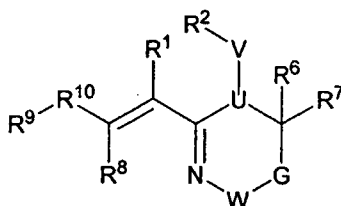
which R<sup>1</sup> was bonded to and the carbon to which R<sup>8</sup> was bonded to, i.e., the compound of formula I is a compound of formula II:



formula II

and R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>11</sup> and R<sup>12</sup> are as defined above).

5 Thus, one embodiment is directed to a compound of formula I:



Formula I

or a pharmaceutically acceptable salt, solvate, ester or prodrug thereof, wherein:

either

10 (i) R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents, (b) said heterocyclyl moiety is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents, and (c) said cycloalkyl, 15 cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents; or

(ii) R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, 20 wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents, (b) said heterocyclyl moiety is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents, and (c) said cycloalkyl,



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cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

(iii)

5 (a)  $R^1$  and  $R^2$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (1) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (2) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and

10 (b)  $R^2$  and  $R^6$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (1) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (2) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; and

15 (c) said  $R^2$  and  $R^6$  cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

(iv)  $R^6$  and either  $R^3$  or  $R^4$  of the  $-C(R^3)(R^4)-$  G moiety, are joined  
20 together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, (b) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (c) said cycloalkyl, cycloalkenyl, heterocyclyl or  
25 heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

(v)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a  
C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8  
30 membered heterocyclenyl moiety, wherein: (a) said cycloalkyl moiety is optionally

substituted with 1-5 independently selected  $R^{21}$  substituents, (b) said heterocycl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (c) said cycloalkyl, cycloalkenyl, heterocycl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from  
 5 the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents;

U is  $\begin{matrix} \diagup \\ \diagdown \end{matrix} -C(R^5) \text{ or } N$ ;

W is selected from the group consisting of a bond; -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, and -C(R<sup>11</sup>)(R<sup>12</sup>)-;

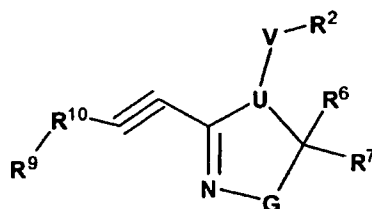
10 G is selected from the group consisting of -C(R<sup>3</sup>)(R<sup>4</sup>)-, -C(O)- and -N(R<sup>13</sup>)-, with the proviso that when W is -O- or -S-, G is not -N(R<sup>13</sup>)- or -C(O)-;

V is selected from the group consisting of a bond, -O-, -C(O)- and -N(R<sup>14</sup>)-;

R<sup>1</sup> (when R<sup>1</sup> is not joined to R<sup>2</sup>), R<sup>2</sup> (when R<sup>2</sup> is not joined to R<sup>1</sup> or R<sup>6</sup>), R<sup>5</sup>, R<sup>6</sup> (when R<sup>6</sup> is not joined to R<sup>2</sup>), and R<sup>7</sup> can be the same or different, each being  
 15 independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocycl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocycl- and heterocyclalkyl- can be unsubstituted or  
 20 optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

or, alternatively, R<sup>1</sup> (when R<sup>1</sup> is not joined to R<sup>2</sup>) and R<sup>8</sup> are taken together to form a bond (i.e., there is a triple bond between the carbon atom to which R<sup>1</sup>  
 25 was bonded to and the carbon to which R<sup>8</sup> was bonded to, i.e., the compound of formula I is a compound of formula II:

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formula II

and  $R^2$ ,  $R^5$ ,  $R^6$ , and  $R^7$  are as defined above, and  $R^3$ ,  $R^4$ ,  $R^{11}$  and  $R^{12}$  are as defined below);

- $R^3$  is selected from the group consisting of H, halo (and in one example, F),
- 5 -OR<sup>15</sup> (and in one example R<sup>15</sup> is H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>,  
 -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>),  
 S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alkyl-,  
 10 alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-,  
 heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, wherein each of  
 said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-,  
 cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-  
 can be unsubstituted or optionally independently substituted with 1-5 substituents  
 15 which can be the same or different, each substituent being independently selected  
 from the group consisting of the moieties shown below; or

- $R^3$  and  $R^6$  taken together form a bond (i.e.,  $R^3$  and  $R^6$  form a bond between  
 G and the carbon to which  $R^6$  is bound), provided that when  $R^3$  and  $R^6$  form a  
 bond: (1) W is not a bond, (2)  $R^2$  and  $R^6$  are not joined together to form a  
 20 cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety (as described in (ii)  
 and (iii) above) (3)  $R^6$  and either  $R^3$  or  $R^4$  of the -C(R<sup>3</sup>)(R<sup>4</sup>)- G moiety are not  
 joined together to form a cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl  
 moiety (as described in (iv) above), and (4)  $R^6$  and  $R^{13}$  of the -N(R<sup>13</sup>)- G moiety  
 are not joined together to form a heterocyclyl or heterocyclenyl moiety (as  
 25 described in (v) above);

$R^4$ ,  $R^{11}$  and  $R^{12}$  can be the same or different, each being independently selected from the group consisting of H, halo (and in one example, F),  $-OR^{15}$  (and in one example  $R^{15}$  is H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
5  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocycl- and heterocyclalkyl-, wherein each of  
10 said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocycl- and heterocyclalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below, and  
15 provided that when one of  $R^3$  or  $R^4$  is selected from the group consisting of:  
 $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , and  $-N_3$ , then the other is not selected from the  
20 group consisting of:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , and  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , and  $-N_3$  (i.e., if one of  $R^3$  or  $R^4$  is  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
25  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , or  $-N_3$ , then the other one is not  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  
and  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  
30  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,

-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>,  
-P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>);

provided that when one of R<sup>11</sup> or R<sup>12</sup> is selected from the group consisting  
of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,

- 5 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>),  
-S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not  
selected from the group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,  
-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
10 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
-S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
=NOR<sup>15</sup>, and -N<sub>3</sub> (i.e., if one of R<sup>11</sup> or R<sup>12</sup> is -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,  
-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
15 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
=NOR<sup>15</sup>, or -N<sub>3</sub>, then the other is not -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,  
-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
-S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
20 =NOR<sup>15</sup>, or -N<sub>3</sub>);

- R<sup>13</sup> is independently selected from the group consisting of H, alkyl,  
arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-,  
arylcycloalkylalkyl-, heteroarylcycloalkylalkyl-, arylheterocycloalkylalkyl-,  
heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylcycloalkyl-,  
25 heterocycloalkyl-, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl,  
arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylcycloalkenyl-,  
heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-,  
alkynyl, arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-,  
heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-,  
30 heterocycloalkylheteroaryl-, cycloalkenylaryl-, heterocycloalkenylaryl-, -OR<sup>15</sup>,

- CN, -C(O)R<sup>8</sup>, -C(O)OR<sup>9</sup>, -S(O)R<sup>10</sup>, -S(O)<sub>2</sub>R<sup>10</sup>, -C(O)N(R<sup>11</sup>)(R<sup>12</sup>),  
 -S(O)N(R<sup>11</sup>)(R<sup>12</sup>), -S(O)<sub>2</sub>N(R<sup>11</sup>)(R<sup>12</sup>), -NO<sub>2</sub>, -N=C(R<sup>8</sup>)<sub>2</sub> and -N(R<sup>8</sup>)<sub>2</sub>; and wherein  
 said R<sup>13</sup> alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-,  
 arylcycloalkylalkyl-, heteroarylcycloalkylalkyl-, arylheterocycloalkylalkyl-,  
 5 heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylcycloalkyl-,  
 heterocycloalkyl, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl,  
 arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylcycloalkenyl-,  
 heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-,  
 alkynyl, arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-,  
 10 heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-,  
 heterocycloalkylheteroaryl-, cycloalkenylaryl-, and heterocycloalkenylaryl- groups  
 are optionally substituted with 1 to 5 groups independently selected from the  
 group consisting of: alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-,  
 cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl,  
 15 heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>,  
 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>,  
 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>,  
 -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>),  
 -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 20 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and  
 -S(O)<sub>2</sub>R<sup>15</sup>;

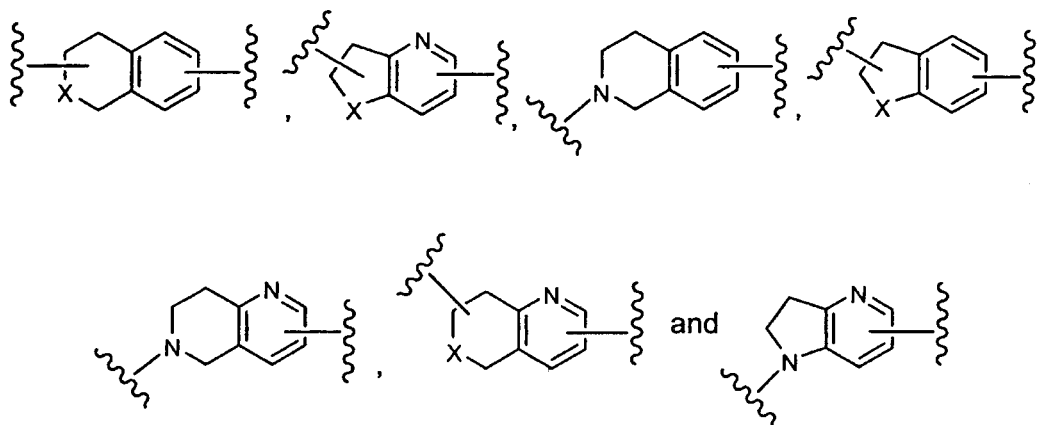
- R<sup>8</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-,  
 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,  
 25 heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, with each of said alkyl-,  
 alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-,  
 heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- being optionally  
 substituted with 1-3 independently selected R<sup>21</sup> substituents;

- R<sup>9</sup> is selected from the group consisting of alkyl-, alkenyl-, alkynyl-,  
 30 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,

heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each  $R^9$  group is optionally substituted with 1-3 independently selected  $R^{21}$  substituents;

$R^{10}$  is selected from the group consisting of a bond, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,

5 heteroarylalkyl-, heterocyclyl-, heterocyclylalkyl- and the moieties:



10 where X is O,  $N(R^{14})$  or S;

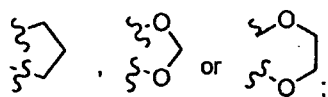
wherein each  $R^{10}$  group (except for the bond) is optionally substituted with 1-3 independently selected  $R^{21}$  substituents;

$R^{14}$  is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, -CN, -C(O) $R^{15}$ , -C(O) $OR^{15}$ ,  
 15 -C(O) $N(R^{15})(R^{16})$ , -S(O) $N(R^{15})(R^{16})$ , -S(O) $_2N(R^{15})(R^{16})$ , -C(=N $OR^{15})R^{16}$ , and -P(O)( $OR^{15}$ )( $OR^{16}$ ), wherein each of said alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, and heteroarylalkyl- is optionally substituted with 1-5 independently  
 20 selected  $R^{21}$  substituents;

$R^{15}$ ,  $R^{16}$  and  $R^{17}$  are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, arylcycloalkyl-, arylheterocyclyl-, ( $R^{18}$ ) $_r$ -alkyl, ( $R^{18}$ ) $_r$ -cycloalkyl, ( $R^{18}$ ) $_r$ -cycloalkylalkyl-, ( $R^{18}$ ) $_r$ -heterocyclyl, ( $R^{18}$ ) $_r$ -

heterocyclalkyl-,  $(R^{18})_r$ -aryl,  $(R^{18})_r$ -arylalkyl-,  $(R^{18})_r$ -heteroaryl and  $(R^{18})_r$ -heteroarylalkyl-; wherein r is 1-5;

- Each  $R^{18}$  is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl-, arylalkenyl-, arylalkynyl-,  $-\text{NO}_2$ , halo, heteroaryl, HO-alkoxyalkyl-,  $-\text{CF}_3$ ,  $-\text{CN}$ , alkyl-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alkyl})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alkyl})(\text{aryl})$ ,  $-\text{C}(\text{O})\text{N}(\text{alkyl})(\text{heteroaryl})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{S}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{S}(\text{O})\text{NH}(\text{aryl})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterocyclalkyl})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alkyl})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alkyl})(\text{aryl})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  $-\text{O-heterocyclalkyl}$ ,  $-\text{O-cycloalkylalkyl}$ ,  $-\text{O-heterocyclalkyl}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alkyl})_2$ ,  $-\text{N}(\text{arylalkyl})_2$ ,  $-\text{N}(\text{arylalkyl})(\text{heteroarylalkyl})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{C}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{C}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alkyl})$ ,  $-\text{NHS}(\text{O})_2\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{S}(\text{O})_2\text{NH}(\text{alkyl})$  and  $-\text{N}(\text{alkyl})\text{S}(\text{O})_2\text{N}(\text{alkyl})(\text{alkyl})$ ;
- or, alternately, two  $R^{18}$  moieties on adjacent carbons can be linked together to form:



$R^{19}$  is selected from the group consisting of: alkyl, cycloalkyl, aryl, arylalkyl- and heteroarylalkyl-;

- $R^{20}$  is selected from the group consisting of: alkyl, cycloalkyl, aryl, halo substituted aryl, arylalkyl-, heteroaryl and heteroarylalkyl-;

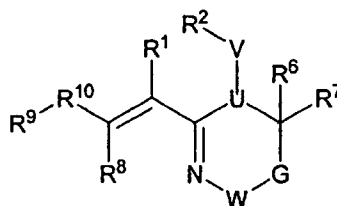
- Each  $R^{21}$  group is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclalkyl, heterocyclalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo,  $-\text{CN}$ ,  $-\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{R}^{15}$ ,  $-\text{C}(\text{O})\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{SR}^{15}$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{CH}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{C}(=\text{NOR}^{15})\text{R}^{16}$ ,  $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ,  $-\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{alkyl-N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{CH}_2-\text{R}^{15}$ ,  $-\text{CH}_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{N}(\text{R}^{16})(\text{R}^{17})$ ,



-N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and  
 -S(O)<sub>2</sub>R<sup>15</sup>; and wherein each of the R<sup>21</sup> alkyl, cycloalkenyl, cycloalkyl,  
 cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl,  
 5 heteroarylalkyl-, alkenyl and alkynyl groups is optionally substituted with 1 to 5  
 independently selected R<sup>22</sup> groups; and

Each R<sup>22</sup> is independently selected from the group consisting of: alkyl,  
 cycloalkyl, cycloalkenyl, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>,  
 -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>),  
 10 -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>),  
 -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and  
 15 -S(O)<sub>2</sub>R<sup>15</sup>.

In another embodiment, the present application discloses a compound, or  
 pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound,  
 said compound having the general structure shown in Formula I:



Formula I

wherein:

R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8  
 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl  
 moiety, with each of said cycloalkyl or heterocyclyl moiety being  
 25 unsubstituted or optionally independently being substituted with 1-5  
 substituents which can be the same or different, each substituent being

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independently selected from the group consisting of the moieties shown below;

U is  $\begin{matrix} \diagup \\ \diagdown \end{matrix} \text{---C(R}^5\text{) or N;}$

W is selected from the group consisting of a bond, -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, and -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G is selected from the group consisting of -C(R<sup>3</sup>)(R<sup>4</sup>)-, -C(O)- and -N(R<sup>13</sup>)-; with the proviso that when W is -O- or -S-; G is not -N(R<sup>13</sup>)- or -C(O)-;

V is selected from the group consisting of a bond, -O-, -C(O)-, and -N(R<sup>14</sup>)-;

R<sup>5</sup>, R<sup>6</sup>, and R<sup>7</sup> can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

R<sup>3</sup> is selected from the group consisting of H, halo (and in one example, F), -OR<sup>15</sup> (and in one example R<sup>15</sup> is H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or

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$R^3$  and  $R^6$  taken together form a bond (i.e.,  $R^3$  and  $R^6$  form a bond between G and the carbon to which  $R^6$  is bound), provided that when  $R^3$  and  $R^6$  form a bond W is not a bond;

$R^4$ ,  $R^{11}$  and  $R^{12}$  can be the same or different, each being independently  
 5 selected from the group consisting of H, halo (and in one example, F),  $-OR^{15}$  (and in one example  $R^{15}$  is H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  
 $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  
 $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  
 10  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-,  
 alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-,  
 heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of  
 said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-,  
 cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-  
 15 can be unsubstituted or optionally independently substituted with 1-5 substituents  
 which can be the same or different, each substituent being independently selected  
 from the group consisting of the moieties shown below,

provided that when one of  $R^3$  or  $R^4$  is selected from the group consisting of:  
 $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  
 20  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , and  $-N_3$ , then the other is not selected from the  
 group consisting of:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , and  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  
 $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 25  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , and  $-N_3$  (i.e., if one of  $R^3$  or  $R^4$  is  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 30  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,

- P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>, then the other one is not -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, and -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>,  
 5 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>);

- provided that when one of R<sup>11</sup> or R<sup>12</sup> is selected from the group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>),  
 10 -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not selected from the group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
 15 =NOR<sup>15</sup>, and -N<sub>3</sub> (i.e., if one of R<sup>11</sup> or R<sup>12</sup> is -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>, then the other is not -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,  
 20 -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>);

- R<sup>13</sup> is independently selected from the group consisting of H, alkyl,  
 25 arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-, arylcycloalkylalkyl-, heteroarylalkyl-, arylheterocycloalkylalkyl-, heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylalkyl-, heterocycloalkyl-, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl, arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylalkenyl-,  
 30 heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-,

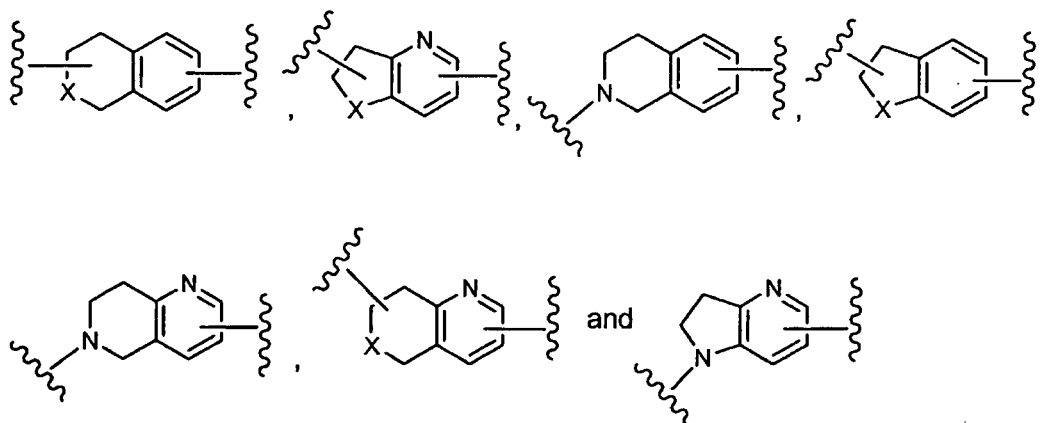
- alkynyl, arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-, heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylaryl-, heterocycloalkenylaryl-, -OR<sup>15</sup>, -CN, -C(O)R<sup>8</sup>, -C(O)OR<sup>9</sup>, -S(O)R<sup>10</sup>, -S(O)<sub>2</sub>R<sup>10</sup>, -C(O)N(R<sup>11</sup>)(R<sup>12</sup>),
- 5 -S(O)N(R<sup>11</sup>)(R<sup>12</sup>), -S(O)<sub>2</sub>N(R<sup>11</sup>)(R<sup>12</sup>), -NO<sub>2</sub>, -N=C(R<sup>8</sup>)<sub>2</sub> and -N(R<sup>8</sup>)<sub>2</sub>; and wherein said R<sup>13</sup> alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-, arylcycloalkylalkyl-, heteroarylalkylalkyl-, arylheterocycloalkylalkyl-, heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylalkyl-, heterocycloalkyl-, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl,
- 10 arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylalkyl-, heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-, heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylaryl-, and heterocycloalkenylaryl- groups
- 15 are optionally substituted with 1 to 5 groups independently selected from the group consisting of: alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>,
- 20 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and
- 25 -S(O)<sub>2</sub>R<sup>15</sup>;
- R<sup>14</sup> is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, and
- 30 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);

$R^8$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, with each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- being

5 unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

$R^{10}$  is selected from the group consisting of a bond, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl-, heterocyclalkyl- and the moieties:

10



15 where X is O, N( $R^{14}$ ) or S;

wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- heterocyclalkyl- for  $R^{10}$  as well as the above-noted moieties for  $R^{10}$  can be unsubstituted or optionally independently substituted with 1-3 substituents which

20 can be the same or different, each being independently selected from the group consisting of the moieties shown below; and

$R^9$  is selected from the group consisting of alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,

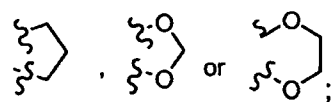
heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-3 substituents which

5 can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

$R^{15}$ ,  $R^{16}$  and  $R^{17}$  are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, arylcycloalkyl-, arylheterocyclyl,  $R^{18}$ -alkyl,  $R^{18}$ -cycloalkyl,  $R^{18}$ -cycloalkylalkyl-,  $R^{18}$ -heterocyclyl,  $R^{18}$ -heterocyclylalkyl-,  $R^{18}$ -aryl,  $R^{18}$ -arylalkyl-,  $R^{18}$ -heteroaryl and  $R^{18}$ -heteroarylalkyl-;

$R^{18}$  is 1-5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl-, arylalkenyl-, arylalkynyl-,  $-\text{NO}_2$ , halo, heteroaryl, HO-alkoxyalkyl,  $-\text{CF}_3$ ,  $-\text{CN}$ , alkyl-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alkyl})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alkyl})(\text{aryl})$ ,  $-\text{C}(\text{O})\text{N}(\text{alkyl})(\text{heteroaryl})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{S}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{S}(\text{O})\text{NH}(\text{aryl})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterocyclyl})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alkyl})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alkyl})(\text{aryl})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  $-\text{O-heterocyclyl}$ ,  $-\text{O-cycloalkylalkyl}$ ,  $-\text{O-heterocyclylalkyl}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alkyl})_2$ ,  $-\text{N}(\text{arylalkyl})_2$ ,  $-\text{N}(\text{arylalkyl})(\text{heteroarylalkyl})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{C}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{C}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alkyl})$ ,  $-\text{NHS}(\text{O})_2\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{S}(\text{O})_2\text{NH}(\text{alkyl})$  and  $-\text{N}(\text{alkyl})\text{S}(\text{O})_2\text{N}(\text{alkyl})(\text{alkyl})$ ;

or, alternately, two  $R^{18}$  moieties on adjacent carbons can be linked together

25 to form: ;

$R^{19}$  is alkyl, cycloalkyl, aryl, arylalkyl- or heteroarylalkyl-;

$R^{20}$  is alkyl, cycloalkyl, aryl, halo substituted aryl, arylalkyl-, heteroaryl or heteroarylalkyl-;

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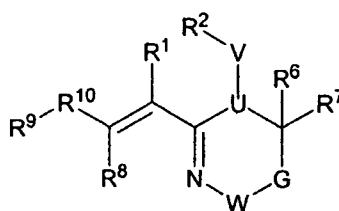
- wherein each of the alkyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, alkylaryl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in  $R^1$ - $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{14}$  is independently unsubstituted or optionally substituted by 1 to 5  $R^{21}$  groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, heterocyclyl, heterocyclylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and -S(O)<sub>2</sub>R<sup>15</sup>;
- wherein each of the alkyl, cycloalkenyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in  $R^{21}$  is independently unsubstituted or substituted by 1 to 5  $R^{22}$  groups independently selected from the group consisting of alkyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and -S(O)<sub>2</sub>R<sup>15</sup>.

In another embodiment, the present application discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in Formula I:



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Formula I

wherein:

- 5  $R^2$  and  $R^6$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

10 U is  $\begin{matrix} \diagup \\ \diagdown \end{matrix} -C(R^5)$  or N;

W is selected from the group consisting of a bond, -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, and -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G is -C(R<sup>3</sup>)(R<sup>4</sup>)-, -C(O)- and -N(R<sup>13</sup>)-; with the proviso that when W is -O- or -S-, G is not -N(R<sup>13</sup>)- or -C(O)-;

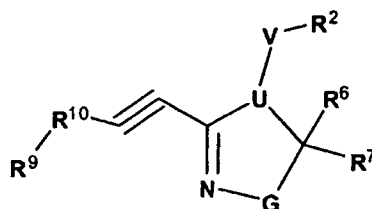
15 V is selected from the group consisting of a bond, -O-, -C(O)-, and -N(R<sup>14</sup>)-;

$R^1$  (when  $R^1$  is not joined to  $R^2$ ),  $R^5$ ,  $R^6$  (when  $R^6$  is not joined to  $R^2$ ), and  $R^7$  can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-,  
 20 wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

25 or, alternatively,  $R^1$  (when  $R^1$  is not joined to  $R^2$ ) and  $R^8$  are taken together to form a bond (i.e., there is a triple bond between the carbon atom to which  $R^1$

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was bonded to and the carbon to which R<sup>8</sup> was bonded to, i.e., the compound of formula I is a compound of formula II:



formula II

and R<sup>2</sup>, R<sup>5</sup>, R<sup>6</sup>, and R<sup>7</sup> are as defined above, and R<sup>3</sup>, R<sup>4</sup>, R<sup>11</sup> and R<sup>12</sup> are as defined below);

R<sup>3</sup> is selected from the group consisting of H, halo (and in one example, F), -OR<sup>15</sup> (and in one example R<sup>15</sup> is H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or

R<sup>4</sup>, R<sup>11</sup> and R<sup>12</sup> can be the same or different, each being independently selected from the group consisting of H, halo (and in one example, F), -OR<sup>15</sup> (and in one example R<sup>15</sup> is H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alkyl-,

alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-

- 5 can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

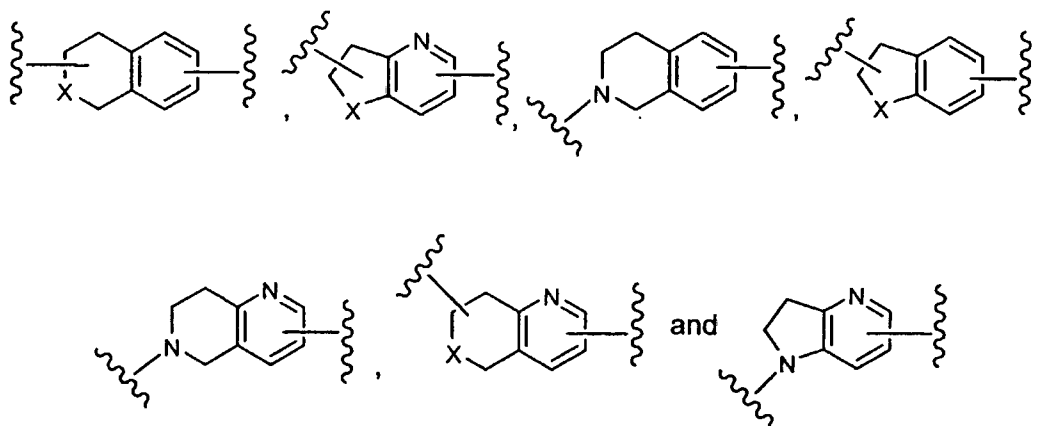
- provided that when one of  $R^3$  or  $R^4$  is selected from the group consisting of:
- 10 -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not selected from the group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, and -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),
- 15 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub> (i.e., if one of  $R^3$  or  $R^4$  is -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,
- 20 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>, then the other one is not -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, and -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>,
- 25 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>;

- provided that when one of  $R^{11}$  or  $R^{12}$  is selected from the group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>),
- 30 -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not

- selected from the group consisting of:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
5  $=NOR^{15}$ , and  $-N_3$  (i.e., if one of  $R^{11}$  or  $R^{12}$  is  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , or  $-N_3$ , then the other is not  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
10  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , or  $-N_3$ );
- $R^{13}$  is independently selected from the group consisting of H, alkyl,  
15 arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-,  
arylcycloalkylalkyl-, heteroarylcycloalkylalkyl-, arylheterocycloalkylalkyl-,  
heteroarylheterocycloalkylalkyl-, cycloalkyl-, arylcycloalkyl-, heteroarylcycloalkyl-,  
heterocycloalkyl-, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl,  
arylalkenyl-, cycloalkenyl-, arylcycloalkenyl-, heteroarylcycloalkenyl-,  
20 heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-,  
alkynyl-, arylalkynyl-, aryl-, cycloalkylaryl-, heterocycloalkylaryl-,  
heterocycloalkenylaryl-, heteroaryl-, cycloalkylheteroaryl-,  
heterocycloalkylheteroaryl-, cycloalkenylaryl-, heterocycloalkenylaryl-,  $-OR^{15}$ ,  
 $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  $-C(O)N(R^{11})(R^{12})$ ,  
25  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  and  $-N(R^8)_2$ ; and wherein  
said  $R^{13}$  alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-,  
arylcycloalkylalkyl-, heteroarylcycloalkylalkyl-, arylheterocycloalkylalkyl-,  
heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylcycloalkyl-,  
heterocycloalkyl, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl,  
30 arylalkenyl, cycloalkenyl, arylcycloalkenyl-, heteroarylcycloalkenyl-,

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- heterocycloalkenyl, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl-, aryl, cycloalkylaryl, heterocycloalkylaryl-, heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylaryl-, and heterocycloalkenylaryl- groups are optionally substituted with 1 to 5 groups
- 5 independently selected from the group consisting of: alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>),
- 10 -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and -S(O)<sub>2</sub>R<sup>15</sup>;
- 15 R<sup>14</sup> is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, and -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);
- 20 R<sup>8</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, with each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- being
- 25 unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;
- R<sup>10</sup> is selected from the group consisting of a bond, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,
- 30 heteroarylalkyl-, heterocyclyl-, heterocyclylalkyl- and the moieties:



where X is O, N(R<sup>14</sup>) or S;

- 5 wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- heterocyclylalkyl- for R<sup>10</sup> as well as the above-noted moieties for R<sup>10</sup> can be unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each being independently selected from the group
- 10 consisting of the moieties shown below;

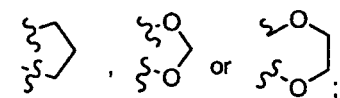
- R<sup>9</sup> is selected from the group consisting of alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-,
- 15 heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

- R<sup>15</sup>, R<sup>16</sup> and R<sup>17</sup> are independently selected from the group consisting of H,
- 20 alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, arylcycloalkyl- arylheterocyclyl-, R<sup>18</sup>-alkyl, R<sup>18</sup>-cycloalkyl, R<sup>18</sup>-cycloalkylalkyl-, R<sup>18</sup>-heterocyclyl, R<sup>18</sup>-heterocyclylalkyl-, R<sup>18</sup>-aryl, R<sup>18</sup>-arylalkyl-, R<sup>18</sup>-heteroaryl and R<sup>18</sup>-heteroarylalkyl-;



$R^{18}$  is 1-5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl-, arylalkenyl-, arylalkynyl-,  $-NO_2$ , halo, heteroaryl, HO-alkoxyalkyl,  $-CF_3$ ,  $-CN$ , alkyl-CN,  $-C(O)R^{19}$ ,  $-C(O)OH$ ,  $-C(O)OR^{19}$ ,  $-C(O)NHR^{20}$ ,  $-C(O)NH_2$ ,  $-C(O)NH_2-C(O)N(alkyl)_2$ ,  $-C(O)N(alkyl)(aryl)$ ,  
 5  $-C(O)N(alkyl)(heteroaryl)$ ,  $-SR^{19}$ ,  $-S(O)_2R^{20}$ ,  $-S(O)NH_2$ ,  $-S(O)NH(alkyl)$ ,  $-S(O)N(alkyl)(alkyl)$ ,  $-S(O)NH(aryl)$ ,  $-S(O)_2NH_2$ ,  $-S(O)_2NHR^{19}$ ,  $-S(O)_2NH(heterocyclyl)$ ,  $-S(O)_2N(alkyl)_2$ ,  $-S(O)_2N(alkyl)(aryl)$ ,  $-OCF_3$ ,  $-OH$ ,  $-OR^{20}$ ,  $-O-heterocyclyl$ ,  $-O-cycloalkylalkyl$ ,  $-O-heterocyclylalkyl$ ,  $-NH_2$ ,  $-NHR^{20}$ ,  $-N(alkyl)_2$ ,  $-N(arylalkyl)_2$ ,  $-N(arylalkyl)-(heteroarylalkyl)$ ,  $-NHC(O)R^{20}$ ,  $-NHC(O)NH_2$ ,  
 10  $-NHC(O)NH(alkyl)$ ,  $-NHC(O)N(alkyl)(alkyl)$ ,  $-N(alkyl)C(O)NH(alkyl)$ ,  $-N(alkyl)C(O)N(alkyl)(alkyl)$ ,  $-NHS(O)_2R^{20}$ ,  $-NHS(O)_2NH(alkyl)$ ,  $-NHS(O)_2N(alkyl)(alkyl)$ ,  $-N(alkyl)S(O)_2NH(alkyl)$  and  $-N(alkyl)S(O)_2N(alkyl)(alkyl)$ ;

or, alternately, two  $R^{18}$  moieties on adjacent carbons can be linked together

15 to form: ;

$R^{19}$  is alkyl, cycloalkyl, aryl, arylalkyl- or heteroarylalkyl-;

$R^{20}$  is alkyl, cycloalkyl, aryl, halo substituted aryl, arylalkyl-, heteroaryl or heteroarylalkyl-;

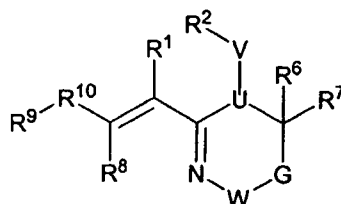
wherein each of the alkyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl-,  
 20 heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, alkylaryl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in  $R^1$ ,  $R^2$ - $R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{14}$  is independently unsubstituted or optionally substituted by 1 to 5  $R^{21}$  groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-,  
 25 aryl, arylalkyl, heteroaryl, heteroarylalkyl-, halo,  $-CN$ ,  $-OR^{15}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-SR^{15}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-CH(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $-N(R^{15})(R^{16})$ ,  $-alkyl-N(R^{15})(R^{16})$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-R^{15}$ ,  $-CH_2N(R^{15})(R^{16})$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-CH_2-N(R^{15})S(O)_2R^{16}$ ,

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-N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and -S(O)<sub>2</sub>R<sup>15</sup>; wherein each of the alkyl, cycloalkenyl-, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclalkyl-, aryl, arylalkyl-,

- 5 heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in R<sup>21</sup> is independently unsubstituted or substituted by 1 to 5 R<sup>22</sup> groups independently selected from the group consisting of alkyl, cycloalkyl, cycloalkenyl-, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),
- 10 -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and -S(O)<sub>2</sub>R<sup>15</sup>.

- 15 In another embodiment, the present application discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in Formula I:



Formula I

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wherein:

- R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being
- 25 unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown



below; and  $R^2$  and  $R^6$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

U is  $\begin{cases} -C(R^5) \text{ or } N; \end{cases}$

W is selected from the group consisting of a bond, -O-, -C(O)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, and -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G is -C(R<sup>3</sup>)(R<sup>4</sup>)-, -C(O)- and -N(R<sup>13</sup>)-; with the proviso that when W is -O- or -S-, G is not -N(R<sup>13</sup>)- or -C(O)- ;

V is selected from the group consisting of a bond, -O-, -C(O)- and -N(R<sup>14</sup>)-;

$R^5$ ,  $R^6$ , and  $R^7$  can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

$R^3$  is selected from the group consisting of H, halo (and in one example, F), -OR<sup>15</sup> (and in one example  $R^{15}$  is H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of

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said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected

5 from the group consisting of the moieties shown below; or

$R^4$ ,  $R^{11}$  and  $R^{12}$  can be the same or different, each being independently selected from the group consisting of H, halo (and in one example, F),  $-OR^{15}$  (and in one example  $R^{15}$  is H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, wherein each of

15 said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

20 provided that when one of  $R^3$  or  $R^4$  is selected from the group consisting of:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , and  $-N_3$ , then the other is not selected from the

25 group consisting of:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , and  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , and  $-N_3$  (i.e., if one of  $R^3$  or  $R^4$  is  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,

30  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,

-N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>,  
 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>, then the other one is not -OR<sup>15</sup>, -CN, -SR<sup>15</sup>,  
 and -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>,  
 5 -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>,  
 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>;

provided that when one of R<sup>11</sup> or R<sup>12</sup> is selected from the group consisting  
 of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 10 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>),  
 -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not  
 selected from the group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,  
 -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 15 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
 =NOR<sup>15</sup>, and -N<sub>3</sub> (i.e., if one of R<sup>11</sup> or R<sup>12</sup> is -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,  
 -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
 20 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
 =NOR<sup>15</sup>, or -N<sub>3</sub>, then the other is not -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,  
 -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
 25 =NOR<sup>15</sup>, or -N<sub>3</sub>;

R<sup>13</sup> is independently selected from the group consisting of H, alkyl,  
 arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-,  
 arylcycloalkylalkyl-, heteroarylalkyl-, arylheterocycloalkylalkyl-,  
 heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylalkyl-,  
 30 heterocycloalkyl-, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl,

- arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroaryl cycloalkenyl-, heterocycloalkenyl, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-, heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylaryl-,
- 5 heterocycloalkenylaryl-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  and  $-N(R^8)_2$ ; and wherein said  $R^{13}$  alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-, arylcycloalkylalkyl-, heteroaryl cycloalkylalkyl-, arylheterocycloalkylalkyl-, heteroarylheterocycloalkylalkyl-, cycloalkyl,
- 10 arylcycloalkyl-, heteroaryl cycloalkyl-, heterocycloalkyl-, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl, arylalkenyl-, cycloalkenyl, arylcycloalkenyl, heteroaryl cycloalkenyl-, heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-, heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-,
- 15 heterocycloalkylheteroaryl-, cycloalkenylaryl-, and heterocycloalkenylaryl- groups are optionally substituted with 1 to 5 groups independently selected from the group consisting of: alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo,  $-CN$ ,  $-OR^{15}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-SR^{15}$ ,
- 20  $-S(O)N(R^{15})(R^{16})$ ,  $-CH(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $-N(R^{15})(R^{16})$ ,  $-alkyl-N(R^{15})(R^{16})$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-R^{15}$ ,  $-CH_2N(R^{15})(R^{16})$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-CH_2-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,
- 25  $-N(R^{15})C(O)OR^{16}$ ,  $-CH_2-N(R^{15})C(O)OR^{16}$ ,  $-S(O)R^{15}$ ,  $=NOR^{15}$ ,  $-N_3$ ,  $-NO_2$  and  $-S(O)_2R^{15}$ ;

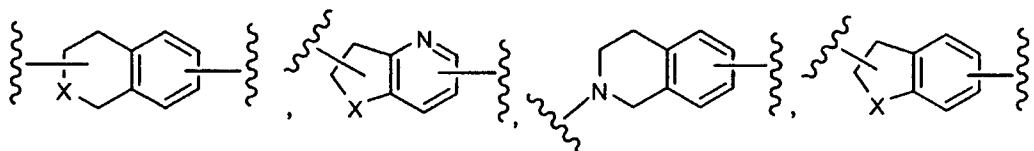
$R^{14}$  is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-,  $-CN$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,

-C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, and -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);

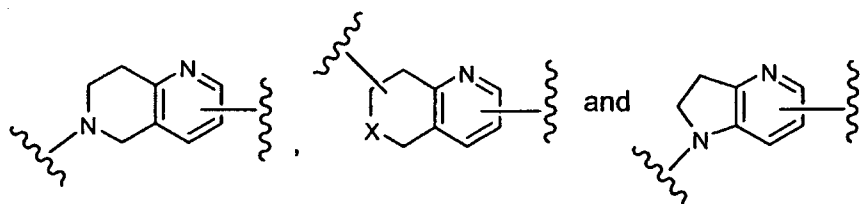
R<sup>8</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,

- 5 heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, with each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- being unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from
- 10 the group consisting of the moieties shown below;

R<sup>10</sup> is selected from the group consisting of a bond, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl-, heterocyclylalkyl- and the moieties:



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where X is O, N(R<sup>14</sup>) or S;

wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl-

- 20 heterocyclylalkyl- for R<sup>10</sup> as well as the above-noted moieties for R<sup>10</sup> can be unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of the moieties shown below; and

R<sup>9</sup> is selected from the group consisting of alkyl-, alkenyl- and alkynyl-,

aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be

5 unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

$R^{15}$ ,  $R^{16}$  and  $R^{17}$  are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, arylcycloalkyl-, arylheterocyclyl-,  $R^{18}$ -alkyl,  $R^{18}$ -cycloalkyl,  $R^{18}$ -cycloalkylalkyl-,  $R^{18}$ -heterocyclyl,  $R^{18}$ -heterocyclylalkyl-,  $R^{18}$ -aryl,  $R^{18}$ -arylalkyl-,  $R^{18}$ -heteroaryl and  $R^{18}$ -heteroarylalkyl-;

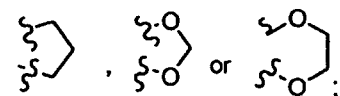
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$R^{18}$  is 1-5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl-, arylalkenyl-, arylalkynyl-,  $-\text{NO}_2$ , halo, heteroaryl, HO-alkoxyalkyl,  $-\text{CF}_3$ ,  $-\text{CN}$ , alkyl-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alkyl})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alkyl})(\text{aryl})$ ,  $-\text{C}(\text{O})\text{N}(\text{alkyl})(\text{heteroaryl})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{S}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{S}(\text{O})\text{NH}(\text{aryl})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterocyclyl})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alkyl})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alkyl})(\text{aryl})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  $-\text{O-heterocyclyl}$ ,  $-\text{O-cycloalkylalkyl}$ ,  $-\text{O-heterocyclylalkyl}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alkyl})_2$ ,  $-\text{N}(\text{arylalkyl})_2$ ,  $-\text{N}(\text{arylalkyl})-(\text{heteroarylalkyl})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{C}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{C}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alkyl})$ ,  $-\text{NHS}(\text{O})_2\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{S}(\text{O})_2\text{NH}(\text{alkyl})$  and  $-\text{N}(\text{alkyl})\text{S}(\text{O})_2\text{N}(\text{alkyl})(\text{alkyl})$ ;

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25 or, alternately, two  $R^{18}$  moieties on adjacent carbons can be linked together

to form: 

$R^{19}$  is alkyl, cycloalkyl, aryl, arylalkyl- or heteroarylalkyl-;

$R^{20}$  is alkyl, cycloalkyl, aryl, halo substituted aryl, arylalkyl-, heteroaryl or heteroarylalkyl-;

wherein each of the alkyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, alkylaryl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in  $R^1$ - $R^2$ ,  $R^2$ - $R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{14}$  is independently unsubstituted or optionally substituted by 1 to 5  $R^{21}$  groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and -S(O)<sub>2</sub>R<sup>15</sup>;

wherein each of the alkyl, cycloalkenyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in  $R^{21}$  is independently unsubstituted or substituted by 1 to 5  $R^{22}$  groups independently selected from the group consisting of alkyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and -S(O)<sub>2</sub>R<sup>15</sup>.

In another embodiment, U is C(R<sup>5</sup>).

In another embodiment, U is N.

In another embodiment, R<sup>2</sup> is H.

- In another embodiment,  $R^2$  is alkyl.
- In another embodiment,  $R^2$  is methyl.
- In another embodiment,  $R^2$  is alkoxyalkyl-.
- In another embodiment,  $R^2$  is 3-methoxypropyl-.
- 5 In another embodiment, U is N and  $R^2$  is 3-methoxypropyl-.
- In another embodiment, W is a bond.
- In another embodiment, W is -O-.
- In another embodiment, W is -C(O)-.
- In another embodiment, W is -S-.
- 10 In another embodiment, W is -S(O)-.
- In another embodiment, W is -S(O<sub>2</sub>)-.
- In another embodiment, W is -C(R<sup>11</sup>)(R<sup>12</sup>)-.
- In another embodiment, =N-W-G- is =N-C(R<sup>11</sup>R<sup>12</sup>)-C(O)-.
- In another embodiment, G is -C(R<sup>3</sup>)(R<sup>4</sup>)-.
- 15 In another embodiment, G is -C(O)-.
- In another embodiment, G is -N(R<sup>13</sup>)-.
- In another embodiment, V is a bond.
- In another embodiment, V is -O-.
- In another embodiment, V is -C(O)-.
- 20 In another embodiment, V is -N(R<sup>14</sup>)-.
- In another embodiment,  $R^2$  is arylalkyl-.
- In another embodiment,  $R^2$  is phenylmethyl-.
- In another embodiment,  $R^2$  is (4-alkoxy)phenylmethyl-.
- In another embodiment,  $R^2$  is (4-methoxy)phenylmethyl-.
- 25 In another embodiment,  $R^1$  is H.
- In another embodiment,  $R^1$  is alkyl.
- In another embodiment,  $R^1$  is methyl.
- In another embodiment,  $R^1$  and  $R^2$  are joined together to form a cyclopentyl ring, which is unsubstituted.



In another embodiment,  $R^1$  and  $R^2$  are joined together to form a cyclopentyl ring, which is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

5 In another embodiment,  $R^1$  and  $R^2$  are joined together to form a cyclohexyl ring, which is unsubstituted.

In another embodiment,  $R^1$  and  $R^2$  are joined together to form a cyclohexyl ring, which is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

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In another embodiment, U is N, and  $R^1$  and  $R^2$  are joined together to form a piperidiny ring including the N of U as the nitrogen of said piperidiny ring, which is unsubstituted.

In another embodiment, U is N, and  $R^1$  and  $R^2$  are joined together to form a piperidiny ring including the N of U as the nitrogen of said piperidiny ring, wherein said piperidiny ring is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

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In another embodiment, U is N, and  $R^1$  and  $R^2$  are joined together to form a pyrrolidiny ring including the N of U as the nitrogen of said pyrrolidiny ring, which is unsubstituted.

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In another embodiment, U is N, and  $R^1$  and  $R^2$  are joined together to form a pyrrolidiny ring including the N of U as the nitrogen of said pyrrolidiny ring, wherein said pyrrolidiny ring is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

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In another embodiment, U is N, and  $R^1$  and  $R^2$  are joined together to form a piperaziny ring including the N of U as a nitrogen of said piperaziny ring, which is unsubstituted.

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In another embodiment, U is N, and R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperaziny ring including the N of U as a nitrogen of said piperaziny ring, wherein said piperaziny ring is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

In another embodiment R<sup>1</sup> and R<sup>2</sup> are joined together to form a ring optionally substituted with 1 to 5 independently selected R<sup>21</sup> substituents, and said ring is fused with an aryl or heteroaryl ring, and said resulting fused ring is optionally substituted with 1 to 5 independently selected R<sup>21</sup> substituents.

In another embodiment R<sup>1</sup> and R<sup>2</sup> are joined together to form a ring substituted with 1 to 5 independently selected R<sup>21</sup> substituents, and said ring is fused with an aryl or heteroaryl ring, and said resulting fused ring is optionally substituted with 1 to 5 independently selected R<sup>21</sup> substituents.

In another embodiment R<sup>1</sup> and R<sup>2</sup> are joined together to form a ring optionally substituted with 1 to 5 independently selected R<sup>21</sup> substituents.

In another embodiment R<sup>1</sup> and R<sup>2</sup> are joined together to form a ring.

In another embodiment R<sup>1</sup> and R<sup>2</sup> are joined together to form a heterocycl ring optionally substituted with 1 to 5 independently selected R<sup>21</sup> substituents.

In another embodiment R<sup>1</sup> and R<sup>2</sup> are joined together to form a heterocycl ring substituted with 1 to 5 independently selected R<sup>21</sup> substituents.

In another embodiment U is N, and R<sup>1</sup> and R<sup>2</sup> are joined together to form a heterocycl ring optionally substituted with 1 to 5 independently selected R<sup>21</sup> substituents.

In another embodiment U is N, and R<sup>1</sup> and R<sup>2</sup> are joined together to form a heterocycl ring substituted with 1 to 5 independently selected R<sup>21</sup> substituents.

In another embodiment R<sup>1</sup> and R<sup>2</sup> are joined together to form a ring, and said ring is fused with an aryl or heteroaryl ring, and said resulting fused ring is optionally substituted with 1 to 5 independently selected R<sup>21</sup> substituents.

In another embodiment R<sup>1</sup> and R<sup>2</sup> are joined together to form a heterocycl ring.

In another embodiment U is N, and R<sup>1</sup> and R<sup>2</sup> are joined together to form a heterocyclyl ring.

In another embodiment R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring optionally substituted with 1 to 5 independently selected R<sup>21</sup> substituents.

5 In another embodiment R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring substituted with 1 to 5 independently selected R<sup>21</sup> substituents.

In another embodiment U is N, and R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring optionally substituted with 1 to 5 independently selected R<sup>21</sup> substituents.

10 In another embodiment U is N, and R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring substituted with 1 to 5 independently selected R<sup>21</sup> substituents.

In another embodiment R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring optionally substituted with a =O moiety.

15 In another embodiment U is N, and R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring optionally substituted with a =O moiety.

In another embodiment R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl.

In another embodiment U is N, and R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring.

20 In another embodiment R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring substituted with a =O moiety.

In another embodiment U is N, and R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring substituted with a =O moiety.

25 In another embodiment R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents, (b) said heterocyclyl moiety is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents, and (c) said cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion  
30 is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents.

In another embodiment:

(a)  $R^1$  and  $R^2$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (1) said cycloalkyl moiety is optionally substituted with 1-5 independently  
5 selected  $R^{21}$  substituents, and (2) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and

(b)  $R^2$  and  $R^6$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (1) said cycloalkyl moiety is optionally substituted with 1-5 independently  
10 selected  $R^{21}$  substituents, and (2) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; and

(c) said  $R^2$  and  $R^6$  cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5  
15 independently selected  $R^{21}$  substituents.

In another embodiment  $R^6$  and either  $R^3$  or  $R^4$  of the  $-C(R^3)(R^4)-G$  moiety, are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$   
20 substituents, (b) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (c) said cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

25 In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-G$  moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (b) said heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the

ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein said heterocyclyl moiety is substituted with 1-5 independently selected  $R^{21}$  substituents.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said heterocyclyl moiety is optionally substituted with a  $=O$ , and (b) said heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein said heterocyclyl moiety is optionally substituted with a  $=O$ .

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein said heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety.

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In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said heterocyclyl moiety is substituted with a =O, and (b) said heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein said heterocyclyl moiety is substituted with a =O.

10 In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein: (a) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (b) said heterocyclyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

20 In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein: (a) said heterocyclyl moiety is optionally substituted with a =O, and (b) said heterocyclyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

25 In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein said heterocyclyl moiety is optionally substituted with a =O.

30 In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein said heterocyclyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety

resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety.

5 In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein: (a) said heterocyclyl moiety is substituted with a  $=O$ , and (b) said heterocyclyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

10 In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein said heterocyclyl moiety is substituted with a  $=O$ .

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a pyrrolidinyl ring, wherein: (a) said pyrrolidinyl ring is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (b) said pyrrolidinyl ring is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

15 In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 pyrrolidinyl ring, wherein said pyrrolidinyl ring is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a pyrrolidinyl ring, wherein: (a) said pyrrolidinyl ring is optionally substituted with a  $=O$ , and (b) said pyrrolidinyl ring is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

20 In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a pyrrolidinyl ring, wherein said pyrrolidinyl ring is optionally substituted with a  $=O$ .

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a pyrrolidinyl ring, wherein said pyrrolidinyl ring is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

5 In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a pyrrolidinyl ring.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a pyrrolidinyl ring, wherein: (a) said pyrrolidinyl ring is substituted with a =O, and (b) said pyrrolidinyl ring is optionally fused with an aryl or  
10 heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a pyrrolidinyl ring, wherein said pyrrolidinyl ring is substituted with a =O.

15 In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein: (a) said heterocyclyl moiety is substituted with 1-5 independently selected  $R^{21}$  substituents, and (b) said heterocyclyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5  
20 independently selected  $R^{21}$  substituents.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein said heterocyclyl moiety is substituted with 1-5 independently selected  $R^{21}$  substituents.

In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined  
25 together to form a pyrrolidinyl ring, wherein: (a) said pyrrolidinyl ring is substituted with 1-5 independently selected  $R^{21}$  substituents, and (b) said pyrrolidinyl ring is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.



In another embodiment  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-G$  moiety, are joined together to form a 5 pyrrolidinyl ring, wherein said pyrrolidinyl ring is substituted with 1-5 independently selected  $R^{21}$  substituents.

In another embodiment,  $R^6$  is H.

5 In another embodiment,  $R^6$  is alkyl.

In another embodiment,  $R^6$  is methyl.

In another embodiment,  $R^7$  is aryl.

In another embodiment,  $R^7$  is an unsubstituted phenyl.

10 In another embodiment,  $R^7$  is a phenyl which is substituted with 1-4 substituents which can be the same or different, each substituent being independently selected from the group consisting of halo, alkyl,  $-CN$ ,  $-NH_2$ ,  $-NH(alkyl)$ ,  $-N(alkyl)_2$ , hydroxy, alkoxy, aryl and heteroaryl groups.

In another embodiment,  $R^7$  is unsubstituted naphthyl.

15 In another embodiment,  $R^7$  is naphthyl which is substituted with 1-4 substituents which can be the same or different, each substituent being independently selected from the group consisting of halo, alkyl,  $-CN$ ,  $-NH_2$ ,  $-NH(alkyl)$ ,  $-N(alkyl)_2$ , hydroxy, alkoxy, aryl and heteroaryl groups.

In another embodiment,  $R^7$  is unsubstituted biphenyl.

20 In another embodiment,  $R^7$  is biphenyl which is substituted with 1-4 substituents which can be the same or different, each substituent being independently selected from the group consisting of halo, alkyl,  $-CN$ ,  $-NH_2$ ,  $-NH(alkyl)$ ,  $-N(alkyl)_2$ , hydroxy and alkoxy groups.

In another embodiment,  $R^7$  is  $3-(1,1'-biphenyl)-yl$ .

In another embodiment,  $R^7$  is  $4-(1,1'-biphenyl)-yl$ .

25 In another embodiment,  $R^6$  is H and  $R^7$  is a biphenyl which can be unsubstituted or optionally independently substituted with 1-4 substituents which can be the same or different, each substituent being independently selected from the group consisting of halo, alkyl,  $-CN$ ,  $-NH_2$ ,  $-NH(alkyl)$ ,  $-N(alkyl)_2$ , hydroxy and alkoxy groups.

In another embodiment,  $R^6$  is methyl, and  $R^7$  is a biphenyl which can be unsubstituted or optionally independently substituted with 1-4 substituents which can be the same or different, each substituent being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

In another embodiment,  $R^6$  is H, and  $R^7$  is a phenyl which can be unsubstituted or optionally independently substituted with 1-4 substituents which can be the same or different, each substituent being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

In another embodiment,  $R^6$  is methyl, and  $R^7$  is a biphenyl which can be unsubstituted or optionally independently substituted with 1-4 substituents which can be the same or different, each substituent being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

In another embodiment,  $R^2$  and  $R^6$  are joined together to form a cyclopentyl ring.

In another embodiment,  $R^2$  and  $R^6$  are joined together to form a cyclopentyl ring, which is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

In another embodiment,  $R^2$  and  $R^6$  are joined together to form a cyclohexyl ring.

In another embodiment,  $R^2$  and  $R^6$  are joined together to form a cyclohexyl ring, which is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

In another embodiment, U is N, and  $R^2$  and  $R^6$  are joined together to form a piperidiny ring including the N of U as the nitrogen of said piperidiny ring, which is unsubstituted.

In another embodiment, U is N, and R<sup>2</sup> and R<sup>6</sup> are joined together to form a piperidinyl ring including the N of U as the nitrogen of said piperidinyl ring, wherein said piperidinyl ring is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

In another embodiment, U is N, and R<sup>2</sup> and R<sup>6</sup> are joined together to form a pyrrolidinyl ring including the N of U as the nitrogen of said pyrrolidinyl ring, which is unsubstituted.

In another embodiment, U is N, and R<sup>2</sup> and R<sup>6</sup> are joined together to form a pyrrolidinyl ring including the N of U as the nitrogen of said pyrrolidinyl ring, wherein said pyrrolidinyl ring is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

In another embodiment, U is N, and R<sup>2</sup> and R<sup>6</sup> are joined together to form a piperazinyl ring including the N of U as a nitrogen of said piperazinyl ring, which is unsubstituted.

In another embodiment, U is N, and R<sup>2</sup> and R<sup>6</sup> are joined together to form a piperazinyl ring including the N of U as a nitrogen of said piperazinyl ring, wherein said piperazinyl ring is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

In another embodiment, R<sup>2</sup> and R<sup>6</sup> are joined together to form a morpholinyl ring which is unsubstituted.

In another embodiment, R<sup>2</sup> and R<sup>6</sup> are joined together to form a morpholinyl ring, which is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

In another embodiment, R<sup>2</sup> and R<sup>6</sup> are joined together to form a pyranyl ring which is unsubstituted.

In another embodiment,  $R^2$  and  $R^6$  are joined together to form a pyranlyl ring, which is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

5 In another embodiment,  $R^2$  and  $R^6$  are joined together to form a pyrrolidinyl ring which is unsubstituted.

In another embodiment,  $R^2$  and  $R^6$  are joined together to form a pyrrolidinyl ring, which is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

10 In another embodiment, both ( $R^1$  and  $R^2$ ) and ( $R^2$  and  $R^6$ ) are joined together to form independent cycloalkyl rings.

In another embodiment, both ( $R^1$  and  $R^2$ ) and ( $R^2$  and  $R^6$ ) are joined together to form independent cycloalkyl rings, each of which is independently optionally substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

15 In another embodiment, both ( $R^1$  and  $R^2$ ) and ( $R^2$  and  $R^6$ ) are joined together to form independent heterocyclyl rings.

20 In another embodiment, both ( $R^1$  and  $R^2$ ) and ( $R^2$  and  $R^6$ ) are joined together to form independent heterocyclyl rings, each of which is independently optionally substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

25 In another embodiment, both ( $R^1$  and  $R^2$ ) and ( $R^2$  and  $R^6$ ) are joined together to form independent cycloalkyl rings.

In another embodiment, both  $R^1$  and  $R^2$  are joined together to form a cycloalkyl ring, and  $R^2$  and  $R^6$  are joined together to form a heterocyclyl ring, each of which is independently optionally substituted with 1-3 substituents which can be the same or different, each being independently selected from the group

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consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

In another embodiment, both R<sup>1</sup> and R<sup>2</sup> are joined together to form a heterocyclyl ring, and R<sup>2</sup> and R<sup>6</sup> are joined together to form a cycloalkyl ring, each  
5 of which is independently optionally substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

In another embodiment, R<sup>7</sup> is aryl.

10 In another embodiment, R<sup>7</sup> is an unsubstituted phenyl.

In another embodiment, R<sup>7</sup> is a phenyl which is substituted with 1-4 substituents which can be the same or different, each substituent being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy, alkoxy, aryl and heteroaryl groups.

15 In another embodiment, R<sup>7</sup> is 4-fluorophenyl.

In another embodiment, R<sup>7</sup> is unsubstituted naphthyl.

In another embodiment, R<sup>7</sup> is naphthyl which is substituted with 1-4 substituents which can be the same or different, each substituent being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>,  
20 -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy, alkoxy, aryl and heteroaryl groups.

In another embodiment, R<sup>7</sup> is unsubstituted biphenyl.

In another embodiment, R<sup>7</sup> is biphenyl which is substituted with 1-4 substituents which can be the same or different, each substituent being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>,  
25 -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

In another embodiment, R<sup>7</sup> is R<sup>7</sup> is 3-(1,1'-biphenyl)-yl.

In another embodiment, R<sup>7</sup> is R<sup>7</sup> is 4-(1,1'-biphenyl)-yl.

In another embodiment, R<sup>8</sup> is H.

In another embodiment, R<sup>8</sup> is alkyl.

30 In another embodiment, R<sup>8</sup> is methyl.

In another embodiment,  $R^{10}$  is aryl.

In another embodiment,  $R^{10}$  is phenyl.

In another embodiment  $R^{10}$  is aryl substituted with 1 halo.

In another embodiment  $R^{10}$  is aryl substituted with 1 halo, and said halo is

5 F.

In another embodiment  $R^{10}$  is aryl substituted with 1 to 3 independently selected  $R^{21}$  moieties.

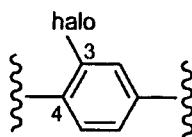
In another embodiment  $R^{10}$  is aryl substituted with 1 to 3  $R^{21}$  moieties, wherein each  $R^{21}$  moiety is the same or different  $-OR^{15}$  group.

10 In another embodiment  $R^{10}$  is aryl substituted with 1  $R^{21}$  moiety.

In another embodiment  $R^{10}$  is phenyl substituted with 1 halo.

In another embodiment  $R^{10}$  is phenyl substituted with 1 halo, and said halo is F.

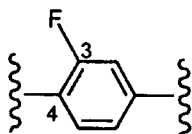
In another embodiment  $R^{10}$  is 3-halo-phenyl:



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(wherein the bond from the carbon labeled as 4 is to the  $R^9$  group).

In another embodiment  $R^{10}$  is 3-F-phenyl:



(wherein the bond from the carbon labeled as 4 is to the  $R^9$  group).

20 In another embodiment  $R^{10}$  is aryl substituted with one  $-OR^{15}$  group.

In another embodiment  $R^{10}$  is aryl substituted with one  $-OR^{15}$  group, and said  $R^{15}$  is alkyl (e.g., methyl).

In another embodiment  $R^{10}$  is phenyl substituted with 1 to 3 independently selected  $R^{21}$  moieties.

25 In another embodiment  $R^{10}$  is phenyl substituted with 1 to 3  $R^{21}$  moieties, wherein each  $R^{21}$  moiety is the same or different  $-OR^{15}$  group.

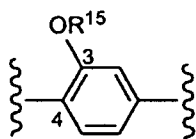
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In another embodiment  $R^{10}$  is phenyl substituted with 1  $R^{21}$  moiety.

In another embodiment  $R^{10}$  is phenyl substituted with one  $-OR^{15}$  group.

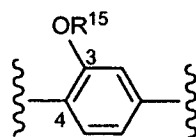
In another embodiment  $R^{10}$  is phenyl substituted with one  $-OR^{15}$  group, and said  $R^{15}$  is alkyl (e.g., methyl).

5 In another embodiment  $R^{10}$  is 3- $OR^{15}$ -phenyl:



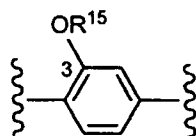
(wherein the bond from the carbon labeled as 4 is to the  $R^9$  group).

In another embodiment  $R^{10}$  is 3- $OR^{15}$ -phenyl:



10 wherein  $R^{15}$  is alkyl (wherein the bond from the carbon labeled as 4 is to the  $R^9$  group).

In another embodiment  $R^{10}$  is 3- $OR^{15}$ -phenyl:



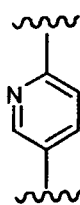
wherein  $R^{15}$  is methyl (i.e.,  $R^{10}$  is 3-methoxy-phenyl).

15 In another embodiment,  $R^{10}$  is heteroaryl.

In another embodiment,  $R^{10}$  is unsubstituted heteroaryl.

In another embodiment  $R^{10}$  is unsubstituted heteroaryl wherein said heteroaryl is pyridyl.

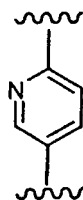
In another embodiment  $R^{10}$  is:



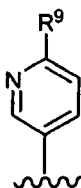
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In another embodiment  $R^{10}$  is:



wherein the  $-R^{10}-R^9$  moiety is:



5 In another embodiment  $R^{10}$  is aryl substituted with 1 to 3  $R^{21}$  moieties, wherein each  $R^{21}$  moiety is the same or different halo.

In another embodiment  $R^{10}$  is aryl substituted with 1 to 3  $R^{21}$  moieties, wherein each  $R^{21}$  moiety is F.

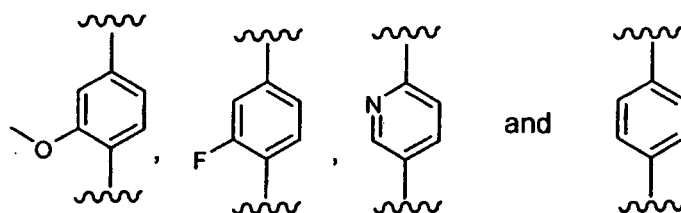
10 In another embodiment  $R^{10}$  is aryl substituted with one  $R^{21}$  moiety, and said  $R^{21}$  moiety is halo.

In another embodiment  $R^{10}$  is aryl substituted with one  $R^{21}$  moiety, said  $R^{21}$  moiety is -halo, and said halo is F.

In another embodiment  $R^{10}$  is phenyl substituted with 1 to 3  $R^{21}$  moieties, wherein each  $R^{21}$  moiety is the same or different halo.

15 In another embodiment  $R^{10}$  is phenyl substituted with 1 to 3  $R^{21}$  moieties, wherein each  $R^{21}$  moiety is F.

In another embodiment  $R^{10}$  is selected from the group consisting of:





In another embodiment of this invention  $R^9$  is selected from the group consisting of heteroaryl and heteroaryl substituted with 1-3  $R^{21}$  groups, and wherein each  $R^{21}$  is independently selected.

In another embodiment,  $R^9$  is unsubstituted heteroaryl.

5 In another embodiment,  $R^9$  is heteroaryl which is substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of halo, alkyl, CN,  $NH_2$ ,  $NH(alkyl)$ ,  $N(alkyl)_2$ , hydroxy and alkoxy groups.

10 In another embodiment,  $R^9$  is heteroaryl substituted with 1 to 3 independently selected alkyl groups.

In another embodiment,  $R^9$  is heteroaryl substituted with one is alkyl group (e.g., methyl).

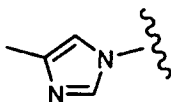
In another embodiment of this invention  $R^9$  is selected from the group consisting of imidazolyl and imidazolyl substituted with 1-3  $R^{21}$  groups, and  
15 wherein each  $R^{21}$  is independently selected.

In another embodiment of this invention  $R^9$  is imidazolyl substituted with 1-3  $R^{21}$  groups, and wherein each  $R^{21}$  is independently selected.

In another embodiment,  $R^9$  is imidazolyl substituted with 1-3 substituents independently selected from the group consisting of halo, alkyl, CN,  $NH_2$ ,  
20  $NH(alkyl)$ ,  $N(alkyl)_2$ , hydroxy and alkoxy groups.

In another embodiment,  $R^9$  is imidazol-1-yl.

In another embodiment,  $R^9$  is 4-methyl-imidazol-1-yl:



In another embodiment,  $R^9$  is 5-chloro-4-methyl-imidazol-1-yl.

25 In another embodiment  $R^{10}$  is selected from the group consisting of aryl and aryl substituted with one or more  $R^{21}$  groups, and  $R^9$  is selected from the group consisting of heteroaryl and heteroaryl substituted with one or more  $R^{21}$  groups, and wherein each  $R^{21}$  is independently selected.

In another embodiment  $R^{10}$  is selected from the group consisting of phenyl and phenyl substituted with 1-3 independently selected  $R^{21}$  groups, and  $R^9$  is selected from the group consisting of imidazolyl and imidazolyl substituted with 1-3 independently selected  $R^{21}$  groups.

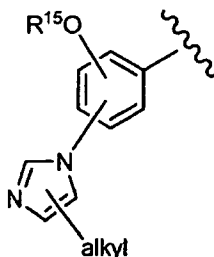
5 In another embodiment  $R^{10}$  is phenyl substituted with 1-3 independently selected  $R^{21}$  groups, and  $R^9$  is selected from the group consisting of imidazolyl and imidazolyl substituted with 1-3 independently selected  $R^{21}$  groups.

In another embodiment  $R^{10}$  is selected from the group consisting of heteroaryl and heteroaryl substituted with 1-3  $R^{21}$  groups, and the  $R^9$  group is  
10 selected from the group consisting of heteroaryl and heteroaryl substituted with 1-3  $R^{21}$  groups, and wherein each  $R^{21}$  is independently selected.

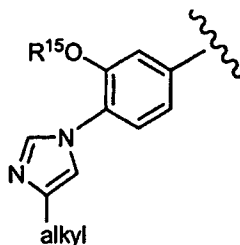
In another embodiment  $R^{10}$  is selected from the group consisting of pyridyl and pyridyl substituted with 1-3  $R^{21}$  groups, and the  $R^9$  group is selected from the group consisting of imidazolyl and imidazolyl substituted with 1-3  $R^{21}$  groups, and  
15 wherein each  $R^{21}$  is independently selected.

In another embodiment  $R^{10}$  is pyridyl, and the  $R^9$  group is imidazolyl substituted with 1-3  $R^{21}$  groups, and wherein each  $R^{21}$  is independently selected.

In another embodiment the  $R^9$ - $R^{10}$ - moiety is:

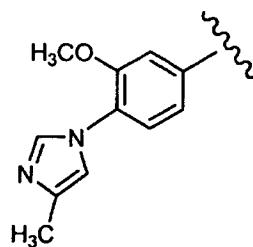


20 In another embodiment the  $R^9$ - $R^{10}$ - moiety is:

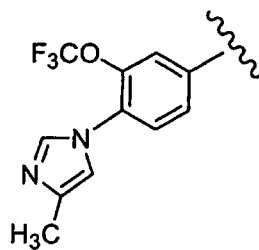


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In another embodiment the R<sup>9</sup>-R<sup>10</sup>- moiety is:

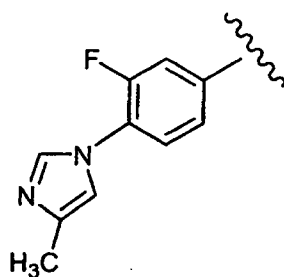


In another embodiment the R<sup>9</sup>-R<sup>10</sup>- moiety is:

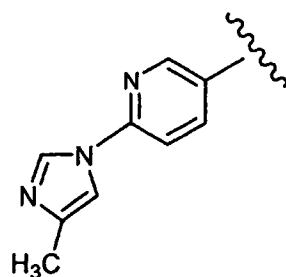


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In another embodiment the R<sup>9</sup>-R<sup>10</sup>- moiety is:



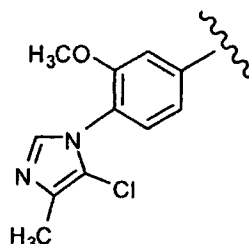
In another embodiment R<sup>9</sup>-R<sup>10</sup>- moiety is:



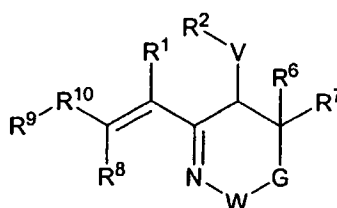
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In another embodiment R<sup>9</sup>-R<sup>10</sup>- moiety is:

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In another embodiment, the present application discloses a compound of formula I, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure of Formula IB:



Formula IB

wherein:

- 10 either (i)  $R^1$  and  $R^2$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being
- 15 independently selected from the group consisting of the moieties shown below; or (ii)  $R^2$  and  $R^6$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5
- 20 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or (iii)  $R^1$  and  $R^2$  are joined together to form a C4-C8 cycloalkyl, C4-

5 C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; and R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

and

15 W is selected from the group consisting of a bond; -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, and -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G is selected from the group consisting of -C(R<sup>3</sup>)(R<sup>4</sup>)-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, -C(O)-O-, and -N(R<sup>13</sup>)-;

V is selected from the group consisting of a bond, -O-, and -N(R<sup>14</sup>)-;

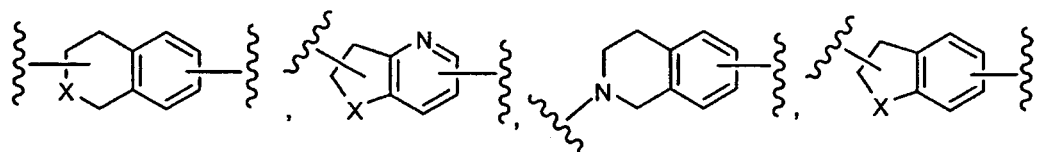
20 R<sup>1</sup> (when R<sup>1</sup> is not joined to R<sup>2</sup>), R<sup>2</sup> (when R<sup>2</sup> is not joined to R<sup>1</sup> or R<sup>6</sup>), R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> (when R<sup>6</sup> is not joined to R<sup>2</sup>), R<sup>7</sup>, R<sup>11</sup> and R<sup>12</sup> can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

- $R^{13}$  is independently selected from the group consisting of H, alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-, arylcycloalkylalkyl-, heteroarylalkyl-, arylheterocycloalkylalkyl-, heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylalkyl-,
- 5 heterocycloalkyl-, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl, arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylalkenyl-, heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl-, aryl, cycloalkylalkyl-, heterocycloalkylalkyl-, heterocycloalkenylalkyl-, heteroaryl, cycloalkylheteroaryl-,
- 10 heterocycloalkylheteroaryl-, cycloalkenylalkyl-, heterocycloalkenylalkyl-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  and  $-N(R^8)_2$ ; and wherein said  $R^{13}$  alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-, arylcycloalkylalkyl-, heteroarylalkyl-, arylheterocycloalkylalkyl-,
- 15 heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylalkyl-, heterocycloalkyl, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl, arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylalkenyl-, heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl-, aryl, cycloalkylalkyl-, heterocycloalkylalkyl-,
- 20 heterocycloalkenylalkyl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylalkyl-, and heterocycloalkenylalkyl- groups are optionally substituted with 1 to 5 groups independently selected from the group consisting of: alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl,
- 25 heteroarylalkyl-, halo,  $-CN$ ,  $-OR^{15}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-SR^{15}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-CH(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $-N(R^{15})(R^{16})$ ,  $-alkyl-N(R^{15})(R^{16})$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-R^{15}$ ,  $-CH_2N(R^{15})(R^{16})$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-CH_2-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,
- 30  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,

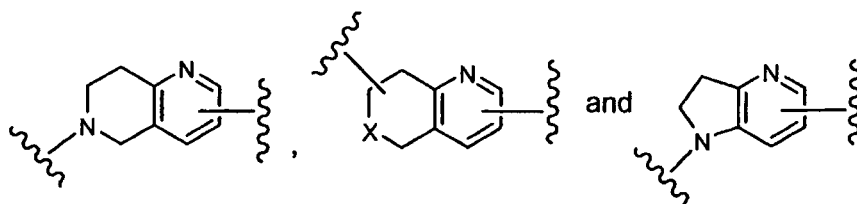
-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and -S(O)<sub>2</sub>R<sup>15</sup>;

R<sup>14</sup> is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>,  
 5 -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, and -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);

R<sup>8</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,  
 10 heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, with each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- being unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from  
 15 the group consisting of the moieties shown below;



20



where X is O, N(R<sup>14</sup>) or S;

wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl-

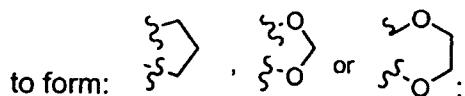
heterocyclalkyl- for  $R^{10}$  as well as the above-noted moieties for  $R^{10}$  can be unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of the moieties shown below; and

- 5  $R^9$  is selected from the group consisting of alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocycl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocycl- and heterocyclalkyl- can be
- 10 unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,
- $R^{15}$ ,  $R^{16}$  and  $R^{17}$  are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, heterocycl-, heterocyclalkyl-, aryl, arylalkyl, heteroaryl, heteroarylalkyl-, arylcycloalkyl-, arylheterocycl-,  $R^{18}$ -alkyl,  $R^{18}$ -cycloalkyl,  $R^{18}$ -cycloalkylalkyl-,  $R^{18}$ -heterocycl-,  $R^{18}$ -heterocyclalkyl-,  $R^{18}$ -aryl,  $R^{18}$ -arylalkyl,  $R^{18}$ -heteroaryl and  $R^{18}$ -heteroarylalkyl-;

- $R^{18}$  is 1-5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl-, arylalkenyl-, arylalkynyl-,  $-NO_2$ , halo,
- 20 heteroaryl, HO-alkoxyalkyl,  $-CF_3$ ,  $-CN$ , alkyl-CN,  $-C(O)R^{19}$ ,  $-C(O)OH$ ,  $-C(O)OR^{19}$ ,  $-C(O)NHR^{20}$ ,  $-C(O)NH_2$ ,  $-C(O)NH_2-C(O)N(alkyl)_2$ ,  $-C(O)N(alkyl)(aryl)$ ,  $-C(O)N(alkyl)(heteroaryl)$ ,  $-SR^{19}$ ,  $-S(O)_2R^{20}$ ,  $-S(O)NH_2$ ,  $-S(O)NH(alkyl)$ ,  $-S(O)N(alkyl)(alkyl)$ ,  $-S(O)NH(aryl)$ ,  $-S(O)_2NH_2$ ,  $-S(O)_2NHR^{19}$ ,  $-S(O)_2NH(heterocycl)$ ,  $-S(O)_2N(alkyl)_2$ ,  $-S(O)_2N(alkyl)(aryl)$ ,  $-OCF_3$ ,  $-OH$ ,  $-OR^{20}$ ,
- 25  $-O-heterocycl$ ,  $-O-cycloalkylalkyl$ ,  $-O-heterocyclalkyl$ ,  $-NH_2$ ,  $-NHR^{20}$ ,  $-N(alkyl)_2$ ,  $-N(arylalkyl)_2$ ,  $-N(arylalkyl)-(heteroarylalkyl)$ ,  $-NHC(O)R^{20}$ ,  $-NHC(O)NH_2$ ,  $-NHC(O)NH(alkyl)$ ,  $-NHC(O)N(alkyl)(alkyl)$ ,  $-N(alkyl)C(O)NH(alkyl)$ ,  $-N(alkyl)C(O)N(alkyl)(alkyl)$ ,  $-NHS(O)_2R^{20}$ ,  $-NHS(O)_2NH(alkyl)$ ,  $-NHS(O)_2N(alkyl)(alkyl)$ ,  $-N(alkyl)S(O)_2NH(alkyl)$  and  $-N(alkyl)S(O)_2N(alkyl)(alkyl)$ ;



or, alternately, two  $R^{18}$  moieties on adjacent carbons can be linked together



$R^{19}$  is alkyl, cycloalkyl, aryl, arylalkyl or heteroarylalkyl;

$R^{20}$  is alkyl, cycloalkyl, aryl, halo substituted aryl, arylalkyl, heteroaryl or

5 heteroarylalkyl;

wherein each of the alkyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl,

heterocyclyl, heterocyclylalkyl, aryl, arylalkyl, alkylaryl, heteroaryl, heteroarylalkyl, alkenyl and alkynyl groups in  $R^1$ ,  $R^2$ ,  $R^1-R^2$ ,  $R^2-R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{14}$  is independently unsubstituted or optionally substituted by 1 to 5

10  $R^{21}$  groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), 15 -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and 20 -S(O)<sub>2</sub>R<sup>15</sup>;

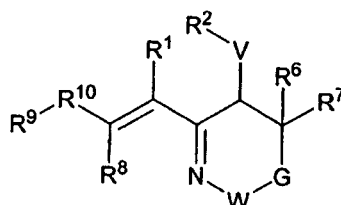
wherein each of the alkyl, cycloalkenyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in  $R^{21}$  is independently unsubstituted or substituted by 1 to 5

25  $R^{22}$  groups independently selected from the group consisting of alkyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),

93

-N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and  
 -S(O)<sub>2</sub>R<sup>15</sup>.

In another embodiment, the present application discloses a compound of  
 5 formula I, or pharmaceutically acceptable salts, solvates, esters or prodrugs of  
 said compound, said compound having the general structure of Formula IB:



Formula IB

wherein:

10 either

(i) R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8  
 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety,  
 wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently  
 selected R<sup>21</sup> substituents, (b) said heterocyclyl moiety is optionally substituted  
 15 with 1-5 independently selected R<sup>21</sup> substituents, and (c) said cycloalkyl,  
 cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl  
 or heteroaryl ring, and the ring moiety resulting from the fusion is optionally  
 substituted with 1-5 independently selected R<sup>21</sup> substituents; or

(ii) R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8  
 20 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety,  
 wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently  
 selected R<sup>21</sup> substituents, (b) said heterocyclyl moiety is optionally substituted  
 with 1-5 independently selected R<sup>21</sup> substituents, and (c) said cycloalkyl,  
 cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl  
 25 or heteroaryl ring, and the ring moiety resulting from the fusion is optionally  
 substituted with 1-5 independently selected R<sup>21</sup> substituents; or

(iii)

- (a)  $R^1$  and  $R^2$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (1) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (2) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and
- (b)  $R^2$  and  $R^6$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (1) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (2) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; and
- (c) said  $R^2$  and  $R^6$  cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or
- (iv)  $R^6$  and either  $R^3$  or  $R^4$  of the  $-C(R^3)(R^4)-G$  moiety, are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, (b) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (c) said cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or
- (v)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-G$  moiety, are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, (b) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (c) said cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from

the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; and

W is selected from the group consisting of a bond, -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, and -C(R<sup>11</sup>)(R<sup>12</sup>)-;

5 G is selected from the group consisting of -C(R<sup>3</sup>)(R<sup>4</sup>)-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, -C(O)-O-, and -N(R<sup>13</sup>)- ;

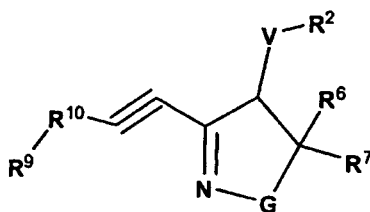
V is selected from the group consisting of a bond, -O-, -C(O)- and -N(R<sup>14</sup>)-;

10  $R^1$  (when  $R^1$  is not joined to  $R^2$ ),  $R^2$  (when  $R^2$  is not joined to  $R^1$  or  $R^6$ ),  $R^5$ ,  $R^6$  (when  $R^6$  is not joined to  $R^2$ ), and  $R^7$  can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocycl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocycl- and heterocyclalkyl- can be unsubstituted or

15 optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

or, alternatively,  $R^1$  (when  $R^1$  is not joined to  $R^2$ ) and  $R^8$  are taken together to form a bond (i.e., there is a triple bond between the carbon atom to which  $R^1$  was bonded to and the carbon to which  $R^8$  was bonded to, i.e., the compound of

20 formula I is a compound of formula IIA:



formula IIA

and  $R^2$ ,  $R^5$ ,  $R^6$ , and  $R^7$  are as defined above, and  $R^3$ ,  $R^4$ ,  $R^{11}$  and  $R^{12}$  are as defined below);

gb

$R^3$  is selected from the group consisting of H, halo (and in one example, F),  $-OR^{15}$  (and in one example  $R^{15}$  is H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or

$R^3$  and  $R^6$  taken together form a bond (i.e.,  $R^3$  and  $R^6$  form a bond between G and the carbon to which  $R^6$  is bound), provided that when  $R^3$  and  $R^6$  form a bond: (1) W is not a bond, (2)  $R^2$  and  $R^6$  are not joined together to form a cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety (as described in (ii) and (iii) above) (3)  $R^6$  and either  $R^3$  or  $R^4$  of the  $-C(R^3)(R^4)-G$  moiety are not joined together to form a cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety (as described in (iv) above), and (4)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-G$  moiety are not joined together to form a heterocyclyl or heterocyclenyl moiety (as described in (v) above);

$R^4$ ,  $R^{11}$  and  $R^{12}$  can be the same or different, each being independently selected from the group consisting of H, halo (and in one example, F),  $-OR^{15}$  (and in one example  $R^{15}$  is H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-,

heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

provided that when one of  $R^3$  or  $R^4$  is selected from the group consisting of:

- OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not selected from the group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, and -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub> (i.e., if one of  $R^3$  or  $R^4$  is -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>, then the other one is not -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, and -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>);

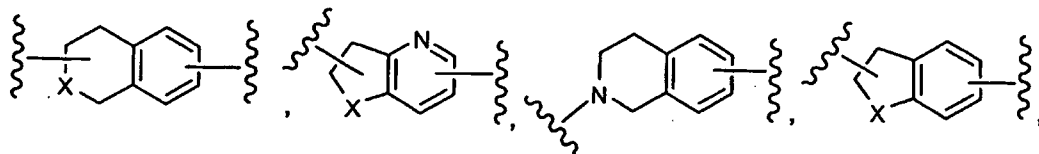
- provided that when one of  $R^{11}$  or  $R^{12}$  is selected from the group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not selected from the group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,

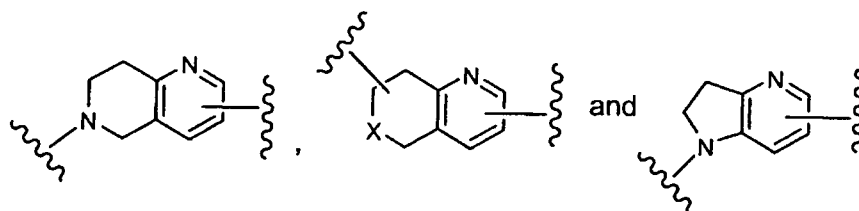
- $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , and  $-N_3$  (i.e., if one of  $R^{11}$  or  $R^{12}$  is  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
5  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , or  $-N_3$ , then the other is not  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
10  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , or  $-N_3$ );

- $R^8$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-,  
 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,  
 15 heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, with each of said alkyl-,  
 alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-,  
 heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- being optionally  
 substituted with 1-3 independently selected  $R^{21}$  substituents;

- $R^9$  is selected from the group consisting of alkyl-, alkenyl-, alkynyl-,  
 20 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,  
 heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, -, wherein each  $R^9$  group is  
 optionally substituted with 1-3 independently selected  $R^{21}$  substituents;

- $R^{10}$  is selected from the group consisting of a bond, alkyl-, alkenyl-,  
 alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,  
 25 heteroarylalkyl-, heterocyclyl-, heterocyclylalkyl- and the moieties:





where X is O, N(R<sup>14</sup>) or S;

wherein each R<sup>10</sup> group (except for the bond) is optionally substituted with 1-3 independently selected R<sup>21</sup> substituents;

- 5 R<sup>13</sup> is independently selected from the group consisting of H, alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-, arylcycloalkylalkyl-, heteroarylalkyl-, arylheterocycloalkylalkyl-, heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylalkyl-, heterocycloalkyl-, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl,
- 10 arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylalkenyl-, heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl-, aryl, cycloalkylalkyl-, heterocycloalkylalkyl-, heterocycloalkenylalkyl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylalkyl-, heterocycloalkenylalkyl-, -OR<sup>15</sup>,
- 15 -CN, -C(O)R<sup>8</sup>, -C(O)OR<sup>9</sup>, -S(O)R<sup>10</sup>, -S(O)<sub>2</sub>R<sup>10</sup>, -C(O)N(R<sup>11</sup>)(R<sup>12</sup>), -S(O)N(R<sup>11</sup>)(R<sup>12</sup>), -S(O)<sub>2</sub>N(R<sup>11</sup>)(R<sup>12</sup>), -NO<sub>2</sub>, -N=C(R<sup>8</sup>)<sub>2</sub> and -N(R<sup>8</sup>)<sub>2</sub>; and wherein said R<sup>13</sup> alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-, arylcycloalkylalkyl-, heteroarylalkyl-, arylheterocycloalkylalkyl-, heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylalkyl-, heterocycloalkyl-, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl,
- 20 arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylalkenyl-, heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl-, aryl, cycloalkylalkyl-, heterocycloalkylalkyl-, heterocycloalkenylalkyl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylalkyl-, and heterocycloalkenylalkyl- groups
- 25 are optionally substituted with 1 to 5 groups independently selected from the group consisting of: alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-,



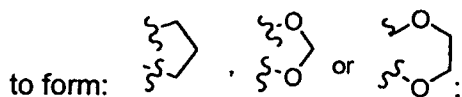
cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>,  
 5 -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and -S(O)<sub>2</sub>R<sup>15</sup>;

- 10 R<sup>14</sup> is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, and -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), wherein each of said alkyl, alkenyl, alkynyl, cycloalkyl,  
 15 cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, and heteroarylalkyl- is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents;

- R<sup>15</sup>, R<sup>16</sup> and R<sup>17</sup> are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-,  
 20 aryl, arylalkyl, heteroaryl, heteroarylalkyl-, arylcycloalkyl-, arylheterocyclyl-, R<sup>18</sup>)-alkyl, R<sup>18</sup>)-cycloalkyl, R<sup>18</sup>)-cycloalkylalkyl-, R<sup>18</sup>)-heterocyclyl, R<sup>18</sup>)-heterocyclylalkyl-, R<sup>18</sup>)-aryl, R<sup>18</sup>)-arylalkyl, R<sup>18</sup>)-heteroaryl and R<sup>18</sup>)-heteroarylalkyl-, wherein r is 1-5;

- Each R<sup>18</sup> is independently selected from the group consisting of alkyl,  
 25 alkenyl, alkynyl, aryl, arylalkyl-, arylalkenyl-, arylalkynyl-, -NO<sub>2</sub>, halo, heteroaryl, HO-alkoxyalkyl, -CF<sub>3</sub>, -CN, alkyl-CN, -C(O)R<sup>19</sup>, -C(O)OH, -C(O)OR<sup>19</sup>, -C(O)NHR<sup>20</sup>, -C(O)NH<sub>2</sub>, -C(O)NH<sub>2</sub>-C(O)N(alkyl)<sub>2</sub>, -C(O)N(alkyl)(aryl), -C(O)N(alkyl)(heteroaryl), -SR<sup>19</sup>, -S(O)<sub>2</sub>R<sup>20</sup>, -S(O)NH<sub>2</sub>, -S(O)NH(alkyl), -S(O)N(alkyl)(alkyl), -S(O)NH(aryl), -S(O)<sub>2</sub>NH<sub>2</sub>, -S(O)<sub>2</sub>NHR<sup>19</sup>,  
 30 -S(O)<sub>2</sub>NH(heterocyclyl), -S(O)<sub>2</sub>N(alkyl)<sub>2</sub>, -S(O)<sub>2</sub>N(alkyl)(aryl), -OCF<sub>3</sub>, -OH, -OR<sup>20</sup>,

- O-heterocyclyl, -O-cycloalkylalkyl, -O-heterocyclylalkyl, -NH<sub>2</sub>, -NHR<sup>20</sup>, -N(alkyl)<sub>2</sub>,  
 -N(arylalkyl)<sub>2</sub>, -N(arylalkyl)-(heteroarylalkyl), -NHC(O)R<sup>20</sup>, -NHC(O)NH<sub>2</sub>,  
 -NHC(O)NH(alkyl), -NHC(O)N(alkyl)(alkyl), -N(alkyl)C(O)NH(alkyl),  
 -N(alkyl)C(O)N(alkyl)(alkyl), -NHS(O)<sub>2</sub>R<sup>20</sup>, -NHS(O)<sub>2</sub>NH(alkyl),  
 5 -NHS(O)<sub>2</sub>N(alkyl)(alkyl), -N(alkyl)S(O)<sub>2</sub>NH(alkyl) and -N(alkyl)S(O)<sub>2</sub>N(alkyl)(alkyl);  
 or, alternately, two R<sup>18</sup> moieties on adjacent carbons can be linked together



R<sup>19</sup> is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl- and heteroarylalkyl-;

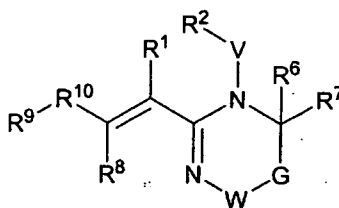
- 10 R<sup>20</sup> is selected from the group consisting of alkyl, cycloalkyl, aryl, halo substituted aryl, arylalkyl-, heteroaryl or heteroarylalkyl-;

- Each R<sup>21</sup> group is independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>,  
 15 -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>),  
 -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>),  
 -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>,  
 -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 20 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and  
 -S(O)<sub>2</sub>R<sup>15</sup>; and wherein each of the R<sup>21</sup> alkyl, cycloalkenyl, cycloalkyl,  
 cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl,  
 heteroarylalkyl-, alkenyl and alkynyl groups is optionally substituted with 1 to 5  
 25 independently selected R<sup>22</sup> groups; and

Each R<sup>22</sup> is independently selected from the group consisting of alkyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>),

-alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and  
 5 -S(O)<sub>2</sub>R<sup>15</sup>.

In another embodiment, this invention discloses a compound of formula I,  
 or pharmaceutically acceptable salts, solvates, esters or prodrugs of said  
 compound, said compound having the general structure of formula IC:



Formula IC

wherein:

- either (i) R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8  
 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl  
 15 moiety, with each of said cycloalkyl or heterocyclyl moiety being  
 unsubstituted or optionally independently being substituted with 1-5  
 substituents which can be the same or different, each substituent being  
 independently selected from the group consisting of the moieties shown  
 below; or (ii) R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-  
 20 C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered  
 heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety  
 being unsubstituted or optionally independently being substituted with 1-5  
 substituents which can be the same or different, each substituent being  
 25 independently selected from the group consisting of the moieties shown  
 below; or (iii) R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-  
 C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered  
 heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety

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being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; and R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

and

W is selected from the group consisting of a bond, -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, and -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G is selected from the group consisting of -C(R<sup>3</sup>)(R<sup>4</sup>)-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, -C(O)-O-, and -N(R<sup>13</sup>)-;

V is selected from the group consisting of a bond, -O-, and -N(R<sup>14</sup>)-;

R<sup>1</sup> (when R<sup>1</sup> is not joined to R<sup>2</sup>), R<sup>2</sup> (when R<sup>2</sup> is not joined to R<sup>1</sup> or R<sup>6</sup>), R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> (when R<sup>6</sup> is not joined to R<sup>2</sup>), R<sup>7</sup>, R<sup>11</sup> and R<sup>12</sup> can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

R<sup>14</sup> is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, heterocyclyl, heterocyclylalkyl, aryl,

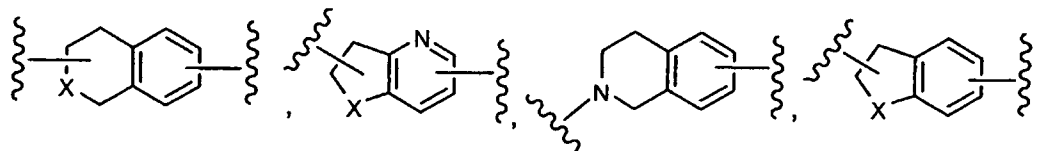
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arylalkyl, heteroaryl, heteroarylalkyl, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, and -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);

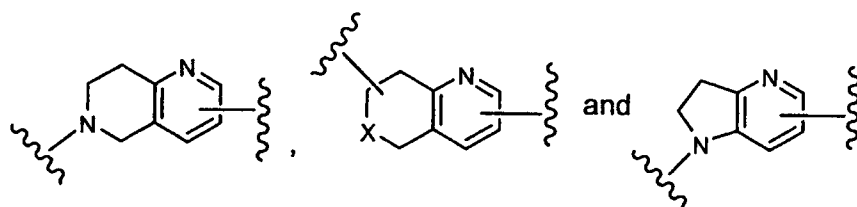
R<sup>8</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,

- 5 heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, with each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- being unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from
- 10 the group consisting of the moieties shown below;

R<sup>10</sup> is selected from the group consisting of a bond, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl-, heterocyclalkyl- and the moieties:



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where X is O, N(R<sup>14</sup>) or S;

wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl-

- 20 heterocyclalkyl- for R<sup>10</sup> as well as the above-noted moieties for R<sup>10</sup> can be unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of the moieties shown below; and

R<sup>9</sup> is selected from the group consisting of alkyl-, alkenyl- and alkynyl-,

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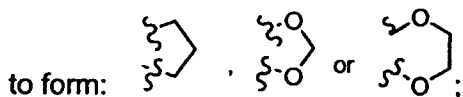
aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be

5 unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

$R^{15}$ ,  $R^{16}$  and  $R^{17}$  are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, arylcycloalkyl-, arylheterocyclyl-,  $R^{18}$ -alkyl,  $R^{18}$ -cycloalkyl,  $R^{18}$ -cycloalkylalkyl,  $R^{18}$ -heterocyclyl,  $R^{18}$ -heterocyclylalkyl,  $R^{18}$ -aryl,  $R^{18}$ -arylalkyl,  $R^{18}$ -heteroaryl and  $R^{18}$ -heteroarylalkyl;

$R^{18}$  is 1-5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl-, arylalkenyl-, arylalkynyl-,  $-\text{NO}_2$ , halo, heteroaryl, HO-alkoxyalkyl,  $-\text{CF}_3$ ,  $-\text{CN}$ , alkyl-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alkyl})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alkyl})(\text{aryl})$ ,  $-\text{C}(\text{O})\text{N}(\text{alkyl})(\text{heteroaryl})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{S}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{S}(\text{O})\text{NH}(\text{aryl})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterocyclyl})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alkyl})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alkyl})(\text{aryl})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  $-\text{O-heterocyclyl}$ ,  $-\text{O-cycloalkylalkyl}$ ,  $-\text{O-heterocyclylalkyl}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alkyl})_2$ ,  $-\text{N}(\text{arylalkyl})_2$ ,  $-\text{N}(\text{arylalkyl})-(\text{heteroarylalkyl})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{C}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{C}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alkyl})$ ,  $-\text{NHS}(\text{O})_2\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{S}(\text{O})_2\text{NH}(\text{alkyl})$  and  $-\text{N}(\text{alkyl})\text{S}(\text{O})_2\text{N}(\text{alkyl})(\text{alkyl})$ ;

25 or, alternately, two  $R^{18}$  moieties on adjacent carbons can be linked together



$R^{19}$  is alkyl, cycloalkyl, aryl, arylalkyl or heteroarylalkyl;

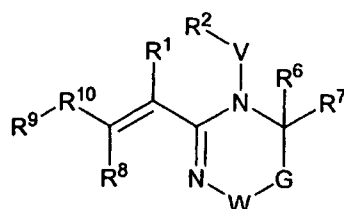
$R^{20}$  is alkyl, cycloalkyl, aryl, halo substituted aryl, arylalkyl, heteroaryl or heteroarylalkyl;

- wherein each of the alkyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, arylalkyl, alkylaryl-, heteroaryl, heteroarylalkyl, alkenyl and alkynyl groups in  $R^1$ ,  $R^2$ ,  $R^1$ - $R^2$ ,  $R^2$ - $R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{14}$  is independently unsubstituted or optionally substituted by 1 to 5
- 5  $R^{21}$  groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>),
- 10 -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and
- 15 -S(O)<sub>2</sub>R<sup>15</sup>;

- wherein each of the alkyl, cycloalkenyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in  $R^{21}$  is independently unsubstituted or substituted by 1 to 5
- 20  $R^{22}$  groups independently selected from the group consisting of alkyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),
- 25 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and -S(O)<sub>2</sub>R<sup>15</sup>.

- In another embodiment, this invention discloses a compound of formula I, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said
- 30 compound, said compound having the general structure of formula IC:

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Formula IC

wherein:

either

- 5 (i) R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents, (b) said heterocyclyl moiety is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents, and (c) said cycloalkyl,
- 10 cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents; or
- (ii) R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety,
- 15 wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents, (b) said heterocyclyl moiety is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents, and (c) said cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally
- 20 substituted with 1-5 independently selected R<sup>21</sup> substituents; or
- (iii)
- (a) R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (1) said cycloalkyl moiety is optionally substituted with 1-5
- 25 independently selected R<sup>21</sup> substituents, and (2) said heterocyclyl moiety is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents, and



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(b)  $R^2$  and  $R^6$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (1) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (2) said heterocyclyl moiety is

5 optionally substituted with 1-5 independently selected  $R^{21}$  substituents; and

(c) said  $R^2$  and  $R^6$  cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

10 (iv)  $R^6$  and either  $R^3$  or  $R^4$  of the  $-C(R^3)(R^4)-G$  moiety, are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, (b) said heterocyclyl moiety is optionally substituted with 1-5 independently

15 selected  $R^{21}$  substituents, and (c) said cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

(v)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-G$  moiety, are joined together to form a

20 C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, (b) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (c) said cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is

25 optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; and

W is selected from the group consisting of a bond, -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, and -C(R<sup>11</sup>)(R<sup>12</sup>)-;

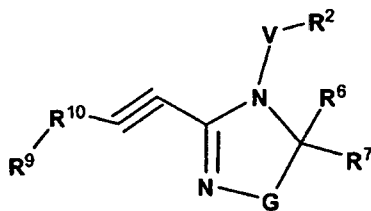
30 G is selected from the group consisting of  $-C(R^3)(R^4)-$ , -C(O)-, -S-, -S(O)-,

-S(O<sub>2</sub>)-, -C(O)-O-, and -N(R<sup>13</sup>)-;

V is selected from the group consisting of a bond, -O-, -C(O)- and -N(R<sup>14</sup>)-;

R<sup>1</sup> (when R<sup>1</sup> is not joined to R<sup>2</sup>), R<sup>2</sup> (when R<sup>2</sup> is not joined to R<sup>1</sup> or R<sup>6</sup>), R<sup>5</sup>, R<sup>6</sup> (when R<sup>6</sup> is not joined to R<sup>2</sup>), and R<sup>7</sup> can be the same or different, each being  
 5 independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or  
 10 optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

or, alternatively, R<sup>1</sup> (when R<sup>1</sup> is not joined to R<sup>2</sup>) and R<sup>8</sup> are taken together to form a bond (i.e., there is a triple bond between the carbon atom to which R<sup>1</sup>  
 15 was bonded to and the carbon to which R<sup>8</sup> was bonded to, i.e., the compound of formula I is a compound of formula II:



formula IIB

and R<sup>2</sup>, R<sup>5</sup>, R<sup>6</sup>, and R<sup>7</sup> are as defined above, and R<sup>3</sup>, R<sup>4</sup>, R<sup>11</sup> and R<sup>12</sup> are as defined below);

20 R<sup>3</sup> is selected from the group consisting of H, halo (and in one example, F), -OR<sup>15</sup> (and in one example R<sup>15</sup> is H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>),  
 25 S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alkyl-,

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alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-  
 5 can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or

$R^3$  and  $R^6$  taken together form a bond (i.e.,  $R^3$  and  $R^6$  form a bond between G and the carbon to which  $R^6$  is bound), provided that when  $R^3$  and  $R^6$  form a  
 10 bond: (1) W is not a bond, (2)  $R^2$  and  $R^6$  are not joined together to form a cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety (as described in (ii) and (iii) above) (3)  $R^6$  and either  $R^3$  or  $R^4$  of the  $-C(R^3)(R^4)-$  G moiety are not joined together to form a cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety (as described in (iv) above), and (4)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety  
 15 are not joined together to form a heterocyclyl or heterocyclenyl moiety (as described in (v) above);

$R^4$ ,  $R^{11}$  and  $R^{12}$  can be the same or different, each being independently selected from the group consisting of H, halo (and in one example, F),  $-OR^{15}$  (and in one example  $R^{15}$  is H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  
 20  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-,  
 25 heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected  
 30 from the group consisting of the moieties shown below,

provided that when one of  $R^3$  or  $R^4$  is selected from the group consisting of:

- OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>,  
 5 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not selected from the  
 group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, and -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
 10 =NOR<sup>15</sup>, and -N<sub>3</sub> (i.e., if one of  $R^3$  or  $R^4$  is -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,  
 -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>,  
 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>, then the other one is not -OR<sup>15</sup>, -CN, -SR<sup>15</sup>,  
 15 and -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>,  
 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>);

provided that when one of  $R^{11}$  or  $R^{12}$  is selected from the group consisting

- 20 of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>),  
 -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not  
 selected from the group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,  
 25 -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
 =NOR<sup>15</sup>, and -N<sub>3</sub> (i.e., if one of  $R^{11}$  or  $R^{12}$  is -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,  
 -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 30 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,

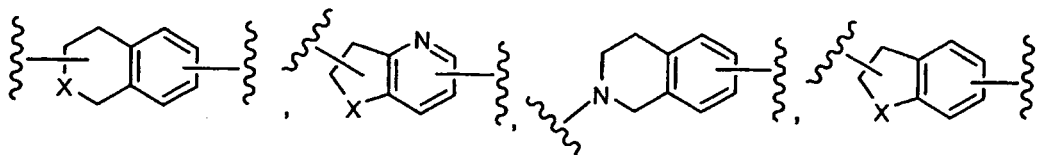
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- 5 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>, then the other is not -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, or -N<sub>3</sub>;

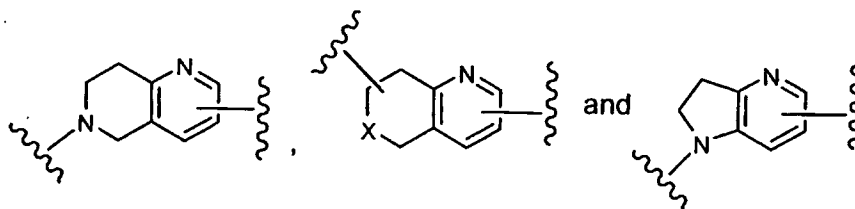
- R<sup>8</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, with each of said alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- being optionally substituted with 1-3 independently selected R<sup>21</sup> substituents;

- R<sup>9</sup> is selected from the group consisting of alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- is optionally substituted with 1-3 independently selected R<sup>21</sup> substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

R<sup>10</sup> is selected from the group consisting of a bond, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl-, heterocyclylalkyl- and the moieties:



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where X is O, N(R<sup>14</sup>) or S;

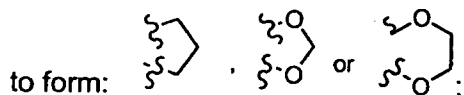
wherein each of said R<sup>10</sup> moieties (except the the bond) is optionally substituted with 1-3 independently selected R<sup>21</sup> substituents which can be the same or different, each being independently selected from the group consisting of the moieties shown below; and

R<sup>14</sup> is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, heterocyclyl, heterocyclylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, and -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), wherein each of said alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, heterocyclyl, heterocyclylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents;

R<sup>15</sup>, R<sup>16</sup> and R<sup>17</sup> are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, arylcycloalkyl-, arylheterocyclyl-, (R<sup>18</sup>)<sub>r</sub>-alkyl, (R<sup>18</sup>)<sub>r</sub>-cycloalkyl, (R<sup>18</sup>)<sub>r</sub>-cycloalkylalkyl, (R<sup>18</sup>)<sub>r</sub>-heterocyclyl, (R<sup>18</sup>)<sub>r</sub>-heterocyclylalkyl, (R<sup>18</sup>)<sub>r</sub>-aryl, (R<sup>18</sup>)<sub>r</sub>-arylalkyl, (R<sup>18</sup>)<sub>r</sub>-heteroaryl and (R<sup>18</sup>)<sub>r</sub>-heteroarylalkyl, wherein r is 1-5;

Each R<sup>18</sup> is independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl-, arylalkenyl-, arylalkynyl-, -NO<sub>2</sub>, halo, heteroaryl, HO-alkoxyalkyl, -CF<sub>3</sub>, -CN, alkyl-CN, -C(O)R<sup>19</sup>, -C(O)OH, -C(O)OR<sup>19</sup>, -C(O)NHR<sup>20</sup>, -C(O)NH<sub>2</sub>, -C(O)NH<sub>2</sub>-C(O)N(alkyl)<sub>2</sub>, -C(O)N(alkyl)(aryl), -C(O)N(alkyl)(heteroaryl), -SR<sup>19</sup>, -S(O)<sub>2</sub>R<sup>20</sup>, -S(O)NH<sub>2</sub>, -S(O)NH(alkyl), -S(O)N(alkyl)(alkyl), -S(O)NH(aryl), -S(O)<sub>2</sub>NH<sub>2</sub>, -S(O)<sub>2</sub>NHR<sup>19</sup>, -S(O)<sub>2</sub>NH(heterocyclyl), -S(O)<sub>2</sub>N(alkyl)<sub>2</sub>, -S(O)<sub>2</sub>N(alkyl)(aryl), -OCF<sub>3</sub>, -OH, -OR<sup>20</sup>,

- O-heterocyclyl, -O-cycloalkylalkyl, -O-heterocyclylalkyl, -NH<sub>2</sub>, -NHR<sup>20</sup>, -N(alkyl)<sub>2</sub>, -N(arylalkyl)<sub>2</sub>, -N(arylalkyl)-(heteroarylalkyl), -NHC(O)R<sup>20</sup>, -NHC(O)NH<sub>2</sub>, -NHC(O)NH(alkyl), -NHC(O)N(alkyl)(alkyl), -N(alkyl)C(O)NH(alkyl), -N(alkyl)C(O)N(alkyl)(alkyl), -NHS(O)<sub>2</sub>R<sup>20</sup>, -NHS(O)<sub>2</sub>NH(alkyl),
- 5 -NHS(O)<sub>2</sub>N(alkyl)(alkyl), -N(alkyl)S(O)<sub>2</sub>NH(alkyl) and -N(alkyl)S(O)<sub>2</sub>N(alkyl)(alkyl); or, alternately, two R<sup>18</sup> moieties on adjacent carbons can be linked together



R<sup>19</sup> is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkyl- and heteroarylalkyl-;

- 10 R<sup>20</sup> is selected from the group consisting of alkyl, cycloalkyl, aryl, halo substituted aryl, arylalkyl-, heteroaryl and heteroarylalkyl-;

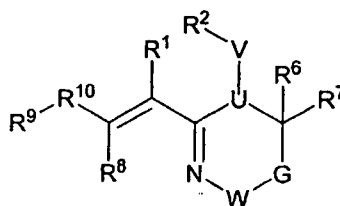
- Each R<sup>21</sup> group independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>,
- 15 -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),
- 20 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and -S(O)<sub>2</sub>R<sup>15</sup>; and wherein each of the R<sup>21</sup> alkyl, cycloalkenyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups is optionally substituted with 1 to 5
- 25 independently selected R<sup>22</sup> groups; and

Each R<sup>22</sup> is independently selected from the group consisting of alkyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>),

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- alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and  
 5 -S(O)<sub>2</sub>R<sup>15</sup>.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

wherein U is C(R<sup>5</sup>);

R<sup>1</sup> is H;

R<sup>2</sup> and R<sup>6</sup> are connected to form a 4-7 membered cycloalkyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

R<sup>8</sup> is H;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

R<sup>10</sup> is phenyl; and

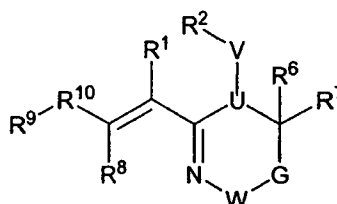
R<sup>9</sup> is imidazol-1-yl, and the other moieties are as defined earlier.



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In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

5

wherein U is C(R<sup>5</sup>);

R<sup>6</sup> is H;

R<sup>1</sup> and R<sup>2</sup> are connected to form a 4-7 membered cycloalkyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

10

R<sup>8</sup> is H;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

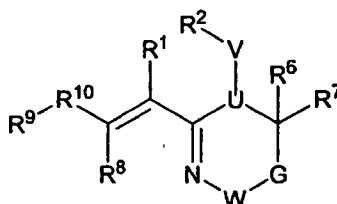
15

R<sup>10</sup> is phenyl; and

20

R<sup>9</sup> is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



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## Formula I

wherein U is C(R<sup>5</sup>) or N;

R<sup>1</sup> is H;

R<sup>2</sup> and R<sup>6</sup> are connected to form a 5-8 membered heterocyclyl ring;

5 R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

R<sup>8</sup> is H;

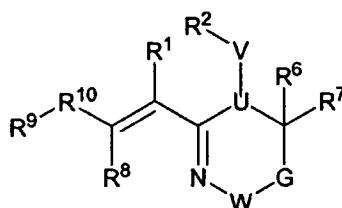
R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and  
 10 alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

15 R<sup>10</sup> is phenyl; and

R<sup>9</sup> is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:

20



Formula I

wherein U is C(R<sup>5</sup>);

R<sup>6</sup> is H;

25 R<sup>1</sup> and R<sup>2</sup> are connected to form a 5-8 membered heterocyclyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

R<sup>8</sup> is H;

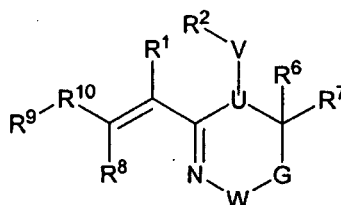
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R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

R<sup>10</sup> is phenyl; and

R<sup>9</sup> is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

wherein U is C(R<sup>5</sup>) or N;

R<sup>1</sup> and R<sup>2</sup> are connected to form a 5-8 membered heterocyclyl ring;

R<sup>2</sup> and R<sup>6</sup> are connected to form a 5-8 membered heterocyclyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

R<sup>8</sup> is H;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same

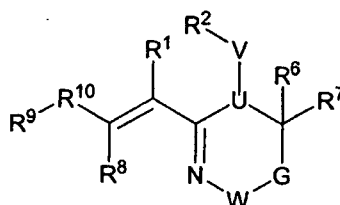
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or different, each substituent being independently selected from the group consisting of moieties described earlier;

$R^{10}$  is phenyl; and

$R^9$  is imidazol-1-yl, and the other moieties are as defined earlier.

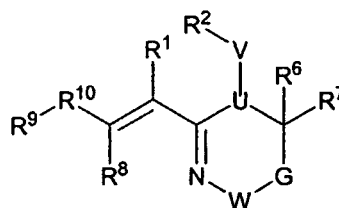
- 5 In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

- 10 wherein U is  $C(R^5)$ ;
- $R^2$  and  $R^6$  are connected to form a 4-7 membered cycloalkyl ring;
- $R^1$  and  $R^2$  are connected to form a 4-7 membered cycloalkyl ring;
- $R^7$  is 3-(1,1'-biphenyl)-yl;
- $R^8$  is H;
- 15  $R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or
- 20 optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;
- $R^{10}$  is phenyl; and
- $R^9$  is imidazol-1-yl, and the other moieties are as defined earlier.
- 25 In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:

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Formula I

wherein U is C(R<sup>5</sup>) or N;

R<sup>1</sup> and R<sup>2</sup> are connected to form a piperidiny ring;

5 R<sup>2</sup> and R<sup>6</sup> are connected to form a piperidiny ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

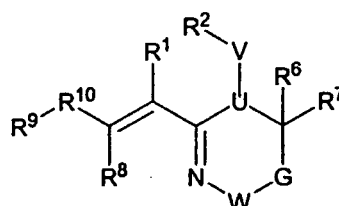
R<sup>8</sup> is H;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-,  
 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-,  
 10 heterocycl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and  
 alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,  
 heteroarylalkyl-, heterocycl- and heterocyclalkyl- can be unsubstituted or  
 optionally independently substituted with 1-5 substituents which can be the same  
 or different, each substituent being independently selected from the group  
 15 consisting of moieties described earlier;

R<sup>10</sup> is phenyl; and

R<sup>9</sup> is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or  
 pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound,  
 20 said compound having the general structure shown in the formula I:



Formula I

wherein U is N;

R<sup>1</sup> and R<sup>2</sup> are connected to form a piperaziny ring;

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$R^2$  and  $R^6$  are connected to form a piperazinyl ring;

$R^7$  is 3-(1,1'-biphenyl)-yl;

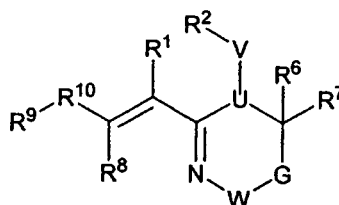
$R^8$  is H;

$R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-,  
 5 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-,  
 heterocyclyl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and  
 alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,  
 heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or  
 optionally independently substituted with 1-5 substituents which can be the same  
 10 or different, each substituent being independently selected from the group  
 consisting of moieties described earlier;

$R^{10}$  is phenyl; and

$R^9$  is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or  
 15 pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound,  
 said compound having the general structure shown in the formula I:



Formula I

wherein U is C( $R^5$ ) or N;

20  $R^1$  and  $R^2$  are connected to form a piperidinyl ring;

$R^2$  and  $R^6$  are connected to form a piperazinyl ring;

$R^7$  is 3-(1,1'-biphenyl)-yl;

$R^8$  is H;

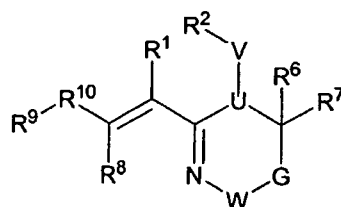
$R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-,  
 25 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-,  
 heterocyclyl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and  
 alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,

heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

5  $R^{10}$  is phenyl; and

$R^9$  is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

wherein U is C( $R^5$ ) or N;

$R^1$  and  $R^2$  are connected to form a piperazinyl ring;

$R^2$  and  $R^6$  are connected to form a piperidnyl ring;

15  $R^7$  is 3-(1,1'-biphenyl)-yl;

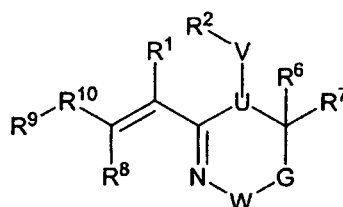
$R^8$  is H;

$R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

25  $R^{10}$  is phenyl; and

$R^9$  is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

5

wherein U is C(R<sup>5</sup>);

R<sup>1</sup> and R<sup>2</sup> are connected to form a cyclohexyl ring;

R<sup>2</sup> and R<sup>6</sup> are connected to form a piperidinyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

10

R<sup>8</sup> is H;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

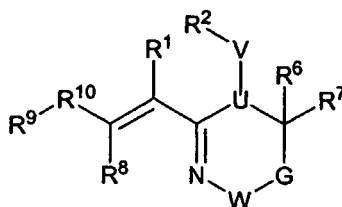
15

R<sup>10</sup> is phenyl; and

20

R<sup>9</sup> is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:





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## Formula I

wherein U is C(R<sup>5</sup>);

R<sup>1</sup> and R<sup>2</sup> are connected to form a cyclohexyl ring;

R<sup>2</sup> and R<sup>6</sup> are connected to form a piperazinyl ring;

5 R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

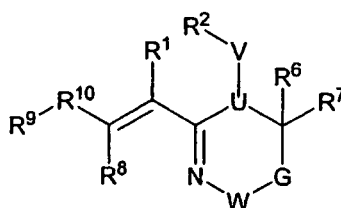
R<sup>8</sup> is H;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and  
10 alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

15 R<sup>10</sup> is phenyl; and

R<sup>9</sup> is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



20

Formula I

wherein U is C(R<sup>5</sup>);

R<sup>1</sup> and R<sup>2</sup> are connected to form a piperidinyl ring;

R<sup>2</sup> and R<sup>6</sup> are connected to form a cyclohexyl ring;

25 R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

R<sup>8</sup> is H;

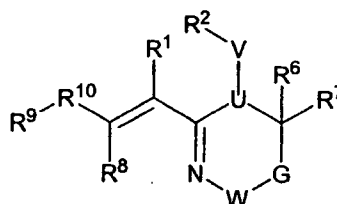


**R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;**

**R<sup>10</sup> is phenyl; and**

10 R<sup>9</sup> is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



### Formula I

15

wherein  $U$  is  $C(R^5)$ ;

**R<sup>1</sup> and R<sup>2</sup> are connected to form a piperazinyl ring;**

**R<sup>2</sup> and R<sup>6</sup> are connected to form a cyclohexyl ring;**

**R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;**

20  $R^8$  is H;

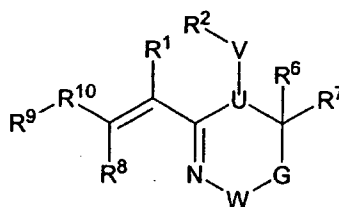
R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same

or different, each substituent being independently selected from the group consisting of moieties described earlier;

$R^{10}$  is phenyl; and

$R^9$  is imidazol-1-yl, and the other moieties are as defined earlier.

- 5 In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

wherein U is C( $R^5$ ) or N;

$R^6$  is H;

$R^1$  and  $R^2$  are connected to form a piperidinyl ring;

$R^7$  is 3-(1,1'-biphenyl)-yl;

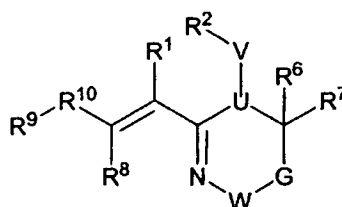
- 15  $R^8$  is H;

$R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

$R^{10}$  is phenyl; and

- 25  $R^9$  is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

5

wherein U is C(R<sup>5</sup>) or N;

R<sup>6</sup> is H;

R<sup>1</sup> and R<sup>2</sup> are connected to form a piperazinyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

10

R<sup>8</sup> is H;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

15

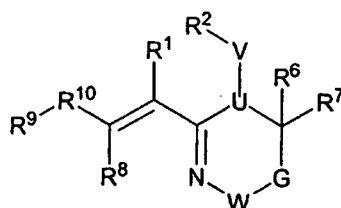
R<sup>10</sup> is phenyl; and

20

R<sup>9</sup> is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:

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Formula I

wherein U is C(R<sup>5</sup>) or N;

R<sup>1</sup> is H;

5 R<sup>6</sup> and R<sup>2</sup> are connected to form a piperidinyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

R<sup>8</sup> is H;

10 R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group

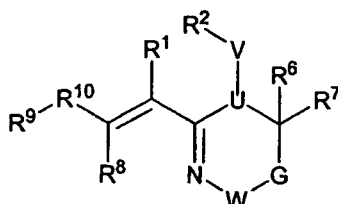
15 consisting of moieties described earlier;

R<sup>10</sup> is phenyl; and

R<sup>9</sup> is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound,

20 said compound having the general structure shown in the formula I:



Formula I

wherein U is C(R<sup>5</sup>) or N;

R<sup>1</sup> is H;

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$R^6$  and  $R^2$  are connected to form a piperazinyl ring;

$R^7$  is 3-(1,1'-biphenyl)-yl;

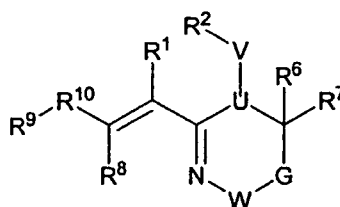
$R^8$  is H;

$R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-,  
 5 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-,  
 heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and  
 alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,  
 heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or  
 optionally independently substituted with 1-5 substituents which can be the same  
 10 or different, each substituent being independently selected from the group  
 consisting of moieties described earlier;

$R^{10}$  is phenyl; and

$R^9$  is imidazol-1-yl, and the other moieties are as defined earlier.

In another embodiment, this invention discloses a compound, or  
 15 pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound,  
 said compound having the general structure shown in the formula I:



Formula I

wherein U is C( $R^5$ );

20  $R^1$  is H;

$R^2$  and  $R^6$  are connected to form a 4-7 membered cycloalkyl ring;

$R^7$  is 3-(1,1'-biphenyl)-yl;

$R^8$  is H;

$R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-,  
 25 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-,  
 heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and  
 alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,

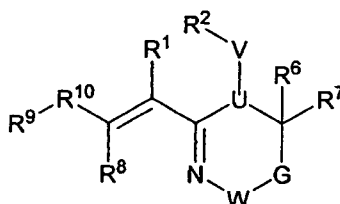
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heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

- 5         $R^{10}$  is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example  $R^{10}$  is 3-methoxy-phenyl, and in another example  $R^{10}$  is 3-F-phenyl);

$R^9$  is 4-methyl-imidazolyl-1-yl.

- 10        In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

wherein U is C( $R^5$ );

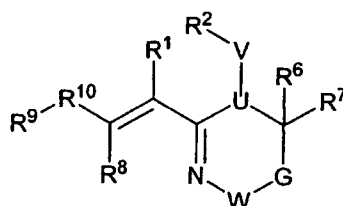
- 15         $R^6$  is H;  
 $R^1$  and  $R^2$  are connected to form a 4-7 membered cycloalkyl ring;  
 $R^7$  is 3-(1,1'-biphenyl)-yl;  
 $R^8$  is H;  
 $R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-,  
20        aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-,  
heterocyclyl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and  
alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,  
heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or  
optionally independently substituted with 1-5 substituents which can be the same  
25        or different, each substituent being independently selected from the group  
consisting of moieties described earlier;

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$R^{10}$  is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example  $R^{10}$  is 3-methoxy-phenyl, and in another example  $R^{10}$  is 3-F-phenyl);

$R^9$  is 4-methyl-imidazolyl-1-yl.

- 5 In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

- 10 wherein U is C( $R^5$ ) or N;

$R^1$  is H;

$R^2$  and  $R^6$  are connected to form a 5-8 membered heterocyclyl ring;

$R^7$  is 3-(1,1'-biphenyl)-yl;

$R^8$  is H;

- 15  $R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or  
 20 optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

- $R^{10}$  is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example  $R^{10}$  is 3-methoxy-phenyl, and in another example  $R^{10}$  is 3-F-phenyl);  
 25

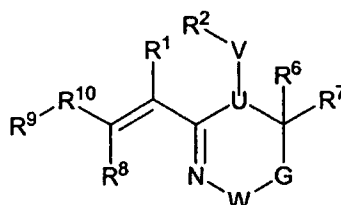
$R^9$  is 4-methyl-imidazolyl-1-yl.



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In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

5

wherein U is C(R<sup>5</sup>);

R<sup>6</sup> is H;

R<sup>1</sup> and R<sup>2</sup> are connected to form a 5-8 membered heterocyclyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

10

R<sup>8</sup> is H;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

R<sup>10</sup> is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example R<sup>10</sup> is 3-methoxy-phenyl, and in another example R<sup>10</sup> is 3-F-phenyl);

20

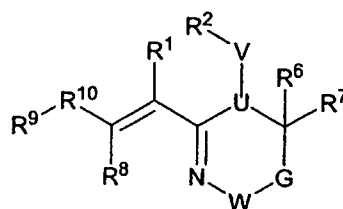
R<sup>9</sup> is 4-methyl-imidazolyl-1-yl.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:

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Formula I

wherein U is C(R<sup>5</sup>) or N;

R<sup>1</sup> and R<sup>2</sup> are connected to form a 5-8 membered heterocyclyl ring;

5 R<sup>2</sup> and R<sup>6</sup> are connected to form a 5-8 membered heterocyclyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

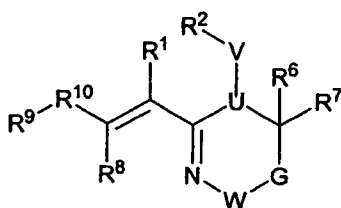
R<sup>8</sup> is H;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-,  
 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-,  
 10 heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and  
 alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,  
 heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or  
 optionally independently substituted with 1-5 substituents which can be the same  
 or different, each substituent being independently selected from the group  
 15 consisting of moieties described earlier;

R<sup>10</sup> is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example R<sup>10</sup> is 3-methoxy-phenyl, and in another example R<sup>10</sup> is 3-F-phenyl);

R<sup>9</sup> is 4-methyl-imidazolyl-1-yl.

20 In another embodiment, this invention discloses a compound, or  
 pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound,  
 said compound having the general structure shown in the formula I:



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## Formula I

wherein U is C(R<sup>5</sup>);

R<sup>2</sup> and R<sup>6</sup> are connected to form a 4-7 membered cycloalkyl ring;

R<sup>1</sup> and R<sup>2</sup> are connected to form a 4-7 membered cycloalkyl ring;

5 R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

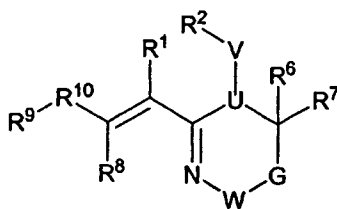
R<sup>8</sup> is H;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocycl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and  
10 alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocycl- and heterocyclalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

15 R<sup>10</sup> is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example R<sup>10</sup> is 3-methoxy-phenyl, and in another example R<sup>10</sup> is 3-F-phenyl);

R<sup>9</sup> is 4-methyl-imidazolyl-1-yl.

In another embodiment, this invention discloses a compound, or  
20 pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

wherein U is C(R<sup>5</sup>) or N;

25 R<sup>1</sup> and R<sup>2</sup> are connected to form a piperidiny ring;

R<sup>2</sup> and R<sup>6</sup> are connected to form a piperidiny ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

135

$R^8$  is H;

$R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and

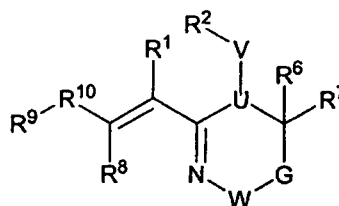
5 alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

10  $R^{10}$  is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example  $R^{10}$  is 3-methoxy-phenyl, and in another example  $R^{10}$  is 3-F-phenyl);

$R^9$  is 4-methyl-imidazolyl-1-yl.

In another embodiment, this invention discloses a compound, or

15 pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

wherein U is N;

20  $R^1$  and  $R^2$  are connected to form a piperazinyl ring;

$R^2$  and  $R^6$  are connected to form a piperazinyl ring;

$R^7$  is 3-(1,1'-biphenyl)-yl;

$R^8$  is H;

$R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-,

25 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,

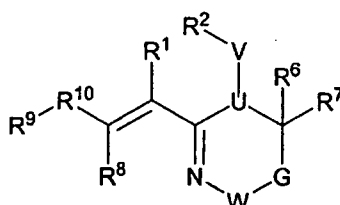
heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

- 5            R<sup>10</sup> is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example R<sup>10</sup> is 3-methoxy-phenyl, and in another example R<sup>10</sup> is 3-F-phenyl);

**R<sup>9</sup> is 4-methyl-imidazolyl-1-yl.**

In another embodiment, this invention discloses a compound, or

- 10 pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound,  
said compound having the general structure shown in the formula I:



### Formula 1

wherein U is  $C(R^5)$  or N;

- 15      R<sup>1</sup> and R<sup>2</sup> are connected to form a piperidinyl ring;  
           R<sup>2</sup> and R<sup>6</sup> are connected to form a piperazinyl ring;  
           R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;  
           R<sup>8</sup> is H;

**R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-,**

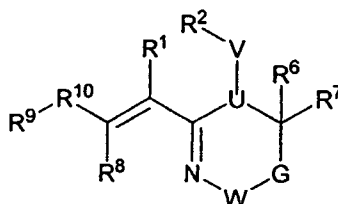
- 20 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same  
25 or different, each substituent being independently selected from the group consisting of moieties described earlier;

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$R^{10}$  is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example  $R^{10}$  is 3-methoxy-phenyl, and in another example  $R^{10}$  is 3-F-phenyl);

$R^9$  is 4-methyl-imidazolyl-1-yl.

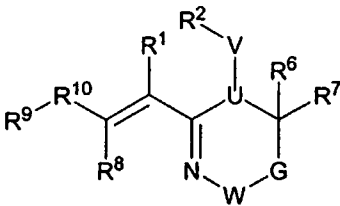
- 5 In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

- 10 wherein U is C( $R^5$ ) or N;  
 $R^1$  and  $R^2$  are connected to form a piperazinyl ring;  
 $R^2$  and  $R^6$  are connected to form a piperidnyl ring;  
 $R^7$  is 3-(1,1'-biphenyl)-yl;  
 $R^8$  is H;  
15  $R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or  
20 optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;  
 $R^{10}$  is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example  $R^{10}$  is 3-methoxy-phenyl, and in another example  $R^{10}$   
25 is 3-F-phenyl);  
 $R^9$  is 4-methyl-imidazolyl-1-yl.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

5

wherein U is C(R<sup>5</sup>);

R<sup>1</sup> and R<sup>2</sup> are connected to form a cyclohexyl ring;

R<sup>2</sup> and R<sup>6</sup> are connected to form a piperidinyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

10

R<sup>8</sup> is H;

15

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

20

R<sup>10</sup> is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example R<sup>10</sup> is 3-methoxy-phenyl, and in another example R<sup>10</sup> is 3-F-phenyl);

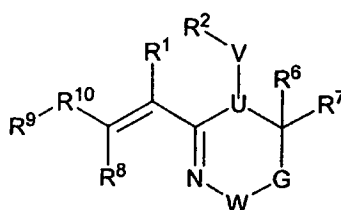
R<sup>9</sup> is 4-methyl-imidazolyl-1-yl.

25

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:

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Formula I

wherein U is C(R<sup>5</sup>);

R<sup>1</sup> and R<sup>2</sup> are connected to form a cyclohexyl ring;

5 R<sup>2</sup> and R<sup>6</sup> are connected to form a piperazinyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

R<sup>8</sup> is H;

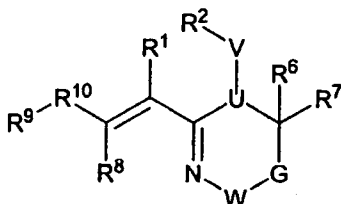
10 R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group

15 consisting of moieties described earlier;

R<sup>10</sup> is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example R<sup>10</sup> is 3-methoxy-phenyl, and in another example R<sup>10</sup> is 3-F-phenyl);

R<sup>9</sup> is 4-methyl-imidazolyl-1-yl.

20 In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I



MO

wherein U is C(R<sup>5</sup>);

R<sup>1</sup> and R<sup>2</sup> are connected to form a piperidinyl ring;

R<sup>2</sup> and R<sup>6</sup> are connected to form a cyclohexyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

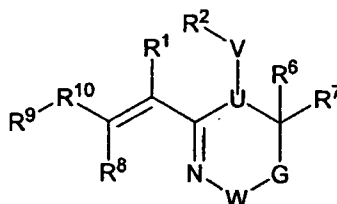
5 R<sup>8</sup> is H;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

10 R<sup>10</sup> is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example R<sup>10</sup> is 3-methoxy-phenyl, and in another example R<sup>10</sup> is 3-F-phenyl);

R<sup>9</sup> is 4-methyl-imidazolyl-1-yl.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, 20 said compound having the general structure shown in the formula I:



Formula I

wherein U is C(R<sup>5</sup>);

R<sup>1</sup> and R<sup>2</sup> are connected to form a piperazinyl ring;

25 R<sup>2</sup> and R<sup>6</sup> are connected to form a cyclohexyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

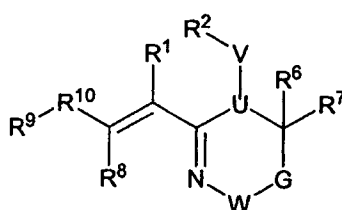
R<sup>8</sup> is H;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

10 R<sup>10</sup> is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example R<sup>10</sup> is 3-methoxy-phenyl, and in another example R<sup>10</sup> is 3-F-phenyl);

R<sup>9</sup> is 4-methyl-imidazolyl-1-yl.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, 15 said compound having the general structure shown in the formula I:



Formula i

wherein U is  $C(R^5)$  or N;

$R^6$  is H;

20 R<sup>1</sup> and R<sup>2</sup> are connected to form a piperidinyl ring;

**R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;**

$R^8$  is  $H$ ;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or

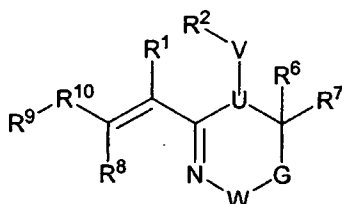
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optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

$R^{10}$  is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example  $R^{10}$  is 3-methoxy-phenyl, and in another example  $R^{10}$  is 3-F-phenyl);

$R^9$  is 4-methyl-imidazolyl-1-yl.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

wherein U is C( $R^5$ ) or N;

$R^6$  is H;

$R^1$  and  $R^2$  are connected to form a piperazinyl ring;

$R^7$  is 3-(1,1'-biphenyl)-yl;

$R^8$  is H;

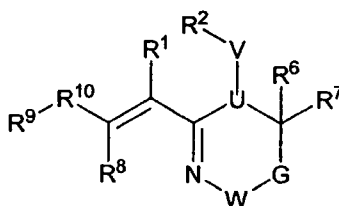
$R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

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$R^{10}$  is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example  $R^{10}$  is 3-methoxy-phenyl, and in another example  $R^{10}$  is 3-F-phenyl);

$R^9$  is 4-methyl-imidazolyl-1-yl.

- 5 In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

wherein U is C( $R^5$ ) or N;

$R^1$  is H;

$R^6$  and  $R^2$  are connected to form a piperidiny ring;

$R^7$  is 3-(1,1'-biphenyl)-yl;

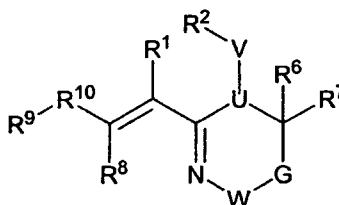
- 15  $R^8$  is H;

- $R^5$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

- 20  $R^{10}$  is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example  $R^{10}$  is 3-methoxy-phenyl, and in another example  $R^{10}$  is 3-F-phenyl);

$R^9$  is 4-methyl-imidazolyl-1-yl.

In another embodiment, this invention discloses a compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula I:



Formula I

wherein U is C(R<sup>5</sup>) or N;

R<sup>1</sup> is H;

R<sup>6</sup> and R<sup>2</sup> are connected to form a piperazinyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

R<sup>8</sup> is H;

R<sup>5</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of moieties described earlier;

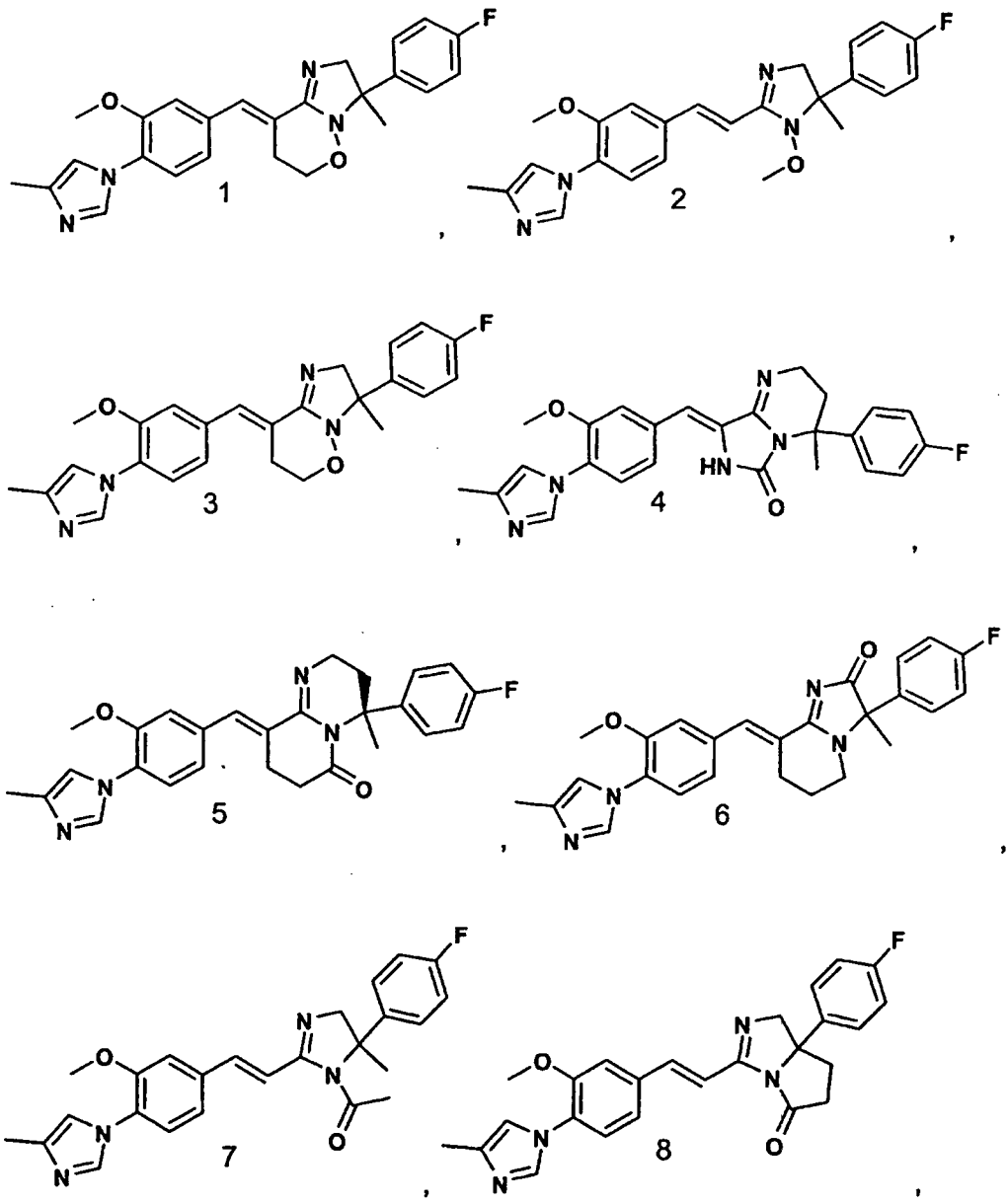
R<sup>10</sup> is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl (and in one example R<sup>10</sup> is 3-methoxy-phenyl, and in another example R<sup>10</sup> is 3-F-phenyl);

R<sup>9</sup> is 4-methyl-imidazolyl-1-yl.

An illustrative group of compounds of the invention are shown in Table 1.

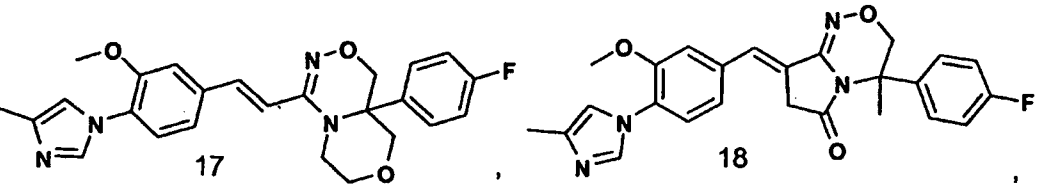
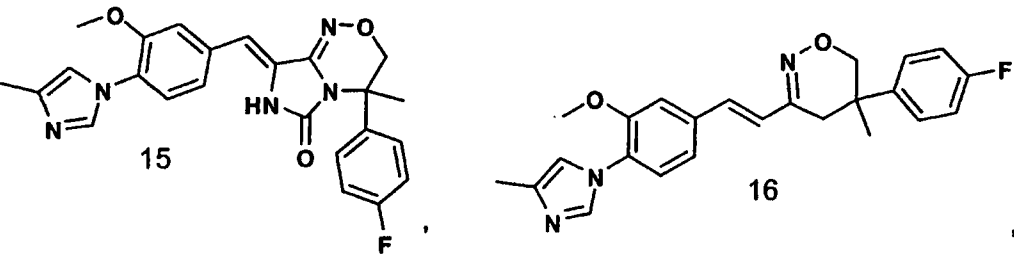
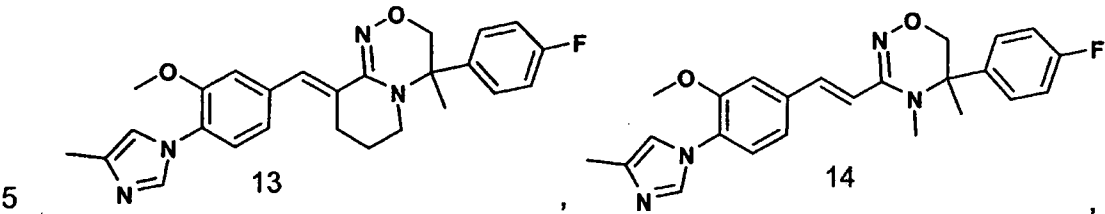
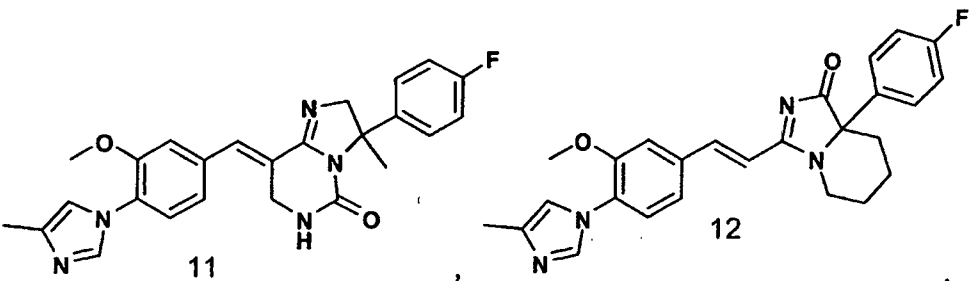
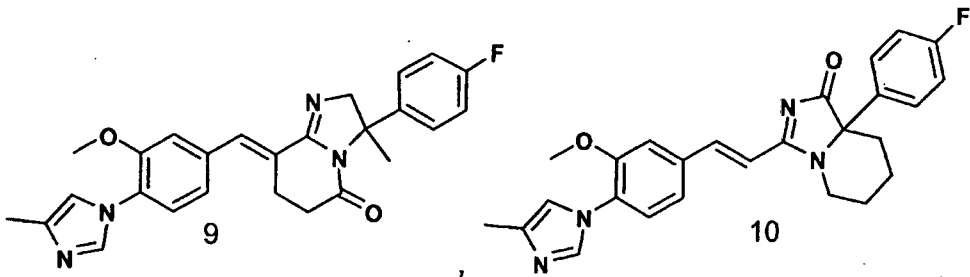
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Table 1



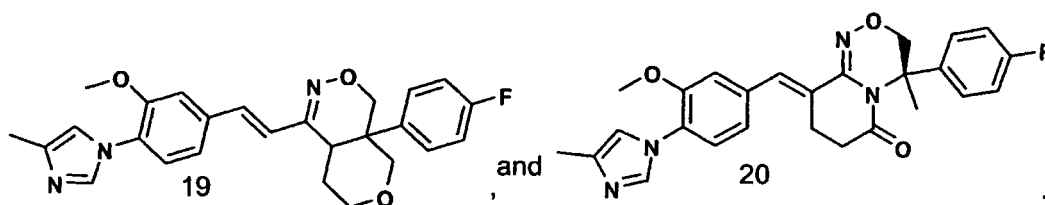
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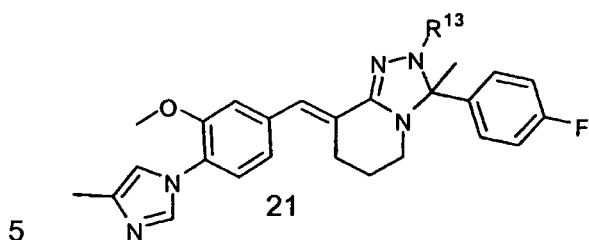


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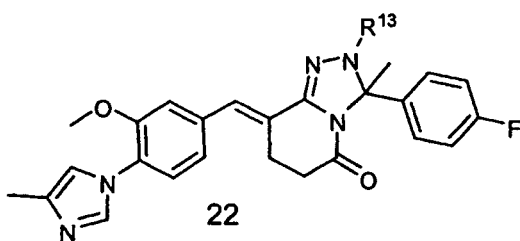
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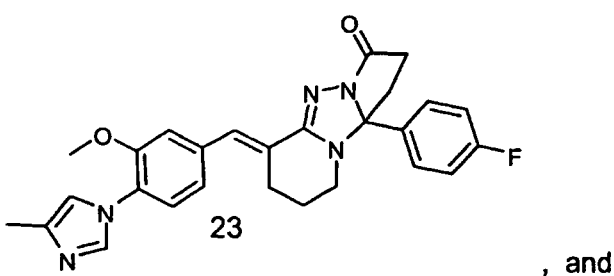
Representative compounds of this invention also include:



wherein R<sup>13</sup> in compound 21 is as defined for formula I (and in one example R<sup>13</sup> is H),



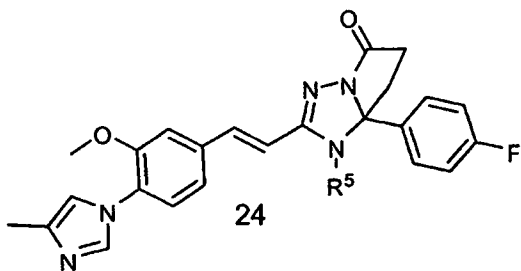
10 wherein R<sup>13</sup> in compound 22 is as defined for formula I (and in one example R<sup>13</sup> is H),





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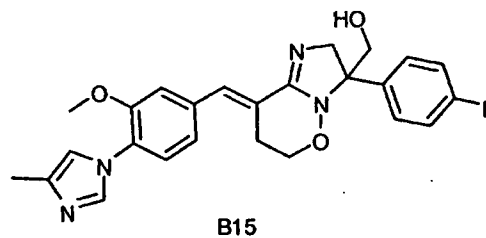
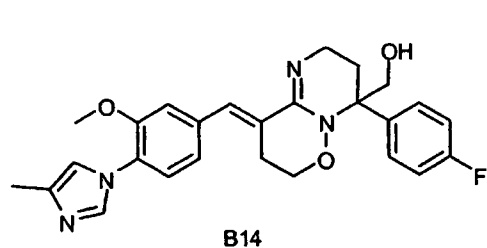
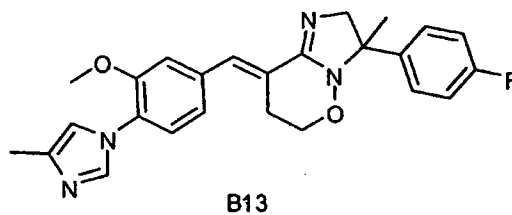
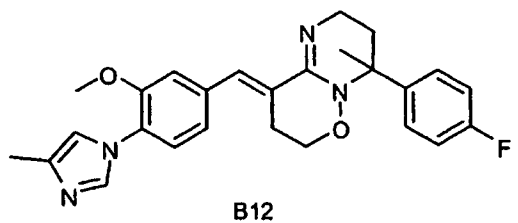
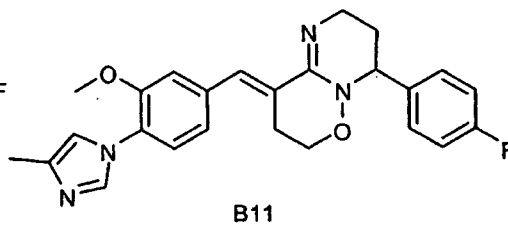
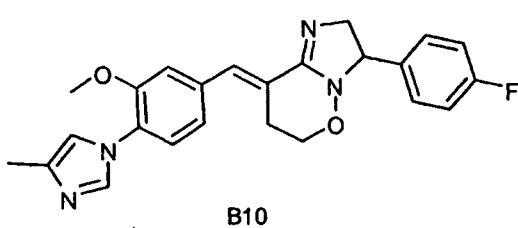
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wherein R<sup>5</sup> in compound 22 is as defined for formula I (and in one example R<sup>5</sup> is H).

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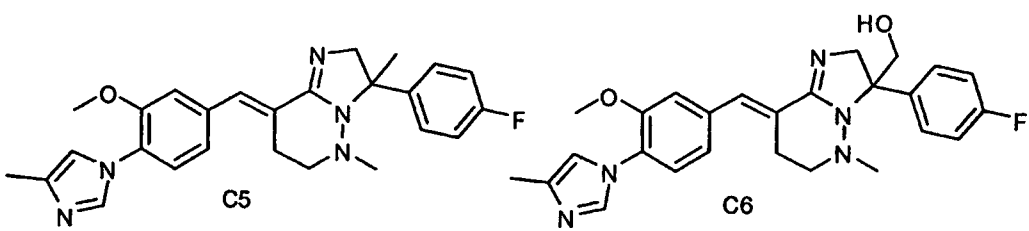
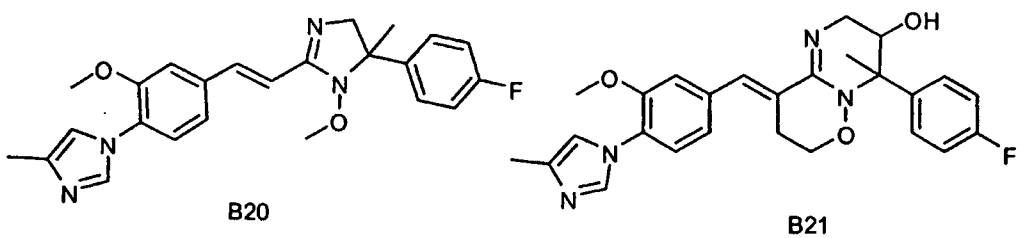
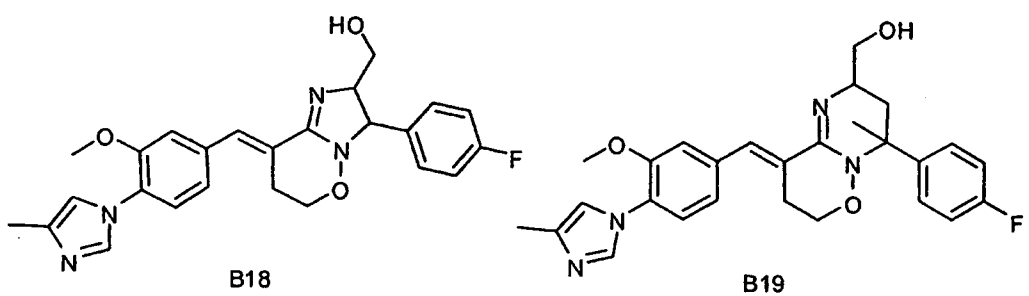
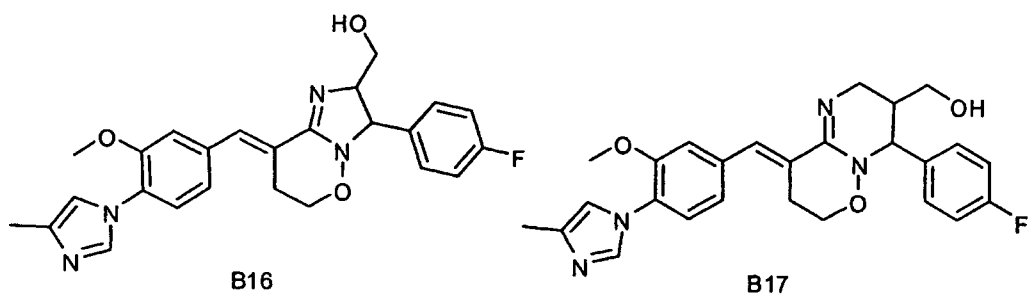
Representative compounds of this invention also include:



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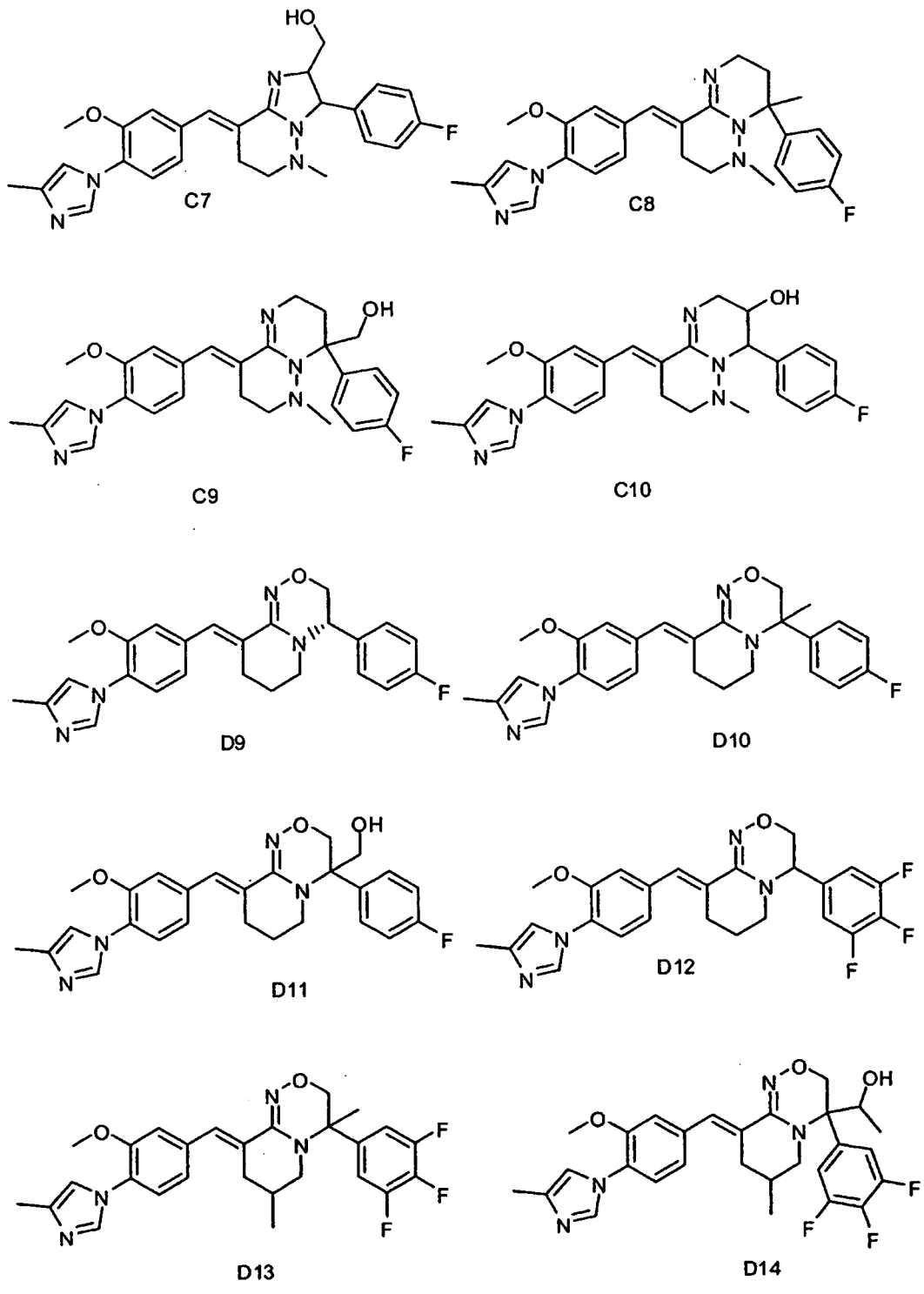
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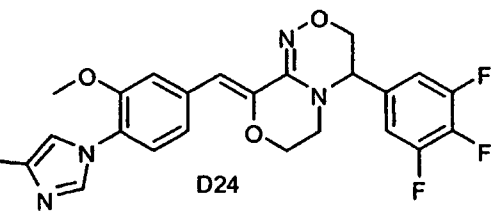
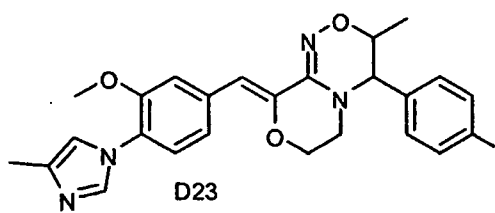
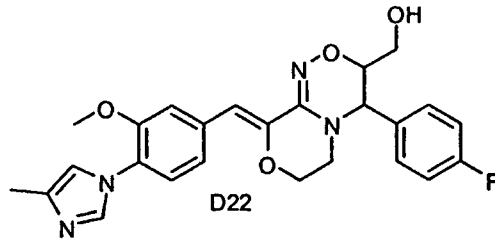
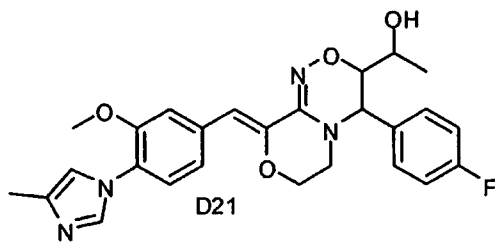
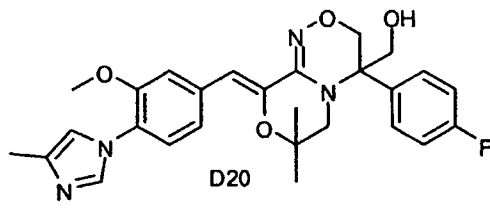
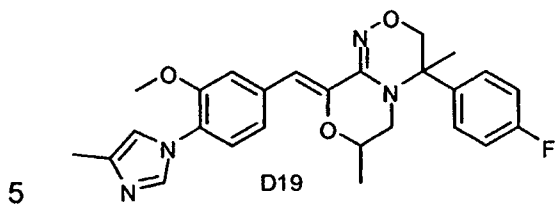
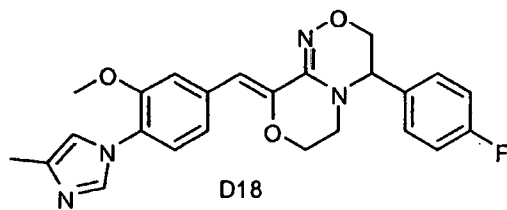
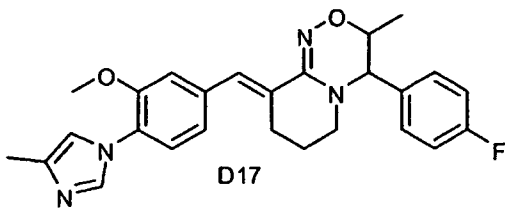
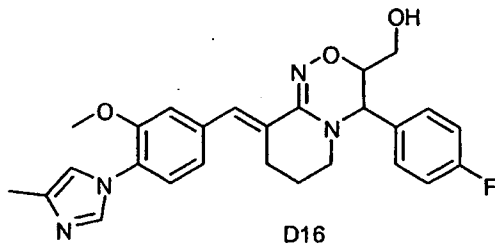
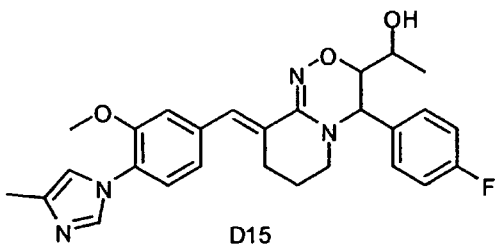


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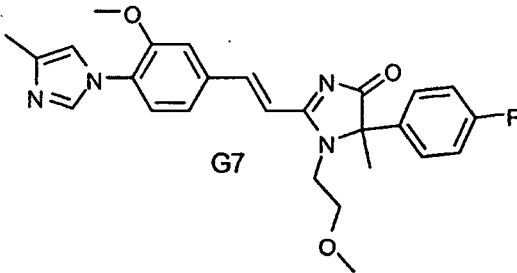
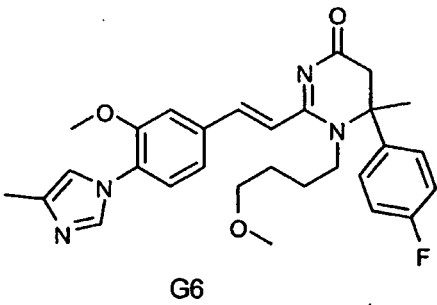
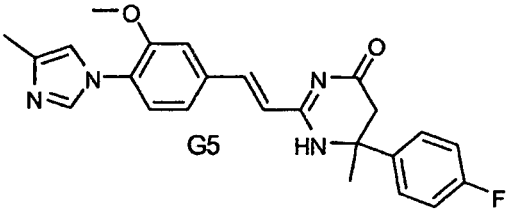
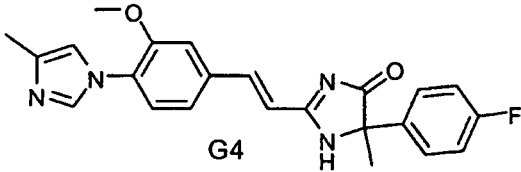
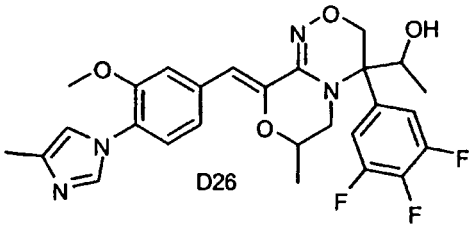
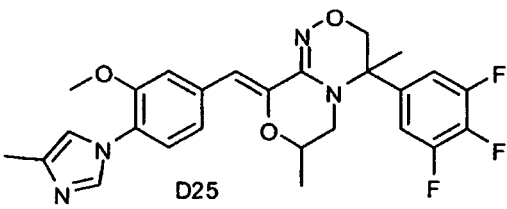
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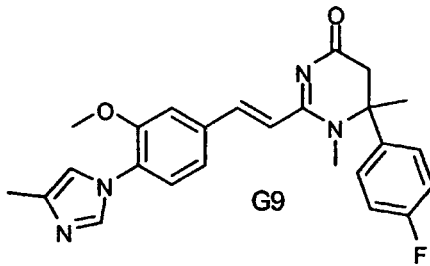
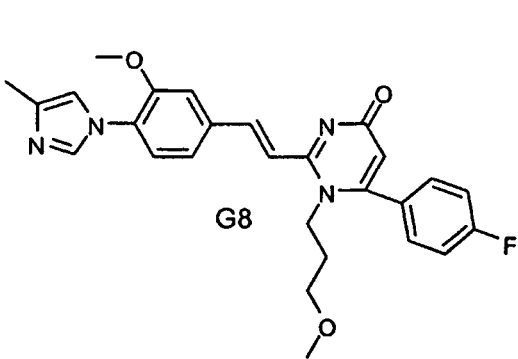


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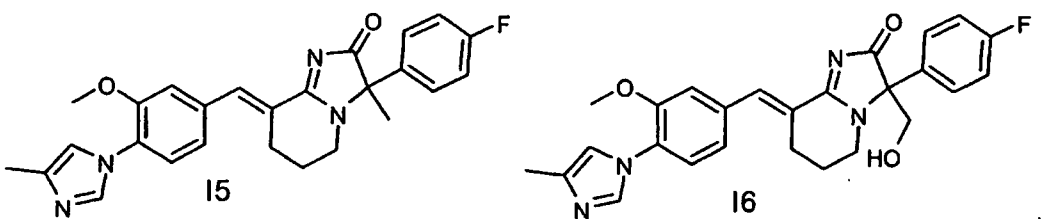
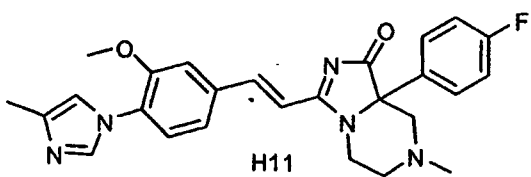
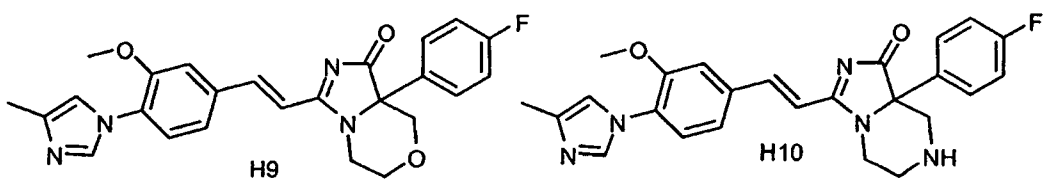
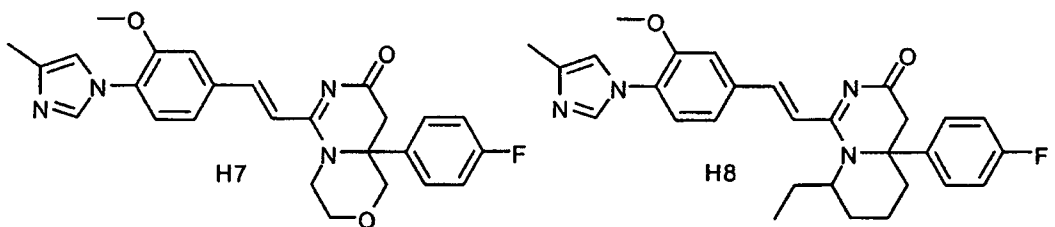
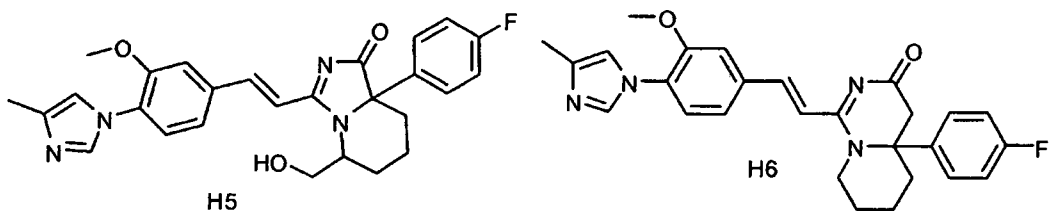
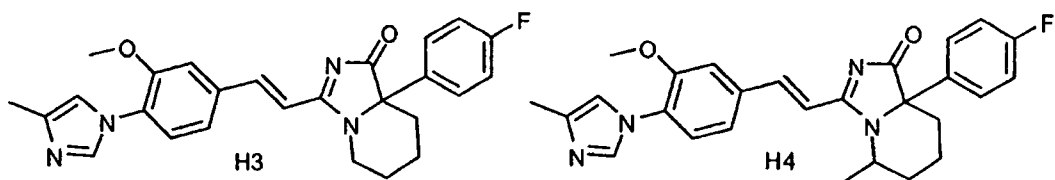


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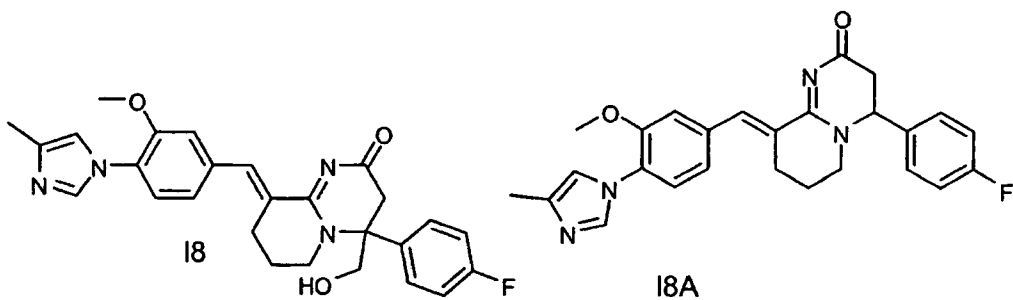
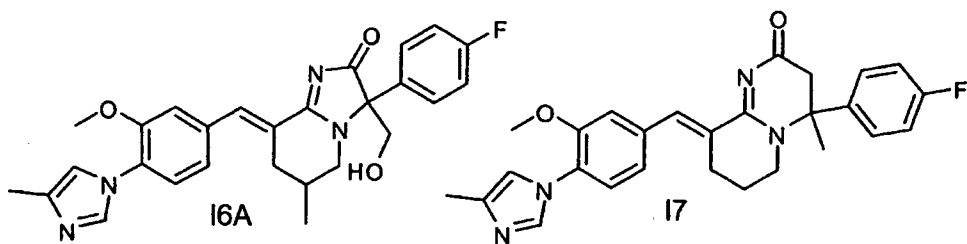


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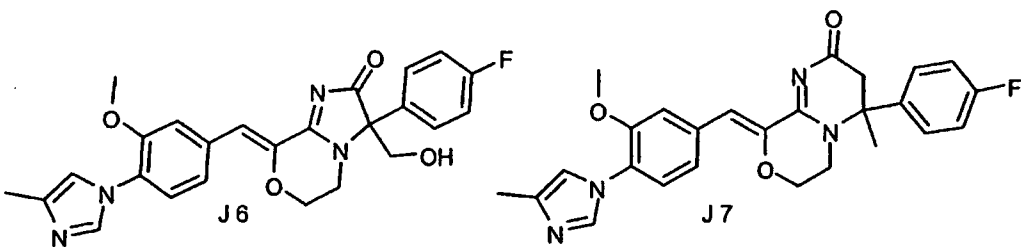
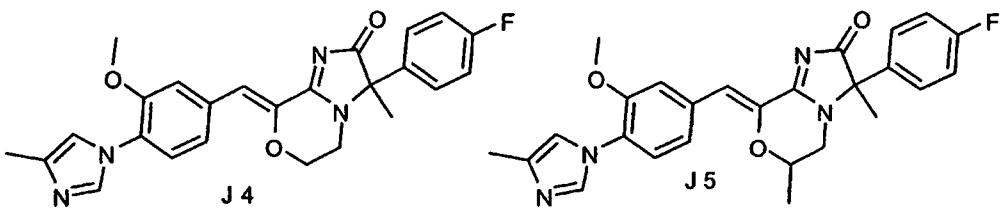
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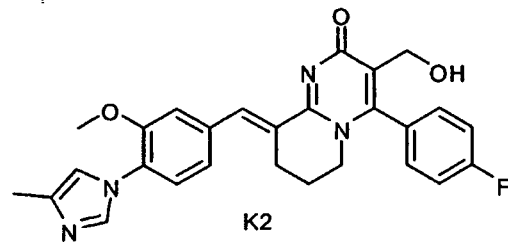
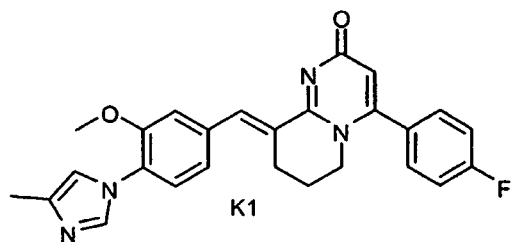
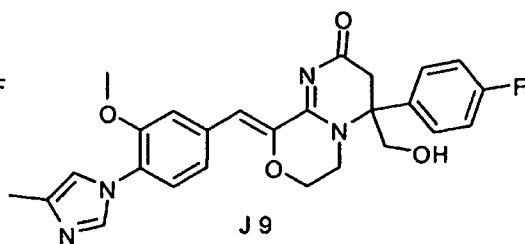
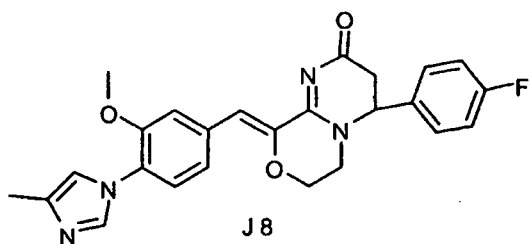


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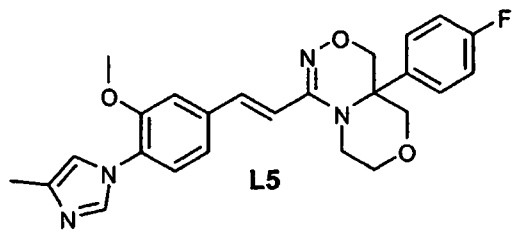
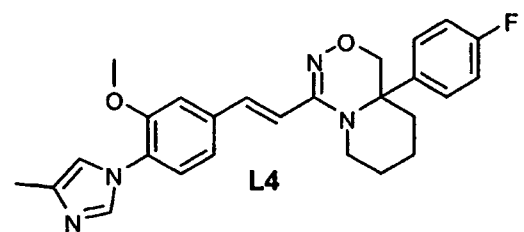
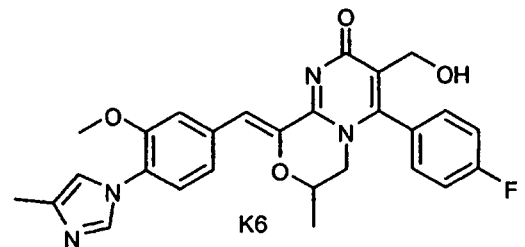
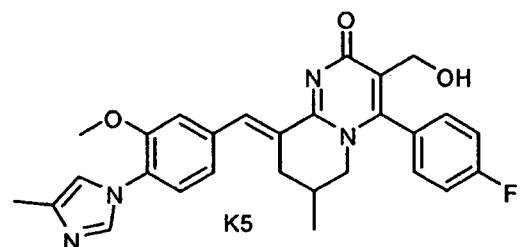
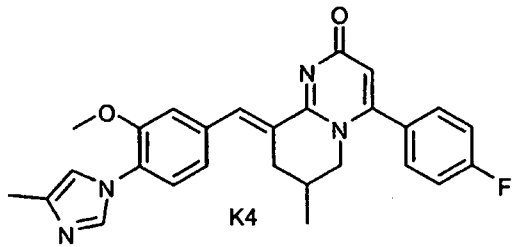
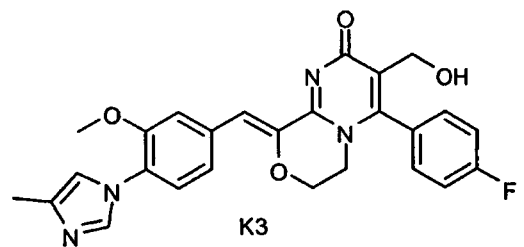


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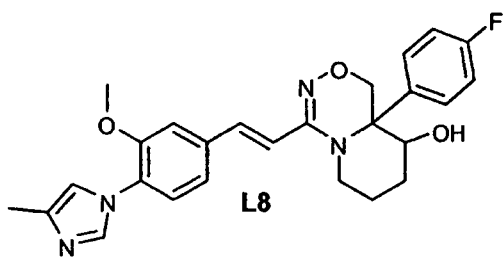
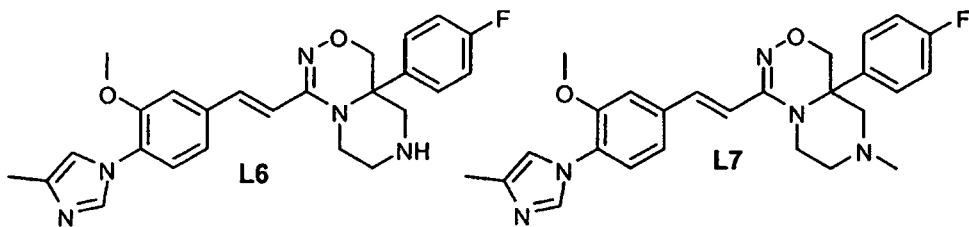


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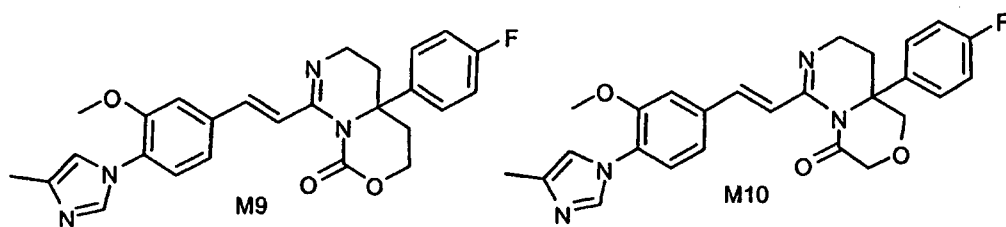
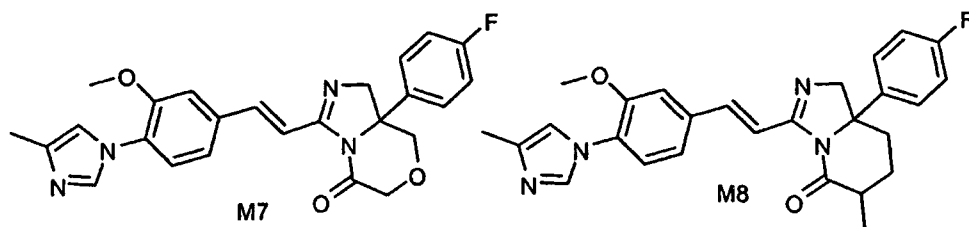
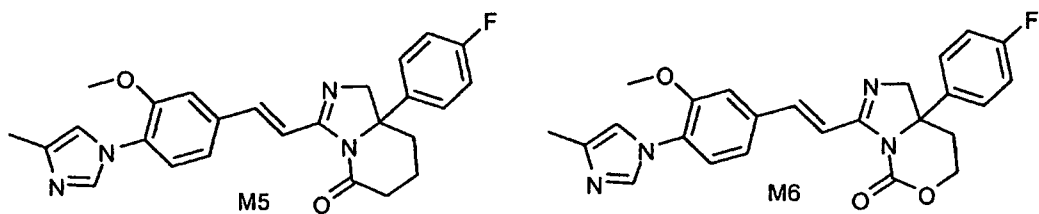


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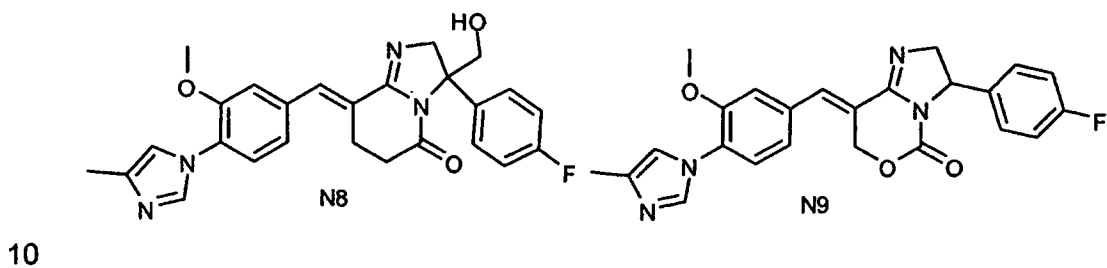
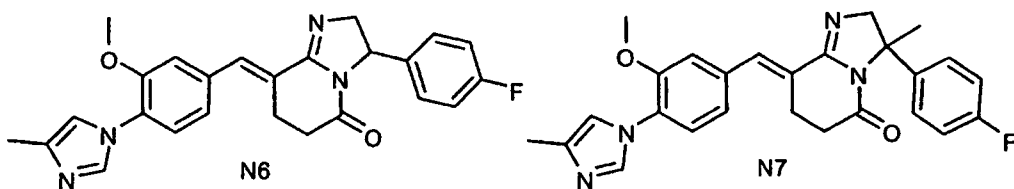
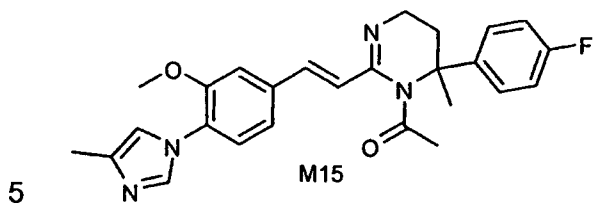
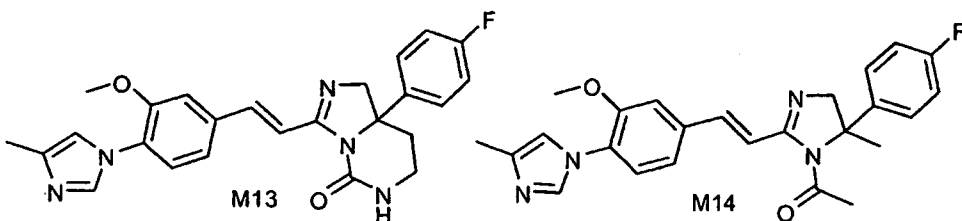
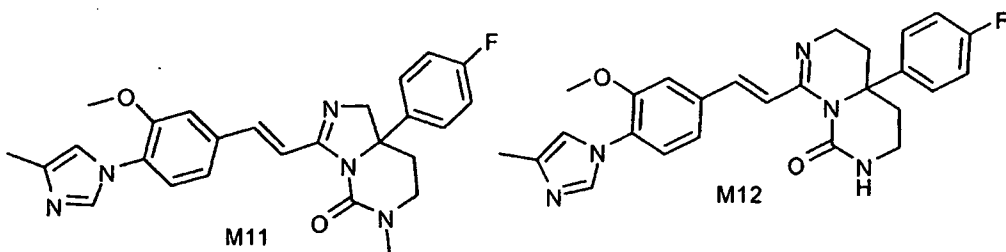
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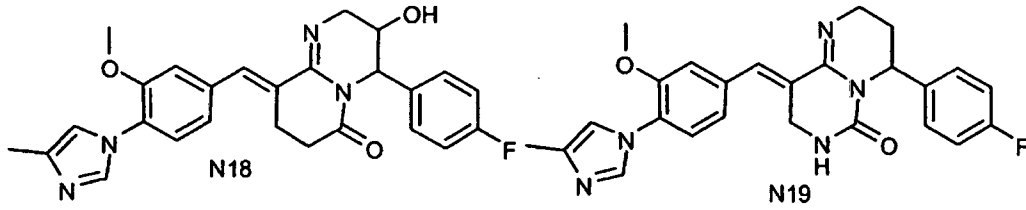
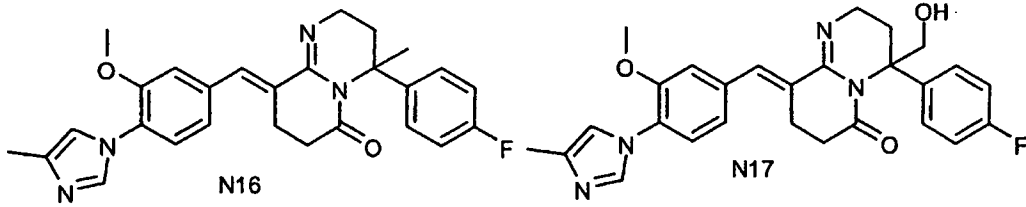
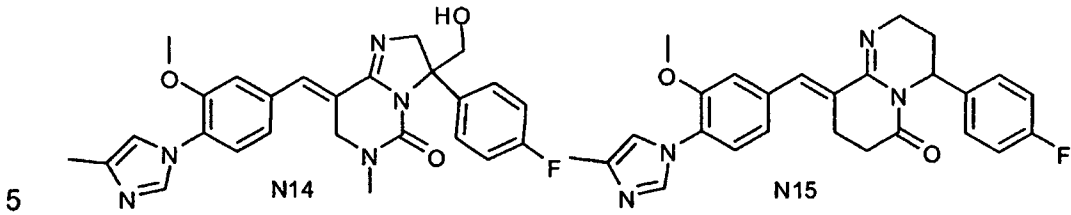
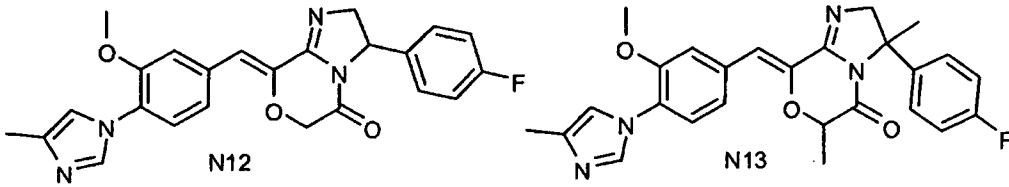
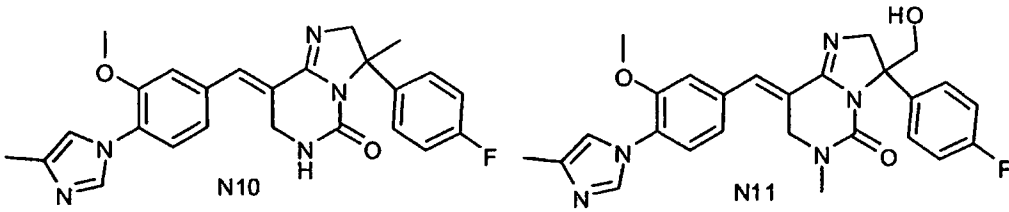
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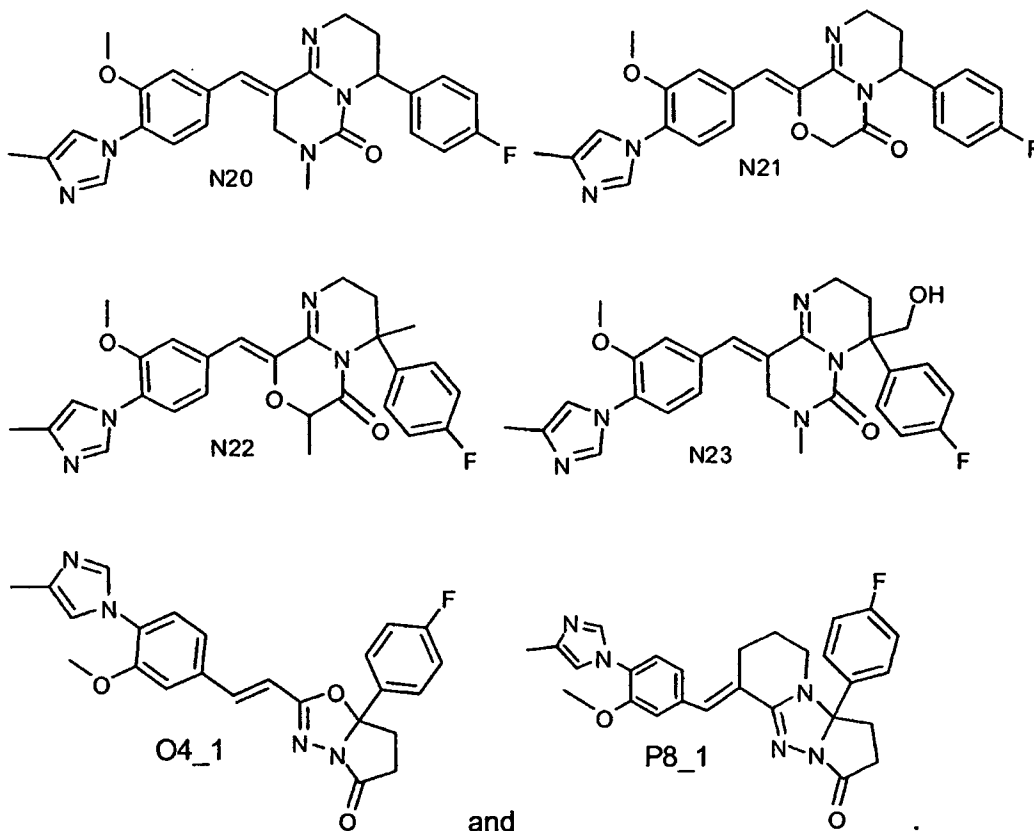
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5

and

One embodiment of this invention is directed to compound 1.

Another embodiment of this invention is directed to compound 2.

Another embodiment of this invention is directed to compound 3.

Another embodiment of this invention is directed to compound 4.

10

Another embodiment of this invention is directed to compound 5.

Another embodiment of this invention is directed to compound 6.

Another embodiment of this invention is directed to compound 7.

Another embodiment of this invention is directed to compound 8.

Another embodiment of this invention is directed to compound 9.

15

Another embodiment of this invention is directed to compound 10.

Another embodiment of this invention is directed to compound 11.

Another embodiment of this invention is directed to compound 12.

Another embodiment of this invention is directed to compound 13.

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- Another embodiment of this invention is directed to compound 14.
- Another embodiment of this invention is directed to compound 15.
- Another embodiment of this invention is directed to compound 16.
- Another embodiment of this invention is directed to compound 17.
- 5 Another embodiment of this invention is directed to compound 18.
- Another embodiment of this invention is directed to compound 19.
- Another embodiment of this invention is directed to compound 20.
- Another embodiment of this invention is directed to compound 21.
- Another embodiment of this invention is directed to compound 22.
- 10 Another embodiment of this invention is directed to compound 23.
- Another embodiment of this invention is directed to compound 24.
- Another embodiment of this invention is directed to compound B10.
- Another embodiment of this invention is directed to compound B11.
- Another embodiment of this invention is directed to compound B12.
- 15 Another embodiment of this invention is directed to compound B13.
- Another embodiment of this invention is directed to compound B14.
- Another embodiment of this invention is directed to compound B15.
- Another embodiment of this invention is directed to compound B16.
- Another embodiment of this invention is directed to compound B17.
- 20 Another embodiment of this invention is directed to compound B18.
- Another embodiment of this invention is directed to compound B19.
- Another embodiment of this invention is directed to compound B20.
- Another embodiment of this invention is directed to compound B21.
- Another embodiment of this invention is directed to compound C5.
- 25 Another embodiment of this invention is directed to compound C6.
- Another embodiment of this invention is directed to compound C7.
- Another embodiment of this invention is directed to compound C8.
- Another embodiment of this invention is directed to compound C9.
- Another embodiment of this invention is directed to compound C10.
- 30 Another embodiment of this invention is directed to compound D9.

- Another embodiment of this invention is directed to compound D10.
- Another embodiment of this invention is directed to compound D11.
- Another embodiment of this invention is directed to compound D12.
- Another embodiment of this invention is directed to compound D13.
- 5 Another embodiment of this invention is directed to compound D14.
- Another embodiment of this invention is directed to compound D15.
- Another embodiment of this invention is directed to compound D16.
- Another embodiment of this invention is directed to compound D17.
- Another embodiment of this invention is directed to compound D18.
- 10 Another embodiment of this invention is directed to compound D19.
- Another embodiment of this invention is directed to compound D20.
- Another embodiment of this invention is directed to compound D21.
- Another embodiment of this invention is directed to compound D22.
- Another embodiment of this invention is directed to compound D23.
- 15 Another embodiment of this invention is directed to compound D24.
- Another embodiment of this invention is directed to compound D25.
- Another embodiment of this invention is directed to compound D26.
- Another embodiment of this invention is directed to compound G4.
- Another embodiment of this invention is directed to compound G5.
- 20 Another embodiment of this invention is directed to compound G6.
- Another embodiment of this invention is directed to compound G7.
- Another embodiment of this invention is directed to compound G8.
- Another embodiment of this invention is directed to compound G9.
- Another embodiment of this invention is directed to compound H3.
- 25 Another embodiment of this invention is directed to compound H4.
- Another embodiment of this invention is directed to compound H5.
- Another embodiment of this invention is directed to compound H6.
- Another embodiment of this invention is directed to compound H7.
- Another embodiment of this invention is directed to compound H8.
- 30 Another embodiment of this invention is directed to compound H9.

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- Another embodiment of this invention is directed to compound H10.
- Another embodiment of this invention is directed to compound H11.
- Another embodiment of this invention is directed to compound I5.
- Another embodiment of this invention is directed to compound I6.
- 5 Another embodiment of this invention is directed to compound I6A.
- Another embodiment of this invention is directed to compound I7.
- Another embodiment of this invention is directed to compound I8.
- Another embodiment of this invention is directed to compound I8A.
- Another embodiment of this invention is directed to compound J4.
- 10 Another embodiment of this invention is directed to compound J5.
- Another embodiment of this invention is directed to compound J6.
- Another embodiment of this invention is directed to compound J7.
- Another embodiment of this invention is directed to compound J8.
- Another embodiment of this invention is directed to compound J9.
- 15 Another embodiment of this invention is directed to compound K1.
- Another embodiment of this invention is directed to compound K2.
- Another embodiment of this invention is directed to compound K3.
- Another embodiment of this invention is directed to compound K4.
- Another embodiment of this invention is directed to compound K5.
- 20 Another embodiment of this invention is directed to compound K6.
- Another embodiment of this invention is directed to compound L4.
- Another embodiment of this invention is directed to compound L5.
- Another embodiment of this invention is directed to compound L6.
- Another embodiment of this invention is directed to compound L7.
- 25 Another embodiment of this invention is directed to compound L8.
- Another embodiment of this invention is directed to compound M5.
- Another embodiment of this invention is directed to compound M6.
- Another embodiment of this invention is directed to compound M7.
- Another embodiment of this invention is directed to compound M8.
- 30 Another embodiment of this invention is directed to compound M9.

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- Another embodiment of this invention is directed to compound M10.
- Another embodiment of this invention is directed to compound M11.
- Another embodiment of this invention is directed to compound M12.
- Another embodiment of this invention is directed to compound M13.
- 5 Another embodiment of this invention is directed to compound M14.
- Another embodiment of this invention is directed to compound M15.
- Another embodiment of this invention is directed to compound N6.
- Another embodiment of this invention is directed to compound N7.
- Another embodiment of this invention is directed to compound N8.
- 10 Another embodiment of this invention is directed to compound N9.
- Another embodiment of this invention is directed to compound N10.
- Another embodiment of this invention is directed to compound N11.
- Another embodiment of this invention is directed to compound N12.
- Another embodiment of this invention is directed to compound N13.
- 15 Another embodiment of this invention is directed to compound N14.
- Another embodiment of this invention is directed to compound N15.
- Another embodiment of this invention is directed to compound N16.
- Another embodiment of this invention is directed to compound N17.
- Another embodiment of this invention is directed to compound N18.
- 20 Another embodiment of this invention is directed to compound N19.
- Another embodiment of this invention is directed to compound N20.
- Another embodiment of this invention is directed to compound N21.
- Another embodiment of this invention is directed to compound N22.
- Another embodiment of this invention is directed to compound N23.
- 25 Another embodiment of this invention is directed to compound O4\_1.
- Another embodiment of this invention is directed to compound P8\_1.

As used above, and throughout this disclosure, the following terms, unless otherwise indicated, shall be understood to have the following meanings:

30 "ADDP" means 1,1'-(azodicarbonyl)dipiperidine.



"AIBN" means 2,2'-azobis(2-methylpropionitrile).

"CAN" means ammonium cerium (IV) nitrate.

"DCC" means N, N'-dicyclohexylcarbodiimide.

"DCM" means dichloromethane.

5 "DMF" means dimethylformamide.

"HOBt" means 1-hydroxybenzotriazole.

"LDA" means lithium diisopropylamide.

"TBAF" means tetra-N-butylammonium fluoride.

"TBSO" means tert-butyldimethylsilyloxy.

10 "TfO" means trifluoromethylsulfonyloxy.

"At least one" means one or more than one, for example, 1, 2 or 3, or in another example, 1 or 2, or in another example 1.

"One or more" with reference to the use of the compounds of this invention means that one or more than one compound is used, for example, 1, 2 or 3, or in  
15 another example, 1 or 2, or in another example 1.

"Patient" includes both human and animals.

"Mammal" means humans and other mammalian animals.

It is noted that the carbons of formula I and other formulas herein may be replaced with 1 to 3 silicon atoms so long as all valency requirements are  
20 satisfied.

"Alkyl" means an aliphatic hydrocarbon group which may be straight or branched and comprising about 1 to about 20 carbon atoms in the chain.

Preferred alkyl groups contain about 1 to about 12 carbon atoms in the chain.

More preferred alkyl groups contain about 1 to about 6 carbon atoms in the chain.

25 Branched means that one or more lower alkyl groups such as methyl, ethyl or propyl, are attached to a linear alkyl chain. "Lower alkyl" means a group having about 1 to about 6 carbon atoms in the chain which may be straight or branched. "Alkyl" may be unsubstituted or optionally substituted by one or more substituents which may be the same or different, each substituent being independently

selected from the group consisting of halo, alkyl, aryl, cycloalkyl, cyano, hydroxy, alkoxy, alkylthio, amino, oxime (e.g., =N-OH), -NH(alkyl), -NH(cycloalkyl), -N(alkyl)<sub>2</sub>, -O-C(O)-alkyl, -O-C(O)-aryl, -O-C(O)-cycloalkyl, carboxy and -C(O)O-alkyl. Non-limiting examples of suitable alkyl groups include

5 methyl, ethyl, n-propyl, isopropyl and t-butyl.

"Alkenyl" means an aliphatic hydrocarbon group containing at least one carbon-carbon double bond and which may be straight or branched and comprising about 2 to about 15 carbon atoms in the chain. Preferred alkenyl groups have about 2 to about 12 carbon atoms in the chain; and more preferably

10 about 2 to about 6 carbon atoms in the chain. Branched means that one or more lower alkyl groups such as methyl, ethyl or propyl, are attached to a linear alkenyl chain. "Lower alkenyl" means about 2 to about 6 carbon atoms in the chain which may be straight or branched. "Alkenyl" may be unsubstituted or optionally substituted by one or more substituents which may be the same or different, each

15 substituent being independently selected from the group consisting of halo, alkyl, aryl, cycloalkyl, cyano, alkoxy and -S(alkyl). Non-limiting examples of suitable alkenyl groups include ethenyl, propenyl, n-butenyl, 3-methylbut-2-enyl, n-pentenyl, octenyl and decenyl.

"Alkene" means a difunctional group obtained by removal of a hydrogen atom from an alkyl group that is defined above. Non-limiting examples of alkene

20 include methylene, ethylene and propylene.

"Alkynyl" means an aliphatic hydrocarbon group containing at least one carbon-carbon triple bond and which may be straight or branched and comprising about 2 to about 15 carbon atoms in the chain. Preferred alkynyl groups have

25 about 2 to about 12 carbon atoms in the chain; and more preferably about 2 to about 4 carbon atoms in the chain. Branched means that one or more lower alkyl groups such as methyl, ethyl or propyl, are attached to a linear alkynyl chain. "Lower alkynyl" means about 2 to about 6 carbon atoms in the chain which may be straight or branched. Non-limiting examples of suitable alkynyl groups include

30 ethynyl, propynyl, 2-butyne and 3-methylbutynyl. "Alkynyl" may be unsubstituted

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or optionally substituted by one or more substituents which may be the same or different, each substituent being independently selected from the group consisting of alkyl, aryl and cycloalkyl.

"Aryl" means an aromatic monocyclic or multicyclic ring system comprising  
5 about 6 to about 14 carbon atoms, preferably about 6 to about 10 carbon atoms. The aryl group can be optionally substituted with one or more "ring system substituents" which may be the same or different, and are as defined herein. Non-limiting examples of suitable aryl groups include phenyl and naphthyl.

"Heteroaryl" means an aromatic monocyclic or multicyclic ring system  
10 comprising about 5 to about 14 ring atoms, preferably about 5 to about 10 ring atoms, in which one or more of the ring atoms is an element other than carbon, for example nitrogen, oxygen or sulfur, alone or in combination. Preferred heteroaryls contain about 5 to about 6 ring atoms. The "heteroaryl" can be optionally substituted by one or more "ring system substituents" which may be the same or  
15 different, and are as defined herein. The prefix aza, oxa or thia before the heteroaryl root name means that at least a nitrogen, oxygen or sulfur atom respectively, is present as a ring atom. A nitrogen atom of a heteroaryl can be optionally oxidized to the corresponding N-oxide. "Heteroaryl" may also include a heteroaryl as defined above fused to an aryl as defined above. Non-limiting  
20 examples of suitable heteroaryls include pyridyl, pyrazinyl, furanyl, thienyl, pyrimidinyl, pyridone (including N-substituted pyridones), isoxazolyl, isothiazolyl, oxazolyl, thiazolyl, pyrazolyl, furazanyl, pyrrolyl, pyrazolyl, triazolyl, 1,2,4-thiadiazolyl, pyrazinyl, pyridazinyl, quinoxaliny, phthalazinyl, oxindolyl, imidazo[1,2-a]pyridinyl, imidazo[2,1-b]thiazolyl, benzofurazanyl, indolyl, azaindolyl,  
25 benzimidazolyl, benzothienyl, quinoliny, imidazolyl, thienopyridyl, quinazolinyl, thienopyrimidyl, pyrrolopyridyl, imidazopyridyl, isoquinoliny, benzoazaindolyl, 1,2,4-triazinyl, benzothiazolyl and the like. The term "heteroaryl" also refers to partially saturated heteroaryl moieties such as, for example, tetrahydroisoquinolyl, tetrahydroquinolyl and the like.

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"Aralkyl" or "arylalkyl" means an aryl-alkyl- group in which the aryl and alkyl are as previously described. Preferred aralkyls comprise a lower alkyl group. Non-limiting examples of suitable aralkyl groups include benzyl, 2-phenethyl and naphthalenylmethyl. The bond to the parent moiety is through the alkyl.

- 5        "Alkylaryl" means an alkyl-aryl- group in which the alkyl and aryl are as previously described. Preferred alkylaryls comprise a lower alkyl group. Non-limiting example of a suitable alkylaryl group is tolyl. The bond to the parent moiety is through the aryl.

- 10        "Cycloalkyl" means a non-aromatic mono- or multicyclic ring system comprising about 3 to about 10 carbon atoms, preferably about 5 to about 10 carbon atoms. Preferred cycloalkyl rings contain about 5 to about 7 ring atoms. The cycloalkyl can be optionally substituted with one or more "ring system substituents" which may be the same or different, and are as defined above. Non-limiting examples of suitable monocyclic cycloalkyls include cyclopropyl, 15 cyclopentyl, cyclohexyl, cycloheptyl and the like. Non-limiting examples of suitable multicyclic cycloalkyls include 1-decalinyl, norbornyl, adamantyl and the like.

"Cycloalkylalkyl" means a cycloalkyl moiety as defined above linked via an alkyl moiety (defined above) to a parent core. Non-limiting examples of suitable cycloalkylalkyls include cyclohexylmethyl, adamantylmethyl and the like.

- 20        "Cycloalkenyl" means a non-aromatic mono or multicyclic ring system comprising about 3 to about 10 carbon atoms, preferably about 5 to about 10 carbon atoms which contains at least one carbon-carbon double bond. Preferred cycloalkenyl rings contain about 5 to about 7 ring atoms. The cycloalkenyl can be optionally substituted with one or more "ring system substituents" which may be 25 the same or different, and are as defined above. Non-limiting examples of suitable monocyclic cycloalkenyls include cyclopentenyl, cyclohexenyl, cyclohepta-1,3-dienyl, and the like. Non-limiting example of a suitable multicyclic cycloalkenyl is norbornylenyl.

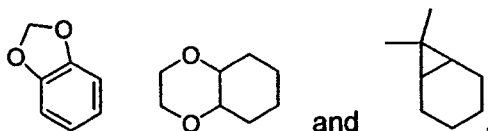
- 30        "Cycloalkenylalkyl" means a cycloalkenyl moiety as defined above linked via an alkyl moiety (defined above) to a parent core. Non-limiting examples of

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suitable cycloalkenylalkyls include cyclopentenylmethyl, cyclohexenylmethyl and the like.

"Halogen" means fluorine, chlorine, bromine, or iodine. Preferred are fluorine, chlorine and bromine. "Halo" refers to fluoro, chloro, bromo or iodo.

- 5 "Ring system substituent" means a substituent attached to an aromatic or non-aromatic ring system which, for example, replaces an available hydrogen on the ring system. Ring system substituents may be the same or different, each being independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, alkylaryl, heteroaralkyl, heteroarylalkenyl, heteroarylalkynyl, alkylheteroaryl, hydroxy, hydroxyalkyl, alkoxy, aryloxy, aralkoxy, acyl, aroyl, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylthio, arylthio, heteroarylthio, aralkylthio, heteroaralkylthio, cycloalkyl, heterocyclyl, -O-C(O)-alkyl, -O-C(O)-aryl, -O-C(O)-cycloalkyl, -C(=N-CN)-NH<sub>2</sub>, -C(=NH)-NH<sub>2</sub>, -C(=NH)-NH(alkyl), oxime (e.g., =N-OH), Y<sub>1</sub>Y<sub>2</sub>N-, Y<sub>1</sub>Y<sub>2</sub>N-alkyl-, Y<sub>1</sub>Y<sub>2</sub>NC(O)-, Y<sub>1</sub>Y<sub>2</sub>NSO<sub>2</sub>- and -SO<sub>2</sub>NY<sub>1</sub>Y<sub>2</sub>, wherein Y<sub>1</sub> and Y<sub>2</sub> can be the same or different and are independently selected from the group consisting of hydrogen, alkyl, aryl, cycloalkyl, and aralkyl. "Ring system substituent" may also mean a single moiety which simultaneously replaces two available hydrogens on two adjacent carbon atoms (one H on each carbon) on a ring system. Examples of such moiety are methylene dioxy, ethylenedioxy, -C(CH<sub>3</sub>)<sub>2</sub>- and the like which form moieties such as, for example:
- 10  
15  
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- "Heteroarylalkyl" means a heteroaryl moiety as defined above linked via an alkyl moiety (defined above) to a parent core. Non-limiting examples of suitable heteroaryls include 2-pyridinylmethyl, quinolinylmethyl and the like.
- 25

"Heterocyclyl" means a non-aromatic saturated monocyclic or multicyclic ring system comprising about 3 to about 10 ring atoms, preferably about 5 to

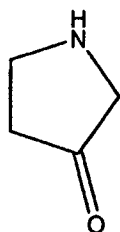
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about 10 ring atoms, in which one or more of the atoms in the ring system is an element other than carbon, for example nitrogen, oxygen or sulfur, alone or in combination. There are no adjacent oxygen and/or sulfur atoms present in the ring system. Preferred heterocycllys contain about 5 to about 6 ring atoms. The prefix

5 aza, oxa or thia before the heterocyclyl root name means that at least a nitrogen, oxygen or sulfur atom respectively is present as a ring atom. Any -NH in a heterocyclyl ring may exist protected such as, for example, as an -N(Boc), -N(CBz), -N(Tos) group and the like; such protections are also considered part of this invention. The heterocyclyl can be optionally substituted by one or more "ring

10 system substituents" which may be the same or different, and are as defined herein. The nitrogen or sulfur atom of the heterocyclyl can be optionally oxidized to the corresponding N-oxide, S-oxide or S,S-dioxide. Non-limiting examples of suitable monocyclic heterocyclyl rings include piperidyl, pyrrolidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, 1,4-dioxanyl, tetrahydrofuranyl,

15 tetrahydrothiophenyl, lactam, lactone, and the like. "Heterocyclyl" may also mean a heterocyclyl ring wherein a single moiety (e.g =O) simultaneously replaces two available hydrogens on the same carbon atom on a ring system. An example of such moiety is pyrrolidone:

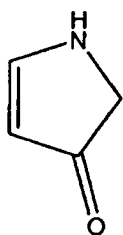


20 "Heterocyclylalkyl" means a heterocyclyl moiety as defined above linked via an alkyl moiety (defined above) to a parent core. Non-limiting examples of suitable heterocyclylalkyls include piperidinylmethyl, piperazinylmethyl and the like.

"Heterocyclenyl" means a non-aromatic monocyclic or multicyclic ring system comprising about 3 to about 10 ring atoms, preferably about 5 to about 10

25 ring atoms, in which one or more of the atoms in the ring system is an element other than carbon, for example nitrogen, oxygen or sulfur atom, alone or in

combination, and which contains at least one carbon-carbon double bond or carbon-nitrogen double bond. There are no adjacent oxygen and/or sulfur atoms present in the ring system. Preferred heterocyclenyl rings contain about 5 to about 6 ring atoms. The prefix aza, oxa or thia before the heterocyclenyl root name means that at least a nitrogen, oxygen or sulfur atom respectively is present as a ring atom. The heterocyclenyl can be optionally substituted by one or more ring system substituents, wherein "ring system substituent" is as defined above. The nitrogen or sulfur atom of the heterocyclenyl can be optionally oxidized to the corresponding N-oxide, S-oxide or S,S-dioxide. Non-limiting examples of suitable heterocyclenyl groups include 1,2,3,4- tetrahydropyridinyl, 1,2-dihydropyridinyl, 1,4-dihydropyridinyl, 1,2,3,6-tetrahydropyridinyl, 1,4,5,6-tetrahydropyrimidinyl, 2-pyrrolinyl, 3-pyrrolinyl, 2-imidazolyl, 2-pyrazolyl, dihydroimidazolyl, dihydrooxazolyl, dihydrooxadiazolyl, dihydrothiazolyl, 3,4-dihydro-2H-pyranyl, dihydrofuranyl, fluorodihydrofuranyl, 7-oxabicyclo[2.2.1]heptenyl, dihydrothiophenyl, dihydrothiopyranyl, and the like. "Heterocyclenyl" may also mean a single moiety (e.g., carbonyl) which simultaneously replaces two available hydrogens on the same carbon atom on a ring system. Example of such moiety is pyrrolidinone:

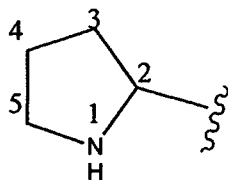


"Heterocyclenylalkyl" means a heterocyclenyl moiety as defined above linked via an alkyl moiety (defined above) to a parent core.

It should be noted that in hetero-atom containing ring systems of this invention, there are no hydroxyl groups on carbon atoms adjacent to a N, O or S, as well as there are no N or S groups on carbon adjacent to another heteroatom. Thus, for example, in the ring:

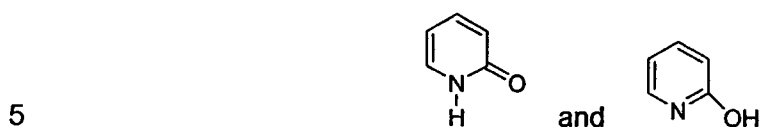
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there is no -OH attached directly to carbons marked 2 and 5.

It should also be noted that tautomeric forms such as, for example, the moieties:



are considered equivalent in certain embodiments of this invention.

"Alkynylalkyl" means an alkynyl-alkyl- group in which the alkynyl and alkyl are as previously described. Preferred alkynylalkyls contain a lower alkynyl and a lower alkyl group. The bond to the parent moiety is through the alkyl. Non-limiting examples of suitable alkynylalkyl groups include propargylmethyl.

"Heteroaralkyl" means a heteroaryl-alkyl- group in which the heteroaryl and alkyl are as previously described. Preferred heteroaralkyls contain a lower alkyl group. Non-limiting examples of suitable aralkyl groups include pyridylmethyl, and quinolin-3-ylmethyl. The bond to the parent moiety is through the alkyl.

15 "Hydroxyalkyl" means a HO-alkyl- group in which alkyl is as previously defined. Preferred hydroxyalkyls contain lower alkyl. Non-limiting examples of suitable hydroxyalkyl groups include hydroxymethyl and 2-hydroxyethyl.

20 "Acyl" means an H-C(O)-, alkyl-C(O)- or cycloalkyl-C(O)-, group in which the various groups are as previously described. The bond to the parent moiety is through the carbonyl. Preferred acyls contain a lower alkyl. Non-limiting examples of suitable acyl groups include formyl, acetyl and propanoyl.

"Aroyl" means an aryl-C(O)- group in which the aryl group is as previously described. The bond to the parent moiety is through the carbonyl. Non-limiting examples of suitable groups include benzoyl and 1-naphthoyl.

25 "Alkoxy" means an alkyl-O- group in which the alkyl group is as previously described. Non-limiting examples of suitable alkoxy groups include methoxy,



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ethoxy, n-propoxy, isopropoxy and n-butoxy. The bond to the parent moiety is through the ether oxygen.

"Aryloxy" means an aryl-O- group in which the aryl group is as previously described. Non-limiting examples of suitable aryloxy groups include phenoxy and naphthoxy. The bond to the parent moiety is through the ether oxygen.

"Aralkyloxy" means an aralkyl-O- group in which the aralkyl group is as previously described. Non-limiting examples of suitable aralkyloxy groups include benzyloxy and 1- or 2-naphthalenemethoxy. The bond to the parent moiety is through the ether oxygen.

"Alkylthio" means an alkyl-S- group in which the alkyl group is as previously described. Non-limiting examples of suitable alkylthio groups include methylthio and ethylthio. The bond to the parent moiety is through the sulfur.

"Arylthio" means an aryl-S- group in which the aryl group is as previously described. Non-limiting examples of suitable arylthio groups include phenylthio and naphthylthio. The bond to the parent moiety is through the sulfur.

"Aralkylthio" means an aralkyl-S- group in which the aralkyl group is as previously described. Non-limiting example of a suitable aralkylthio group is benzylthio. The bond to the parent moiety is through the sulfur.

"Alkoxy carbonyl" means an alkyl-O-CO- group. Non-limiting examples of suitable alkoxy carbonyl groups include methoxy carbonyl and ethoxy carbonyl. The bond to the parent moiety is through the carbonyl.

"Aryloxy carbonyl" means an aryl-O-C(O)- group. Non-limiting examples of suitable aryloxy carbonyl groups include phenoxy carbonyl and naphthoxy carbonyl. The bond to the parent moiety is through the carbonyl.

"Aralkoxy carbonyl" means an aralkyl-O-C(O)- group. Non-limiting example of a suitable aralkoxy carbonyl group is benzyloxy carbonyl. The bond to the parent moiety is through the carbonyl.

"Alkylsulfonyl" means an alkyl-S(O<sub>2</sub>)- group. Preferred groups are those in which the alkyl group is lower alkyl. The bond to the parent moiety is through the sulfonyl.

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"Arylsulfonyl" means an aryl-S(O<sub>2</sub>)- group. The bond to the parent moiety is through the sulfonyl.

The term "substituted" means that one or more hydrogens on the designated atom is replaced with a selection from the indicated group, provided  
5 that the designated atom's normal valency under the existing circumstances is not exceeded, and that the substitution results in a stable compound. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds. By "stable compound" or "stable structure" is meant a compound that is sufficiently robust to survive isolation to a useful degree of purity  
10 from a reaction mixture, and formulation into an efficacious therapeutic agent.

The term "optionally substituted" means optional substitution with the specified groups, radicals or moieties.

The term "purified", "in purified form" or "in isolated and purified form" for a compound refers to the physical state of said compound after being isolated from  
15 a synthetic process (e.g. from a reaction mixture), or natural source or combination thereof. Thus, the term "purified", "in purified form" or "in isolated and purified form" for a compound refers to the physical state of said compound after being obtained from a purification process or processes described herein or well known to the skilled artisan (e.g., chromatography, recrystallization and the like) ,  
20 in sufficient purity to be characterizable by standard analytical techniques described herein or well known to the skilled artisan.

It should also be noted that any carbon as well as heteroatom with unsatisfied valences in the text, schemes, examples and Tables herein is assumed to have the sufficient number of hydrogen atom(s) to satisfy the  
25 valences.

When a functional group in a compound is termed "protected", this means that the group is in modified form to preclude undesired side reactions at the protected site when the compound is subjected to a reaction. Suitable protecting groups will be recognized by those with ordinary skill in the art as well as by

reference to standard textbooks such as, for example, T. W. Greene *et al*, *Protective Groups in organic Synthesis* (1991), Wiley, New York.

When any variable (e.g., aryl, heterocycle, R<sup>2</sup>, etc.) occurs more than one time in any constituent or in Formula I, its definition on each occurrence is  
5 independent of its definition at every other occurrence.

As used herein, the term "composition" is intended to encompass a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combination of the specified ingredients in the specified amounts.

10 Prodrugs and solvates of the compounds of the invention are also contemplated herein. A discussion of prodrugs is provided in T. Higuchi and V. Stella, *Pro-drugs as Novel Delivery Systems* (1987) 14 of the A.C.S. Symposium Series, and in *Bioreversible Carriers in Drug Design*, (1987) Edward B. Roche, ed., American Pharmaceutical Association and Pergamon Press. The term  
15 "prodrug" means a compound (e.g., a drug precursor) that is transformed *in vivo* to yield a compound of Formula (I) or a pharmaceutically acceptable salt, hydrate or solvate of the compound. The transformation may occur by various mechanisms (e.g., by metabolic or chemical processes), such as, for example, through hydrolysis in blood. A discussion of the use of prodrugs is provided by T.  
20 Higuchi and W. Stella, "Pro-drugs as Novel Delivery Systems," Vol. 14 of the A.C.S. Symposium Series, and in *Bioreversible Carriers in Drug Design*, ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987.

For example, if a compound of Formula (I) or a pharmaceutically  
25 acceptable salt, hydrate or solvate of the compound contains a carboxylic acid functional group, a prodrug can comprise an ester formed by the replacement of the hydrogen atom of the acid group with a group such as, for example, (C<sub>1</sub>–C<sub>8</sub>)alkyl, (C<sub>2</sub>–C<sub>12</sub>)alkanoyloxymethyl, 1-(alkanoyloxy)ethyl having from 4 to 9 carbon atoms, 1-methyl-1-(alkanoyloxy)-ethyl having from 5 to 10 carbon atoms,  
30 alkoxycarbonyloxymethyl having from 3 to 6 carbon atoms, 1-

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(alkoxycarbonyloxy)ethyl having from 4 to 7 carbon atoms, 1-methyl-1-(alkoxycarbonyloxy)ethyl having from 5 to 8 carbon atoms, N-(alkoxycarbonyl)aminomethyl having from 3 to 9 carbon atoms, 1-(N-(alkoxycarbonyl)amino)ethyl having from 4 to 10 carbon atoms, 3-phthalidyl, 4-crotonolactonyl, gamma-butyrolacton-4-yl, di-N,N-(C<sub>1</sub>-C<sub>2</sub>)alkylamino(C<sub>2</sub>-C<sub>3</sub>)alkyl (such as  $\beta$ -dimethylaminoethyl), carbamoyl-(C<sub>1</sub>-C<sub>2</sub>)alkyl, N,N-di (C<sub>1</sub>-C<sub>2</sub>)alkylcarbamoyl-(C<sub>1</sub>-C<sub>2</sub>)alkyl and piperidino-, pyrrolidino- or morpholino(C<sub>2</sub>-C<sub>3</sub>)alkyl, and the like.

Similarly, if a compound of Formula (I) contains an alcohol functional group, a prodrug can be formed by the replacement of the hydrogen atom of the alcohol group with a group such as, for example, (C<sub>1</sub>-C<sub>6</sub>)alkanoyloxymethyl, 1-((C<sub>1</sub>-C<sub>6</sub>)alkanoyloxy)ethyl, 1-methyl-1-((C<sub>1</sub>-C<sub>6</sub>)alkanoyloxy)ethyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonyloxymethyl, N-(C<sub>1</sub>-C<sub>6</sub>)alkoxycarbonylaminomethyl, succinoyl, (C<sub>1</sub>-C<sub>6</sub>)alkanoyl,  $\alpha$ -amino(C<sub>1</sub>-C<sub>4</sub>)alkanyl, arylacyl and  $\alpha$ -aminoacyl, or  $\alpha$ -aminoacyl- $\alpha$ -aminoacyl, where each  $\alpha$ -aminoacyl group is independently selected from the naturally occurring L-amino acids, P(O)(OH)<sub>2</sub>, -P(O)(O(C<sub>1</sub>-C<sub>6</sub>)alkyl)<sub>2</sub> or glycosyl (the radical resulting from the removal of a hydroxyl group of the hemiacetal form of a carbohydrate), and the like.

If a compound of Formula (I) incorporates an amine functional group, a prodrug can be formed by the replacement of a hydrogen atom in the amine group with a group such as, for example, R-carbonyl, RO-carbonyl, NRR'-carbonyl where R and R' are each independently (C<sub>1</sub>-C<sub>10</sub>)alkyl, (C<sub>3</sub>-C<sub>7</sub>) cycloalkyl, benzyl, or R-carbonyl is a natural  $\alpha$ -aminoacyl or natural  $\alpha$ -aminoacyl, —C(OH)C(O)OY<sup>1</sup> wherein Y<sup>1</sup> is H, (C<sub>1</sub>-C<sub>6</sub>)alkyl or benzyl, —C(OY<sup>2</sup>)Y<sup>3</sup> wherein Y<sup>2</sup> is (C<sub>1</sub>-C<sub>4</sub>) alkyl and Y<sup>3</sup> is (C<sub>1</sub>-C<sub>6</sub>)alkyl, carboxy (C<sub>1</sub>-C<sub>6</sub>)alkyl, amino(C<sub>1</sub>-C<sub>4</sub>)alkyl or mono-N— or di-N,N-(C<sub>1</sub>-C<sub>6</sub>)alkylaminoalkyl, —C(Y<sup>4</sup>)Y<sup>5</sup> wherein Y<sup>4</sup> is H or methyl and Y<sup>5</sup> is mono-N— or di-N,N-(C<sub>1</sub>-C<sub>6</sub>)alkylamino morpholino, piperidin-1-yl or pyrrolidin-1-yl, and the like.

One or more compounds of the invention may exist in unsolvated as well as solvated forms with pharmaceutically acceptable solvents such as water,

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ethanol, and the like, and it is intended that the invention embrace both solvated and unsolvated forms. "Solvate" means a physical association of a compound of this invention with one or more solvent molecules. This physical association involves varying degrees of ionic and covalent bonding, including hydrogen  
5 bonding. In certain instances the solvate will be capable of isolation, for example when one or more solvent molecules are incorporated in the crystal lattice of the crystalline solid. "Solvate" encompasses both solution-phase and isolatable solvates. Non-limiting examples of suitable solvates include ethanolates, methanolates, and the like. "Hydrate" is a solvate wherein the solvent molecule is  
10 H<sub>2</sub>O.

One or more compounds of the invention may optionally be converted to a solvate. Preparation of solvates is generally known. Thus, for example, M. Caira *et al*, *J. Pharmaceutical Sci.*, 93(3), 601-611 (2004) describe the preparation of the solvates of the antifungal fluconazole in ethyl acetate as well as from water.  
15 Similar preparations of solvates, hemisolvate, hydrates and the like are described by E. C. van Tonder *et al*, *AAPS PharmSciTech.*, 5(1), article 12 (2004); and A. L. Bingham *et al*, *Chem. Commun.*, 603-604 (2001). A typical, non-limiting, process involves dissolving the inventive compound in desired amounts of the desired solvent (organic or water or mixtures thereof) at a higher than ambient  
20 temperature, and cooling the solution at a rate sufficient to form crystals which are then isolated by standard methods. Analytical techniques such as, for example I. R. spectroscopy, show the presence of the solvent (or water) in the crystals as a solvate (or hydrate).

"Effective amount" or "therapeutically effective amount" is meant to  
25 describe an amount of compound or a composition of the present invention effective in inhibiting the above-noted diseases and thus producing the desired therapeutic, ameliorative, inhibitory or preventative effect.

The compounds of Formula I can form salts which are also within the scope of this invention. Reference to a compound of Formula I herein is understood to  
30 include reference to salts thereof, unless otherwise indicated. The term "salt(s)",

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as employed herein, denotes acidic salts formed with inorganic and/or organic acids, as well as basic salts formed with inorganic and/or organic bases. In addition, when a compound of Formula I contains both a basic moiety, such as, but not limited to a pyridine or imidazole, and an acidic moiety, such as, but not limited to a carboxylic acid, zwitterions ("inner salts") may be formed and are included within the term "salt(s)" as used herein. Pharmaceutically acceptable (i.e., non-toxic, physiologically acceptable) salts are preferred, although other salts are also useful. Salts of the compounds of the Formula I may be formed, for example, by reacting a compound of Formula I with an amount of acid or base, such as an equivalent amount, in a medium such as one in which the salt precipitates or in an aqueous medium followed by lyophilization.

Exemplary acid addition salts include acetates, ascorbates, benzoates, benzenesulfonates, bisulfates, borates, butyrates, citrates, camphorates, camphorsulfonates, fumarates, hydrochlorides, hydrobromides, hydroiodides, lactates, maleates, methanesulfonates, naphthalenesulfonates, nitrates, oxalates, phosphates, propionates, salicylates, succinates, sulfates, tartarates, thiocyanates, toluenesulfonates (also known as tosylates,) and the like. Additionally, acids which are generally considered suitable for the formation of pharmaceutically useful salts from basic pharmaceutical compounds are discussed, for example, by P. Stahl *et al*, Camille G. (eds.) *Handbook of Pharmaceutical Salts. Properties, Selection and Use*. (2002) Zurich: Wiley-VCH; S. Berge *et al*, *Journal of Pharmaceutical Sciences* (1977) 66(1) 1-19; P. Gould, *International J. of Pharmaceutics* (1986) 33 201-217; Anderson *et al*, *The Practice of Medicinal Chemistry* (1996), Academic Press, New York; and in *The Orange Book* (Food & Drug Administration, Washington, D.C. on their website). These disclosures are incorporated herein by reference thereto.

Exemplary basic salts include ammonium salts, alkali metal salts such as sodium, lithium, and potassium salts, alkaline earth metal salts such as calcium and magnesium salts, salts with organic bases (for example, organic amines) such as dicyclohexylamines, t-butyl amines, and salts with amino acids such as

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arginine, lysine and the like. Basic nitrogen-containing groups may be quarternized with agents such as lower alkyl halides (e.g. methyl, ethyl, and butyl chlorides, bromides and iodides), dialkyl sulfates (e.g. dimethyl, diethyl, and dibutyl sulfates), long chain halides (e.g. decyl, lauryl, and stearyl chlorides, bromides and iodides), aralkyl halides (e.g. benzyl and phenethyl bromides), and others.

All such acid salts and base salts are intended to be pharmaceutically acceptable salts within the scope of the invention and all acid and base salts are considered equivalent to the free forms of the corresponding compounds for purposes of the invention.

Pharmaceutically acceptable esters of the present compounds include the following groups: (1) carboxylic acid esters obtained by esterification of the hydroxy groups, in which the non-carbonyl moiety of the carboxylic acid portion of the ester grouping is selected from straight or branched chain alkyl (for example, acetyl, n-propyl, t-butyl, or n-butyl), alkoxyalkyl (for example, methoxymethyl), aralkyl (for example, benzyl), aryloxyalkyl (for example, phenoxymethyl), aryl (for example, phenyl optionally substituted with, for example, halogen, C<sub>1-4</sub>alkyl, or C<sub>1-4</sub>alkoxy or amino); (2) sulfonate esters, such as alkyl- or aralkylsulfonyl (for example, methanesulfonyl); (3) amino acid esters (for example, L-valyl or L-isoleucyl); (4) phosphonate esters and (5) mono-, di- or triphosphate esters. The phosphate esters may be further esterified by, for example, a C<sub>1-20</sub> alcohol or reactive derivative thereof, or by a 2,3-di (C<sub>6-24</sub>)acyl glycerol.

Compounds of Formula I, and salts, solvates, esters and prodrugs thereof, may exist in their tautomeric form (for example, as an amide, enol, keto or imino ether). All such tautomeric forms are contemplated herein as part of the present invention.

The compounds of Formula (I) may contain asymmetric or chiral centers, and, therefore, exist in different stereoisomeric forms. It is intended that all stereoisomeric forms of the compounds of Formula (I) as well as mixtures thereof, including racemic mixtures, form part of the present invention. In addition, the

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present invention embraces all geometric and positional isomers. For example, if a compound of Formula (I) incorporates a double bond or a fused ring, both the cis- and trans-forms, as well as mixtures, are embraced within the scope of the invention.

5 Diastereomeric mixtures can be separated into their individual diastereomers on the basis of their physical chemical differences by methods well known to those skilled in the art, such as, for example, by chromatography and/or fractional crystallization. Enantiomers can be separated by converting the enantiomeric mixture into a diastereomeric mixture by reaction with an appropriate  
10 optically active compound (e.g., chiral auxiliary such as a chiral alcohol or Mosher's acid chloride), separating the diastereomers and converting (e.g., hydrolyzing) the individual diastereomers to the corresponding pure enantiomers. Also, some of the compounds of Formula (I) may be atropisomers (e.g., substituted biaryls) and are considered as part of this invention. Enantiomers can  
15 also be separated by use of chiral HPLC column.

It is also possible that the compounds of Formula (I) may exist in different tautomeric forms, and all such forms are embraced within the scope of the invention. Also, for example, all keto-enol and imine-enamine forms of the compounds are included in the invention.

20 All stereoisomers (for example, geometric isomers, optical isomers and the like) of the present compounds (including those of the salts, solvates, esters and prodrugs of the compounds as well as the salts, solvates and esters of the prodrugs), such as those which may exist due to asymmetric carbons on various substituents, including enantiomeric forms (which may exist even in the absence  
25 of asymmetric carbons), rotameric forms, atropisomers, and diastereomeric forms, are contemplated within the scope of this invention, as are positional isomers (such as, for example, 4-pyridyl and 3-pyridyl). (For example, if a compound of Formula (I) incorporates a double bond or a fused ring, both the cis- and trans-forms, as well as mixtures, are embraced within the scope of the invention. Also,  
30 for example, all keto-enol and imine-enamine forms of the compounds are



included in the invention.) Individual stereoisomers of the compounds of the invention may, for example, be substantially free of other isomers, or may be admixed, for example, as racemates or with all other, or other selected, stereoisomers. The chiral centers of the present invention can have the S or R  
5 configuration as defined by the *IUPAC* 1974 Recommendations. The use of the terms "salt", "solvate", "ester", "prodrug" and the like, is intended to equally apply to the salt, solvate, ester and prodrug of enantiomers, stereoisomers, rotamers, tautomers, positional isomers, racemates or prodrugs of the inventive compounds.

The present invention also embraces isotopically-labelled compounds of  
10 the present invention which are identical to those recited herein, but for the fact that one or more atoms are replaced by an atom having an atomic mass or mass number different from the atomic mass or mass number usually found in nature. Examples of isotopes that can be incorporated into compounds of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, fluorine and  
15 chlorine, such as  $^2\text{H}$ ,  $^3\text{H}$ ,  $^{13}\text{C}$ ,  $^{14}\text{C}$ ,  $^{15}\text{N}$ ,  $^{18}\text{O}$ ,  $^{17}\text{O}$ ,  $^{31}\text{P}$ ,  $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^{18}\text{F}$ , and  $^{36}\text{Cl}$ , respectively.

Certain isotopically-labelled compounds of Formula (I) (e.g., those labeled with  $^3\text{H}$  and  $^{14}\text{C}$ ) are useful in compound and/or substrate tissue distribution assays. Tritiated (i.e.,  $^3\text{H}$ ) and carbon-14 (i.e.,  $^{14}\text{C}$ ) isotopes are particularly  
20 preferred for their ease of preparation and detectability. Further, substitution with heavier isotopes such as deuterium (i.e.,  $^2\text{H}$ ) may afford certain therapeutic advantages resulting from greater metabolic stability (e.g., increased in vivo half-life or reduced dosage requirements) and hence may be preferred in some circumstances. Isotopically labelled compounds of Formula (I) can generally be  
25 prepared by following procedures analogous to those disclosed in the Schemes and/or in the Examples hereinbelow, by substituting an appropriate isotopically labelled reagent for a non-isotopically labelled reagent.

Polymorphic forms of the compounds of Formula I, and of the salts, solvates, esters and prodrugs of the compounds of Formula I, are intended to be  
30 included in the present invention.

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The compounds according to the invention can have pharmacological properties; in particular, the compounds of Formula I can be modulators of gamma secretase (including inhibitors, antagonists and the like).

5 More specifically, the compounds of Formula I can be useful in the treatment of a variety of disorders of the central nervous system including, for example, including, but not limited to, Alzheimer's disease, AIDS-related dementia, Parkinson's disease, amyotrophic lateral sclerosis, retinitis pigmentosa, spinal muscular atrophy and cerebellar degeneration and the like.

10 Another aspect of this invention is a method of treating a mammal (e.g., human) having a disease or condition of the central nervous system by administering a therapeutically effective amount of at least one compound of Formula I, or a pharmaceutically acceptable salt, solvate, ester or prodrug of said compound to the mammal.

15 A preferred dosage is about 0.001 to 500 mg/kg of body weight/day of the compound of Formula I. An especially preferred dosage is about 0.01 to 25 mg/kg of body weight/day of a compound of Formula I, or a pharmaceutically acceptable salt or solvate of said compound.

20 The compounds of this invention may also be useful in combination (administered together or sequentially) with one or more additional agents listed above.

The compounds of this invention may also be useful in combination (administered together or sequentially) with one or more compounds selected from the group consisting of A $\beta$  antibody inhibitors, gamma secretase inhibitors and beta secretase inhibitors.

25 If formulated as a fixed dose, such combination products employ the compounds of this invention within the dosage range described herein and the other pharmaceutically active agent or treatment within its dosage range.

30 Accordingly, in an aspect, this invention includes combinations comprising an amount of at least one compound of Formula I, or a pharmaceutically acceptable salt, solvate, ester or prodrug thereof, and an amount of one or more



additional agents listed above wherein the amounts of the compounds/ treatments result in desired therapeutic effect.

The pharmacological properties of the compounds of this invention may be confirmed by a number of pharmacological assays. Certain assays are

5 exemplified later in this document.

This invention is also directed to pharmaceutical compositions which comprise at least one compound of Formula I, or a pharmaceutically acceptable salt, solvate, ester or prodrug of said compound and at least one pharmaceutically acceptable carrier.

10 Other embodiments of this invention are directed to pharmaceutically acceptable salts of any one of the embodiments above directed to any one of compounds 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

15 Other embodiments of this invention are directed to pharmaceutically acceptable esters of any one of the embodiments above directed to any one of compounds 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

20 Other embodiments of this invention are directed to solvates of any one of the embodiments above directed to any one of compounds 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

One embodiment of this invention is directed to a compound of formula I.

Another embodiment of this invention is directed to a pharmaceutically acceptable salt of a compound of formula I.

25 Another embodiment of this invention is directed to a pharmaceutically acceptable ester of a compound of formula I.

Another embodiment of this invention is directed to a solvate of a compound of formula I.

30 Another embodiment of this invention is directed to a compound of formula I in isolated form.



Another embodiment of this invention is directed to a compound of formula I in pure form.

Another embodiment of this invention is directed to a compound of formula I in pure and isolated form.

5 Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds of formula I and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of a pharmaceutically acceptable salt  
10 of one or more (e.g., one) compounds of formula I and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of a pharmaceutically acceptable ester of one or more (e.g., one) compounds of formula I and a pharmaceutically  
15 acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of a solvate of one or more (e.g., one) compounds of formula I and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical  
20 composition comprising an effective amount of one or more (e.g., one) compounds of formula I, and an effective amount of one or more (e.g., one) other pharmaceutically active ingredients (e.g.,) drugs, and a pharmaceutically acceptable carrier. Examples of the other pharmaceutically active ingredients include, but are not limited to drugs selected from the group consisting of: (a)  
25 drugs useful for the treatment of Alzheimer's disease, (b) drugs useful for inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), (c) drugs useful for treating neurodegenerative diseases, and (d) drugs useful for inhibiting gamma-secretase.

Another embodiment of this invention is directed to a pharmaceutical  
30 composition comprising an effective amount of one or more (e.g., one)

compounds of formula I, and effective amount of one or more BACE inhibitors, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one)  
5 compounds of formula I, and effective amount of one or more cholinesterase inhibitors (e.g., acetyl- and/or butyrylcholinesterase inhibitors), and a pharmaceutically acceptable carrier.

The compounds of formula I can be useful as gamma secretase modulators and can be useful in the treatment and prevention of diseases such as, for  
10 example, central nervous system disorders such as Alzheimers disease and Downs Syndrome.

Thus, another embodiment of this invention is directed to a method for modulating (including inhibiting, antagonizing and the like) gamma-secretase comprising administering an effective amount of one or more (e.g., one)  
15 compounds of formula I to a patient in need of such treatment.

Another embodiment of this invention is directed to a method for modulating (including inhibiting, antagonizing and the like) gamma-secretase, comprising administering an effective amount of a compound of formula I to a patient in need of treatment.

20 Another embodiment of this invention is directed to a method of treating one or more neurodegenerative diseases, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

Another embodiment of this invention is directed to a method of treating  
25 one or more neurodegenerative diseases, comprising administering an effective amount of a compound of formula I to a patient in need of treatment.

Another embodiment of this invention is directed to a method of inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), comprising administering an effective amount

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of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

Another embodiment of this invention is directed to a method of inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around  
5 neurological tissue (e.g., the brain), comprising administering an effective amount of a compound of formula I to a patient in need of treatment.

Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

10 Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of a compound of formula I to a patient in need of treatment.

This invention also provides combination therapies for (1) modulating gamma-secretase, or (2) treating one or more neurodegenerative diseases, or (3)  
15 inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), or (4) treating Alzheimer's disease. The combination therapies are directed to methods comprising the administration of an effective amount of one or more (e.g. one) compounds of formula I and the administration of an effective amount of one or more (e.g., one) other  
20 pharmaceutical active ingredients (e.g., drugs). The compounds of formula I and the other drugs can be administered separately (i.e., each is in its own separate dosage form), or the compounds of formula I can be combined with the other drugs in the same dosage form.

Thus, other embodiments of this invention are directed to any one of the  
25 methods of treatment, or methods of inhibiting, described herein, wherein an effective amount of the compound of formula I is used in combination with an effective amount of one or more other pharmaceutically active ingredients selected from the group consisting of: BACE inhibitors (beta secretase inhibitors), muscarinic antagonists (e.g.,  $m_1$  agonists or  $m_2$  antagonists), cholinesterase  
30 inhibitors (e.g., acetyl- and/or butyrylcholinesterase inhibitors); gamma secretase

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inhibitors; gamma secretase modulators; HMG-CoA reductase inhibitors; non-steroidal anti-inflammatory agents; N-methyl-D-aspartate receptor antagonists; anti-amyloid antibodies; vitamin E; nicotinic acetylcholine receptor agonists; CB1 receptor inverse agonists or CB1 receptor antagonists; an antibiotic; growth  
5 hormone secretagogues; histamine H3 antagonists; AMPA agonists; PDE4 inhibitors; GABA<sub>A</sub> inverse agonists; inhibitors of amyloid aggregation; glycogen synthase kinase beta inhibitors; promoters of alpha secretase activity; PDE-10 inhibitors and cholesterol absorption inhibitors (e.g., ezetimibe).

Another embodiment of this invention is directed to a method of treating  
10 Alzheimer's disease, comprising administering an effective amount of one or more (e.g., one) compounds of formula I, in combination with an effective (i.e., therapeutically effective) amount of one or more cholinesterase inhibitors (such as, for example, (±)-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1 *H*-inden-1-one hydrochloride, i.e., donepezil hydrochloride,  
15 available as the Aricept® brand of donepezil hydrochloride), to a patient in need of treatment.

Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of a compound of formula I, in combination with an effective amount of one or more (e.g., one)  
20 cholinesterase inhibitors (such as, for example, (±)-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1 *H*-inden-1-one hydrochloride, i.e., donepezil hydrochloride, available as the Aricept® brand of donepezil hydrochloride), to a patient in need of treatment.

Another embodiment of this invention is directed to a method of treating  
25 Alzheimer's disease, comprising administering an effective amount of one or more (e.g., one) compounds of formula I, in combination with an effective amount of one or more compounds selected from the group consisting of Aβ antibody inhibitors, gamma secretase inhibitors and beta secretase inhibitors.

Another embodiment of this invention is directed to a method of treating  
30 Alzheimer's disease, comprising administering an effective amount of one or more

(e.g., one) compounds of formula I, in combination with an effective amount of one or more BACE inhibitors.

Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more  
5 compounds of formula I, in combination with an effective amount of Exelon (rivastigmine).

Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of Cognex  
10 (tacrine).

Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of a Tau kinase inhibitor.

15 Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more Tau kinase inhibitor (e.g., GSK3beta inhibitor, cdk5 inhibitor, ERK inhibitor).

This invention also provides a method of treating Alzheimer's disease,  
20 comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one anti-Abeta vaccination (active immunization).

Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more  
25 compounds of formula I, in combination with an effective amount of one or more APP ligands.

Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more  
30 agents that upregulate insulin degrading enzyme and/or neprilysin.



Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more cholesterol lowering agents (for example, statins such as Atorvastatin, Fluvastatin, 5 Lovastatin, Mevastatin, Pitavastatin, Pravastatin, Rosuvastatin, Simvastatin, and cholesterol absorption inhibitor such as Ezetimibe).

This invention also provides a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more fibrates (for 10 example, clofibrate, Clofibrade, Etofibrate, Aluminium Clofibrate).

Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more LXR agonists.

15 Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more LRP mimics.

Another embodiment of this invention is directed to a method of treating 20 Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more 5-HT<sub>6</sub> receptor antagonists.

Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more 25 compounds of formula I, in combination with an effective amount of one or more nicotinic receptor agonists.

Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more 30 H<sub>3</sub> receptor antagonists.

This invention also provides a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more histone deacetylase inhibitors.

- 5 Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more hsp90 inhibitors.

- 10 Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more m1 muscarinic receptor agonists.

- 15 Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more 5-HT6 receptor antagonists mGluR1 or mGluR5 positive allosteric modulators or agonists

- 20 Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more mGluR2/3 antagonists.

- 25 Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more anti-inflammatory agents that can reduce neuroinflammation.

Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more Prostaglandin EP2 receptor antagonists.

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This invention also provides a method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more PAI-1 inhibitors.

This invention also provides a method of treating Alzheimer's disease,  
5 comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more agents that can induce Abeta efflux such as gelsolin.

This invention also provides a method of treating Downs syndrome, comprising administering an effective amount of one or more (e.g., one)  
10 compounds of formula I to a patient in need of treatment.

This invention also provides a method of treating Downs syndrome, comprising administering an effective amount of a compound of formula I to a patient in need of treatment.

This invention also provides a method of treating Downs syndrome,  
15 comprising administering an effective amount of one or more (e.g., one) compounds of formula I, in combination with an effective amount of one or more cholinesterase inhibitors (such as, for example, (±)-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidiny]methyl]-1 H -inden-1-one hydrochloride, i.e., donepezil hydrochloride, available as the Aricept® brand of donepezil  
20 hydrochloride), to a patient in need of treatment.

This invention also provides a method of treating Downs syndrome, comprising administering an effective amount of a compound of formula I, in combination with an effective amount of one or more (e.g., one) cholinesterase inhibitors (such as, for example, (±)-2,3-dihydro-5,6-dimethoxy-2-[[1-  
25 (phenylmethyl)-4-piperidiny]methyl]-1 H -inden-1-one hydrochloride, i.e., donepezil hydrochloride, available as the Aricept® brand of donepezil hydrochloride), to a patient in need of treatment.

This invention also provides a method of treating mild cognitive impairment, comprising administering an effective amount of one or more (e.g., one)  
30 compounds of formula I to a patient in need of treatment.

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This invention also provides a method of treating glaucoma, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

5 This invention also provides a method of treating cerebral amyloid angiopathy, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

This invention also provides a method of treating stroke, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

10 This invention also provides a method of treating dementia, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

This invention also provides a method of treating microgliosis, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

15 This invention also provides a method of treating brain inflammation, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

This invention also provides a method of treating olfactory function loss, comprising administering an effective amount of one or more (e.g., one) compounds of formula I to a patient in need of treatment.

20 This invention also provides combinations (i.e., pharmaceutical compositions) comprising an effective amount of one or more (e.g., one) compounds of formula I, in combination with an effective amount of one or more compounds selected from the group consisting of cholinesterase inhibitors (such as, for example, ( $\pm$ )-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1 H -inden-1-one hydrochloride, i.e., donepezil hydrochloride, available as the Aricept<sup>®</sup> brand of donepezil hydrochloride), A $\beta$  antibody inhibitors, gamma secretase inhibitors and beta secretase inhibitors. The pharmaceutical

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30 compositions also comprise a pharmaceutically acceptable carrier.

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This invention also provides a kit comprising, in separate containers, in a single package, pharmaceutical compositions for use in combination, wherein one container comprises an effective amount of a compound of formula I in a pharmaceutically acceptable carrier, and another container (i.e., a second  
5 container) comprises an effective amount of another pharmaceutically active ingredient (as described above), the combined quantities of the compound of formula I and the other pharmaceutically active ingredient being effective to: (a) treat Alzheimer's disease, or (b) inhibit the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), or (c)  
10 treat neurodegenerative diseases, or (d) modulate the activity of gamma-secretase.

Another embodiment of this invention is directed to a pharmaceutically acceptable salt of a compound of formula (I), said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9,  
15 H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a pharmaceutically acceptable ester of a compound of formula (I), said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9,  
20 H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a solvate of a compound of formula (I), said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6,  
25 I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a compound of formula (I) in isolated form, said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

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Another embodiment of this invention is directed to a compound of formula (I) in pure form, said compound of formula (I) being selected from the group consisting of: said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a compound of formula (I) in pure and isolated form, said compound of formula (I) being selected from the group consisting of: said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds of formula (I) and a pharmaceutically acceptable carrier, said compound of formula (I) being selected from the group consisting of: said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment is directed to a pharmaceutical composition comprising an effective amount of a pharmaceutically acceptable salt of one or more (e.g., one) compounds of formula (I) and a pharmaceutically acceptable carrier, said compound of formula (I) being selected from the group consisting of: said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment is directed to a pharmaceutical composition comprising an effective amount of a pharmaceutically acceptable ester of one or more (e.g., one) compounds of formula (I) and a pharmaceutically acceptable carrier, said compound of formula (I) being selected from the group consisting of: said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

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Another embodiment is directed to a pharmaceutical composition comprising an effective amount of a solvate of one or more (e.g., one) compounds of formula (I) and a pharmaceutically acceptable carrier, said compound of formula (I) being selected from the group consisting of: said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds of formula (I), and an effective amount of one or more (e.g., one) other pharmaceutically active ingredients (e.g., drugs), and a pharmaceutically acceptable carrier. Examples of the other pharmaceutically active ingredients include, but are not limited to drugs selected from the group consisting of: (a) drugs useful for the treatment of Alzheimer's disease, (b) drugs useful for inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), (c) drugs useful for treating neurodegenerative diseases, and (d) drugs useful for inhibiting gamma-secretase, said compound of formula (I) being selected from the group consisting of: said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds of formula (I), and effective amount of one or more BACE inhibitors, and a pharmaceutically acceptable carrier, said compound of formula (I) being selected from the group consisting of: said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one)

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compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and an effective amount of one or more cholinesterase inhibitors (e.g., acetyl- and/or butyrylcholinesterase inhibitors), and a

5 pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-  
10 N23, O4\_1, and P8\_1, and effective amount of one or more muscarinic antagonists (e.g., m<sub>1</sub> agonists or m<sub>2</sub> antagonists), and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-  
15 N23, O4\_1, and P8\_1, and effective amount of Exelon (rivastigmine), and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-  
20 N23, O4\_1, and P8\_1, and effective amount of Cognex (tacrine), and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-  
25 N23, O4\_1, and P8\_1, and effective amount of a Tau kinase inhibitor, and a  
30 pharmaceutically acceptable carrier.



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Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more Tau kinase inhibitor (e.g., GSK3beta inhibitor, cdk5 inhibitor, ERK inhibitor), and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one anti-Abeta vaccine (active immunization), and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more APP ligands, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more agents that upregulate insulin degrading enzyme and/or neprilysin, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-

N23, O4\_1, and P8\_1, and effective amount of one or more cholesterol lowering agents (for example, statins such as Atorvastatin, Fluvastatin, Lovastatin, Mevastatin, Pitavastatin, Pravastatin, Rosuvastatin, Simvastatin, and cholesterol absorption inhibitor such as Ezetimibe), and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more fibrates (for example, clofibrate, Clofibrade, Etofibrate, Aluminium Clofibrate), and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more LXR agonists, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more LRP mimics, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more 5-HT6 receptor antagonists, and a pharmaceutically acceptable carrier.

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Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more nicotinic receptor agonists, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more H3 receptor antagonists, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more histone deacetylase inhibitors, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more hsp90 inhibitors, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more m1 muscarinic receptor agonists, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more 5-HT6 receptor antagonists mGluR1 or mGluR5 positive allosteric modulators or agonists, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more one mGluR2/3 antagonists, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more anti-inflammatory agents that can reduce neuroinflammation, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more Prostaglandin EP2 receptor antagonists, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one) compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-



N23, O4\_1, and P8\_1, and effective amount of one or more PAI-1 inhibitors, and a pharmaceutically acceptable carrier.

Another embodiment of this invention is directed to a pharmaceutical composition comprising an effective amount of one or more (e.g., one)  
5 compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and effective amount of one or more agents that can induce Abeta efflux such as gelsolin, and a pharmaceutically acceptable carrier.

The compounds of formula I selected from the group consisting of: 1 to 24,  
10 B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1 can be useful as gamma secretase modulators and can be useful in the treatment and prevention of diseases such as, for example, central nervous system disorders (such as Alzheimers disease and  
Downs Syndrome), and treating mild cognitive impairment, glaucoma, cerebral  
15 amyloid angiopathy, stroke, dementia, microgliosis, brain inflammation, and olfactory function loss.

Thus, another embodiment of this invention is directed to a method for modulating (including inhibiting, antagonizing and the like) gamma-secretase comprising administering an effective (i.e., therapeutically effective) amount of one  
20 or more (e.g., one) compounds of formula (I) to a patient in need of such treatment, said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a method for  
25 modulating (including inhibiting, antagonizing and the like) gamma-secretase, comprising administering an effective (i.e., therapeutically effective) amount of a compound of formula (I) to a patient in need of treatment, said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15,  
30 N6-N23, O4\_1, and P8\_1.

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Another embodiment of this invention is directed to a method of treating one or more neurodegenerative diseases, comprising administering an effective (i.e., therapeutically effective) amount of one or more (e.g., one) compounds of formula (I) to a patient in need of treatment, said compound of formula (I) being  
5 selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a method of treating one or more neurodegenerative diseases, comprising administering an effective  
10 (i.e., therapeutically effective) amount of a compound of formula (I) to a patient in need of treatment, said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a method of inhibiting  
15 the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), comprising administering an effective (i.e., therapeutically effective) amount of one or more (e.g., one) compounds of formula (I) to a patient in need of treatment, said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11,  
20 I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a method of inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), comprising administering an effective (i.e.,  
therapeutically effective) amount of a compound of formula (I) to a patient in need  
25 of treatment, said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective (i.e., therapeutically  
30 effective) amount of one or more (e.g., one) compounds of formula (I) to a patient

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in need of treatment, said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a method of treating  
5 Alzheimer's disease, comprising administering an effective (i.e., therapeutically effective) amount of a compound of formula (I) to a patient in need of treatment, said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

10 Another embodiment of this invention is directed to a method of treating mild cognitive impairment, glaucoma, cerebral amyloid angiopathy, stroke, dementia, microgliosis, brain inflammation, or olfactory function loss, comprising administering an effective (i.e., therapeutically effective) amount of one or more (e.g., one) compounds of formula (I) to a patient in need of treatment, said  
15 compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Another embodiment of this invention is directed to a method of treating mild cognitive impairment, glaucoma, cerebral amyloid angiopathy, stroke,  
20 dementia, microgliosis, brain inflammation, or olfactory function loss, comprising administering an effective (i.e., therapeutically effective) amount of a compound of formula (I) to a patient in need of treatment, said compound of formula (I) being selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and  
25 P8\_1.

This invention also provides combination therapies for (1) modulating gamma-secretase, or (2) treating one or more neurodegenerative diseases, or (3) inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), or (4) treating Alzheimer's disease.  
30 The combination therapies are directed to methods comprising the administration



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of one or more (e.g. one) compounds of formula (I), and the administration of one or more (e.g., one) other pharmaceutical active ingredients (e.g., drugs). The compounds of formula (I), and the other drugs can be administered separately (i.e., each is in its own separate dosage form), or the compounds of formula (I) can be combined with the other drugs in the same dosage form.

Thus, other embodiments of this invention are directed to any one of the methods of treatment, or methods of inhibiting, described herein, wherein the compounds of formula (I) are used in combination with an effective amount of one or more other pharmaceutically active ingredients selected from the group consisting of: BACE inhibitors (beta secretase inhibitors); muscarinic antagonists (e.g., m<sub>1</sub> agonists or m<sub>2</sub> antagonists); cholinesterase inhibitors (e.g., acetyl- and/or butyrylcholinesterase inhibitors); gamma secretase inhibitors; gamma secretase modulators; HMG-CoA reductase inhibitors; non-steroidal anti-inflammatory agents; N-methyl-D-aspartate receptor antagonists; anti-amyloid antibodies; vitamin E; nicotinic acetylcholine receptor agonists; CB1 receptor inverse agonists or CB1 receptor antagonists; an antibiotic; growth hormone secretagogues; histamine H3 antagonists; AMPA agonists; PDE4 inhibitors; GABA<sub>A</sub> inverse agonists; inhibitors of amyloid aggregation; glycogen synthase kinase beta inhibitors; promoters of alpha secretase activity; PDE-10 inhibitors; Exelon (rivastigmine); Cognex (tacrine); Tau kinase inhibitors (e.g., GSK3beta inhibitors, cdk5 inhibitors, or ERK inhibitors); anti-Abeta vaccine; APP ligands; agents that upregulate insulin cholesterol lowering agents (for example, statins such as Atorvastatin, Fluvastatin, Lovastatin, Mevastatin, Pitavastatin, Pravastatin, Rosuvastatin, Simvastatin); cholesterol absorption inhibitors (such as Ezetimibe); fibrates (such as, for example, clofibrate, Clofibrade, Etofibrate, and Aluminium Clofibrate); LXR agonists; LRP mimics; nicotinic receptor agonists; H3 receptor antagonists; histone deacetylase inhibitors; hsp90 inhibitors; m1 muscarinic receptor agonists; 5-HT6 receptor antagonists; mGluR1; mGluR5; positive allosteric modulators or agonists; mGluR2/3 antagonists; anti-inflammatory agents that can reduce neuroinflammation; Prostaglandin EP2

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receptor antagonists; PAI-1 inhibitors; and agents that can induce Abeta efflux such as gelsolin.

This invention also provides combination therapies for (1) modulating gamma-secretase, or (2) treating one or more neurodegenerative diseases, or (3) inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), or (4) treating Alzheimer's disease. The combination therapies are directed to methods comprising the administration of one or more (e.g. one) compounds of formula (I) selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and the administration of one or more (e.g., one) other pharmaceutical active ingredients (e.g., drugs). The compounds of formula 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, and the other drugs can be administered separately (i.e., each is in its own separate dosage form), or the compounds of formula 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1 can be combined with the other drugs in the same dosage form.

Thus, other embodiments of this invention are directed to any one of the methods of treatment, or methods of inhibiting, described herein, wherein the compounds of formula (I), selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1 are used in combination with an effective amount of one or more other pharmaceutically active ingredients selected from the group consisting of: BACE inhibitors (beta secretase inhibitors), muscarinic antagonists (e.g., agonists or m<sub>2</sub> antagonists), cholinesterase inhibitors (e.g., acetyl- and/or butyrylcholinesterase inhibitors); gamma secretase inhibitors; gamma secretase modulators; HMG-CoA reductase inhibitors; non-steroidal anti-inflammatory agents; N-methyl-D-aspartate receptor antagonists; anti-amyloid antibodies; vitamin E; nicotinic acetylcholine receptor agonists; CB1 receptor inverse agonists

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or CB1 receptor antagonists; an antibiotic; growth hormone secretagogues; histamine H3 antagonists; AMPA agonists; PDE4 inhibitors; GABA<sub>A</sub> inverse agonists; inhibitors of amyloid aggregation; glycogen synthase kinase beta inhibitors; promoters of alpha secretase activity; PDE-10 inhibitors; Exelon (rivastigmine); Cognex (tacrine); Tau kinase inhibitors (e.g., GSK3beta inhibitors, cdk5 inhibitors, or ERK inhibitors); anti-Abeta vaccine; APP ligands; agents that upregulate insulin cholesterol lowering agents (for example, statins such as Atorvastatin, Fluvastatin, Lovastatin, Mevastatin, Pitavastatin, Pravastatin, Rosuvastatin, Simvastatin); cholesterol absorption inhibitors (such as Ezetimibe); fibrates (such as, for example, clofibrate, Clofibrate, Etofibrate, and Aluminium Clofibrate); LXR agonists; LRP mimics; nicotinic receptor agonists; H3 receptor antagonists; histone deacetylase inhibitors; hsp90 inhibitors; m1 muscarinic receptor agonists; 5-HT6 receptor antagonists; mGluR1; mGluR5; positive allosteric modulators or agonists; mGluR2/3 antagonists; anti-inflammatory agents that can reduce neuroinflammation; Prostaglandin EP2 receptor antagonists; PAI-1 inhibitors; and agents that can induce Aβ efflux such as gelsolin.

Other embodiments of this invention are directed to any one of the methods of treatment, or methods of inhibiting, described herein, wherein the compounds of formula (I), selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1 are used in combination with an effective amount of one or more other pharmaceutically active ingredients selected from the group consisting of: BACE inhibitors (beta secretase inhibitors), muscarinic antagonists (e.g., m<sub>1</sub> agonists or m<sub>2</sub> antagonists), cholinesterase inhibitors (e.g., acetyl- and/or butyrylcholinesterase inhibitors); gamma secretase inhibitors; gamma secretase modulators; HMG-CoA reductase inhibitors; non-steroidal anti-inflammatory agents; N-methyl-D-aspartate receptor antagonists; anti-amyloid antibodies; vitamin E; nicotinic acetylcholine receptor agonists; CB1 receptor inverse agonists or CB1 receptor antagonists; an antibiotic; growth hormone secretagogues;



histamine H3 antagonists; AMPA agonists; PDE4 inhibitors; GABA<sub>A</sub> inverse agonists; inhibitors of amyloid aggregation; glycogen synthase kinase beta inhibitors; promoters of alpha secretase activity; PDE-10 inhibitors; and cholesterol absorption inhibitors (e.g., ezetimibe).

- 5 Other embodiments of this invention are directed to any one of the methods of treatment, or methods of inhibiting, described herein, wherein the compounds of formula (I), selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1 are used in combination with an effective amount of one
- 10 or more other pharmaceutically active ingredients selected from the group consisting of: Exelon (rivastigmine); Cognex (tacrine); Tau kinase inhibitors (e.g., GSK3beta inhibitors, cdk5 inhibitors, or ERK inhibitors); anti-Abeta vaccine; APP ligands; agents that upregulate insulin cholesterol lowering agents (for example, statins such as Atorvastatin, Fluvastatin, Lovastatin, Mevastatin, Pitavastatin,
- 15 Pravastatin, Rosuvastatin, Simvastatin); cholesterol absorption inhibitors (such as Ezetimibe); fibrates (such as, for example, for example, clofibrate, Clofibrade, Etofibrate, and Aluminium Clofibrate); LXR agonists; LRP mimics; nicotinic receptor agonists; H3 receptor antagonists; histone deacetylase inhibitors; hsp90 inhibitors; m1 muscarinic receptor agonists; 5-HT6 receptor antagonists; mGluR1;
- 20 mGluR5; positive allosteric modulators or agonists; mGluR2/3 antagonists; anti-inflammatory agents that can reduce neuroinflammation; Prostaglandin EP2 receptor antagonists; PAI-1 inhibitors; and agents that can induce Abeta efflux such as gelsolin.

- Another embodiment of this invention is directed to a method of treating
- 25 Alzheimer's disease, comprising administering an effective (i.e., therapeutically effective) amount of one or more (e.g., one) compounds of formula (I) selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, in combination with an effective (i.e., therapeutically effective) amount of one or
- 30 more cholinesterase inhibitors (such as, for example, (±)-2,3-dihydro-5,6-

dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1 *H*-inden-1-one hydrochloride, i.e., donepezil hydrochloride, available as the Aricept® brand of donepezil hydrochloride), to a patient in need of treatment.

- Another embodiment of this invention is directed to a method of treating
- 5 Alzheimer's disease, comprising administering an effective (i.e., therapeutically effective) amount of a compound of formula (I) selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, in combination with an effective (i.e., therapeutically effective) amount of one or more (e.g., one)
- 10 cholinesterase inhibitors (such as, for example, (±)-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1 *H*-inden-1-one hydrochloride, i.e., donepezil hydrochloride, available as the Aricept® brand of donepezil hydrochloride), to a patient in need of treatment.

- Another embodiment of this invention is directed to a method of treating
- 15 Alzheimer's disease, comprising administering an effective (i.e., therapeutically effective) amount of one or more (e.g., one) compounds of formula (I) selected from the group consisting of: in combination with an effective (i.e., therapeutically effective) amount of one or more compounds selected from the group consisting of Aβ antibody inhibitors, gamma secretase inhibitors and beta secretase
- 20 inhibitors.

- Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective (i.e., therapeutically effective) amount of one or more (e.g., one) compounds of formula (I) selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11,
- 25 I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, in combination with an effective (i.e., therapeutically effective) amount of one or more BACE inhibitors.

- Another embodiment of this invention is directed to a method of treating Alzheimer's disease, comprising administering an effective (i.e., therapeutically
- 30 effective) amount of a compound of formula (I) selected from the group consisting

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of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, in combination with an effective (i.e., therapeutically effective) amount of one or more BACE inhibitors.

Another embodiment of this invention is directed to a method of treating  
5 Downs syndrome, comprising administering an effective (i.e., therapeutically effective) amount of one or more (e.g., one) compounds of formula (I) selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1 to a patient in need of treatment.

10 Another embodiment of this invention is directed to a method of treating Downs syndrome, comprising administering an effective (i.e., therapeutically effective) amount of a compound of formula (I) selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, to a patient in need of  
15 treatment.

Another embodiment of this invention is directed to a method of treating Downs syndrome, comprising administering an effective (i.e., therapeutically effective) amount of one or more (e.g., one) compounds of formula (I) selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11,  
20 I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, in combination with an effective (i.e., therapeutically effective) amount of one or more cholinesterase inhibitors (such as, for example, ( $\pm$ )-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1 *H*-inden-1-one hydrochloride, i.e., donepezil hydrochloride, available as the Aricept® brand of  
25 donepezil hydrochloride), to a patient in need of treatment.

Another embodiment of this invention is directed to a method of treating Downs syndrome, comprising administering an effective (i.e., therapeutically effective) amount of a compound of formula (I) selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-  
30 J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1, in combination with an

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effective (i.e., therapeutically effective) amount of one or more (e.g., one) cholinesterase inhibitors (such as, for example, ( $\pm$ )-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1 *H*-inden-1-one hydrochloride, i.e., donepezil hydrochloride, available as the Aricept<sup>®</sup> brand of donepezil hydrochloride), to a patient in need of treatment.

Another embodiment of this invention is directed to combinations (i.e., pharmaceutical compositions) comprising an effective (i.e., therapeutically effective) amount of one or more (e.g., one) compounds of formula (I) selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1 in combination with an effective (i.e., therapeutically effective) amount of one or more compounds selected from the group consisting of cholinesterase inhibitors (such as, for example, ( $\pm$ )-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1 *H*-inden-1-one hydrochloride, i.e., donepezil hydrochloride, available as the Aricept<sup>®</sup> brand of donepezil hydrochloride), A $\beta$  antibody inhibitors, gamma secretase inhibitors and beta secretase inhibitors. The pharmaceutical compositions also comprise a pharmaceutically acceptable carrier.

This invention also provides a kit comprising, in separate containers, in a single package, pharmaceutical compositions for use in combination, wherein one container comprises an effective amount of one or more (e.g., one) compounds of formula (I) (e.g., compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1 in a pharmaceutically acceptable carrier, and another container (i.e., a second container) comprises an effective amount of another pharmaceutically active ingredient (as described above), the combined quantities of the compounds of formula (I) and the other pharmaceutically active ingredient being effective to: (a) treat Alzheimer's disease, or (b) inhibit the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), or (c) treat neurodegenerative diseases, or (d) modulate the activity of gamma-secretase.

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This invention also provides a kit comprising, in separate containers, in a single package, pharmaceutical compositions for use in combination, wherein one container comprises an effective amount of a compound selected from the group consisting of the compounds of formulas (I) (e.g. the compounds selected from the group consisting of: 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1) in a pharmaceutically acceptable carrier, and another container (i.e., a second container) comprises an effective amount of another pharmaceutically active ingredient (as described above), the combined quantities of the compound of formulas (I) and the other pharmaceutically active ingredient being effective to: (a) treat Alzheimer's disease, or (b) inhibit the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue (e.g., the brain), or (c) treat neurodegenerative diseases, or (d) modulate the activity of gamma-secretase.

Other embodiments of this invention are directed to any one of the above methods of treatment, pharmaceutical compositions, or kits wherein the compound of formula I is any one of the compounds 1 to 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, and P8\_1.

Examples of cholinesterase inhibitors are tacrine, donepezil, rivastigmine, galantamine, pyridostigmine and neostigmine, with tacrine, donepezil, rivastigmine and galantamine being preferred.

Examples of  $m_1$  agonists are known in the art. Examples of  $m_2$  antagonists are also known in the art; in particular,  $m_2$  antagonists are disclosed in US patents 5,883,096; 6,037,352; 5,889,006; 6,043,255; 5,952,349; 5,935,958; 6,066,636; 5,977,138; 6,294,554; 6,043,255; and 6,458,812; and in WO 03/031412, all of which are incorporated herein by reference.

Examples of BACE inhibitors include those described in: US2005/0119227 published 06/02/2005 (see also WO2005/016876 published 02/24/2005), US2005/0043290 published 02/24/2005 (see also WO2005/014540 published



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02/17/2005 ), WO2005/058311 published 06/30/2005 (see also US2007/0072852 published 03/29/2007), US2006/0111370 published 05/25/2006 (see also WO2006/065277 published 06/22/2006), US Application Serial No. 11/710582 filed 02/23/2007, US2006/0040994 published 02/23/2006 (see also

5 WO2006/014762 published 02/09/2006), WO2006/014944 published 02/09/2006 (see also US2006/0040948 published 02/23/2006), WO2006/138266 published 12/28/2006 (see also US2007/0010667 published 01/11/2007), WO2006/138265 published 12/28/2006, WO2006/138230 published 12/28/2006, WO2006/138195 published 12/28/2006 (see also US2006/0281729 published 12/14/2006),

10 WO2006/138264 published 12/28/2006 (see also US2007/0060575 published 03/15/2007), WO2006/138192 published 12/28/2006 (see also US2006/0281730 published 12/14/2006), WO2006/138217 published 12/28/2006 (see also US2006/0287294 published 12/21/2006), US2007/0099898 published 05/03/2007 (see also WO2007/050721 published 05/03/2007), WO2007/053506 published

15 05/10/2007 (see also US2007/099875 published 05/03/2007), U.S. Application Serial No. 11/759336 filed 06/07/2007, U.S. Application Serial No. 60/874362 filed 12/12/2006, and U.S. Application Serial No. 60/874419 filed 12/12/2006, the disclosures of each being incorporated herein by reference thereto.

20 For preparing pharmaceutical compositions from the compounds described by this invention, inert, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, dispersible granules, capsules, cachets and suppositories. The powders and tablets may be comprised of from about 5 to about 95 percent active ingredient. Suitable solid carriers are

25 known in the art, e.g., magnesium carbonate, magnesium stearate, talc, sugar or lactose. Tablets, powders, cachets and capsules can be used as solid dosage forms suitable for oral administration. Examples of pharmaceutically acceptable carriers and methods of manufacture for various compositions may be found in A. Gennaro (ed.), *Remington's Pharmaceutical Sciences*, 18<sup>th</sup> Edition, (1990), Mack

30 Publishing Co., Easton, Pennsylvania.

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Liquid form preparations include solutions, suspensions and emulsions. As an example may be mentioned water or water-propylene glycol solutions for parenteral injection or addition of sweeteners and opacifiers for oral solutions, suspensions and emulsions. Liquid form preparations may also include solutions  
5 for intranasal administration.

Aerosol preparations suitable for inhalation may include solutions and solids in powder form, which may be in combination with a pharmaceutically acceptable carrier, such as an inert compressed gas, e.g. nitrogen.

Also included are solid form preparations that are intended to be converted,  
10 shortly before use, to liquid form preparations for either oral or parenteral administration. Such liquid forms include solutions, suspensions and emulsions.

The compounds of the invention may also be deliverable transdermally. The transdermal compositions can take the form of creams, lotions, aerosols and/or emulsions and can be included in a transdermal patch of the matrix or  
15 reservoir type as are conventional in the art for this purpose.

The compounds of this invention may also be delivered subcutaneously. Preferably the compound is administered orally.

Preferably, the pharmaceutical preparation is in a unit dosage form. In such form, the preparation is subdivided into suitably sized unit doses containing  
20 appropriate quantities of the active component, e.g., an effective amount to achieve the desired purpose.

The quantity of active compound in a unit dose of preparation may be varied or adjusted from about 1 mg to about 100 mg, preferably from about 1 mg to about 50 mg, more preferably from about 1 mg to about 25 mg, according to the  
25 particular application.

The actual dosage employed may be varied depending upon the requirements of the patient and the severity of the condition being treated. Determination of the proper dosage regimen for a particular situation is within the skill of the art. For convenience, the total daily dosage may be divided and  
30 administered in portions during the day as required.

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The amount and frequency of administration of the compounds of the invention and/or the pharmaceutically acceptable salts thereof will be regulated according to the judgment of the attending clinician considering such factors as age, condition and size of the patient as well as severity of the symptoms being  
5 treated. A typical recommended daily dosage regimen for oral administration can range from about 1 mg/day to about 500 mg/day, preferably 1 mg/day to 200 mg/day, in two to four divided doses.

Another aspect of this invention is a kit comprising a therapeutically effective amount of at least one compound of Formula I, or a pharmaceutically  
10 acceptable salt, solvate, ester or prodrug of said compound and a pharmaceutically acceptable carrier, vehicle or diluent.

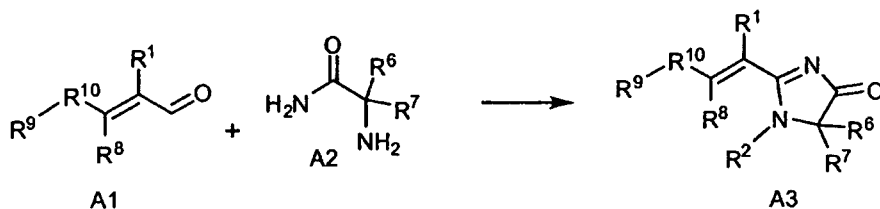
Yet another aspect of this invention is a kit comprising an amount of at least one compound of Formula I, or a pharmaceutically acceptable salt, solvate, ester or prodrug of said compound and an amount of at least one additional agent  
15 listed above, wherein the amounts of the two or more ingredients result in desired therapeutic effect.

The invention disclosed herein is exemplified by the following illustrative example which should not be construed to limit the scope of the disclosure. Alternative mechanistic pathways and analogous structures will be apparent to  
20 those skilled in the art.

Where NMR data are presented,  $^1\text{H}$  spectra were obtained on either a Varian VXR-200 (200 MHz,  $^1\text{H}$ ), Varian Gemini-300 (300 MHz) or XL-400 (400 MHz) and are reported as ppm down field from  $\text{Me}_4\text{Si}$  with number of protons, multiplicities, and coupling constants in Hertz indicated parenthetically. Where  
25 LC/MS data are presented, analyses was performed using an Applied Biosystems API-100 mass spectrometer and Shimadzu SCL-10A LC column: Altech platinum C18, 3 micron, 33mm x 7mm ID; gradient flow: 0 min – 10%  $\text{CH}_3\text{CN}$ , 5 min – 95%  $\text{CH}_3\text{CN}$ , 7 min – 95%  $\text{CH}_3\text{CN}$ , 7.5 min – 10%  $\text{CH}_3\text{CN}$ , 9 min – stop. The observed  
30 parent ion is given.

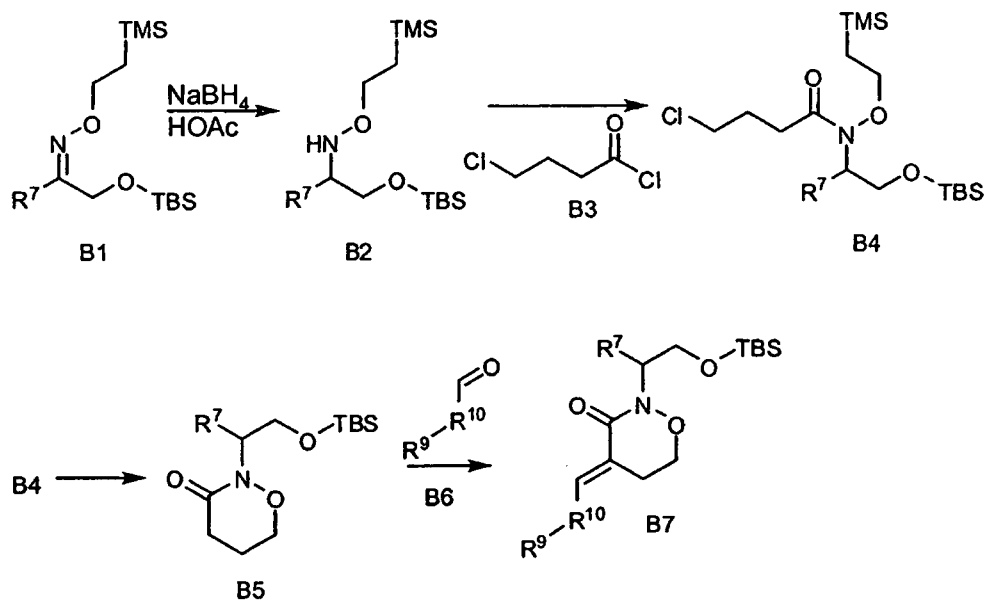
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**Method A**

- 5 To a dichloromethane solution of **A1** ( $R^1 = H$ ,  $R^8 = H$ ,  $R^{10} = 3$ -(methoxy)phenyl,  $R^9 = 4$ -(4-Me-imidazol-yl) and **A2** ( $R^6 = Me$ ,  $R^7 = 4$ -fluorophenyl) is added N-chlorosuccinimide and the reaction mixture is stirred overnight and then is worked up to give compound **A3** ( $R^2 = H$ ,  $R^8 = H$ ,  $R^{10} = 3$ -(methoxy)phenyl,  $R^9 = 4$ -(4-Me-imidazol-yl),  $R^6 = Me$ ,  $R^7 = 4$ -fluorophenyl).

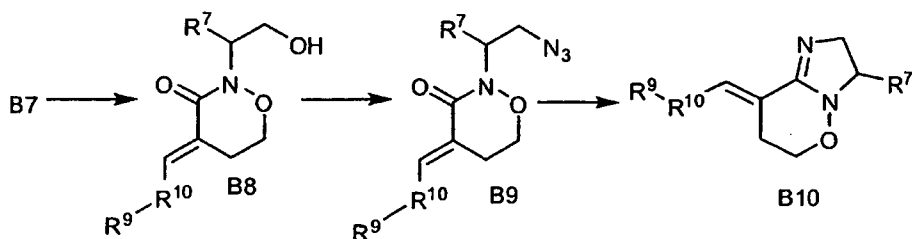
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**Method B**

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**Method B, Step 1;**

Compound **B1** ( $R^7 = p\text{-F-Ph}$ ), which is obtained from the corresponding ketone and oxime, is reduced to hydroxylamine using  $\text{NaBH}_4$  and  $\text{HOAc}$  as the solvent to give compound **B2** ( $R^7 = p\text{-F-Ph}$ ).

**Method B, Step 2;**

Compound **B2** ( $R^7 = p\text{-F-Ph}$ ) is converted to **B4** ( $R^7 = p\text{-F-Ph}$ ) using standard amide formation conditions.

**Method B, Step 3;**

Compound **B4** ( $R^7 = p\text{-F-Ph}$ ) is treated with 1.5 eq. of TBAF to generate compound **B5** ( $R^7 = p\text{-F-Ph}$ ) through selective deprotection of trimethylsilylethyl group which is followed by cyclization.

**Method B, Step 4**

Compound **B5** ( $R^7 = p\text{-F-Ph}$ ) is treated with LDA followed by compound **B6** ( $R^9 = 4\text{-(4'-methylimidazol-1-yl)}$  and  $R^{10} = 3\text{-MeOPhenyl}$ ) to give compound **B7** ( $R^7 = p\text{-F-Ph}$ ,  $R^9 = 4\text{-(4-methylimidazol-1-yl)}$  and  $R^{10} = 3\text{-MeOPhenyl}$ ).

**Method B, Step 5**

Compound **B7** ( $R^7 = p\text{-F-Ph}$ ,  $R^9 = 4\text{-(4-methylimidazol-1-yl)}$  and  $R^{10} = 3\text{-MeOPhenyl}$ ) is treated with TFA to give compound **B8** ( $R^7 = p\text{-F-Ph}$ ,  $R^9 = 4\text{-(4-methylimidazol-1-yl)}$  and  $R^{10} = 3\text{-MeOPhenyl}$ ).

**Method B, Step 6**

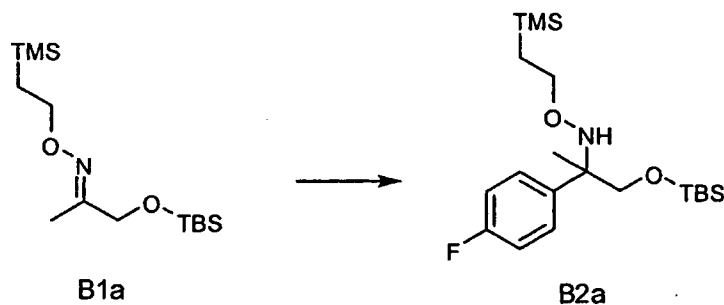
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Compound **B8** ( $R^7 = p\text{-F-Ph}$ , 4-(4-methylimidazol-1-yl) and  $R^{10} = 3\text{-MeOPhenyl}$ ) is treated with DPPA to give compound **B9** ( $R^7 = p\text{-F-Ph}$ ,  $R^9 = 4\text{-(4'-methylimidazol-1-yl)}$  and  $R^{10} = 3\text{-MeOPhenyl}$ )

#### 5 Method B, Step 7

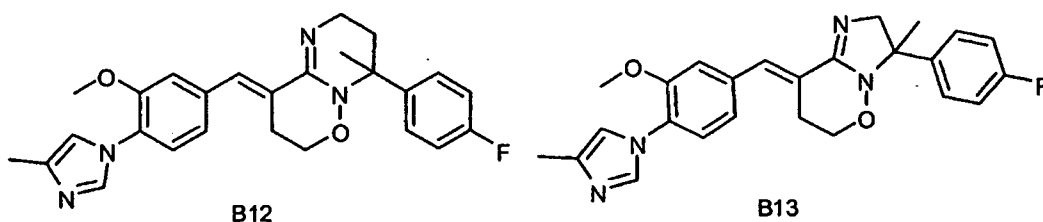
Compound **B9** ( $R^7 = p\text{-F-Ph}$ ,  $R^9 = 4\text{-(4'-methylimidazol-1-yl)}$  and  $R^{10} = 3\text{-MeOPhenyl}$ ) is treated with tributylphosphine in reflux toluene to give compound **B10A** ( $R^7 = p\text{-F-Ph}$ ,  $R^9 = 4\text{-(4'-methylimidazol-1-yl)}$  and  $R^{10} = 3\text{-MeOPhenyl}$ ).

10 Alternatively, Analogs of **B2** can be generated using a method similar to the following: *Diastereoselective additions of organolithium reagents to the C=N bond of protected erythrulose oxime ethers. Synthesis of enantiopure  $\alpha,\alpha$ -disubstituted  $\alpha$ -amino acids* Marco, J. Alberto; Carda, Miguel; Murga, Juan; Gonzalez, Florenci; Falomir, Eva. *Tetrahedron Letters* (1997), **38**(10), 1841-1844.

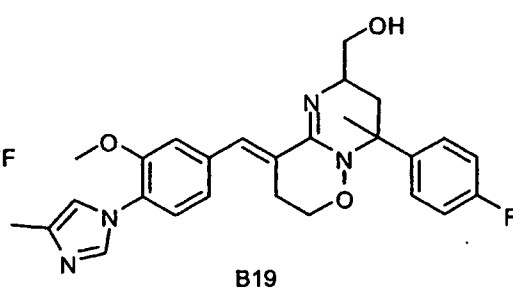
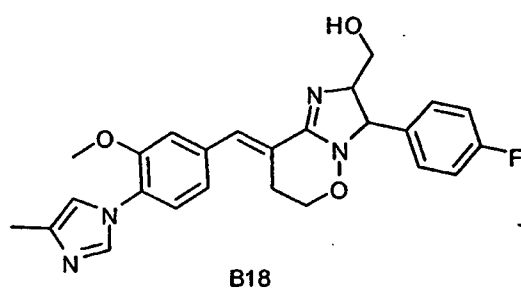
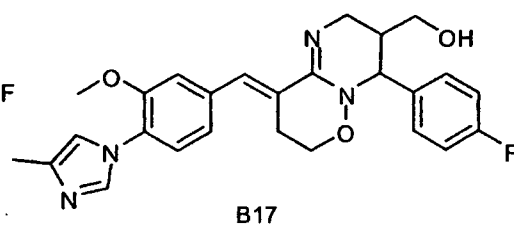
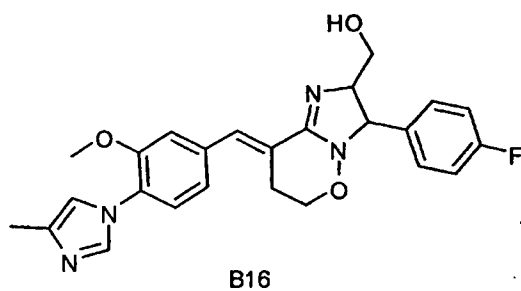
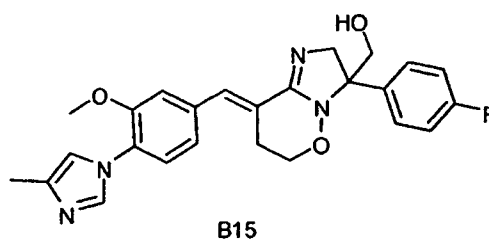
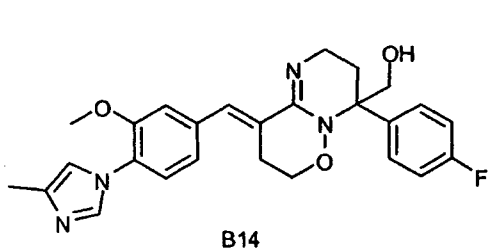


To an ether solution of **B1a** is added phenyl lithium to give compound **B2a** which is applied to the rest of the synthetic route in Method B.

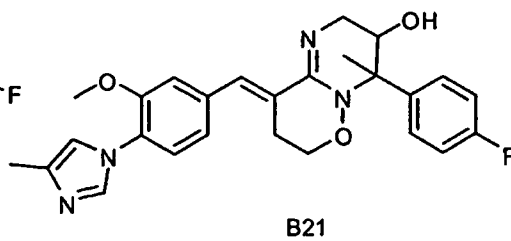
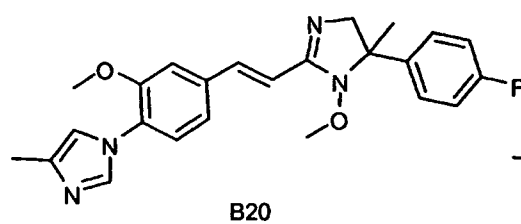
The following compounds are synthesized using method similar to Method B.



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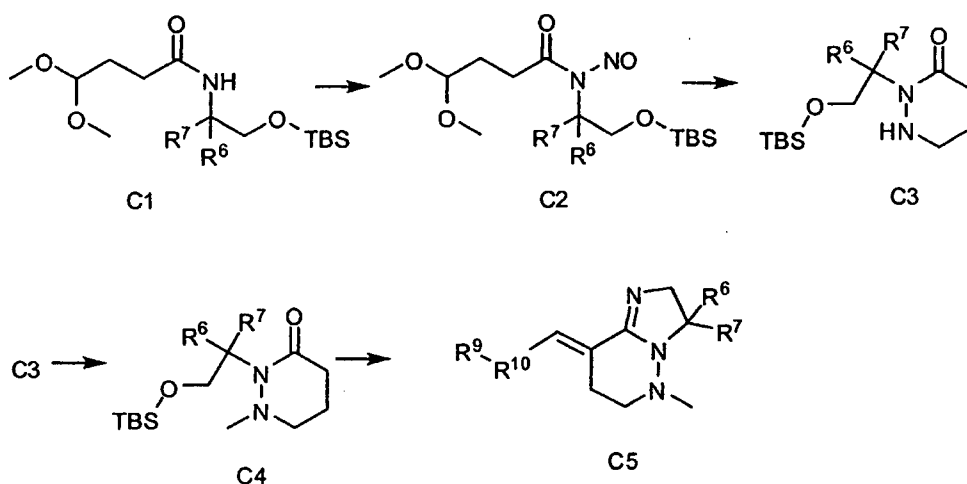


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**Method C**

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**Method C, Step 1**

Compound **C1** ( $R^6 = \text{Me}$ ,  $R^7 = \text{p-F-phenyl}$ ), which is obtained using corresponding acid and amine through amide coupling chemistry, is converted to N-nitroso product **C2** ( $R^6 = \text{Me}$ ,  $R^7 = \text{p-F-phenyl}$ ) using conditions similar to the following literature: *Enantioselective syntheses of carbocyclic ribavirin and its analogs: linear versus convergent approaches*. Kuang, R.; Ganguly, A. K.; Chan, T.-M.; Pramanik, B. N.; Blythin, D. J.; McPhail, A. T.; Saksena, A. K. *Tetrahedron Letters* (2000), **41**(49), 9575-9579.

15 **Method C, Step 2**

**C2** ( $R^6 = \text{Me}$ ,  $R^7 = \text{p-F-phenyl}$ ) is treated with  $\text{Zn}/\text{HOAc}/\text{H}_2\text{O}$  to give compound **C3** ( $R^6 = \text{Me}$ ,  $R^7 = \text{p-F-phenyl}$ ).

**Method C, Step 3**

20 Compound **C3** ( $R^6 = \text{Me}$ ,  $R^7 = \text{p-F-phenyl}$ ) is treated with  $\text{NaH}$  which is followed by  $\text{MeI}$  to give compound **C4** ( $R^6 = \text{Me}$ ,  $R^7 = \text{p-F-phenyl}$ ).



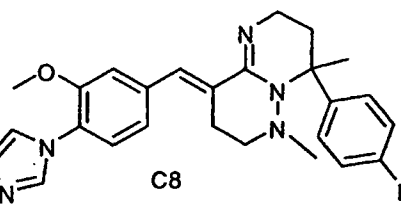
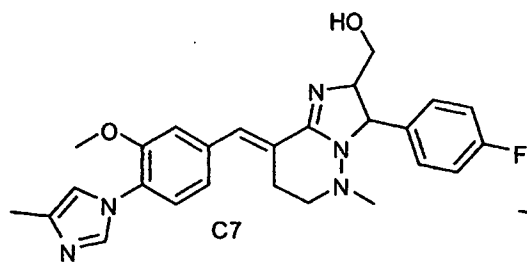
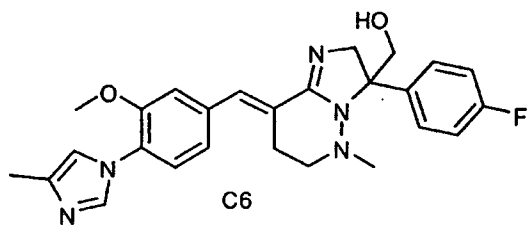
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**Method C, Step 4**

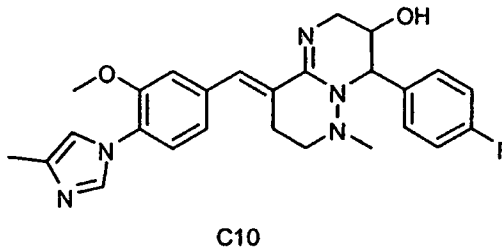
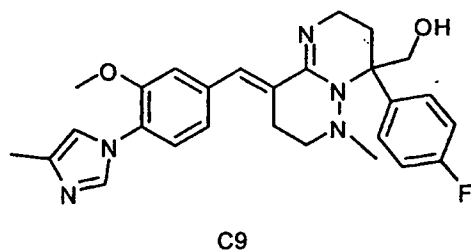
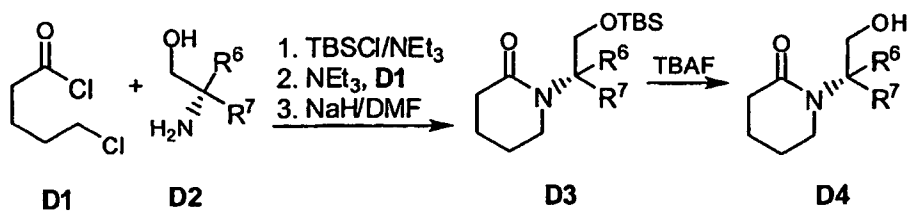
Compound **C4** ( $R^6 = \text{Me}$ ,  $R^7 = p\text{-F-phenyl}$ ) is converted to compound **C5** ( $R^6 = \text{Me}$ ,  $R^7 = p\text{-F-phenyl}$ ,  $R^8 = 4\text{-(4-methylimidazol-1-yl)}$ ,  $R^{10} = 3\text{-MeOphenyl}$ ) using a procedure similar to Method B Steps 4, 5, 6 and 7.

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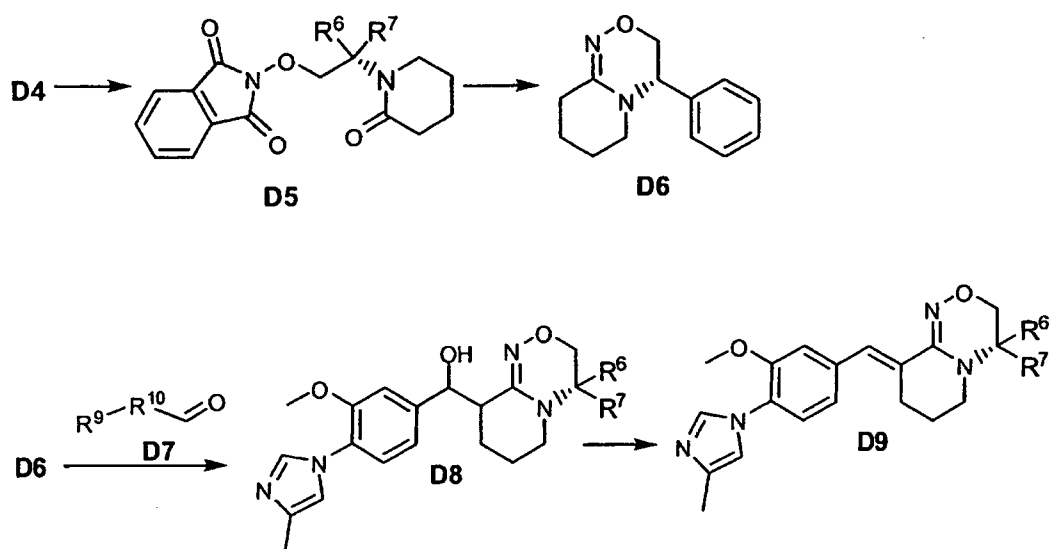
The following compounds are obtained using methods similar to Method C:



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**Method D**

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**Method D, STEP 1:**

TBSCl (5.6 g, 37.2 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added dropwise to a solution of D2 ((S), R<sup>6</sup> = H, R<sup>7</sup> = Ph) (5.1 g, 37.2 mmol), NEt<sub>3</sub> (10.4 mL, 74.4 mmol) and DMAP (20 mg) in CH<sub>2</sub>Cl<sub>2</sub> (20) at room temperature. The mixture was then stirred over night. The mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (200 mL) and NH<sub>4</sub>Cl solution (30 mL). The organic layer was washed with water, brine, dried over MgSO<sub>4</sub>, and concentrated to give the crude product (6.0 g) which was taken up in CH<sub>2</sub>Cl<sub>2</sub> (50 mL) and treated with NEt<sub>3</sub> (3.8 mL, 27.45 mmol). Compound D1 was added dropwise to the mixture at 0°C. The resulting reaction mixture was stirred at room temperature over night. The mixture was diluted with EtOAc (200 mL) and NaHCO<sub>3</sub> solution (40 mL). The organic layer was washed with water, brine, dried over MgSO<sub>4</sub>, and concentrated to give the crude product. The crude residue was dissolved in DMF (50 mL) and treated with NaH (1.25 g, 28.6 mmol, 60% in paraffin) at room temperature. The resulting mixture was then heated at 60°C over night. The mixture was diluted with EtOAc (200 mL) and aq. NH<sub>4</sub>Cl solution (40 mL). The organic layer was washed with water (3x), brine, dried over MgSO<sub>4</sub>, and concentrated to give the crude product which was purified by column

chromatography eluting with EtOAc/hexanes to yield compound **D3** ((S),  $R^6 = H$ ,  $R^7 = Ph$ ; 5.0 g).

**Method D, STEP 2:**

- 5           TBAF (3.15 mL, 3.15 mmol, 1.0 M in THF) was added dropwise to a solution of compound **D3** ((S),  $R^6 = H$ ,  $R^7 = Ph$ ; 0.7 g, 2.1 mmol) in THF (10 mL). The mixture was stirred for 2 hours before it was diluted with EtOAc (100 mL) and HCl solution (20 mL, 0.5 M). The organic layer was washed with water, brine, dried over  $MgSO_4$ , and concentrated to give the crude product which was purified
- 10 by column chromatography eluting with EtOAc/hexanes to yield hydroxyl compound **D4** ((S),  $R^6 = H$ ,  $R^7 = Ph$ ; 0.44 g).

**Method D, STEP 3:**

- $PBu_3$  (0.2 mL, 0.82 mmol) was added to a solution of compound **D4** ((S),  $R^6 = H$ ,  $R^7 = Ph$ ; 0.1 g, 0.457 mmol), ADDP (0.2 g, 0.82 mmol) and phthalimide (0.12 g, 0.685 mmol) in THF (5 mL) at room temperature. The resulting mixture was then heated at 80°C for 2 hours. The mixture was diluted with EtOAc (100 mL) and  $NaHCO_3$  solution (20 mL). The organic layer was washed with  $NaHCO_3$  solution, brine, dried over  $MgSO_4$ , and concentrated to give the crude product
- 20 which was purified by column chromatography eluting with EtOAc/hexanes to yield compound **D5** ((S),  $R^6 = H$ ,  $R^7 = Ph$ ; 0.1 g, 0.457 mmol, 0.14 g).

**Method D, STEP 4,**

- $NH_2NH_2 \cdot xH_2O$  (54.4  $\mu L$ , 1.12 mmol) was added to a solution of compound
- 25 **D5** ((S),  $R^6 = H$ ,  $R^7 = Ph$ ; 0.14 g, 0.373 mmol) in MeOH (2.0 mL) and  $CH_2Cl_2$  (2.0 mL) at room temperature. The resulting mixture was stirred for 2 hours before it was diluted with EtOAc (50 mL) and  $NaHCO_3$  solution (10 mL). The organic layer was washed with water, brine, dried over  $MgSO_4$ , and concentrated to give the crude product which was dissolved in EtOH (3.0 mL) and treated with  $P_2O_5$  (0.53
- 30 g, 3.72 mmol). The resulting mixture was heated at 80 °C over night. The mixture

was cooled and diluted with EtOAc (50 mL) and NaHCO<sub>3</sub> solution (20 mL). The organic layer was washed with NaHCO<sub>3</sub> solution, brine, dried over MgSO<sub>4</sub>, and concentrated to give the crude product which was purified by column chromatography eluting with EtOAc/hexanes to yield compound **D6** ((S), R<sup>6</sup> = H, R<sup>7</sup> = Ph; 46 mg).

<sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 7.43-7.32 (m, 5 H); 4.30 (dd, J = 5.0, 4.0 Hz, 1 H); 4.16 (AB quart, J = 11.5, 4.0 Hz, 1 H); 3.96 (AB quart, J = 11.5, 5.0 Hz, 1 H); 3.07 (m, 1 H); 2.89 (m, 1 H); 2.50 (m, 2 H); 1.84 (m, 2 H); 1.76 (m, 2 H). Electrospray LCMS: Obs. Mass: 217.2.

#### Method D, STEP 5,

t-BuLi (0.188 mL, 0.32 mmol, 1.7 M) was added dropwise to a solution of compound **D6** ((S), R<sup>6</sup> = H, R<sup>7</sup> = Ph; 46 mg, 0.21 mmol) in THF (1.5 mL) at -78 °C. The mixture was stirred for 45 minutes before compound **D7** (R<sup>10</sup> = 3-MeO-Phenyl, R<sup>9</sup> = 4-(4-methylimidazol-1-yl)) was added in THF (1.0 mL) in fast drops. The resulting mixture was stirred for 2 hours before it was diluted with EtOAc (50 mL) and NH<sub>4</sub>Cl solution (10 mL). The organic layer was washed with brine, dried over MgSO<sub>4</sub>, and concentrated to give the crude product which was purified by column chromatography eluting with EtOAc/hexanes to yield compound **D8** ((S), R<sup>6</sup> = H, R<sup>7</sup> = Ph; R<sup>10</sup> = 3-MeO-Phenyl, R<sup>9</sup> = 4-(4-methylimidazol-1-yl)).

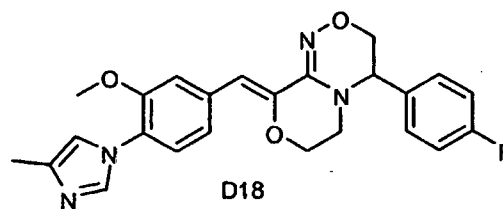
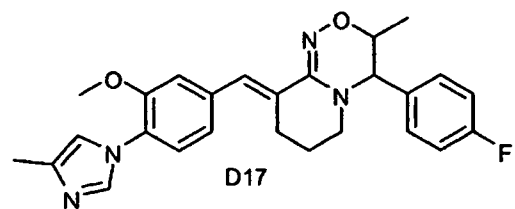
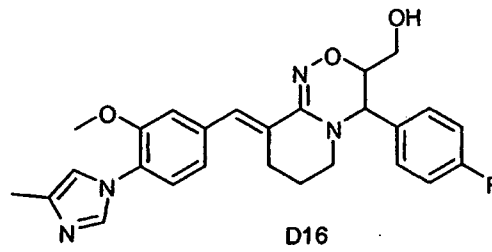
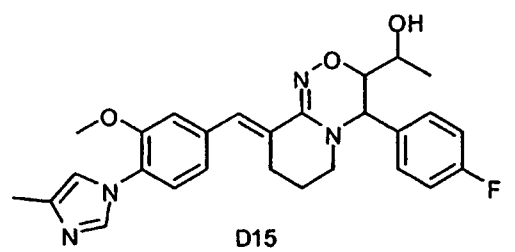
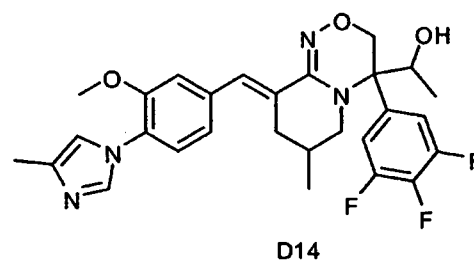
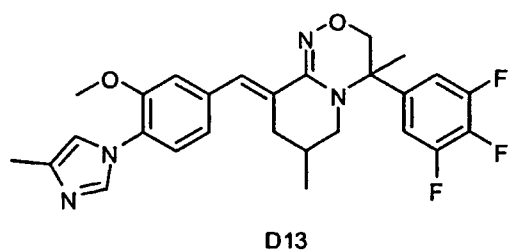
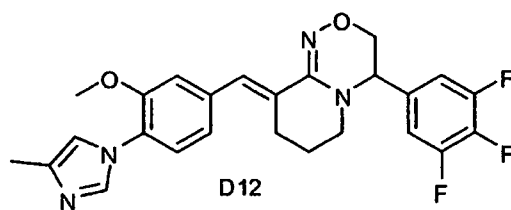
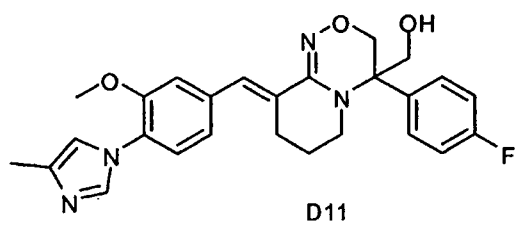
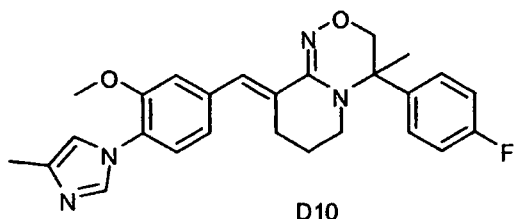
#### Method D, STEP 7,

Compound **D8** ((S), R<sup>6</sup> = H, R<sup>7</sup> = Ph; R<sup>10</sup> = 3-MeO-Phenyl, R<sup>9</sup> = 4-(4-methylimidazol-1-yl)) will be dissolved in toluene and treated with p-TSA (10 mol%). The mixture will be heated at reflux condition with a Dean-Stark apparatus over night. The solvent will be removed and crude residue will be purified with column chromatography to give compound **D9** ((S), R<sup>6</sup> = H, R<sup>7</sup> = Ph; R<sup>10</sup> = 3-MeO-Phenyl, R<sup>9</sup> = 4-(4-methylimidazol-1-yl)).

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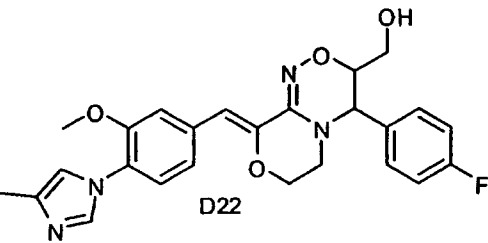
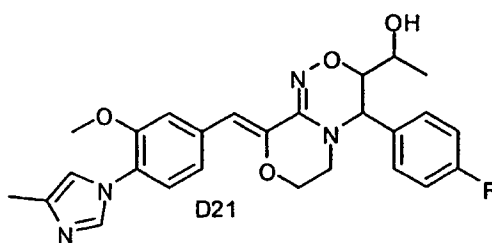
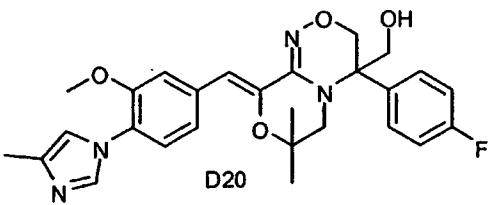
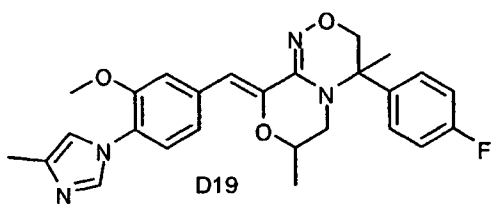
The following compounds are synthesized using methods similar to method

D:

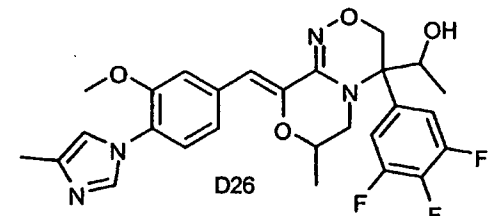
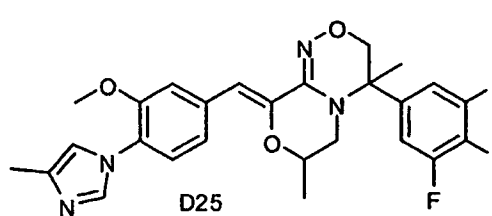
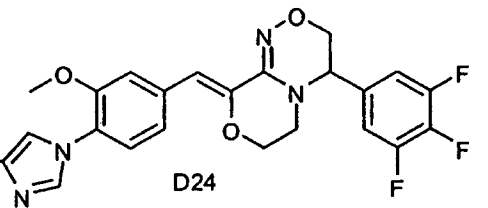
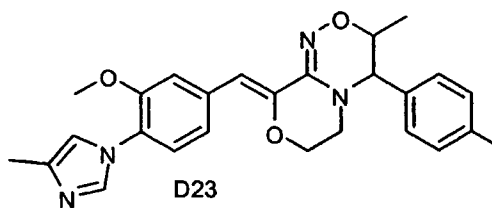


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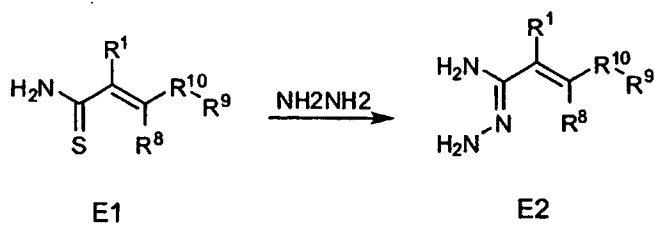


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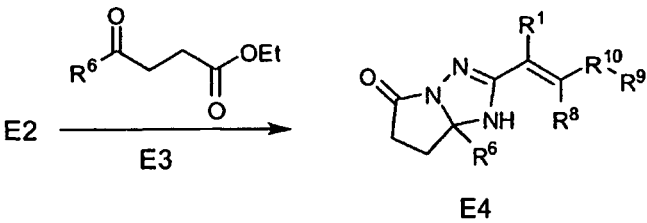
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**Method E**



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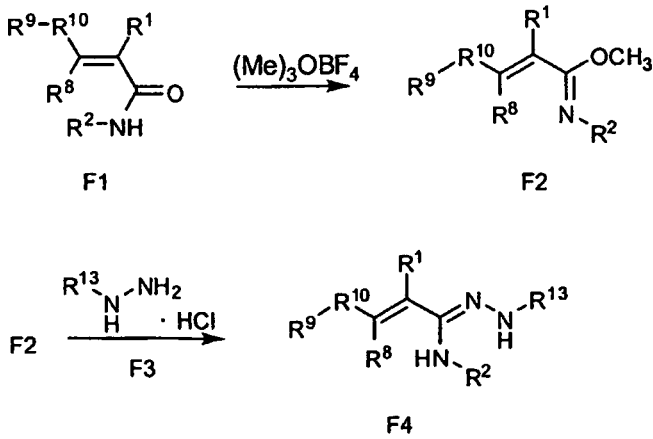
Method E, Step 1.

Compounds of E1 ( $R^1 = R^8 = H$ ,  $R^{10} = 3\text{-MeOPhenyl}$ ,  $R^9 = 4\text{-(4-Me-imidazol-1-yl)}$ ) are prepared from the corresponding thioamides or nitriles by treatment with hydrazine with a catalytic amount of acid in a solvent such as ethanol with heating.

Method E, Step 2.

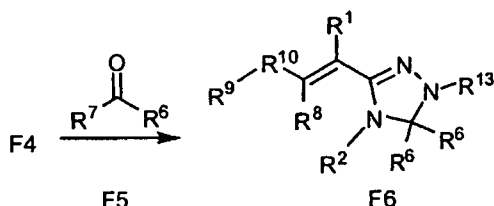
E1 ( $R^1 = R^8 = H$ ,  $R^{10} = 3\text{-MeOPhenyl}$ ,  $R^9 = 4\text{-(4-Me-imidazol-1-yl)}$ ) is reacted with keto esters of E3 ( $R^6 = p\text{-F-phenyl}$ ) under dehydrating conditions such as treatment with a catalytic amount of acid (e.g. TsOH, or AcOH) in solvents such as Toluene or DCM. In some cases heating in toluene to remove water through azeotropic distillation will facilitate the reaction to produce compounds E4 ( $R^1 = R^8 = H$ ,  $R^{10} = 3\text{-MeOPhenyl}$ ,  $R^9 = 4\text{-(4-Me-imidazol-1-yl)}$ ,  $R^6 = p\text{-F-phenyl}$ ).

Method F.



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**Method F, Step1,**

- 5 To a dichloromethane solution of F1 (R<sup>1</sup> = H, R<sup>2</sup>=H, R<sup>8</sup> = H, R<sup>10</sup> = 3-(methoxy)phenyl, R<sup>9</sup> = 4-(4-Me-imidazol-1-yl) is added trimethyloxonium tetrafluoroborate, and the reaction mixture is stirred at room temperature overnight. The solvent is evaporated to yield the crude iminoether B2 as its tetrafluoroborate salt. Optionally, the crude tetrafluoroborate salt is triturated with
- 10 ether and the resulting precipitated tetrafluoroborate salt of F2 (R<sup>1</sup> = H, R<sup>2</sup>=H, R<sup>8</sup> = H, R<sup>10</sup> = 3-(methoxy)phenyl, R<sup>9</sup> = 4-(4-Me-imidazol-1-yl) is filtered and is dried. This is converted to the free base by partitioning between dichloromethane and excess 1M NaOH. The methylene chloride layer is dried over K<sub>2</sub>CO<sub>3</sub> and is evaporated to give the free base of F2 (R<sup>1</sup> = H, R<sup>2</sup>=H, R<sup>8</sup> = H, R<sup>10</sup> = 3-
- 15 (methoxy)phenyl, R<sup>9</sup> = 4-(4-Me-imidazol-1-yl)), which is used immediately.

**Method F, Step 2:**

- F2 (R<sup>1</sup> = H, R<sup>2</sup>=H, R<sup>8</sup> = H, R<sup>10</sup> = 3-(methoxy)phenyl, R<sup>9</sup> = 4-(4-Me-imidazol-1-yl)) is treated with hydrazine F3 (R<sup>13</sup>=H) optionally as the hydrochloride or
- 20 hydrate in refluxing methanol overnight. The reaction mixture is neutralized with sodium bicarbonate, filtered and evaporated to give the crude amidohyrazide F4 (R<sup>1</sup> = H, R<sup>2</sup>=H, R<sup>13</sup>=H, R<sup>8</sup> = H, R<sup>10</sup> = 3-(methoxy)phenyl, R<sup>9</sup> = 4-(4-Me-imidazol-1-yl)).

**25 Method F, Step 3:**

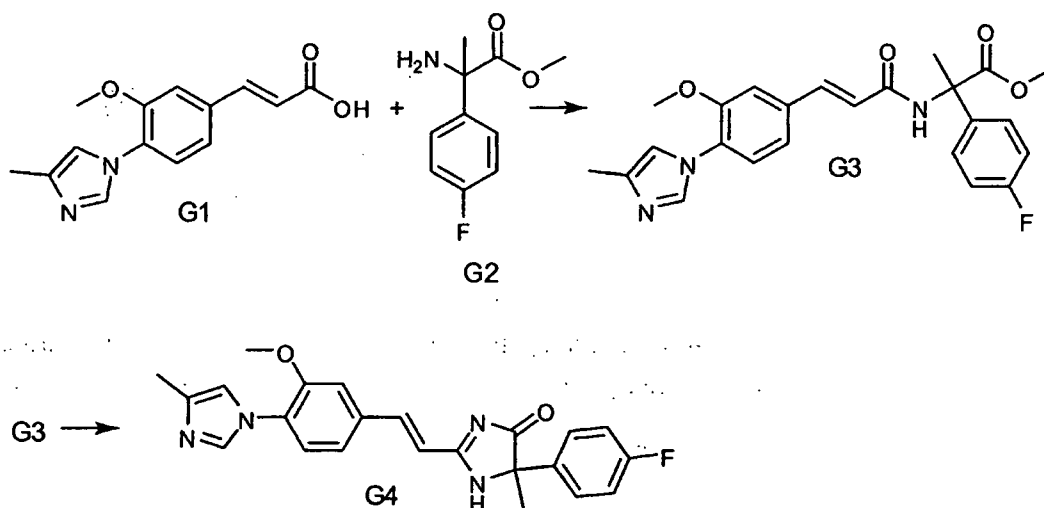
F4 (R<sup>1</sup> = H, R<sup>2</sup>=H, R<sup>13</sup>=H, R<sup>8</sup> = H, R<sup>10</sup> = 3-(methoxy)phenyl, R<sup>9</sup> = 4-(4-Me-imidazol-1-yl)) is treated with ketone F5 (R<sup>6</sup> = Me, R<sup>7</sup> = 4-fluorophenyl) and p-



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toluenesulfonic acid in refluxing ethanol overnight to give, after neutralization and evaporation, compound **F6** ( $R^1 = H$ ,  $R^2 = H$ ,  $R^{13} = H$ ,  $R^8 = H$ ,  $R^{10} = 3$ -(methoxy)phenyl,  $R^9 = 4$ -(4-Me-imidazol-1-yl),  $R^6 = Me$ ,  $R^7 = 4$ -fluorophenyl).

## 5 **Method G**



## 10 **Method G, Step 1**

Compound **G1** (200 mg), generated from the corresponding aldehyde and carbomethoxymethyl diethylphosphonate, followed by LiOH hydrolysis, was reacted with compound **G2** (230 mg) with HOBT (135 mg) and EDCI (197 mg) in 10 mL DMF to give compound **G3** after routine work-up and purification in 66% yield.

$^1\text{H}$  NMR of **G3** ( $\text{CDCl}_3$ , ppm);  $\delta$  7.35 s, 1H; 7.55 d, 1H; 7.45 m, 2H; 7.25, d, 1H; 7.15, m, 3H; 7.10, m, 1H; 6.95, s, 1H; 6.5, s, 1H; 3.9 s, 3H; 3.75 s, 3H; 2.3 s, 3H; 2.15 s, 3H.

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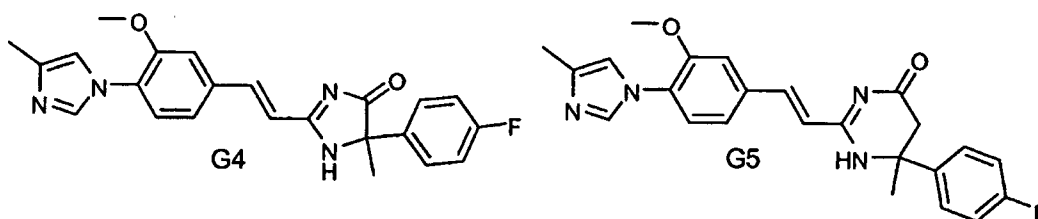
## **Method G, Step 2**

A solution of ammonia in THF was treated with  $\text{Me}_3\text{Al}$  in hexane before compound **G3** was added slowly. The final mixture was refluxed overnight before

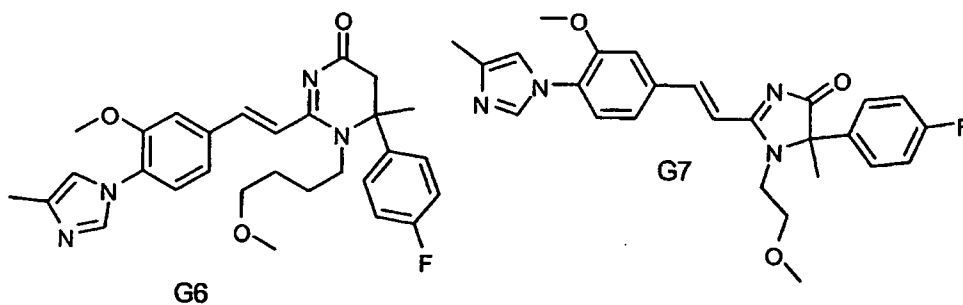
it was quenched with sat. aqueous ammonium chloride and extracted with EtOAc. The organic layer was washed with brine, dried over and solvent evaporated. The residue was chromatographed to give the corresponding amide. The product amide was dissolved in 1mL EtOH and 2mL of 1N NaOH. After the starting material disappeared, the reaction mixture was partitioned in DCM/sat. aq ammonim chloride. The organic layer was dried and solvent evaporated. The residue was chromatographed to give compound **G4**.

<sup>1</sup>H NMR of G4 (CDCl<sub>3</sub>, ppm); δ 10.5 br. 1H; 7.9, s, 1H, 7.6 m, 2H, 7.4, m, 1H; 7.3, m 2H; 7.2, m, 1H; 7.05, m, 2H; 7.0 s, 1H; 6.9 m 1H; 3.9 s, 3H; 2.3 s, 3H.

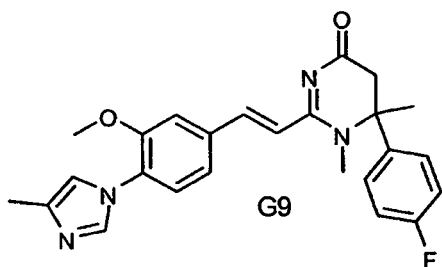
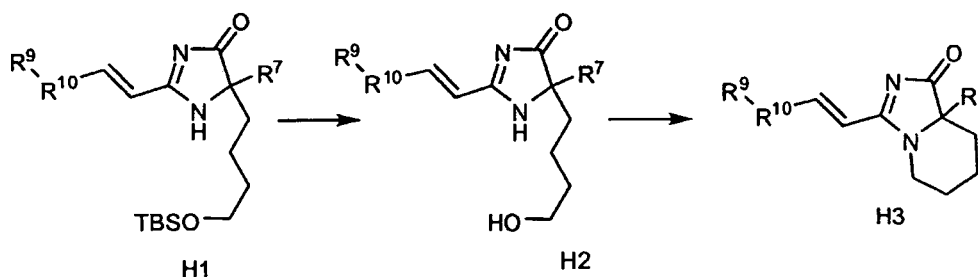
The following compounds are obtained using methods similar to method G:



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**Method H****5 Method H, Step 1**

Compound **H1** ( $R^7 = p\text{-F-phenyl}$ ,  $R^{10} = 3\text{-MeO-Phenyl}$ ,  $R^9 = 4\text{-(4-methyl-imidazol-1-yl)}$ ), is prepared using methods similar to method G, is treated with TBAF to give compound **H2** ( $R^7 = p\text{-F-phenyl}$ ,  $R^{10} = 3\text{-MeO-Phenyl}$ ,  $R^9 = 4\text{-(4-methyl-imidazol-1-yl)}$ ) after purification.

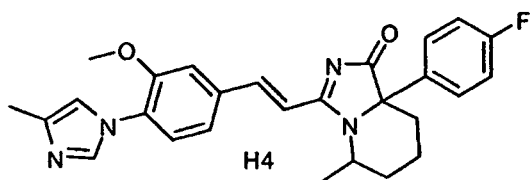
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**Method H, Step 2**

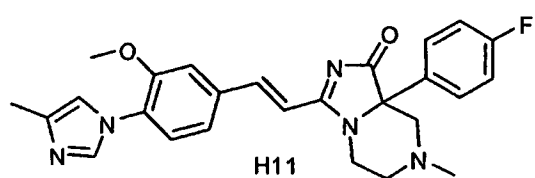
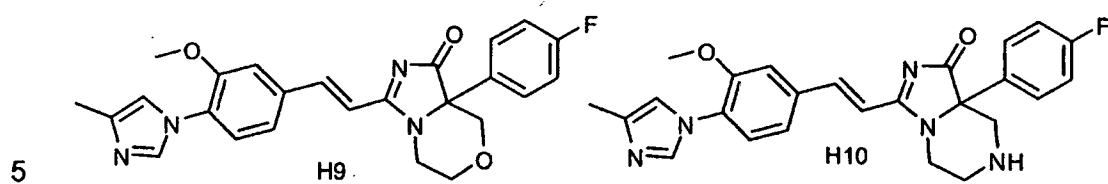
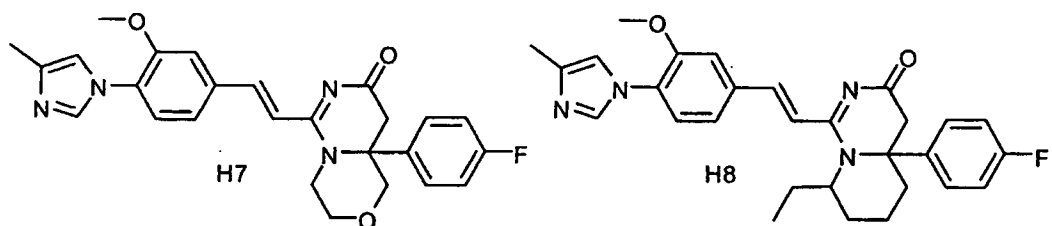
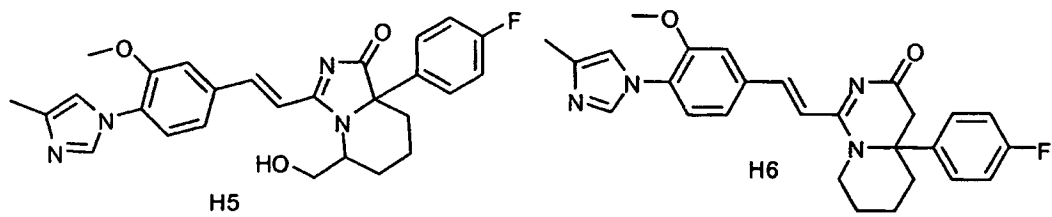
Compound **H2** ( $R^7 = p\text{-F-phenyl}$ ,  $R^{10} = 3\text{-MeO-Phenyl}$ ,  $R^9 = 4\text{-(4-methyl-imidazol-1-yl)}$ ) is converted to the triflate. The product triflate is treated with NaH in DMF to give compound **H3** ( $R^7 = p\text{-F-phenyl}$ ,  $R^{10} = 3\text{-MeO-Phenyl}$ ,  $R^9 = 4\text{-(4-methyl-imidazol-1-yl)}$ ) after routing work up and purification.

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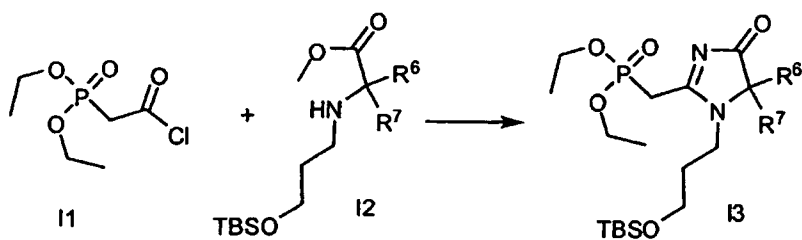
The following compounds are obtained using methods similar to method H:



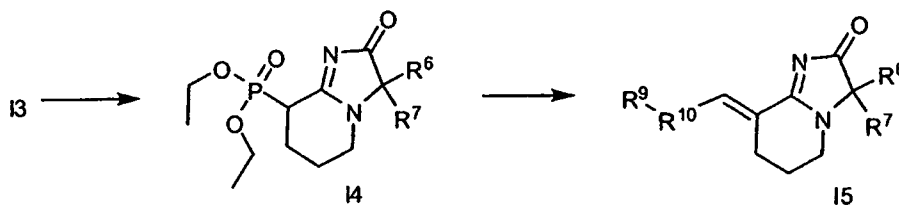
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## 10 Method I



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**Method I, Step 1**

Compound **13** ( $R^6 = p\text{-F-Phenyl}$ ,  $R^7 = \text{Me}$ ) is obtained using methods similar  
 5 to method G using starting material **11** and **12** ( $R^6 = p\text{-F-Phenyl}$ ,  $R^7 = \text{Me}$ ).

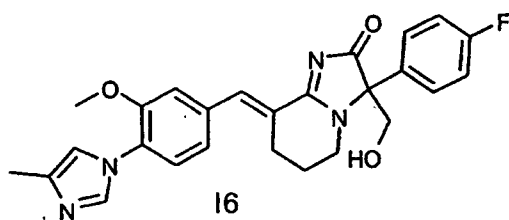
**Method I, Step 2**

Compound **13** ( $R^6 = p\text{-F-Phenyl}$ ,  $R^7 = \text{Me}$ ) is treated with TBAF which is  
 followed by purification to give the corresponding alcohol which is transformed into  
 10 triflate. The triflate is treated with NaH in DMF to give compound **14** ( $R^6 = p\text{-F-Phenyl}$ ,  $R^7 = \text{Me}$ ).

**Method I, Step 3**

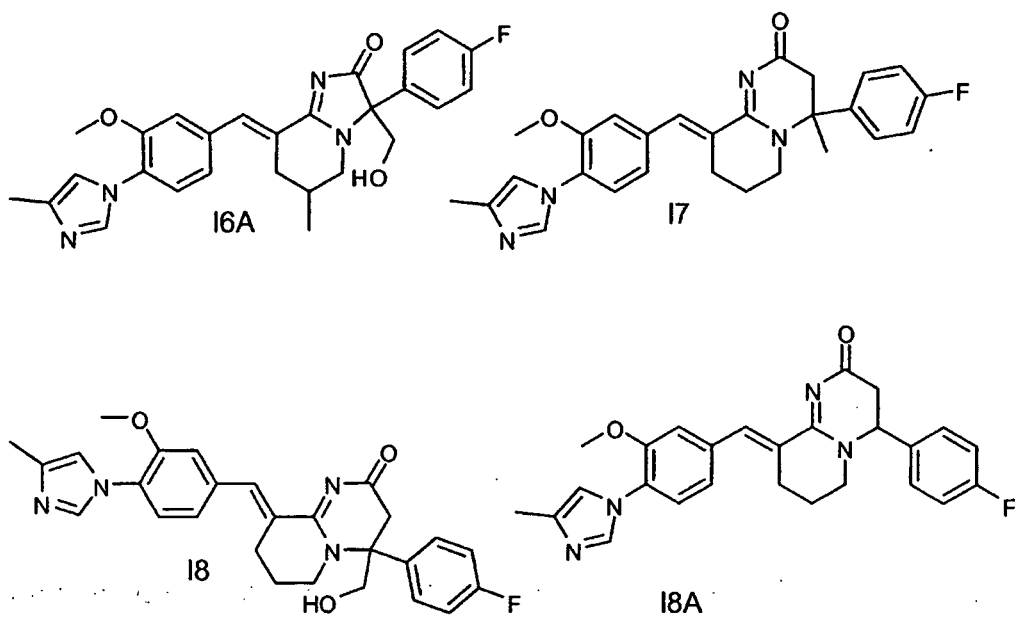
Compound **15** ( $R^6 = p\text{-F-Phenyl}$ ,  $R^7 = \text{Me}$ ,  $R^{10} = 3\text{-MeOphenyl}$ ,  $R^9 = 4\text{-(4-methylimidazol-1-yl)}$ ) is obtained using compound **14** ( $R^6 = p\text{-F-Phenyl}$ ,  $R^7 = \text{Me}$ )  
 15 reacting with **D7** ( $R^{10} = 3\text{-MeOphenyl}$ ,  $R^9 = 4\text{-(4-methylimidazol-1-yl)}$ ) and a base  
 after purification.

The following compounds are obtained using method similar to method I.

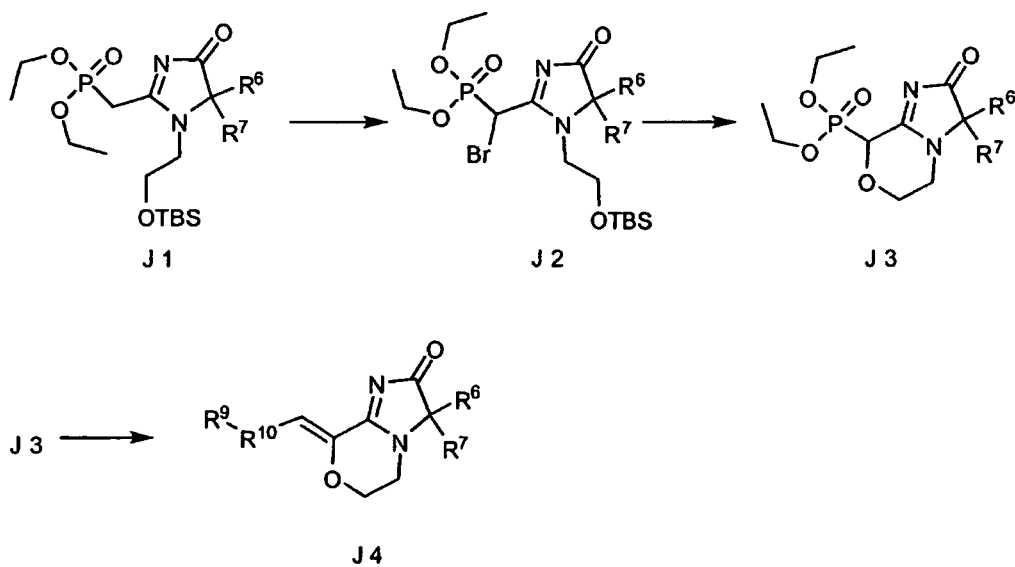


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## 5 Method J



### Method J, Step 1

- 10 Compound J1 ( $R^6 = p\text{-F-Ph}$  and  $R^7 = \text{methyl}$ ), which is obtained using a method similar to Method I, Step 1, is treated with NBS in Benzene with a radical

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initiator (such as AIBN) under reflux to give compound **J2** ( $R^6 = p\text{-F-Ph}$  and  $R^7 = \text{methyl}$ ).

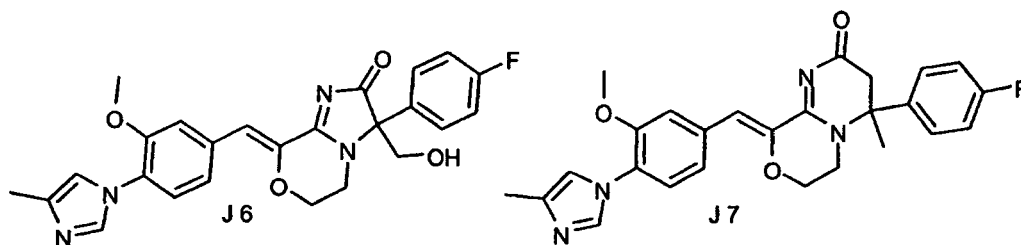
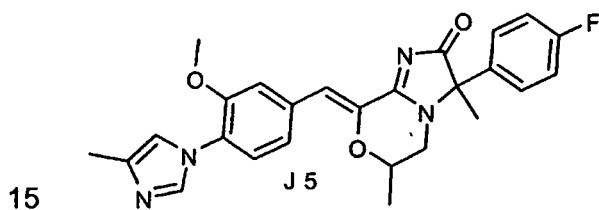
**Method J, step 2**

- 5        Compound **J2** ( $R^6 = p\text{-F-Ph}$  and  $R^7 = \text{methyl}$ ) is treated with TBAF in DMF to give compound **J3** ( $R^6 = p\text{-F-Ph}$  and  $R^7 = \text{methyl}$ ) after purification.

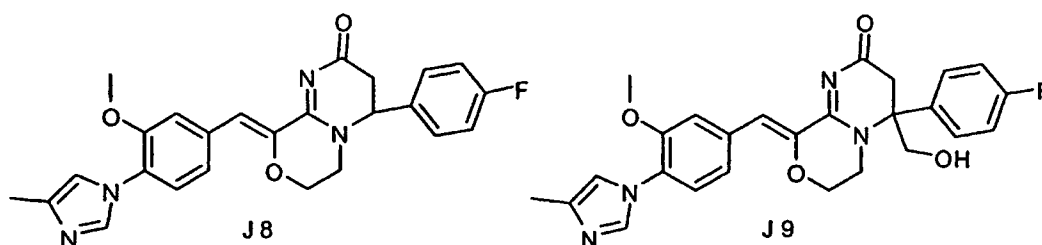
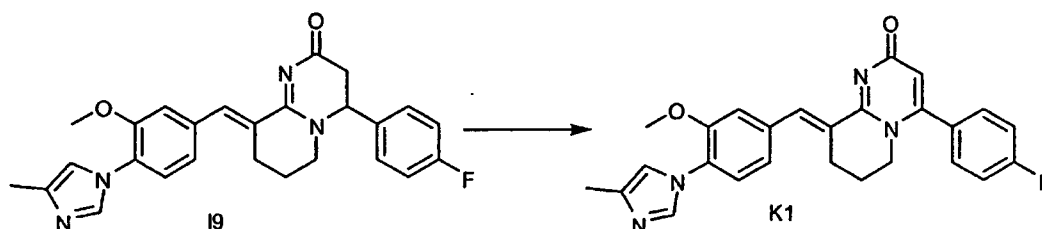
**Method J Step3**

- 10        Compound **J4** ( $R^6 = p\text{-F-Ph}$  and  $R^7 = \text{methyl}$ ,  $R^{10} = 3\text{-MeOphenyl}$ ,  $R^9 = 4\text{-(4-methylimidazol-1-yl)}$ ) is obtained using method similar to method Method I step 3.

The following compounds are obtained using methods similar to Method J:



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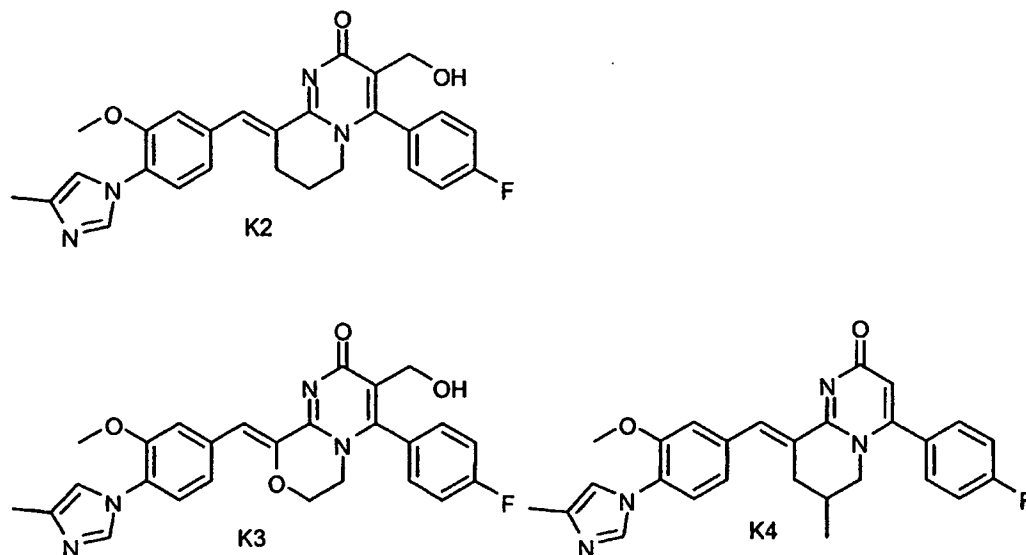
**Method K**

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Compound I9 is treated with 1.2 eq of LDA at -78 C before it is reacted with phenylselenium bromide. After the reaction is warmed to r.t. it is treated with H<sub>2</sub>O<sub>2</sub> and is worked up, and is purified to give compound K1.

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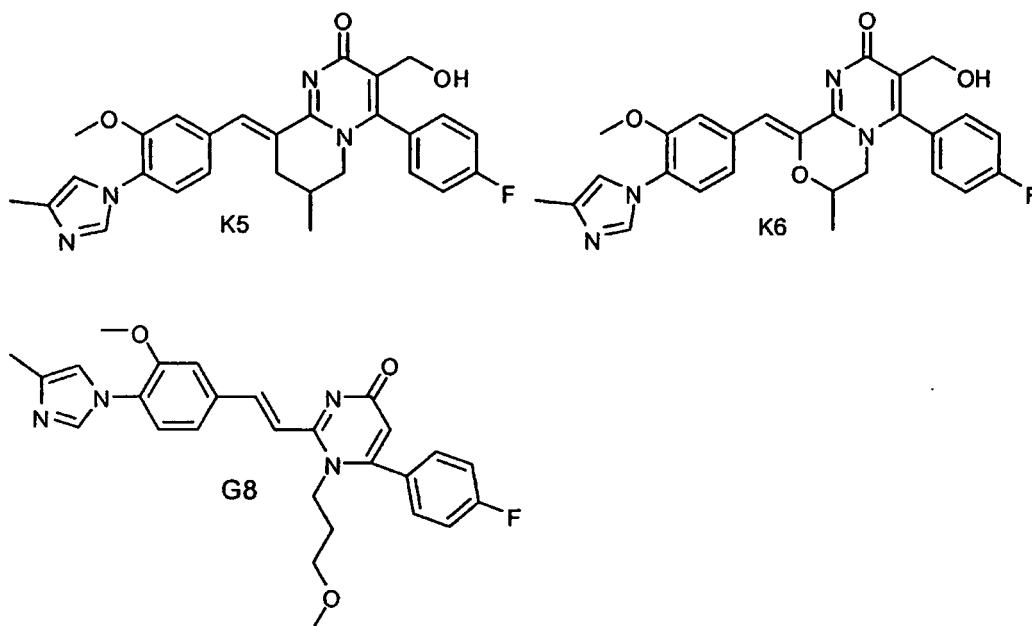
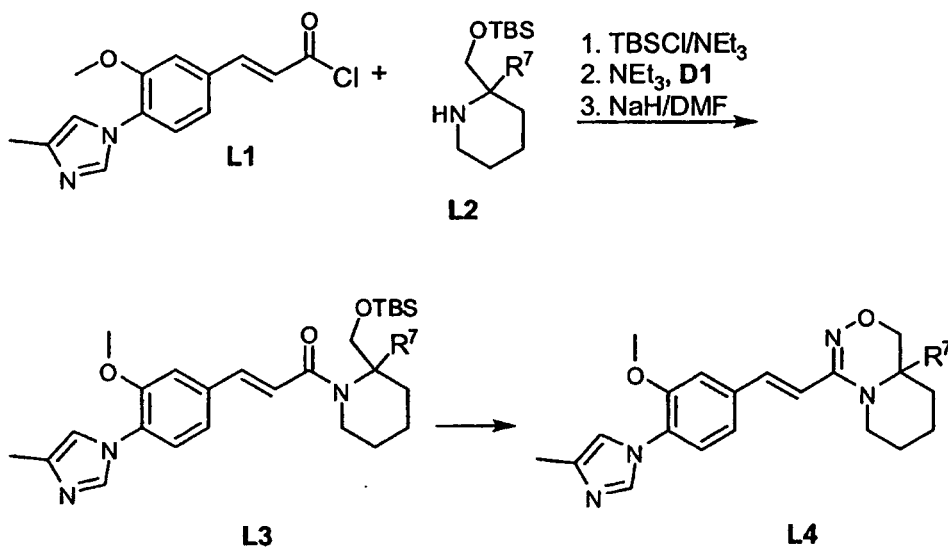
The following compounds are obtained using methods similar to Method K:





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5 **Method L****Method L, Step 1**

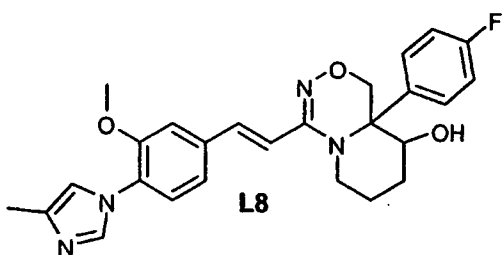
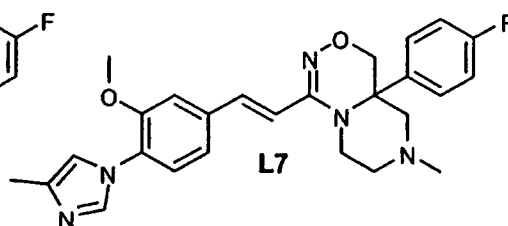
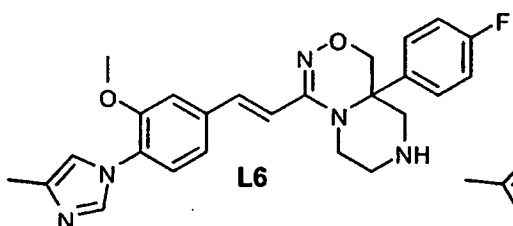
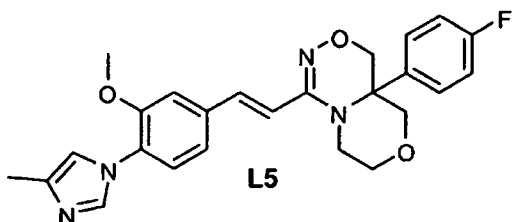
- 10 Compound L3 (R<sup>7</sup> = p-F-Phenyl) is obtained using amide coupling chemistry from L1 and L2

7b6

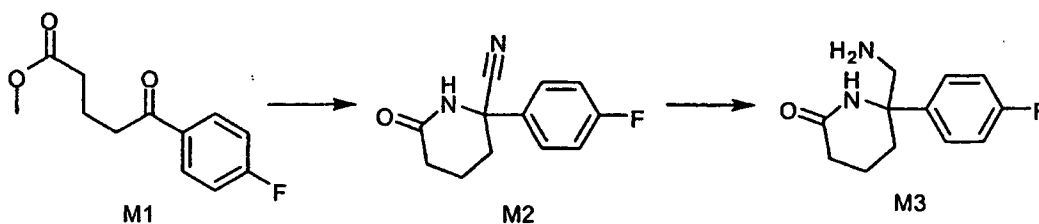
**Method L, Step 2**

Compound **L4** ( $R^7 = p\text{-F-Phenyl}$ ) is obtained using methods similar to method D, Steps 2 to 5.

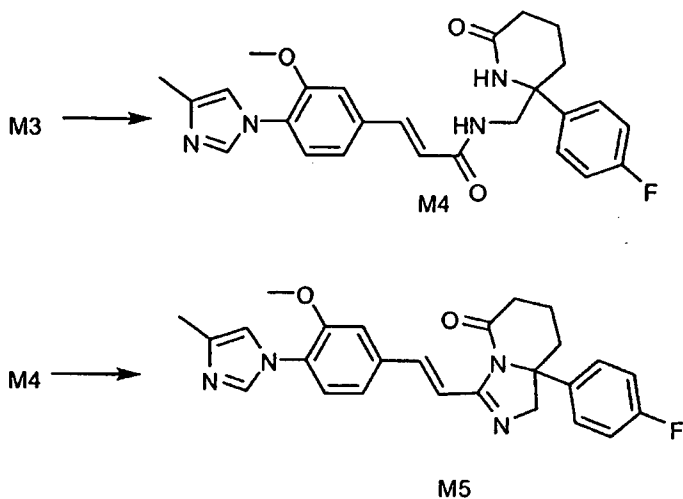
5 The following compounds are obtained using methods similar to method L:



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**Method M**

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**5 Method M, step 1**

Compound **M1** is converted to **M2** through Strecker amine synthesis by reacting **M1** with Ammonium Cyanide in alcohol.

**Method M, Step 2**

10 Compound **M3** is obtained using a Ni mediated hydrogenation of **M2**.

**Method M, Step 3**

Compound **M4** is obtained using a normal amide coupling conditions.

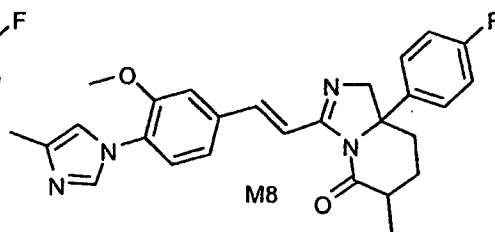
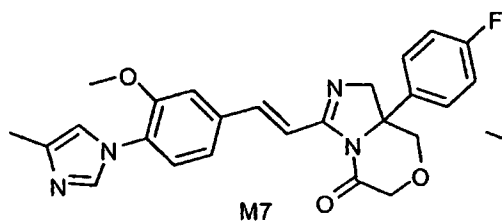
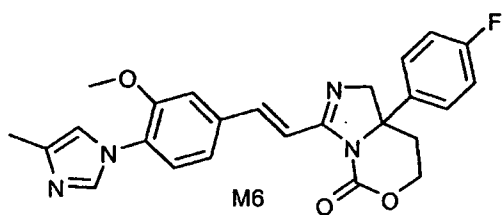
**15 Method M, Step 4**

Compound **M5** is obtained through treatment of **M4** with POCl<sub>3</sub> in reflux toluene.

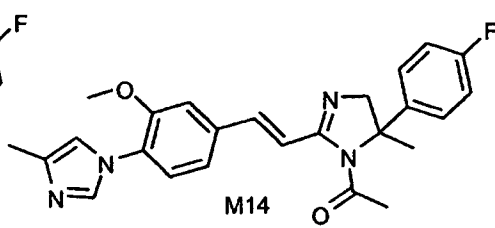
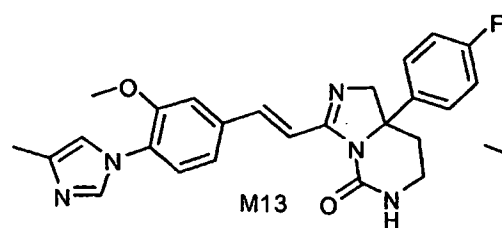
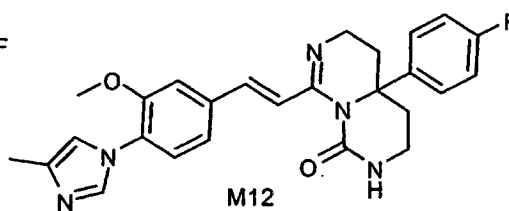
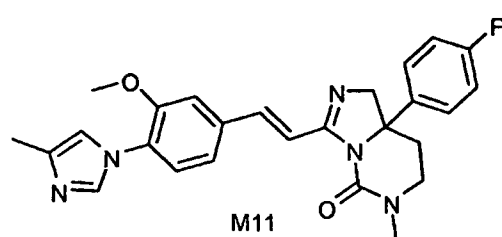
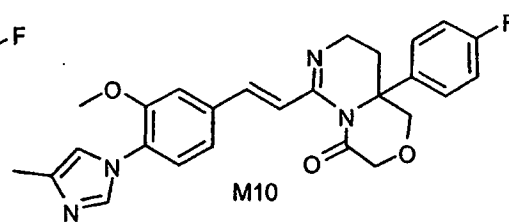
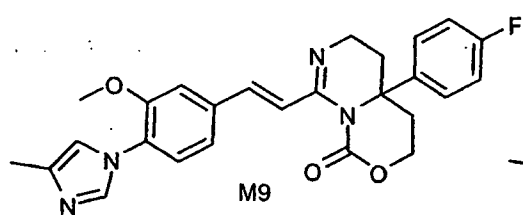
The following compounds will be obtained using method similar to method M.

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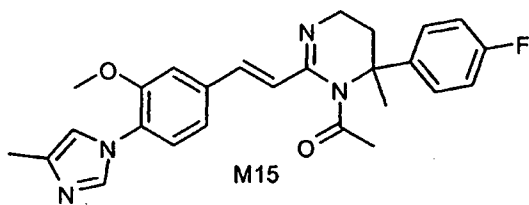
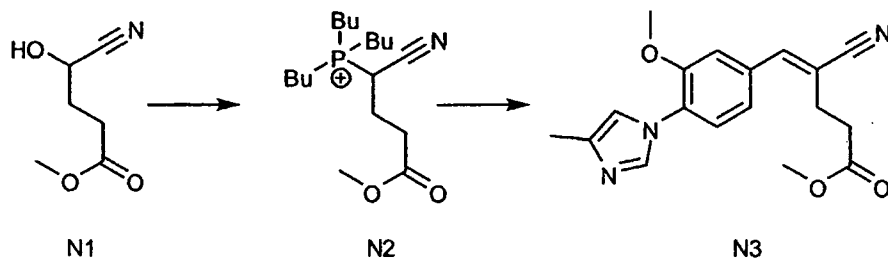
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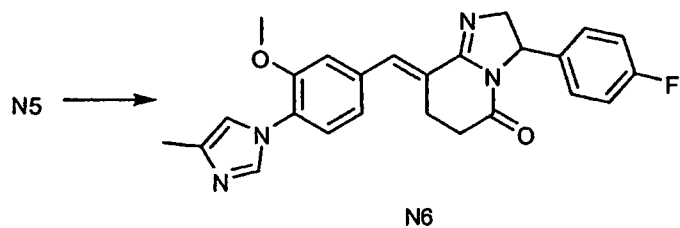
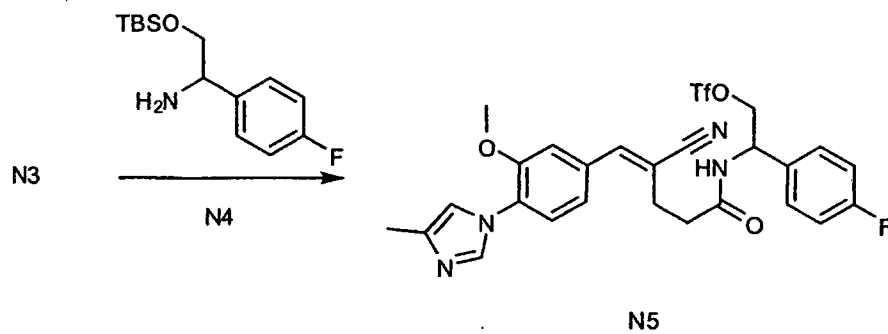
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**Method N**

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**10 Method N, Step 1**

N2 is obtained from N1 after the triflate ester generation which is followed by tributylphosphine treatment.

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**Method N, Step 2**

Compound **N3** is obtained through Wittig reaction with appropriate aldehyde with **N2**

**5 Method N, Step 3**

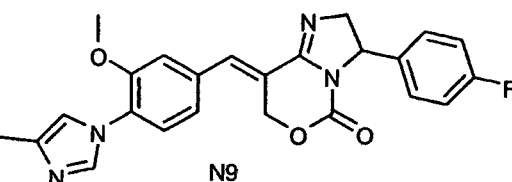
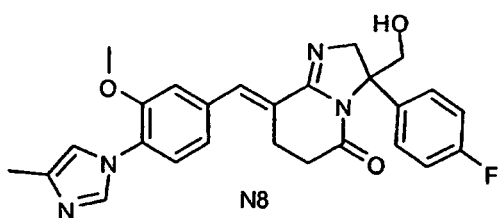
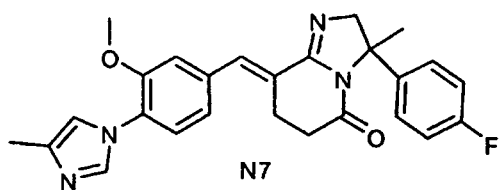
Compound **N5** is obtained through hydrolysis of **N3** to its corresponding acid which is followed by standard amide coupling with compound **N4** which is followed by TBS deprotection and triflate generation.

**10 Method N, Step 4**

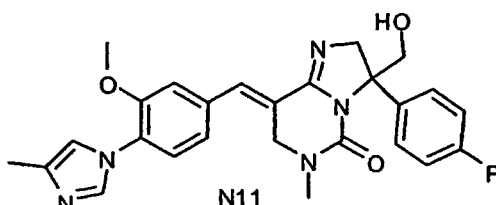
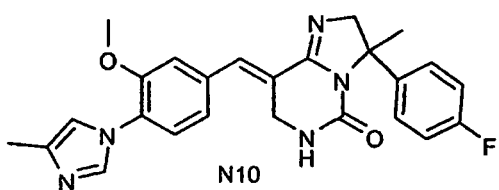
Compound **N6** is obtained using compound **N5** following treatment of NaH in DMF.

The following compounds are obtained using methods similar to method N:

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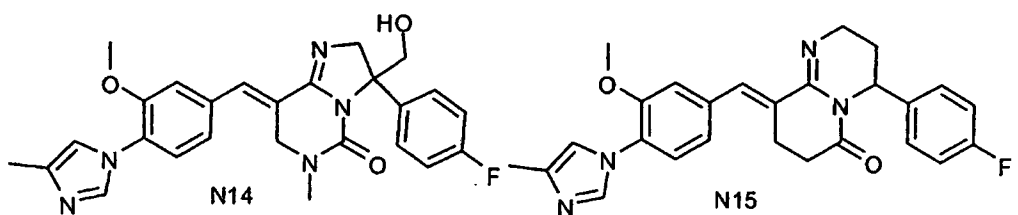
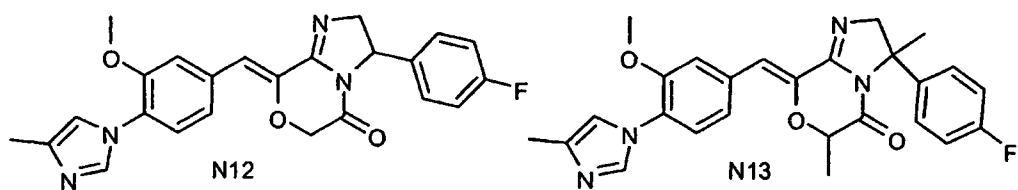


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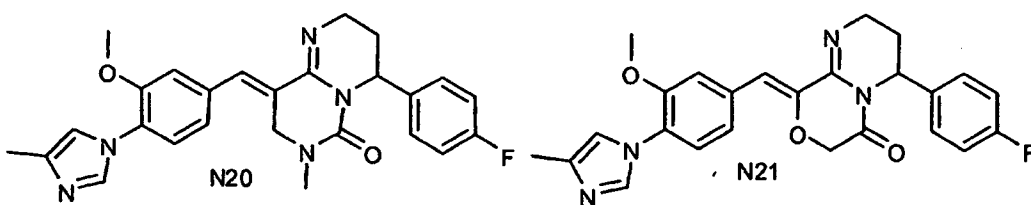
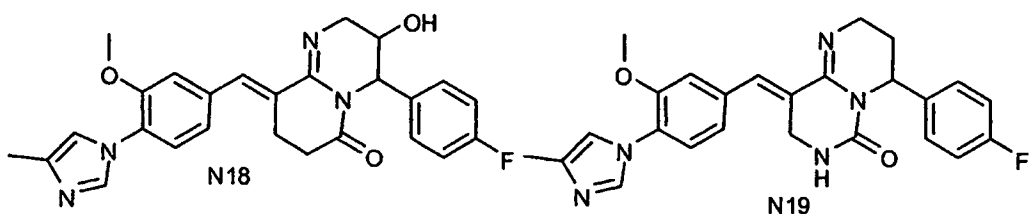
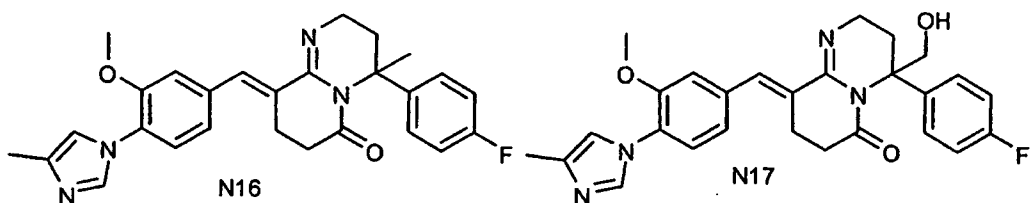


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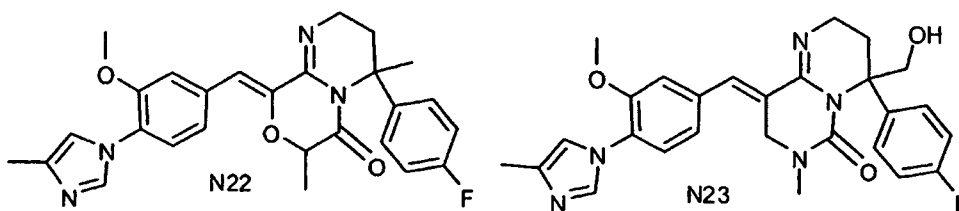
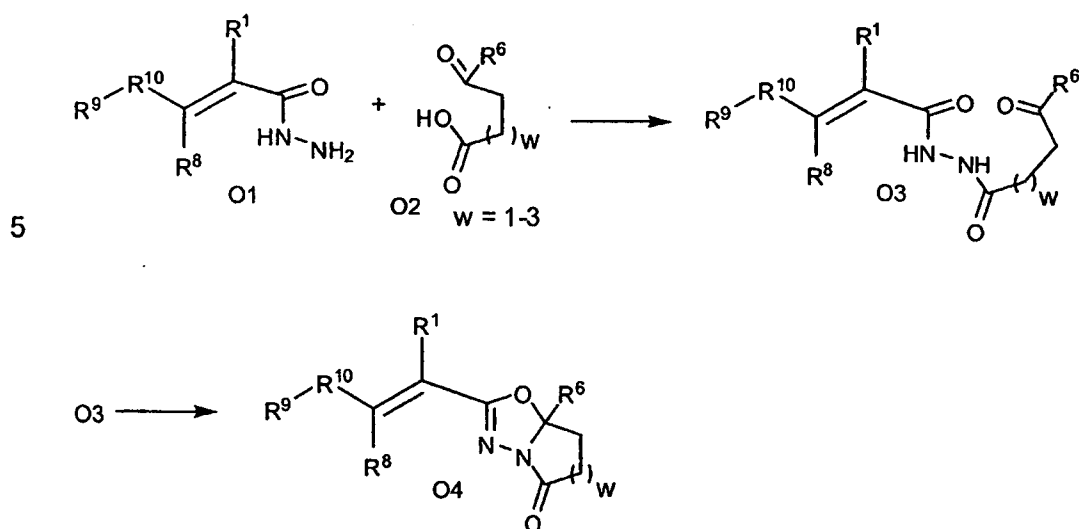


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**Method O**

10 The reaction of acylhydrazines **O1** (which are prepared by coupling the corresponding acid with hydrazine under peptide coupling conditions, or by reaction of hydrazine with the appropriate methyl ester) with keto acids (**O2**) is performed using standard carbodiimide conditions or other coupling procedures widely used to make an amide bond in peptide chemistry. The subsequent

15 dehydration of compound **O3** is accomplished by treatment with a catalytic amount of acid such as TsOH, or AcOH in solvents such as Toluene or DCM. In some cases heating in toluene to azeotrope off the H<sub>2</sub>O will facilitate the reaction to produce compounds of Formula **O4**.

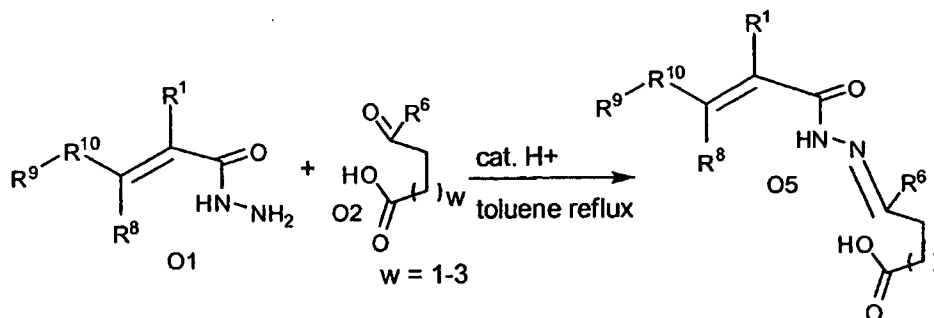
Alternatively, a modified scheme can be used wherein the ketone **O2** is first condensed with the amine **O1** to give the imine **O5**. Subsequent treatment of



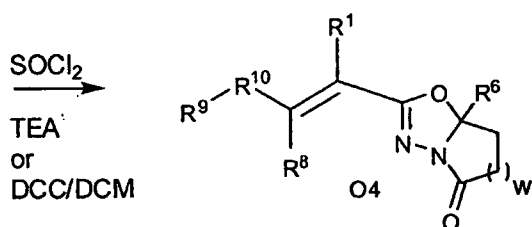
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**O5** with a dehydrating agent such as  $\text{SOCl}_2$ ,  $\text{Ac}_2\text{O}$ , or a carbodiimide will provide compounds of formula **O4**

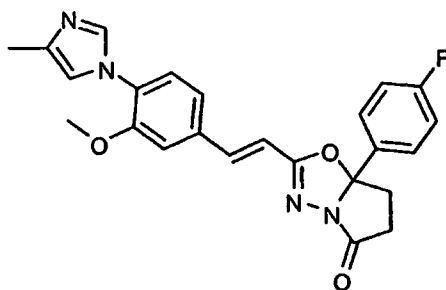


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#### Example Method O

(E)-7a-(4-fluorophenyl)-2-(3-methoxy-4-(4-methyl-1H-imidazol-1-yl)styryl)-7,7a-dihydropyrrolo[2,1-b][1,3,4]oxadiazol-5(6H)-one

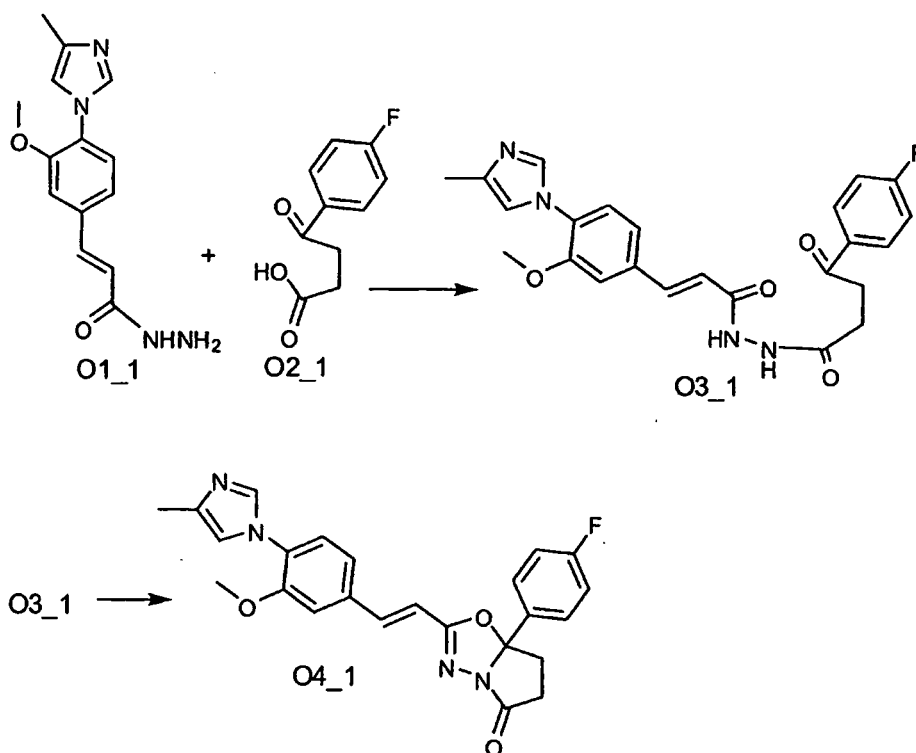


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**O4\_1**

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**Step 1: Reaction Scheme**

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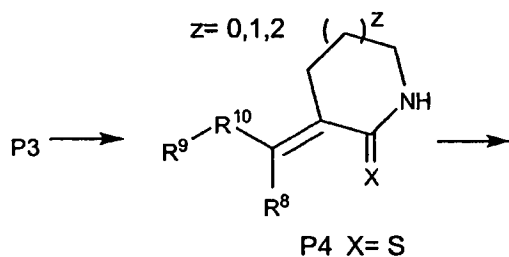
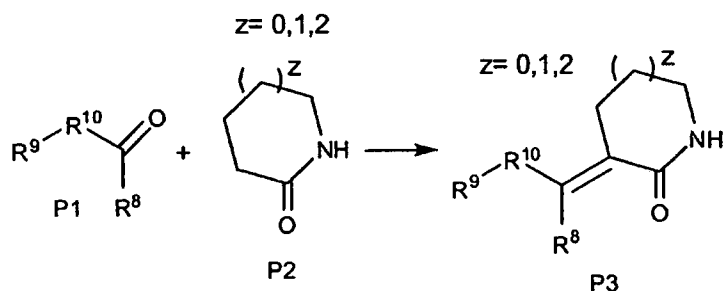
**Step 1**

Compound **O3\_1** is prepared by treating a solution of 1 gram of compound **O1\_1** in DCM (100 ml), and 1 equivalent of DCC with 1 equivalent of known compound **O2\_1**. After stirring for 12 hrs, add brine (100 ml) and separate the organic layer. Evaporate this to dryness and purify the residue by flash chromatography to obtain **O3\_1**. Treat compound **O3\_1** in toluene with TsOH (0.1 equivalents) and heat to reflux under a Dean Stark trap overnight. After cooling to room temperature add dilute NaHCO<sub>3</sub> solution and brine and separate the organic layer. Evaporate this to dryness and purify the residue by flash chromatography to obtain the compound **O4\_1**.

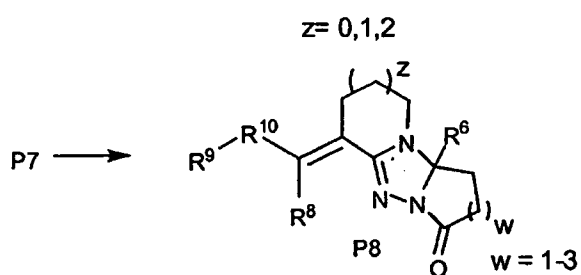
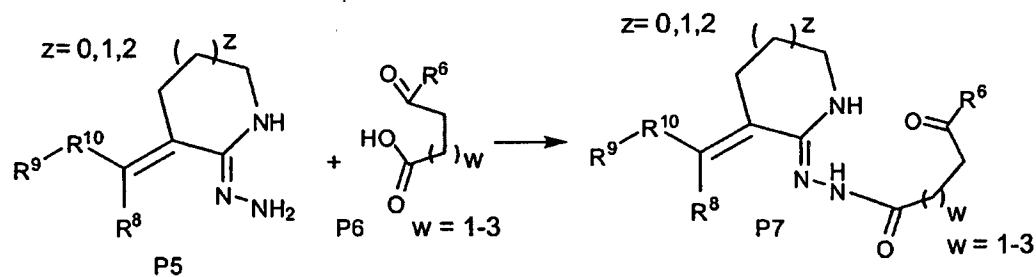
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**METHOD P**

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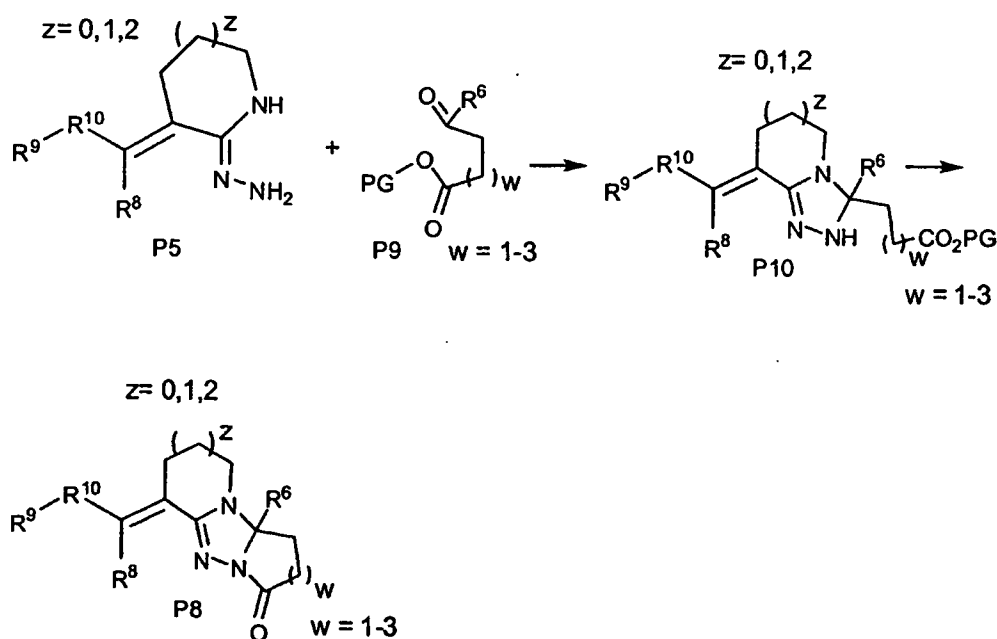


The condensation of a carbonyl containing compound such as **P1** with the  
lactams **P2** under basic conditions (using for example NaH and LDA to form the  
dianion of **P2**, and then treatment with **P1**) will provide compounds **P3**. Reaction

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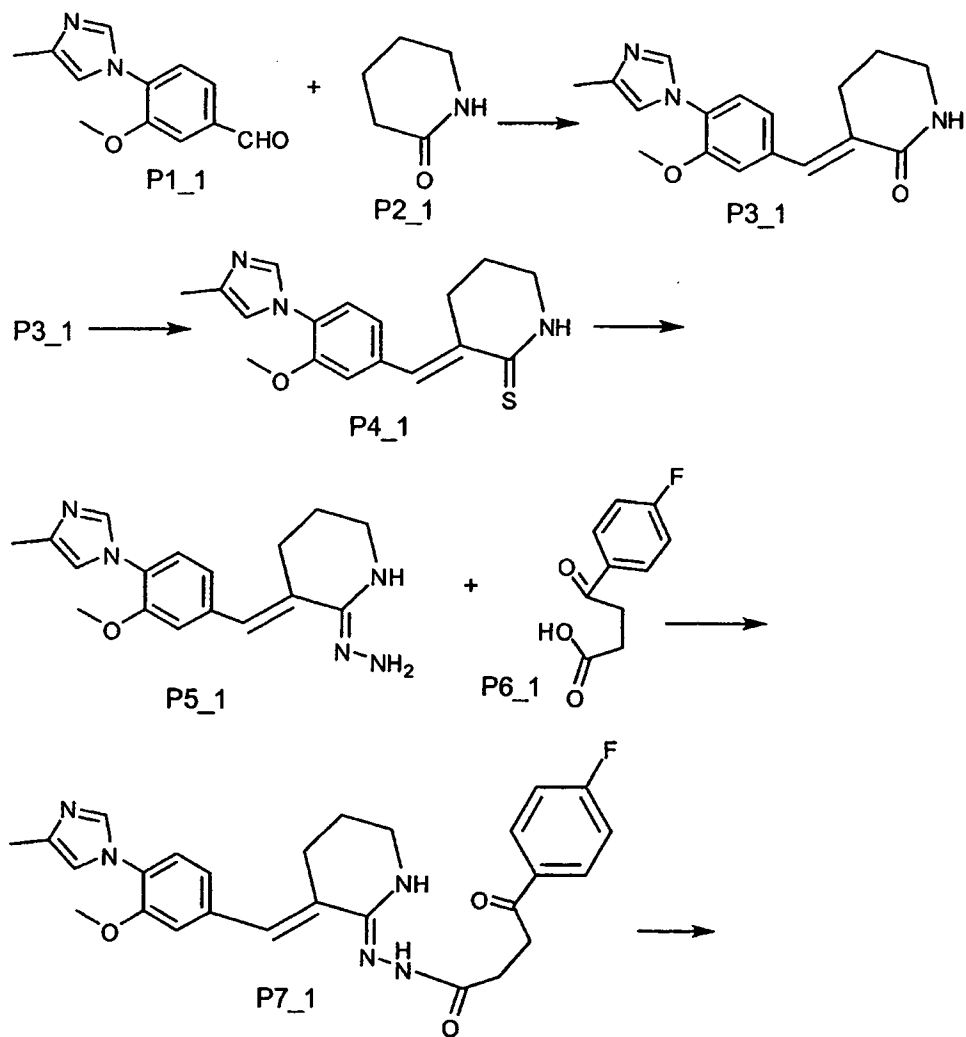
of **P3** with Lawesson's reagent provides the thioamides **P4**. These can be converted into the compounds of type **P5**, by direct treatment with hydrazine in a solvent such as isopropanol or toluene. Alternatively, in some cases the reaction may be facilitated by first reacting **P4** with MeI to prepare the thiomethyl ether as an intermediate which is then treated with hydrazine to provide compounds of type **P5**. Reaction of **P5** with a keto acid **P6** and a dehydrating agent such as DCC in DCM will provide an intermediate **P7** which can be converted into compounds of formula **P8** upon further heating or use of an acid catalyst such as TsOH in refluxing toluene.

Alternatively, a modified reaction scheme will provide compounds of formula **P8**. For example, the amine **P5** can be reacted with the ketone **P9** (where PG is a protecting group such as a tBu, Et, TMSCH<sub>2</sub>CH<sub>2</sub>) under dehydrating conditions to provide the triazine **P10**. After removing the PG, the acid is converted in compounds of formula **P8** by treatment with DCC in DCM or other dehydrating reaction conditions.

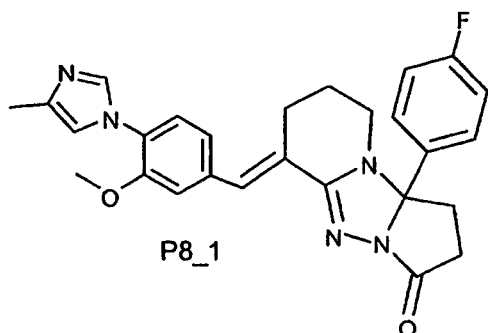


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In some cases it will be beneficial to protect the NH of the starting lactams P2 with a protecting group such as a p-methoxy phenyl, or trityl. In these cases the p-methoxy phenyl, or trityl protecting group can be removed (by treatment with CAN or Acid respectively) from the intermediates P5, P3 or P4 and the sequence  
5 completed as above.

**METHOD P EXAMPLES**

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**Step 1**

- Add a solution of the lactam **P2\_1** (1 gram) in THF (100 mls) to a suspension of NaH (1.5 equivalents) in THF at RT under an inert atmosphere.
- 5 After stirring for 15 minutes, cool the reaction mixture to -78 C and then add to this 1 equivalent of LDA in THF via syringe. Allow this to warm to 0 C for 1 hr then recool this to -78 C and add a THF solution of the aldehyde **P1\_1** via syringe. Allow the reaction mixture to warm to room temperature followed by addition of a saturated solution of NH<sub>4</sub>Cl. Partition the mixture with EtOAc,
- 10 separate the organic layer, evaporate to dryness and purify by flash chromatography to provide compound **P3\_1**.

**Step 2**

- Treat 1 gram of compound **P3\_1** with 1 equivalent of Lawesson's reagent
- 15 in toluene (100 ml) at between 50 and 100 C overnight. After cooling to room temperature partition with brine and separate the organic layer. Evaporate this to dryness and purify the residue by flash chromatography to obtain the intermediate **P4\_1**.

20 **Step 3:**

Treat 1 gram of compound **P4\_1** in DCM (100 ml) with 1 equivalent of MeI and 1 equivalent of triethylamine. After 3 hrs at RT, concentrate to dryness, and redissolve the residue in dioxane and add an excess of hydrazine. After heating for 6 hrs at 50 C cool to room temperature, evaporate to dryness and partition the

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residue between DCM and brine. Separate the organic layer, evaporate this to dryness and purify the residue by flash chromatography to obtain the intermediate **P5\_1**.

5 **Step 4**

Compound **P8\_1** can be prepared by treating a solution of 1 gram of compound **P5\_1** in DCM (100 ml), and 1 equivalent of DCC with 1 equivalent of known acid **P6\_1**. After stirring for 12 hrs, add brine (100 ml) and separate the organic layer. Evaporate this to dryness and purify the residue by flash chromatography to obtain the intermediate **P7\_1**. Treat compound **P7\_1** in toluene (100 mls) with TsOH (0.1 equivalents) and heat to reflux under a Dean Stark trap overnight. After cooling to room temperature, add dilute NaHCO<sub>3</sub> solution and brine and separate the organic layer. Evaporate this to dryness and purify the residue by flash chromatography to obtain the desired compound **P8\_1**.

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**Assay:**

Secretase Reaction and A $\beta$  Analysis in Whole Cells: HEK293 cells overexpressing APP with Swedish and London mutations were treated with the specified compounds for 5 hour at 37 °C in 100 ml of DMEM medium containing 10% fetal bovine serum. At the end of the incubation, total A $\beta$ , A $\beta$ 40 and A $\beta$ 42 were measured using electrochemiluminescence (ECL) based sandwich immunoassays. Total A $\beta$  was determined using a pair of antibodies TAG-W02 and biotin-4G8, A $\beta$ 40 was identified with antibody pairs TAG-G2-10 and biotin- 4G8, while A $\beta$ 42 was identified with TAG-G2-11 and biotin-4G8. The ECL signal was measured using Sector Imager 2400 (Meso Scale Discovery).

25

MS Analysis of A $\beta$  Profile: A $\beta$  profile in conditioned media was determined using surface enhanced laser desorption/ionization (SELDI) mass spectrometry. Conditioned media was incubated with antibody W02 coated PS20 ProteinChip array. Mass spectra of A $\beta$  captured on the array were read on SELDI ProteinChip Reader (Bio-Rad) according to manufacture's instructions.

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CSF A $\beta$  Analysis: A $\beta$  in rat CSF was determined using MSD technology as described above. A $\beta$ 40 was measured using antibody pair Tag-G2-10 and biotin-4G8, while A $\beta$ 42 was measured using Tag-anti A $\beta$ 42 (Meso Scale Discovery) and biotin-4G8. The ECL signal was measured using Sector Imager 2400 (Meso

5 Scale Discovery).

Matrix-assisted laser desorption/ionization mass spectrometric (MALDI MS) analysis of A $\beta$  is performed on a Voyager-DE STR mass spectrometer (ABI, Framingham, MA). The instrument is equipped with a pulsed nitrogen laser (337 nm). Mass spectra are acquired in the linear mode with an acceleration voltage of

10 20 kV. Each spectrum presented in this work represents an average of 256 laser shots. To prepare the sample-matrix solution, 1  $\mu$ L of immunoprecipitated A $\beta$  sample is mixed with 3  $\mu$ L of saturated  $\alpha$ -cyano-4-hydroxycinnamic acid solution in 0.1% TFA/acetonitrile. The sample-matrix solution is then applied to the sample plate and dried at ambient temperature prior to mass spectrometric analysis. All

15 the spectra are externally calibrated with a mixture of bovine insulin and ACTH (18-39 clip).

Compound G4 had an Ab42 IC50 of 1114 nM with an Abtotal/Ab42 selectivity of 11 fold.

20 While the present invention has been described with in conjunction with the specific embodiments set forth above, many alternatives, modifications and other variations thereof will be apparent to those of ordinary skill in the art. All such alternatives, modifications and variations are intended to fall within the spirit and scope of the present invention.

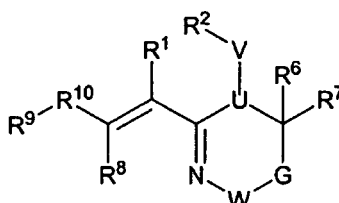


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**WHAT IS CLAIMED IS:**

1. A compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula:



Formula I

wherein:

- 10 either (i) R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or (ii) R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or (iii) R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; and R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-

C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered  
 heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety  
 being unsubstituted or optionally independently being substituted with 1-5  
 substituents which can be the same or different, each substituent being  
 5 independently selected from the group consisting of the moieties shown  
 below; or (iv)  $R^6$  and either  $R^3$  or  $R^4$  of the  $-C(R^3)(R^4)-$  G moiety, are joined  
 together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered  
 heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said  
 cycloalkyl or heterocyclyl moiety being unsubstituted or optionally  
 10 independently being substituted with 1-5 substituents which can be the  
 same or different, each substituent being independently selected from the  
 group consisting of the moieties shown below; or (v)  $R^6$  and  $R^{13}$  of the  
 $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl  
 or 5-8 membered heterocyclenyl moiety, with said heterocyclyl moiety  
 15 being unsubstituted or optionally independently being substituted with 1-5  
 substituents which can be the same or different, each substituent being  
 independently selected from the group consisting of the moieties shown  
 below; and

U is  $\begin{matrix} \diagup \\ \diagdown \end{matrix} -C(R^5)$  or N;

20 W is selected from the group consisting of a bond, -O-, -C(O)-, -S-, -S(O)-,  
 -S(O<sub>2</sub>)-, and  $-C(R^{11})(R^{12})-$ ;

G is selected from the group consisting of  $-C(R^3)(R^4)-$ , -C(O)- and  
 $-N(R^{13})-$ , with the proviso that when W is -O- or -S-, G is not  $-N(R^{13})-$  or -C(O)-;

V is selected from the group consisting of a bond, -O-, -C(O)- and  $-N(R^{14})-$ ;

25  $R^1$  (when  $R^1$  is not joined to  $R^2$ ),  $R^2$  (when  $R^2$  is not joined to  $R^1$  or  $R^6$ ),  $R^5$ ,  
 $R^6$  (when  $R^6$  is not joined to  $R^2$ ), and  $R^7$  can be the same or different, each being  
 independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-,  
 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-,  
 heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and  
 30 alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,

heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

5 or, alternatively,  $R^1$  (when  $R^1$  is not joined to  $R^2$ ) and  $R^8$  are taken together to form a bond;

$R^3$  is selected from the group consisting of H, halo,  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  
 10  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-,  
 15 cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or

$R^3$  and  $R^6$  taken together form a bond, provided that when  $R^3$  and  $R^6$  form  
 20 a bond: (1) W is not a bond, (2)  $R^2$  and  $R^6$  are not joined together to form a cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety (as described in (ii) and (iii) above) (3)  $R^6$  and either  $R^3$  or  $R^4$  of the  $-C(R^3)(R^4)-$  G moiety are not joined together to form a cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety (as described in (iv) above), and (4)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety  
 25 are not joined together to form a heterocyclyl or heterocyclenyl moiety (as described in (v) above);

$R^4$ ,  $R^{11}$  and  $R^{12}$  can be the same or different, each being independently selected from the group consisting of H, halo,  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 30  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,

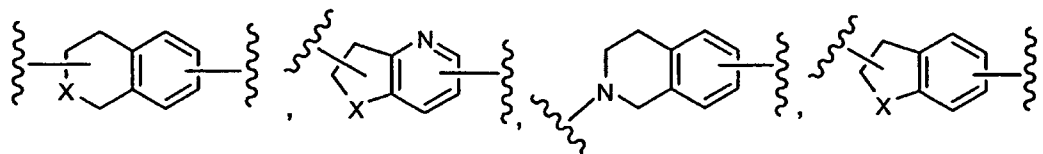
- C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>),  
 -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alkyl-,  
 alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-,  
 heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of  
 5 said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-,  
 cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-  
 can be unsubstituted or optionally independently substituted with 1-5 substituents  
 which can be the same or different, each substituent being independently selected  
 from the group consisting of the moieties shown below,
- 10 provided that when one of R<sup>3</sup> or R<sup>4</sup> is selected from the group consisting of:  
 -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>,  
 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not selected from the  
 15 group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, and -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
 =NOR<sup>15</sup>, and -N<sub>3</sub>;
- 20 provided that when one of R<sup>11</sup> or R<sup>12</sup> is selected from the group consisting  
 of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>),  
 -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not  
 25 selected from the group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,  
 -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
 =NOR<sup>15</sup>, and -N<sub>3</sub>;

- $R^{13}$  is independently selected from the group consisting of H, alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-, arylcycloalkylalkyl-, heteroarylcyaloalkylalkyl-, arylheterocycloalkylalkyl-, heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylcyaloalkyl-, heterocycloalkyl-, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl, arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylcyaloalkenyl-, heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-, heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylaryl-, heterocycloalkenylaryl-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  and  $-N(R^8)_2$ ; and wherein said  $R^{13}$  alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-, arylcycloalkylalkyl-, heteroarylcyaloalkylalkyl-, arylheterocycloalkylalkyl-, heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylcyaloalkyl-, heterocycloalkyl, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl, arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylcyaloalkenyl-, heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-, heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylaryl-, and heterocycloalkenylaryl- groups are optionally substituted with 1 to 5 groups independently selected from the group consisting of: alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo,  $-CN$ ,  $-OR^{15}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-SR^{15}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-CH(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $-N(R^{15})(R^{16})$ ,  $-alkyl-N(R^{15})(R^{16})$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-R^{15}$ ,  $-CH_2N(R^{15})(R^{16})$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-CH_2-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,

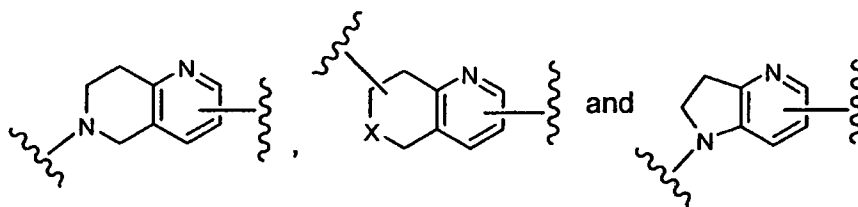
$-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{OR}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{OR}^{16}$ ,  $-\text{S}(\text{O})\text{R}^{15}$ ,  $=\text{NOR}^{15}$ ,  $-\text{N}_3$ ,  $-\text{NO}_2$  and  $-\text{S}(\text{O})_2\text{R}^{15}$ ;

$\text{R}^{14}$  is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-,  $-\text{CN}$ ,  $-\text{C}(\text{O})\text{R}^{15}$ ,  $-\text{C}(\text{O})\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{C}(=\text{NOR}^{15})\text{R}^{16}$ , and  $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ;

$\text{R}^8$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, with each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- being unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;



20



where X is O,  $\text{N}(\text{R}^{14})$  or S;

wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl-

heterocyclalkyl- for  $R^{10}$  as well as the above-noted moieties for  $R^{10}$  can be unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of the moieties shown below; and

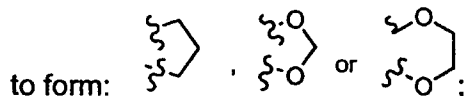
- 5  $R^9$  is selected from the group consisting of alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocycl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocycl- and heterocyclalkyl- can be
- 10 unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

- $R^{15}$ ,  $R^{16}$  and  $R^{17}$  are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, heterocycl-, heterocyclalkyl-,
- 15 aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, arylcycloalkyl-, arylheterocycl-,  $R^{18}$ -alkyl,  $R^{18}$ -cycloalkyl,  $R^{18}$ -cycloalkylalkyl-,  $R^{18}$ -heterocycl-,  $R^{18}$ -heterocyclalkyl-,  $R^{18}$ -aryl,  $R^{18}$ -arylalkyl-,  $R^{18}$ -heteroaryl and  $R^{18}$ -heteroarylalkyl-;

- $R^{18}$  is 1-5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl-, arylalkenyl-, arylalkynyl-,  $-NO_2$ , halo,
- 20 heteroaryl, HO-alkoxyalkyl-,  $-CF_3$ ,  $-CN$ , alkyl-CN,  $-C(O)R^{19}$ ,  $-C(O)OH$ ,  $-C(O)OR^{19}$ ,  $-C(O)NHR^{20}$ ,  $-C(O)NH_2$ ,  $-C(O)NH_2-C(O)N(alkyl)_2$ ,  $-C(O)N(alkyl)(aryl)$ ,  $-C(O)N(alkyl)(heteroaryl)$ ,  $-SR^{19}$ ,  $-S(O)_2R^{20}$ ,  $-S(O)NH_2$ ,  $-S(O)NH(alkyl)$ ,  $-S(O)N(alkyl)(alkyl)$ ,  $-S(O)NH(aryl)$ ,  $-S(O)_2NH_2$ ,  $-S(O)_2NHR^{19}$ ,  $-S(O)_2NH(heterocycl)$ ,  $-S(O)_2N(alkyl)_2$ ,  $-S(O)_2N(alkyl)(aryl)$ ,  $-OCF_3$ ,  $-OH$ ,  $-OR^{20}$ ,
- 25  $-O-heterocycl$ ,  $-O-cycloalkylalkyl$ ,  $-O-heterocyclalkyl$ ,  $-NH_2$ ,  $-NHR^{20}$ ,  $-N(alkyl)_2$ ,  $-N(arylalkyl)_2$ ,  $-N(arylalkyl)-(heteroarylalkyl)$ ,  $-NHC(O)R^{20}$ ,  $-NHC(O)NH_2$ ,  $-NHC(O)NH(alkyl)$ ,  $-NHC(O)N(alkyl)(alkyl)$ ,  $-N(alkyl)C(O)NH(alkyl)$ ,  $-N(alkyl)C(O)N(alkyl)(alkyl)$ ,  $-NHS(O)_2R^{20}$ ,  $-NHS(O)_2NH(alkyl)$ ,  $-NHS(O)_2N(alkyl)(alkyl)$ ,  $-N(alkyl)S(O)_2NH(alkyl)$  and
- 30  $-N(alkyl)S(O)_2N(alkyl)(alkyl)$ ;

25b

or, alternately, two  $R^{18}$  moieties on adjacent carbons can be linked together



$R^{19}$  is alkyl, cycloalkyl, aryl, arylalkyl- or heteroarylalkyl-;

$R^{20}$  is alkyl, cycloalkyl, aryl, halo substituted aryl, arylalkyl-, heteroaryl or

5 heteroarylalkyl-;

wherein each of the alkyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl-,

heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, alkylaryl-, heteroaryl,

heteroarylalkyl-, alkenyl and alkynyl groups in  $R^1$ ,  $R^2$ ,  $R^1$ - $R^2$ ,  $R^2$ - $R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{14}$  is independently unsubstituted or optionally

10 substituted by 1 to 5  $R^{21}$  groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>),

15 -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and

20 -S(O)<sub>2</sub>R<sup>15</sup>;

wherein each of the alkyl, cycloalkenyl, cycloalkyl, cycloalkylalkyl-,

heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in  $R^{21}$  is independently unsubstituted or substituted by 1 to 5

25  $R^{22}$  groups independently selected from the group consisting of alkyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,

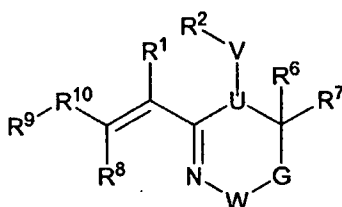


250

-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and  
 -S(O)<sub>2</sub>R<sup>15</sup>.

5

2. A compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula:



10 wherein:

R<sup>1</sup> and R<sup>2</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5  
 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

15

U is  $\begin{matrix} \diagup \\ \diagdown \end{matrix} \text{---C(R}^5\text{) or N;}$

20

W is selected from the group consisting of a bond, -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, and -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G is -C(R<sup>3</sup>)(R<sup>4</sup>)-; -C(O)- and -N(R<sup>13</sup>)-; with the proviso that when W is -O- or -S-, G is not -N(R<sup>13</sup>)- or -C(O)-;

V is selected from the group consisting of a bond, -O-, -C(O)- and -N(R<sup>14</sup>)-;

25

R<sup>5</sup>, R<sup>6</sup>, and R<sup>7</sup> can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-,

alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be

5 unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

$R^3$  is selected from the group consisting of H, halo,  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,

10  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-,

15 wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; or

20  $R^3$  and  $R^6$  taken together form a bond, provided that when  $R^3$  and  $R^6$  form a bond W is not a bond;

$R^4$ ,  $R^{11}$  and  $R^{12}$  can be the same or different, each being independently selected from the group consisting of H, halo,  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,

25  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of

30 said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-,

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cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

5 provided that when one of  $R^3$  or  $R^4$  is selected from the group consisting of:

-OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>,  
-N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>,  
-P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not selected from the

10 group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, and -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>,  
-N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
-S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
=NOR<sup>15</sup>, and -N<sub>3</sub>;

15 provided that when one of  $R^{11}$  or  $R^{12}$  is selected from the group consisting

of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>),  
-S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not

20 selected from the group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,  
-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
-S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
=NOR<sup>15</sup>, and -N<sub>3</sub>;

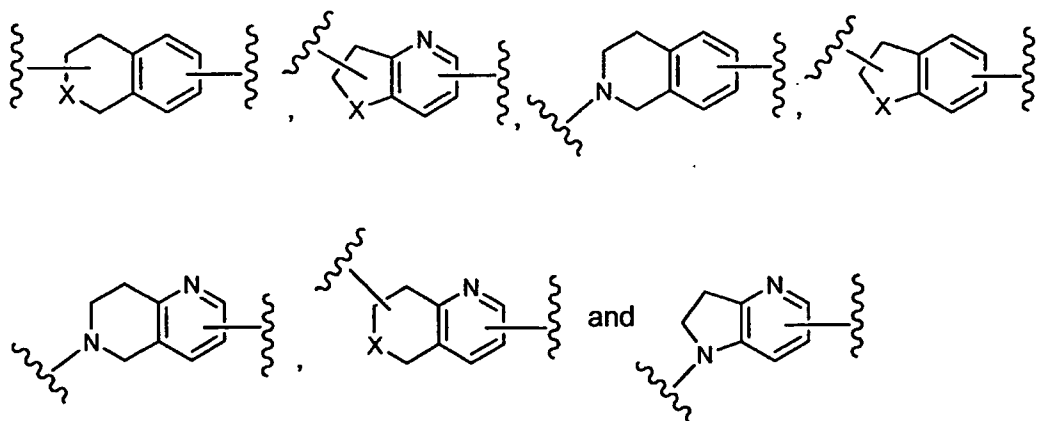
25  $R^{13}$  is independently selected from the group consisting of H, alkyl,

arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-,  
arylcycloalkylalkyl-, heteroarylcycloalkylalkyl-, arylheterocycloalkylalkyl-,  
heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylcycloalkyl-,  
heterocycloalkyl, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl,  
30 arylalkenyl, cycloalkenyl, arylcycloalkenyl-, heteroarylcycloalkenyl-,

- heterocycloalkenyl, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-, heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylaryl-, heterocycloalkenylaryl-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  and  $-N(R^8)_2$ ; and wherein said  $R^{13}$  alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-, arylcycloalkylalkyl-, heteroarylalkyl-, arylheterocycloalkylalkyl-, heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylalkyl-, heterocycloalkyl, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl, arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylalkyl-, heterocycloalkenyl, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-, heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylaryl-, and heterocycloalkenylaryl- groups are optionally substituted with 1 to 5 groups independently selected from the group consisting of: alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo,  $-CN$ ,  $-OR^{15}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-SR^{15}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-CH(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $-N(R^{15})(R^{16})$ ,  $-alkyl-N(R^{15})(R^{16})$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-R^{15}$ ,  $-CH_2N(R^{15})(R^{16})$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-CH_2-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-CH_2-N(R^{15})C(O)OR^{16}$ ,  $-S(O)R^{15}$ ,  $=NOR^{15}$ ,  $-N_3$ ,  $-NO_2$  and  $-S(O)_2R^{15}$ ;
- $R^{14}$  is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-,  $-CN$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ , and  $-P(O)(OR^{15})(OR^{16})$ ;

$R^8$  is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, with each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- being unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

$R^{10}$  is selected from the group consisting of a bond, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl-, heterocyclylalkyl- and the moieties:



where X is O, N( $R^{14}$ ) or S;

wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- heterocyclylalkyl- for  $R^{10}$  as well as the above-noted moieties for  $R^{10}$  can be unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of the moieties shown below; and

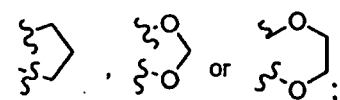
$R^9$  is selected from the group consisting of alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,

heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-3 substituents which  
5 can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

$R^{15}$ ,  $R^{16}$  and  $R^{17}$  are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, arylcycloalkyl-, arylheterocyclyl-,  $R^{18}$ -alkyl,  $R^{18}$ -cycloalkyl,  $R^{18}$ -cycloalkylalkyl-,  $R^{18}$ -heterocyclyl,  $R^{18}$ -heterocyclylalkyl-,  
10  $R^{18}$ -aryl,  $R^{18}$ -arylalkyl,  $R^{18}$ -heteroaryl and  $R^{18}$ -heteroarylalkyl-;

$R^{18}$  is 1-5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl-, arylalkenyl-, arylalkynyl-,  $-\text{NO}_2$ , halo, heteroaryl, HO-alkoxyalkyl-,  $-\text{CF}_3$ ,  $-\text{CN}$ , alkyl-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  
15  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2\text{-C}(\text{O})\text{N}(\text{alkyl})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alkyl})(\text{aryl})$ ,  $-\text{C}(\text{O})\text{N}(\text{alkyl})(\text{heteroaryl})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{S}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{S}(\text{O})\text{NH}(\text{aryl})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterocyclyl})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alkyl})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alkyl})(\text{aryl})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  $-\text{O-heterocyclyl}$ ,  $-\text{O-cycloalkylalkyl}$ ,  $-\text{O-heterocyclylalkyl}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alkyl})_2$ ,  
20  $-\text{N}(\text{arylalkyl})_2$ ,  $-\text{N}(\text{arylalkyl})\text{-(heteroarylalkyl)}$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{C}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{C}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alkyl})$ ,  $-\text{NHS}(\text{O})_2\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{S}(\text{O})_2\text{NH}(\text{alkyl})$  and  $-\text{N}(\text{alkyl})\text{S}(\text{O})_2\text{N}(\text{alkyl})(\text{alkyl})$ ;

or, alternately, two  $R^{18}$  moieties on adjacent carbons can be linked together

25 to form: ;

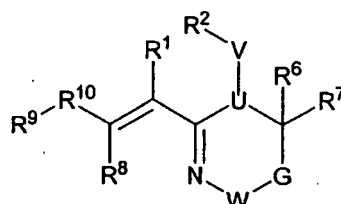
$R^{19}$  is alkyl, cycloalkyl, aryl, arylalkyl or heteroarylalkyl;

$R^{20}$  is alkyl, cycloalkyl, aryl, halo substituted aryl, arylalkyl, heteroaryl or heteroarylalkyl;

wherein each of the alkyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, alkylaryl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in  $R^1$ - $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{14}$  is independently unsubstituted or optionally substituted by 1 to 5  $R^{21}$  groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and -S(O)<sub>2</sub>R<sup>15</sup>;

wherein each of the alkyl, cycloalkenyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in  $R^{21}$  is independently unsubstituted or substituted by 1 to 5  $R^{22}$  groups independently selected from the group consisting of alkyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and -S(O)<sub>2</sub>R<sup>15</sup>.

3. A compound, or pharmaceutically acceptable salts, solvates, esters or prodrugs of said compound, said compound having the general structure shown in the formula:



5 wherein:

R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

U is  $\begin{matrix} \diagup \\ \diagdown \end{matrix} \text{---C(R}^5\text{) or N}$ ;

W is selected from the group consisting of a bond, -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)- and -C(R<sup>11</sup>)(R<sup>12</sup>)-;

15 G is -C(R<sup>3</sup>)(R<sup>4</sup>)-; -C(O)- and -N(R<sup>13</sup>)-; with the proviso that when W is -O- or -S-, G is not -N(R<sup>13</sup>)- or -C(O)-;

V is selected from the group consisting of a bond, -O-, -C(O)- and -N(R<sup>14</sup>)-;

R<sup>1</sup> (when R<sup>1</sup> is not joined to R<sup>2</sup>), R<sup>5</sup>, R<sup>6</sup> (when R<sup>6</sup> is not joined to R<sup>2</sup>), and R<sup>7</sup> can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;



or, alternatively,  $R^1$  (when  $R^1$  is not joined to  $R^2$ ) and  $R^8$  are taken together to form a bond;

- $R^3$  is selected from the group consisting of H, halo,  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  
 5  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-,  
 10 wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;
- 15  $R^4$ ,  $R^{11}$  and  $R^{12}$  can be the same or different, each being independently selected from the group consisting of H, halo,  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  
 20  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-  
 25 can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

- provided that when one of  $R^3$  or  $R^4$  is selected from the group consisting of:  
 30  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,

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- N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>,  
 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not selected from the  
 group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, and -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 5 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
 =NOR<sup>15</sup>, and -N<sub>3</sub>;

- provided that when one of R<sup>11</sup> or R<sup>12</sup> is selected from the group consisting  
 of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 10 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>),  
 -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, and -N<sub>3</sub>, then the other is not  
 selected from the group consisting of: -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>,  
 -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 15 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>,  
 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
 =NOR<sup>15</sup>, and -N<sub>3</sub>;

- R<sup>13</sup> is independently selected from the group consisting of H, alkyl,  
 arylalkyl, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-,  
 20 arylcycloalkylalkyl-, heteroarylalkyl-, arylheterocycloalkylalkyl-,  
 heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylalkyl-,  
 heterocycloalkyl, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl,  
 arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylalkenyl-,  
 heterocycloalkenyl, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl,  
 25 arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-, heterocycloalkenylaryl-,  
 heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylaryl-,  
 heterocycloalkenylaryl-, -OR<sup>15</sup>, -CN, -C(O)R<sup>8</sup>, -C(O)OR<sup>9</sup>, -S(O)R<sup>10</sup>, -S(O)<sub>2</sub>R<sup>10</sup>,  
 -C(O)N(R<sup>11</sup>)(R<sup>12</sup>), -S(O)N(R<sup>11</sup>)(R<sup>12</sup>), -S(O)<sub>2</sub>N(R<sup>11</sup>)(R<sup>12</sup>), -NO<sub>2</sub>, -N=C(R<sup>8</sup>)<sub>2</sub> and  
 -N(R<sup>8</sup>)<sub>2</sub>; and wherein said R<sup>13</sup> alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-,  
 30 heterocycloalkylalkyl-, arylcycloalkylalkyl-, heteroarylalkyl-,

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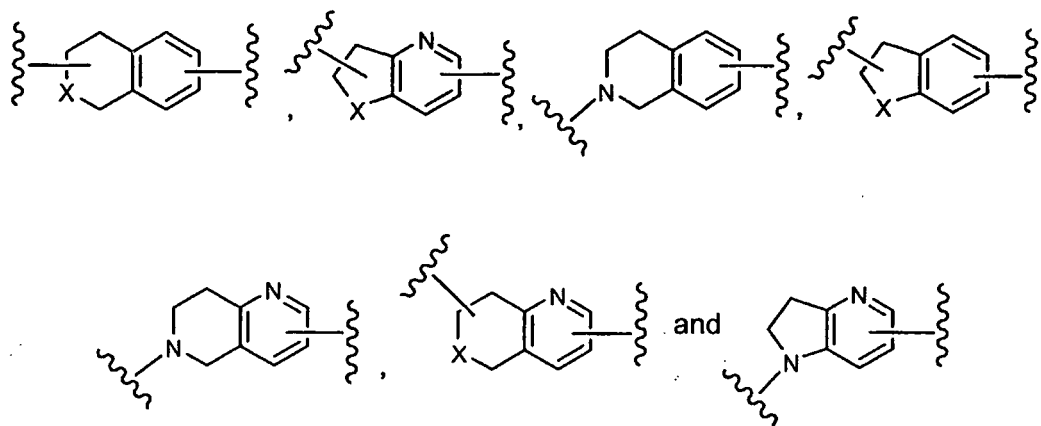
arylheterocycloalkylalkyl-, heteroarylheterocycloalkylalkyl-, cycloalkyl,  
 arylcycloalkyl-, heteroarylcycloalkyl-, heterocycloalkyl, arylheterocycloalkyl-,  
 heteroarylheterocycloalkyl-, alkenyl, arylalkenyl-, cycloalkenyl, arylcycloalkenyl-,  
 heteroarylcycloalkenyl-, heterocycloalkenyl, arylheterocycloalkenyl-,  
 5 heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl, aryl, cycloalkylaryl-,  
 heterocycloalkylaryl-, heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-,  
 heterocycloalkylheteroaryl-, cycloalkenylaryl-, and heterocycloalkenylaryl- groups  
 are optionally substituted with 1 to 5 groups independently selected from the  
 group consisting of: alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-,  
 10 cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl,  
 heteroarylalkyl, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>,  
 -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>,  
 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>,  
 -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>),  
 15 -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and  
 -S(O)<sub>2</sub>R<sup>15</sup>;

R<sup>14</sup> is selected from the group consisting of H, alkyl, alkenyl, alkynyl,  
 20 cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl,  
 arylalkyl-, heteroaryl, heteroarylalkyl-, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>,  
 -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, and  
 -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);

R<sup>8</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-,  
 25 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-,  
 heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, with each of said alkyl-,  
 alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-,  
 heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- being  
 unsubstituted or optionally independently substituted with 1-3 substituents which

can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

- $R^{10}$  is selected from the group consisting of a bond, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl-, heterocyclalkyl- and the moieties:



where X is O, N( $R^{14}$ ) or S;

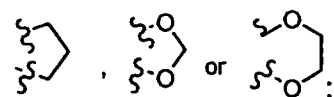
- 10 wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- heterocyclalkyl- for  $R^{10}$  as well as the above-noted moieties for  $R^{10}$  can be unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each being independently selected from the group
- 15 consisting of the moieties shown below; and

- $R^9$  is selected from the group consisting of alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-,
- 20 heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclalkyl- can be unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

$R^{15}$ ,  $R^{16}$  and  $R^{17}$  are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, arylcycloalkyl, arylheterocyclyl-,  $R^{18}$ -alkyl-,  $R^{18}$ -cycloalkyl-,  $R^{18}$ -cycloalkylalkyl-,  $R^{18}$ -heterocyclyl-,  
 5  $R^{18}$ -heterocyclalkyl-,  $R^{18}$ -aryl-,  $R^{18}$ -arylalkyl-,  $R^{18}$ -heteroaryl- and  $R^{18}$ -heteroarylalkyl-;

$R^{18}$  is 1-5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, arylalkenyl, arylalkynyl,  $-\text{NO}_2$ , halo, heteroaryl, HO-alkoxyalkyl,  $-\text{CF}_3$ ,  $-\text{CN}$ , alkyl-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  
 10  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alkyl})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alkyl})(\text{aryl})$ ,  $-\text{C}(\text{O})\text{N}(\text{alkyl})(\text{heteroaryl})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{S}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{S}(\text{O})\text{NH}(\text{aryl})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterocyclyl})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alkyl})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alkyl})(\text{aryl})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  $-\text{O-heterocyclyl}$ ,  $-\text{O-cycloalkylalkyl}$ ,  $-\text{O-heterocyclalkyl}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alkyl})_2$ ,  
 15  $-\text{N}(\text{arylalkyl})_2$ ,  $-\text{N}(\text{arylalkyl})-(\text{heteroarylalkyl})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{C}(\text{O})\text{NH}(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{C}(\text{O})\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alkyl})$ ,  $-\text{NHS}(\text{O})_2\text{N}(\text{alkyl})(\text{alkyl})$ ,  $-\text{N}(\text{alkyl})\text{S}(\text{O})_2\text{NH}(\text{alkyl})$  and  $-\text{N}(\text{alkyl})\text{S}(\text{O})_2\text{N}(\text{alkyl})(\text{alkyl})$ ;

or, alternately, two  $R^{18}$  moieties on adjacent carbons can be linked together

20 to form: ;

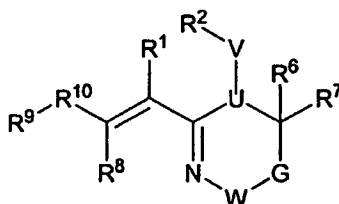
$R^{19}$  is alkyl, cycloalkyl, aryl, arylalkyl or heteroarylalkyl;

$R^{20}$  is alkyl, cycloalkyl, aryl, halo substituted aryl, arylalkyl, heteroaryl or heteroarylalkyl;

wherein each of the alkyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl-,  
 25 heterocyclyl, heterocyclalkyl-, aryl, arylalkyl-, alkylaryl-, heteroaryl, heteroarylalkyl-, alkenyl and alkynyl groups in  $R^1$ ,  $R^2$ - $R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{14}$  is independently unsubstituted or optionally substituted by 1 to 5  $R^{21}$  groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclalkyl-,

- aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>,  
 -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>),  
 -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>),  
 -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>,  
 5 -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>; -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and  
 -S(O)<sub>2</sub>R<sup>15</sup>;  
 10 wherein each of the alkyl, cycloalkenyl, cycloalkyl, cycloalkylalkyl-,  
 heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, alkenyl  
 and alkynyl groups in R<sup>21</sup> is independently unsubstituted or substituted by 1 to 5  
 R<sup>22</sup> groups independently selected from the group consisting of alkyl, cycloalkyl,  
 cycloalkenyl, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>,  
 15 -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>),  
 -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>),  
 -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 20 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and  
 -S(O)<sub>2</sub>R<sup>15</sup>.

4. A compound, or pharmaceutically acceptable salts, solvates, esters  
 or prodrugs of said compound, said compound having the general structure shown  
 25 in the formula:



wherein:

5  $R^1$  and  $R^2$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below; and  $R^2$  and  $R^6$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

15 U is  $\begin{matrix} \diagup \\ \diagdown \end{matrix} -C(R^5)$  or N;

W is selected from the group consisting of a bond, -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, and -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G is -C(R<sup>3</sup>)(R<sup>4</sup>)-; -C(O)- and -N(R<sup>13</sup>)-; with the proviso that when W is -O- or -S-, G is not -N(R<sup>13</sup>)- or -C(O)-;

20 V is selected from the group consisting of a bond, -O-, -C(O)- and -N(R<sup>14</sup>)-;

$R^5$ ,  $R^6$ , and  $R^7$  can be the same or different, each being independently selected from the group consisting of H, alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

- $R^3$  is selected from the group consisting of H, halo,  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;
- $R^4$ ,  $R^{11}$  and  $R^{12}$  can be the same or different, each being independently selected from the group consisting of H, halo,  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alkyl-, alkenyl-, alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be unsubstituted or optionally independently substituted with 1-5 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,
- provided that when one of  $R^3$  or  $R^4$  is selected from the group consisting of:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , and  $-N_3$ , then the other is not selected from the



group consisting of:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , and  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  
 $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
5  $=NOR^{15}$ , and  $-N_3$ ;

provided that when one of  $R^{11}$  or  $R^{12}$  is selected from the group consisting  
of:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  
 $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  
10  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , and  $-N_3$ , then the other is not  
selected from the group consisting of:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
15  $=NOR^{15}$ , and  $-N_3$ ;

$R^{13}$  is independently selected from the group consisting of H, alkyl,  
arylalkyl, heteroarylalkyl-, cycloalkylalkyl-, heterocycloalkylalkyl-,  
arylcycloalkylalkyl-, heteroarylcycloalkylalkyl-, arylheterocycloalkylalkyl-,  
heteroarylheterocycloalkylalkyl-, cycloalkyl, arylcycloalkyl-, heteroarylcycloalkyl-,  
20 heterocycloalkyl, arylheterocycloalkyl-, heteroarylheterocycloalkyl-, alkenyl,  
arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylcycloalkenyl-,  
heterocycloalkenyl, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl,  
arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-, heterocycloalkenylaryl-,  
heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylaryl-,  
25 heterocycloalkenylaryl-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  
 $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  and  
 $-N(R^8)_2$ ; and wherein said  $R^{13}$  alkyl, arylalkyl-, heteroarylalkyl-, cycloalkylalkyl-,  
heterocycloalkylalkyl-, arylcycloalkylalkyl-, heteroarylcycloalkylalkyl-,  
arylheterocycloalkylalkyl-, heteroarylheterocycloalkylalkyl-, cycloalkyl,  
30 arylcycloalkyl-, heteroarylcycloalkyl-, heterocycloalkyl, arylheterocycloalkyl-,

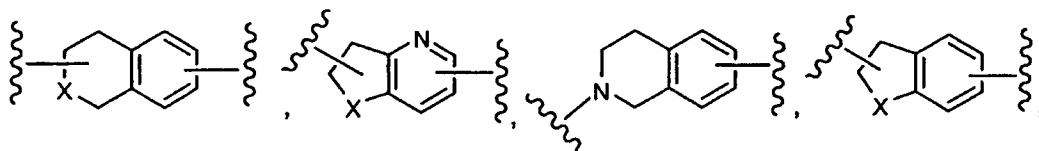
heteroarylheterocycloalkyl-, alkenyl, arylalkenyl-, cycloalkenyl, arylcycloalkenyl-, heteroarylcyaloalkenyl-, heterocycloalkenyl-, arylheterocycloalkenyl-, heteroarylheterocycloalkenyl-, alkynyl, arylalkynyl-, aryl, cycloalkylaryl-, heterocycloalkylaryl-, heterocycloalkenylaryl-, heteroaryl, cycloalkylheteroaryl-, heterocycloalkylheteroaryl-, cycloalkenylaryl-, and heterocycloalkenylaryl- groups

are optionally substituted with 1 to 5 groups independently selected from the group consisting of: alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and -S(O)<sub>2</sub>R<sup>15</sup>;

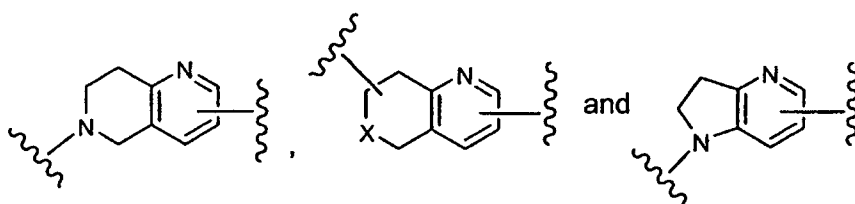
R<sup>14</sup> is selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, and -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);

R<sup>8</sup> is selected from the group consisting of H, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, with each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- being unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below;

$R^{10}$  is selected from the group consisting of a bond, alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl-, heterocyclylalkyl- and the moieties:



5



where X is O,  $N(R^{14})$  or S;

wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl-

10 heterocyclylalkyl- for  $R^{10}$  as well as the above-noted moieties for  $R^{10}$  can be unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of the moieties shown below; and

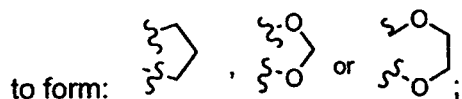
$R^9$  is selected from the group consisting of alkyl-, alkenyl- and alkynyl-,  
 15 aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl-, wherein each of said alkyl-, alkenyl- and alkynyl-, aryl-, arylalkyl-, alkylaryl-, cycloalkyl-, cycloalkylalkyl-, heteroaryl-, heteroarylalkyl-, heterocyclyl- and heterocyclylalkyl- can be  
 20 unsubstituted or optionally independently substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of the moieties shown below,

$R^{15}$ ,  $R^{16}$  and  $R^{17}$  are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl-, heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, arylcycloalkyl-, arylheterocyclyl-,  $R^{18}$ -

alkyl-, R<sup>18</sup>-cycloalkyl-, R<sup>18</sup>-cycloalkylalkyl-, R<sup>18</sup>-heterocyclyl-,  
R<sup>18</sup>-heterocyclylalkyl-, R<sup>18</sup>-aryl-, R<sup>18</sup>-arylalkyl-, R<sup>18</sup>-heteroaryl- and  
R<sup>18</sup>-heteroarylalkyl

- R<sup>18</sup> is 1-5 substituents independently selected from the group consisting of
- 5 alkyl, alkenyl, alkynyl, aryl, arylalkyl-, arylalkenyl-, arylalkynyl-, -NO<sub>2</sub>, halo,  
heteroaryl, HO-alkoxyalkyl-, -CF<sub>3</sub>, -CN, alkyl-CN, -C(O)R<sup>19</sup>, -C(O)OH, -C(O)OR<sup>19</sup>,  
-C(O)NHR<sup>20</sup>, -C(O)NH<sub>2</sub>, -C(O)NH<sub>2</sub>-C(O)N(alkyl)<sub>2</sub>, -C(O)N(alkyl)(aryl),  
-C(O)N(alkyl)(heteroaryl), -SR<sup>19</sup>, -S(O)<sub>2</sub>R<sup>20</sup>, -S(O)NH<sub>2</sub>, -S(O)NH(alkyl),  
-S(O)N(alkyl)(alkyl), -S(O)NH(aryl), -S(O)<sub>2</sub>NH<sub>2</sub>, -S(O)<sub>2</sub>NHR<sup>19</sup>,  
10 -S(O)<sub>2</sub>NH(heterocyclyl), -S(O)<sub>2</sub>N(alkyl)<sub>2</sub>, -S(O)<sub>2</sub>N(alkyl)(aryl), -OCF<sub>3</sub>, -OH, -OR<sup>20</sup>,  
-O-heterocyclyl, -O-cycloalkylalkyl, -O-heterocyclylalkyl, -NH<sub>2</sub>, -NHR<sup>20</sup>, -N(alkyl)<sub>2</sub>,  
-N(arylalkyl)<sub>2</sub>, -N(arylalkyl)-(heteroarylalkyl), -NHC(O)R<sup>20</sup>, -NHC(O)NH<sub>2</sub>,  
-NHC(O)NH(alkyl), -NHC(O)N(alkyl)(alkyl), -N(alkyl)C(O)NH(alkyl),  
-N(alkyl)C(O)N(alkyl)(alkyl), -NHS(O)<sub>2</sub>R<sup>20</sup>, -NHS(O)<sub>2</sub>NH(alkyl),  
15 -NHS(O)<sub>2</sub>N(alkyl)(alkyl), -N(alkyl)S(O)<sub>2</sub>NH(alkyl) and -N(alkyl)S(O)<sub>2</sub>N(alkyl)(alkyl);

or, alternately, two R<sup>18</sup> moieties on adjacent carbons can be linked together



R<sup>19</sup> is alkyl, cycloalkyl, aryl, arylalkyl- or heteroarylalkyl-;

- R<sup>20</sup> is alkyl, cycloalkyl, aryl, halo substituted aryl, arylalkyl-, heteroaryl or  
20 heteroarylalkyl-;

- wherein each of the alkyl, cycloalkyl, cycloalkenyl, cycloalkylalkyl,  
heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, alkyaryl-, heteroaryl,  
heteroarylalkyl-, alkenyl and alkynyl groups in R<sup>1</sup>-R<sup>2</sup>, R<sup>2</sup>-R<sup>6</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>,  
R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>14</sup> is independently unsubstituted or optionally substituted by 1  
25 to 5 R<sup>21</sup> groups independently selected from the group consisting of alkyl, alkenyl,  
alkynyl, cycloalkyl, cycloalkylalkyl-, cycloalkenyl, heterocyclyl, heterocyclylalkyl-,  
aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>,  
-C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>),  
-S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>),

- alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>,  
 -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>; -CH<sub>2</sub>-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 5 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> and  
 -S(O)<sub>2</sub>R<sup>15</sup>;

wherein each of the alkyl, cycloalkenyl, cycloalkyl, cycloalkylalkyl-,  
 heterocyclyl, heterocyclylalkyl-, aryl, arylalkyl-, heteroaryl, heteroarylalkyl-, alkenyl  
 and alkynyl groups in R<sup>21</sup> is independently unsubstituted or substituted by 1 to 5 .

- 10 R<sup>22</sup> groups independently selected from the group consisting of alkyl, cycloalkyl,  
 cycloalkenyl, heterocyclyl, aryl, heteroaryl, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>,  
 -C(O)OR<sup>15</sup>, -alkyl-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>),  
 -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>),  
 -alkyl-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 15 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> and  
 -S(O)<sub>2</sub>R<sup>15</sup>.

- 20 5. The compound of claim 1, wherein R<sup>1</sup> is H.
6. The compound of claim 1, wherein R<sup>1</sup> is alkyl.
7. The compound of claim 1, wherein R<sup>1</sup> is methyl.
- 25 8. The compound of claim 1, wherein U is C(R<sup>5</sup>).
9. The compound of claim 1, wherein U is N.
- 30 10. The compound of claim 1, wherein W is a bond.

11. The compound of claim 1, wherein W is -O-.
12. The compound of claim 1, wherein R<sup>2</sup> and R<sup>6</sup> are joined together to  
5 form a cyclohexyl ring.
13. The compound of claim 1, wherein W is -C(O)-.
14. The compound of claim 1, wherein =N-W-G- is =N-C(R<sup>11</sup>R<sup>12</sup>)-C(O)-.  
10
15. The compound of claim 1, wherein W is -C(R<sup>11</sup>)(R<sup>12</sup>)-.
16. The compound of claim 1, wherein:  
(a) U is N, and R<sup>2</sup> and R<sup>6</sup> are joined together to form a pyrrolidinyl  
15 ring including the N of U as the nitrogen of said pyrrolidinyl ring, which is  
unsubstituted; or  
(b) U is N, and R<sup>2</sup> and R<sup>6</sup> are joined together to form a pyrrolidinyl  
ring including the N of U as the nitrogen of said pyrrolidinyl ring, wherein said  
pyrrolidinyl ring is substituted with 1-3 substituents which can be the same or  
20 different, each being independently selected from the group consisting of halo,  
alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups; or  
(c) U is N, and R<sup>2</sup> and R<sup>6</sup> are joined together to form a piperazinyl  
ring including the N of U as a nitrogen of said piperazinyl ring, which is  
unsubstituted; or  
25 (d) U is N, and R<sup>2</sup> and R<sup>6</sup> are joined together to form a piperazinyl  
ring including the N of U as a nitrogen of said piperazinyl ring, wherein said  
piperazinyl ring is substituted with 1-3 substituents which can be the same or  
different, each being independently selected from the group consisting of halo,  
alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups; or

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(e)  $R^2$  and  $R^6$  are joined together to form a morpholinyl ring which is unsubstituted; or

(f)  $R^2$  and  $R^6$  are joined together to form a morpholinyl ring, which is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl,  $-CN$ ,  $-NH_2$ ,  $-NH(alkyl)$ ,  $-N(alkyl)_2$ , hydroxy and alkoxy groups; or

(g)  $R^2$  and  $R^6$  are joined together to form a pyranlyl ring which is unsubstituted; or

(h)  $R^2$  and  $R^6$  are joined together to form a pyranlyl ring, which is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl,  $-CN$ ,  $-NH_2$ ,  $-NH(alkyl)$ ,  $-N(alkyl)_2$ , hydroxy and alkoxy groups; or

(i)  $R^2$  and  $R^6$  are joined together to form a pyrrolidinyl ring which is unsubstituted; or

(j)  $R^2$  and  $R^6$  are joined together to form a pyrrolidinyl ring, which is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl,  $-CN$ ,  $-NH_2$ ,  $-NH(alkyl)$ ,  $-N(alkyl)_2$ , hydroxy and alkoxy groups.

17. The compound of claim 1, wherein:

(a) U is N and  $R^1$  and  $R^2$  are joined together to form a pyrrolidinyl ring, which is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl,  $-CN$ ,  $-NH_2$ ,  $-NH(alkyl)$ ,  $-N(alkyl)_2$ , hydroxy and alkoxy groups; or

(b) U is N and  $R^1$  and  $R^2$  are joined together to form a piperidinyl ring, which is substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl,  $-CN$ ,  $-NH_2$ ,  $-NH(alkyl)$ ,  $-N(alkyl)_2$ , hydroxy and alkoxy groups; or

(c) U is N and  $R^1$  and  $R^2$  are joined together to form a piperazinyl ring, which is substituted with 1-3 substituents which can be the same or different,

each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.

5                   18.    The compound of claim 1, wherein R<sup>7</sup> is 4-fluorophenyl.

                  19.    The compound of claim 1, wherein:  
                          (a) U is N, R<sup>1</sup> and R<sup>2</sup> are joined together to form a pyrrolidiny ring, which ring is unsubstituted or optionally substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups, and R<sup>2</sup> and R<sup>6</sup> are joined together to form a pyrrolidiny ring, which ring is unsubstituted or optionally substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups; or  
10                   (b) U is N, R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidiny ring, which ring is unsubstituted or optionally substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups, and R<sup>2</sup> and R<sup>6</sup> are joined together to form a piperidiny ring, which ring is  
15                   unsubstituted or optionally substituted with 1-3 substituents which can be the same or different, each being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.  
20

                  20.    The compound of claim 1, wherein:  
25                   (a) R<sup>7</sup> is unsubstituted biphenyl; or  
                          (b) R<sup>7</sup> is biphenyl which is substituted with 1-4 substituents which can be the same or different, each substituent being independently selected from the group consisting of halo, alkyl, -CN, -NH<sub>2</sub>, -NH(alkyl), -N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups;  
30                   (c) R<sup>7</sup> is 3-(1,1'-biphenyl)-yl; or



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(d) R<sup>7</sup> is 4-(1,1'-biphenyl)-yl.

21. The compound of claim 1, wherein R<sup>8</sup> is H.
- 5 22. The compound of claim 1, wherein R<sup>8</sup> is alkyl.
23. The compound of claim 1, wherein R<sup>8</sup> is methyl.
24. The compound of claim 1, wherein R<sup>10</sup> is aryl.
- 10 25. The compound of claim 1, wherein R<sup>10</sup> is phenyl.
26. The compound of claim 1, wherein R<sup>10</sup> is heteroaryl.
- 15 27. The compound of claim 1, wherein R<sup>9</sup> is unsubstituted heteroaryl.
28. The compound of claim 1, wherein R<sup>9</sup> is heteroaryl which is substituted with 1-3 substituents which can be the same or different, each substituent being independently selected from the group consisting of halo, alkyl, 20 CN, NH<sub>2</sub>, NH(alkyl), N(alkyl)<sub>2</sub>, hydroxy and alkoxy groups.
29. The compound of claim 1, wherein R<sup>9</sup> is imidazol-1-yl.
30. The compound of claim 1, wherein R<sup>9</sup> is 4-methyl-imidazol-1-yl.
- 25 31. The compound of claim 1, wherein R<sup>9</sup> is 5-chloro-4-methyl-imidazol-1-yl.
32. The compound of claim 1 wherein:
- 30 (a)

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- U is C(R<sup>5</sup>);  
R<sup>1</sup> is H;  
R<sup>2</sup> and R<sup>6</sup> are connected to form a 4-7 membered cycloalkyl ring;  
R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;  
5 R<sup>8</sup> is H;  
R<sup>10</sup> is selected from the group consisting of: 3-methoxy-phenyl and  
3-F-phenyl; and  
R<sup>9</sup> is 4-methyl-imidazolyl-1-yl; or  
(b)  
10 U is C(R<sup>5</sup>) or N;  
R<sup>1</sup> is H;  
R<sup>2</sup> and R<sup>6</sup> are connected to form a 5-8 membered heterocyclyl ring;  
R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;  
R<sup>8</sup> is H;  
15 R<sup>10</sup> is selected from the group consisting of: 3-methoxy-phenyl and  
3-F-phenyl; and  
R<sup>9</sup> is 4-methyl-imidazolyl-1-yl; or  
(c)  
U is C(R<sup>5</sup>) or N;  
20 R<sup>1</sup> and R<sup>2</sup> are connected to form a 5-8 membered heterocyclyl ring;  
R<sup>2</sup> and R<sup>6</sup> are connected to form a 5-8 membered heterocyclyl ring;  
R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;  
R<sup>8</sup> is H;  
R<sup>10</sup> is selected from the group consisting of: 3-methoxy-phenyl and  
25 3-F-phenyl; and  
R<sup>9</sup> is 4-methyl-imidazolyl-1-yl; or  
(d)  
U is C(R<sup>5</sup>);  
R<sup>2</sup> and R<sup>6</sup> are connected to form a 4-7 membered cycloalkyl ring;  
30 R<sup>1</sup> and R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

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$R^8$  is H;

$R^{10}$  is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl; and

$R^9$  is 4-methyl-imidazolyl-1-yl; or

5 (e)

U is C( $R^5$ ) or N;

$R^1$  and  $R^2$  are connected to form a piperidinyl ring;

$R^2$  and  $R^6$  are connected to form a piperidinyl ring;

$R^7$  is 3-(1,1'-biphenyl)-yl;

10  $R^8$  is H;

$R^{10}$  is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl; and

$R^9$  is 4-methyl-imidazolyl-1-yl; or

(f)

15 U is C( $R^5$ ) or N;

$R^1$  and  $R^2$  are connected to form a piperazinyl ring;

$R^2$  and  $R^6$  are connected to form a piperazinyl ring;

$R^7$  is 3-(1,1'-biphenyl)-yl;

$R^8$  is H;

20  $R^{10}$  is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl; and

$R^9$  is 4-methyl-imidazolyl-1-yl; or

(g)

U is C( $R^5$ ) or N;

25  $R^1$  and  $R^2$  are connected to form a piperidinyl ring;

$R^2$  and  $R^6$  are connected to form a piperazinyl ring;

$R^7$  is 3-(1,1'-biphenyl)-yl;

$R^8$  is H;

30  $R^{10}$  is selected from the group consisting of: 3-methoxy-phenyl and 3-F-phenyl; and

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R<sup>9</sup> is 4-methyl-imidazolyl-1-yl; or

(h)

U is N;

R<sup>1</sup> and R<sup>2</sup> are connected to form a piperazinyl ring;

5 R<sup>2</sup> and R<sup>6</sup> are connected to form a piperidnyl ring;

R<sup>7</sup> is 3-(1,1'-biphenyl)-yl;

R<sup>8</sup> is H;

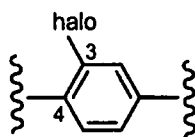
R<sup>10</sup> is selected from the group consisting of: 3-methoxy-phenyl and  
3-F-phenyl; and

10 R<sup>9</sup> is 4-methyl-imidazolyl-1-yl.

33. The compound of claim 1 wherein R<sup>10</sup> is phenyl substituted with 1  
halo.

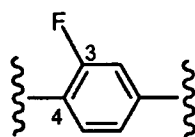
15 34. The compound of claim 1 wherein R<sup>10</sup> is phenyl substituted with 1  
halo, and said halo is F.

35. The compound of claim 1 wherein R<sup>10</sup> is:



20 (wherein the bond from the carbon labeled as 4 is to the R<sup>9</sup> group).

36. The compound of claim 1 wherein R<sup>10</sup> is:



(wherein the bond from the carbon labeled as 4 is to the R<sup>9</sup> group).

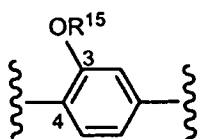
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37. The compound of claim 1 wherein  $R^{10}$  is phenyl substituted with one  $-OR^{15}$  group.

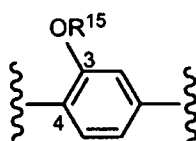
38. The compound of claim 1 wherein  $R^{10}$  is phenyl substituted with one  $-OR^{15}$  group, and said  $R^{15}$  is alkyl.

39. The compound of claim 1 wherein  $R^{10}$  is:



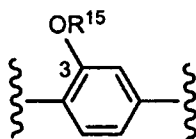
(wherein the bond from the carbon labeled as 4 is to the  $R^9$  group).

40. The compound of claim 1 wherein  $R^{10}$  is:



wherein  $R^{15}$  is alkyl (wherein the bond from the carbon labeled as 4 is to the  $R^9$  group).

41. The compound of claim 1 wherein  $R^{10}$  is:



wherein  $R^{15}$  is methyl (i.e.,  $R^{10}$  is 3-methoxy-phenyl).

42. The compound of claim 1 wherein  $R^9$  is heteroaryl substituted with 1 to 3 independently selected alkyl groups.

43. The compound of claim 1 wherein  $R^9$  is heteroaryl substituted with one is alkyl group.

44. The compound of claim 1 wherein:

(a)  $R^1$  and  $R^2$  are joined together to form a ring optionally substituted with 1 to 5 independently selected  $R^{21}$  substituents, and said ring is fused with an aryl or heteroaryl ring, and said resulting fused ring is optionally substituted with 1 to 5 independently selected  $R^{21}$  substituents; or

(b)  $R^1$  and  $R^2$  are joined together to form a ring substituted with 1 to 5 independently selected  $R^{21}$  substituents, and said ring is fused with an aryl or heteroaryl ring, and said resulting fused ring is optionally substituted with 1 to 5 independently selected  $R^{21}$  substituents; or

(c)  $R^1$  and  $R^2$  are joined together to form a ring optionally substituted with 1 to 5 independently selected  $R^{21}$  substituents; or

(d)  $R^1$  and  $R^2$  are joined together to form a ring; or

(e)  $R^1$  and  $R^2$  are joined together to form a ring, and said ring is fused with an aryl or heteroaryl ring, and said resulting fused ring is optionally substituted with 1 to 5 independently selected  $R^{21}$  substituents.

45. The compound of claim 1 wherein:

(a)  $R^1$  and  $R^2$  are joined together to form a heterocyclyl ring optionally substituted with 1 to 5 independently selected  $R^{21}$  substituents; or

(b)  $R^1$  and  $R^2$  are joined together to form a heterocyclyl ring substituted with 1 to 5 independently selected  $R^{21}$  substituents; or

(c) U is N, and  $R^1$  and  $R^2$  are joined together to form a heterocyclyl ring optionally substituted with 1 to 5 independently selected  $R^{21}$  substituents; or

(d) U is N, and  $R^1$  and  $R^2$  are joined together to form a heterocyclyl ring substituted with 1 to 5 independently selected  $R^{21}$  substituents; or

(e)  $R^1$  and  $R^2$  are joined together to form a heterocyclyl ring; or

(f) U is N, and  $R^1$  and  $R^2$  are joined together to form a heterocyclyl ring.

46. The compound of claim 1 wherein:

(a) R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring optionally substituted with 1 to 5 independently selected R<sup>21</sup> substituents; or

5 (b) R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring substituted with 1 to 5 independently selected R<sup>21</sup> substituents; or

(c) R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring optionally substituted with 1 to 5 independently selected R<sup>21</sup> substituents; or

(d) U is N, and R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring substituted with 1 to 5 independently selected R<sup>21</sup> substituents; or

10 (e) R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring optionally substituted with a =O moiety; or

(f) U is N, and R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring optionally substituted with a =O moiety; or

(g) R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl; or

15 (h) U is N, and R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring; or

(i) R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring substituted with a =O moiety; or

20 (j) U is N, and R<sup>1</sup> and R<sup>2</sup> are joined together to form a piperidinyl ring substituted with a =O moiety.

47. The compound of claim 1 wherein R<sup>2</sup> and R<sup>6</sup> are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents, (b) said heterocyclyl moiety is optionally substituted with 1-5 independently selected R<sup>21</sup> substituents, and (c) said cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected R<sup>21</sup>

30 substituents.

48. The compound of claim 1 wherein:

(a)  $R^1$  and  $R^2$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (1) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (2) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and

(b)  $R^2$  and  $R^6$  are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (1) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (2) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; and

(c) said  $R^2$  and  $R^6$  cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

49. The compound of claim 1 wherein  $R^6$  and either  $R^3$  or  $R^4$  of the  $-C(R^3)(R^4)-G$  moiety, are joined together to form a C4-C8 cycloalkyl, C4-C8 cycloalkenyl, 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (a) said cycloalkyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, (b) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (c) said cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents.

50. The compound of claim 1 wherein:

(a)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-G$  moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (1)



said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (2) said heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

5 (b)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

(c)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a  
10 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein said heterocyclyl moiety is substituted with 1-5 independently selected  $R^{21}$  substituents; or

(d)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety; or

15 (e)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (1) said heterocyclyl moiety is optionally substituted with a =O, and (2) said heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5  
20 independently selected  $R^{21}$  substituents; or

(f)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein said heterocyclyl moiety is optionally substituted with a =O; or

(g)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a  
25 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein said heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

(h)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a  
30 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety;

(i)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein: (1) said heterocyclyl moiety is substituted with a =O, and (2) said heterocyclyl or heterocyclenyl moiety is optionally fused with an aryl or heteroaryl ring, and the  
5 ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents;

(j)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5-8 membered heterocyclyl or 5-8 membered heterocyclenyl moiety, wherein said heterocyclyl moiety is substituted with a =O.

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51. The compound of claim 1 wherein:

(a)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein: (1) said heterocyclyl moiety is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and  
15 (2) said heterocyclyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

(b)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein said heterocyclyl moiety is optionally  
20 substituted with 1-5 independently selected  $R^{21}$  substituents; or

(c)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein: (1) said heterocyclyl moiety is optionally substituted with a =O, and (2) said heterocyclyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion  
25 is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

(d)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein said heterocyclyl moiety is optionally substituted with a =O; or

(e)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a  
30 5 membered heterocyclyl moiety, wherein said heterocyclyl moiety is optionally

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fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

(f)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety; or

5 (g)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein: (1) said heterocyclyl moiety is substituted with a =O, and (2) said heterocyclyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

10 (h)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein said heterocyclyl moiety is substituted with a =O; or

(i)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein: (1) said heterocyclyl moiety is substituted with 1-5 independently selected  $R^{21}$  substituents, and (2) said heterocyclyl moiety is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

15 (j)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 membered heterocyclyl moiety, wherein said heterocyclyl moiety is substituted with 1-5 independently selected  $R^{21}$  substituents.

52. The compound of claim 1 wherein:

25 (a)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a pyrrolidinyl ring, wherein: (1) said pyrrolidinyl ring is optionally substituted with 1-5 independently selected  $R^{21}$  substituents, and (2) said pyrrolidinyl ring is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

(b)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 pyrrolidinyl ring, wherein said pyrrolidinyl ring is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

(c)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 pyrrolidinyl ring, wherein: (1) said pyrrolidinyl ring is optionally substituted with a  $=O$ , and (2) said pyrrolidinyl ring is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

(d)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 10 pyrrolidinyl ring, wherein said pyrrolidinyl ring is optionally substituted with a  $=O$ ; or

(e)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a pyrrolidinyl ring, wherein said pyrrolidinyl ring is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally 15 substituted with 1-5 independently selected  $R^{21}$  substituents; or

(f)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a pyrrolidinyl ring; or

(g)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a pyrrolidinyl ring, wherein: (1) said pyrrolidinyl ring is substituted with a  $=O$ , and (2) 20 said pyrrolidinyl ring is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

(h)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a pyrrolidinyl ring, wherein said pyrrolidinyl ring is substituted with a  $=O$ ; or

(i)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 25 pyrrolidinyl ring, wherein: (1) said pyrrolidinyl ring is substituted with 1-5 independently selected  $R^{21}$  substituents, and (2) said pyrrolidinyl ring is optionally fused with an aryl or heteroaryl ring, and the ring moiety resulting from the fusion is optionally substituted with 1-5 independently selected  $R^{21}$  substituents; or

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(j)  $R^6$  and  $R^{13}$  of the  $-N(R^{13})-$  G moiety, are joined together to form a 5 pyrrolidinyl ring, wherein said pyrrolidinyl ring is substituted with 1-5 independently selected  $R^{21}$  substituents.

5            53.    The compound of claim 1 wherein:

(a)  $R^{10}$  is selected from the group consisting of aryl and aryl substituted with one or more  $R^{21}$  groups, and  $R^9$  is selected from the group consisting of heteroaryl and heteroaryl substituted with one or more  $R^{21}$  groups, and wherein each  $R^{21}$  is independently selected; or

10            (b)  $R^{10}$  is selected from the group consisting of phenyl and phenyl substituted with 1-3 independently selected  $R^{21}$  groups, and  $R^9$  is selected from the group consisting of imidazolyl and imidazolyl substituted with 1-3 independently selected  $R^{21}$  groups; or

15            (c)  $R^{10}$  is phenyl substituted with 1-3 independently selected  $R^{21}$  groups, and  $R^9$  is selected from the group consisting of imidazolyl and imidazolyl substituted with 1-3 independently selected  $R^{21}$  groups; or

20            (d)  $R^{10}$  is selected from the group consisting of heteroaryl and heteroaryl substituted with 1-3  $R^{21}$  groups, and the  $R^9$  group is selected from the group consisting of heteroaryl and heteroaryl substituted with 1-3  $R^{21}$  groups, and wherein each  $R^{21}$  is independently selected; or

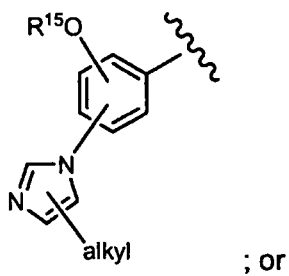
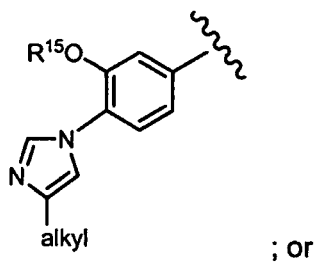
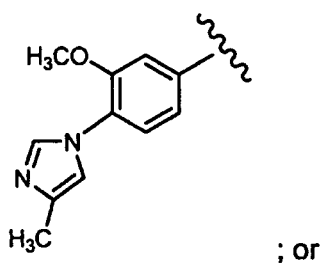
(e)  $R^{10}$  is selected from the group consisting of pyridyl and pyridyl substituted with 1-3  $R^{21}$  groups, and the  $R^9$  group is selected from the group consisting of imidazolyl and imidazolyl substituted with 1-3  $R^{21}$  groups, and wherein each  $R^{21}$  is independently selected; or

25            (f)  $R^{10}$  is pyridyl, and the  $R^9$  group is imidazolyl substituted with 1-3  $R^{21}$  groups, and wherein each  $R^{21}$  is independently selected; or

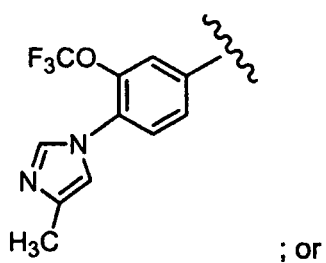
(g) the  $R^9-R^{10}$ - moiety is:

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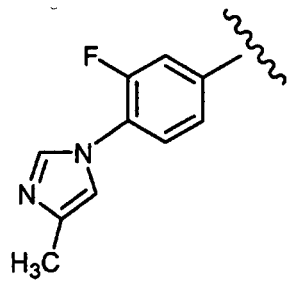
(h)  $R^9-R^{10}$ - moiety is:(i) the  $R^9-R^{10}$ - moiety is:

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(j) the  $R^9-R^{10}$ - moiety is:(k) the  $R^9-R^{10}$ - moiety is:

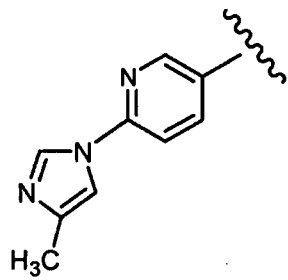
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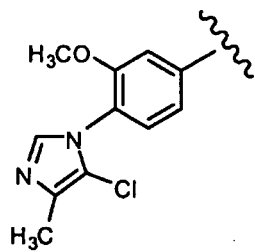
; or

(l) R<sup>9</sup>-R<sup>10</sup>- moiety is:



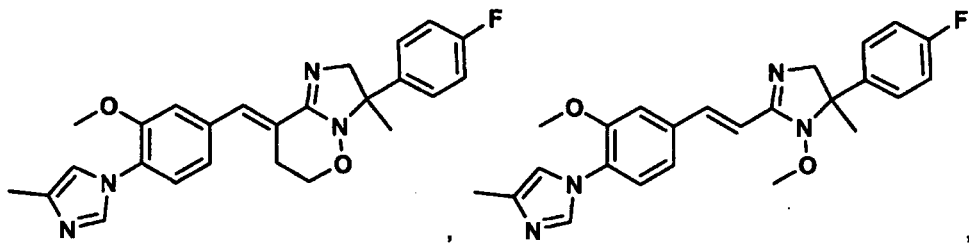
; or

(m) the R<sup>9</sup>-R<sup>10</sup>- moiety is:



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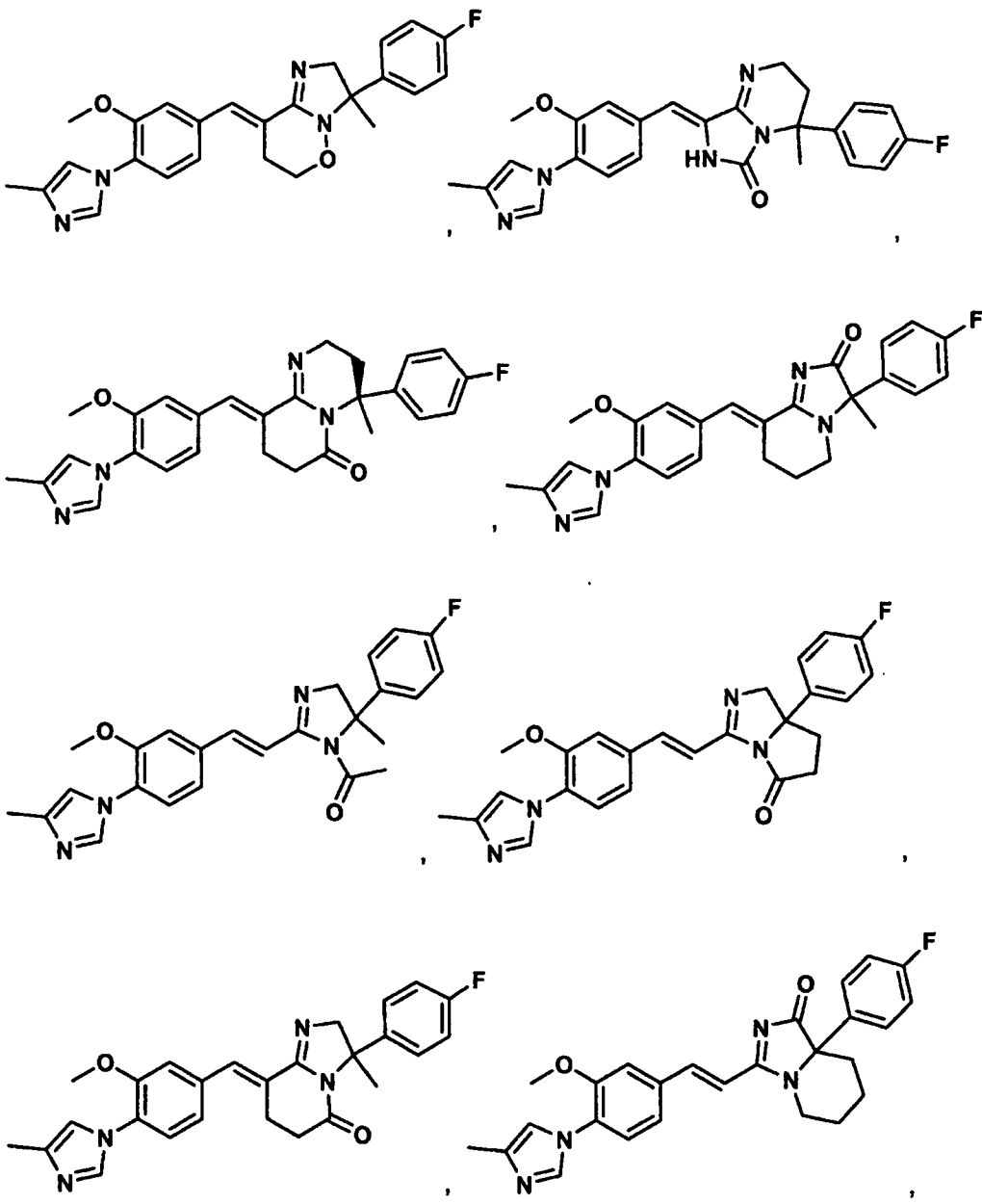
54. A compound of the formula:



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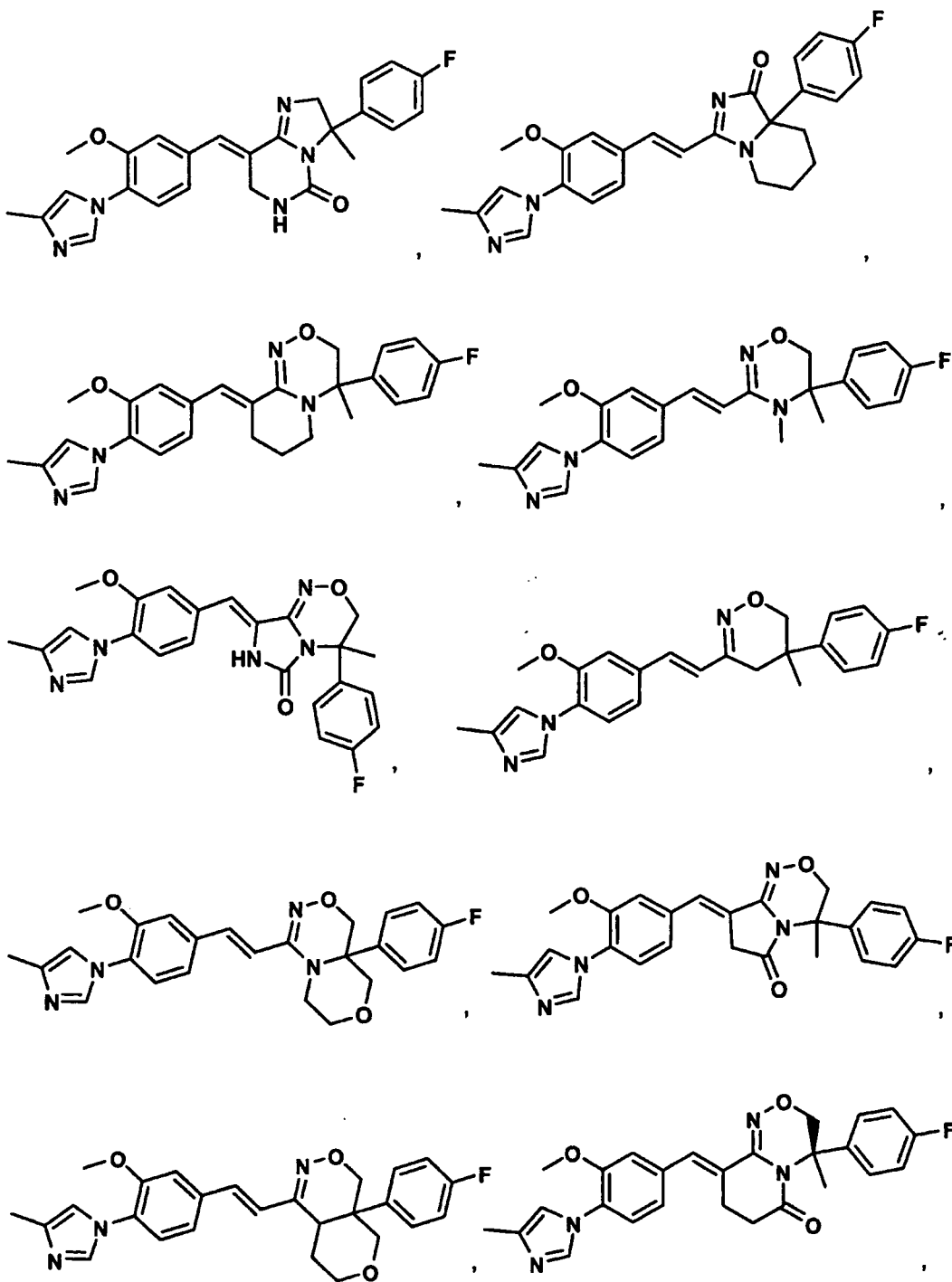
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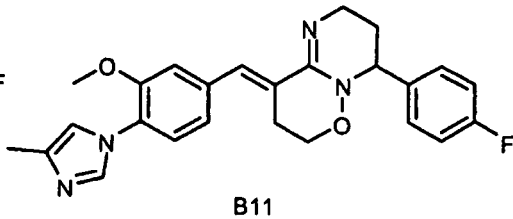
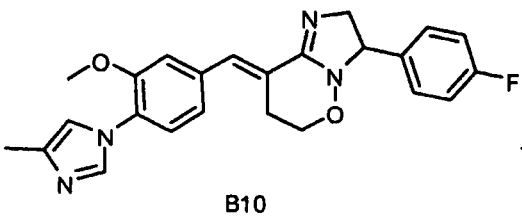
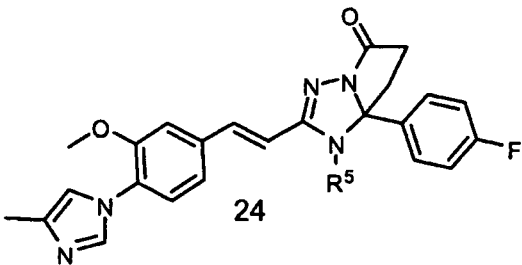
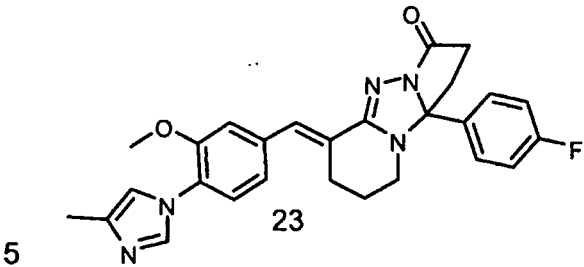
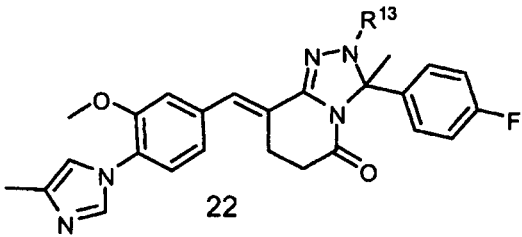
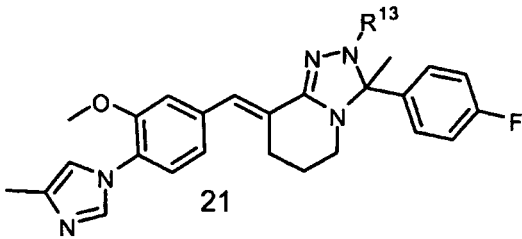


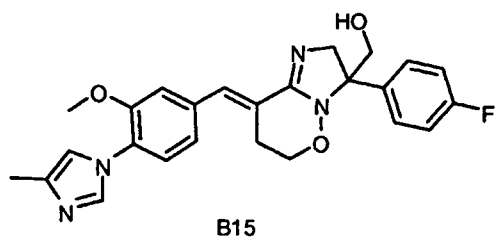
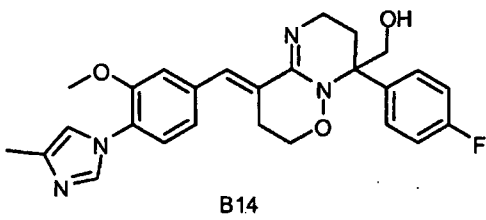
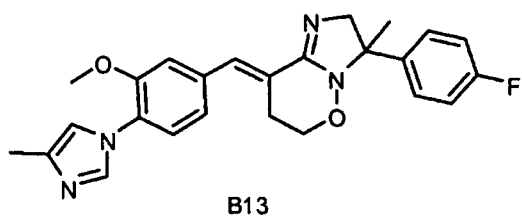
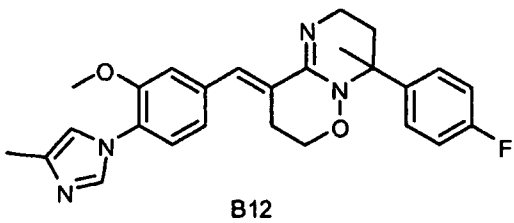
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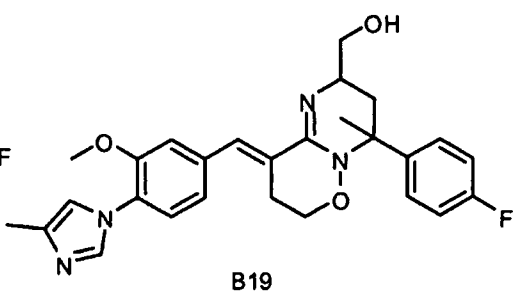
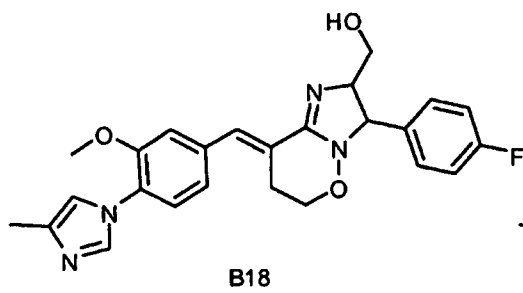
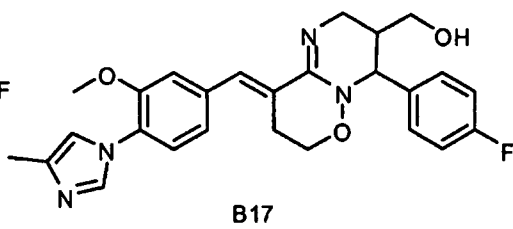
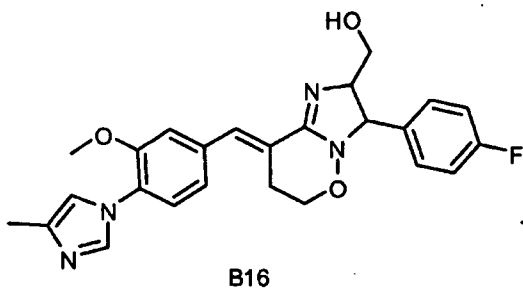
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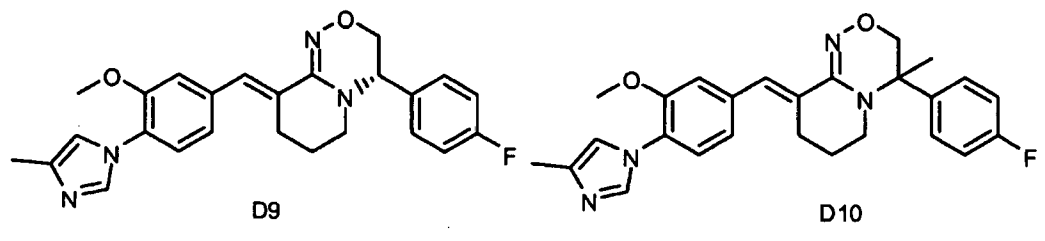
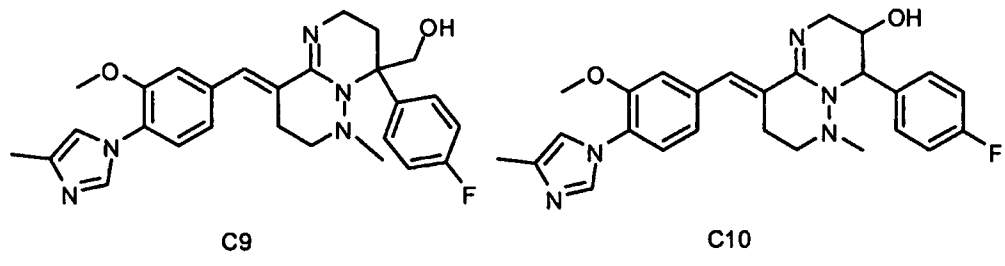
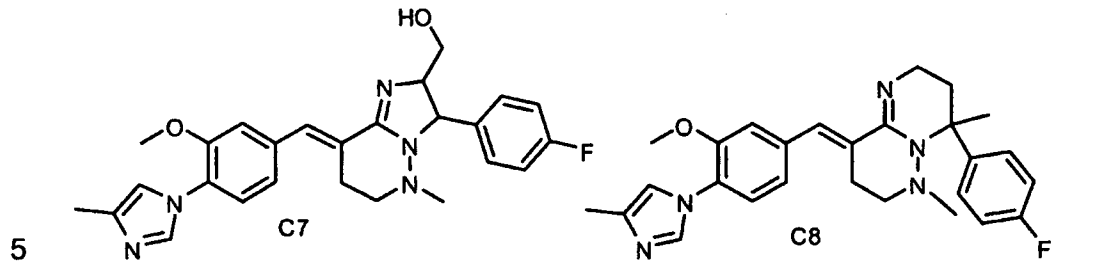
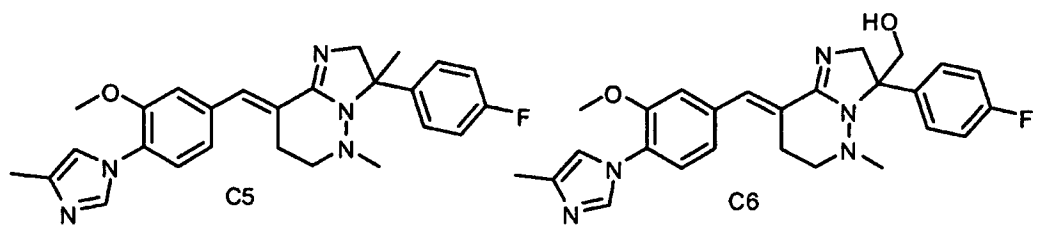
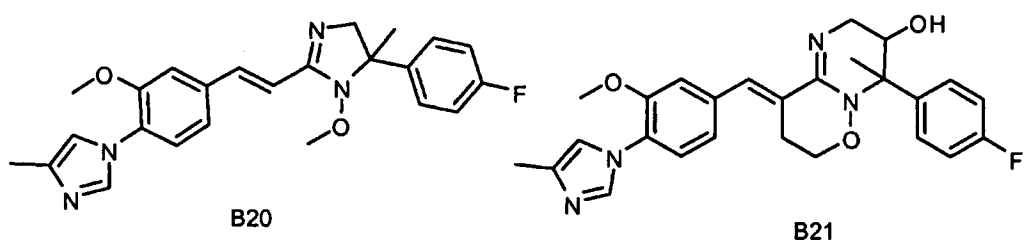


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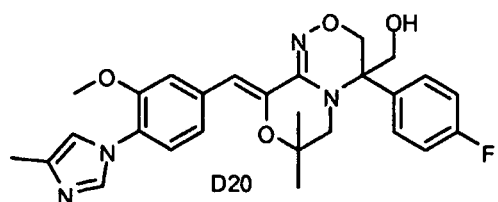
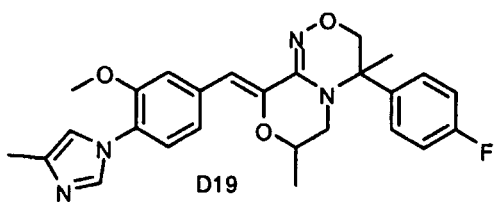
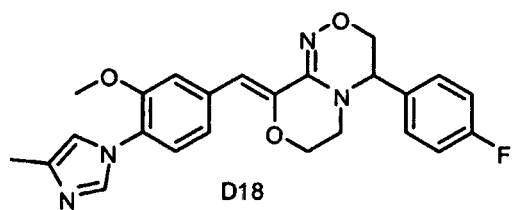
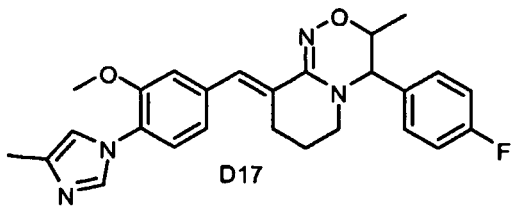
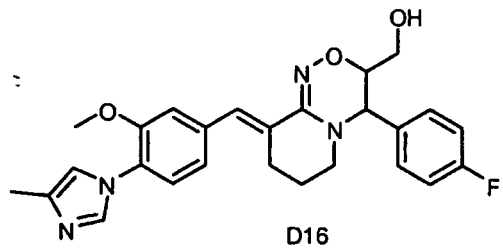
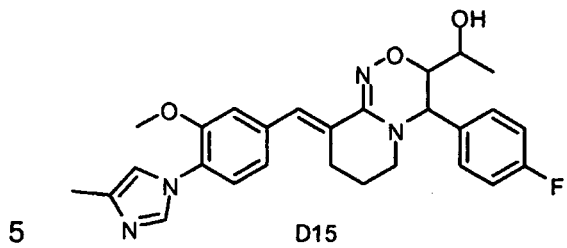
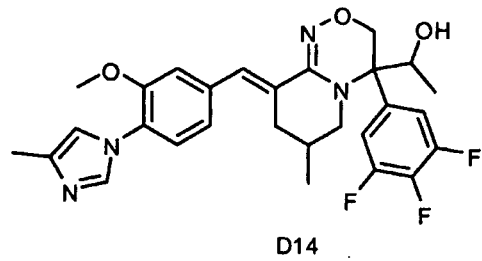
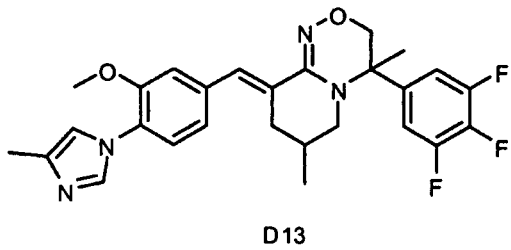
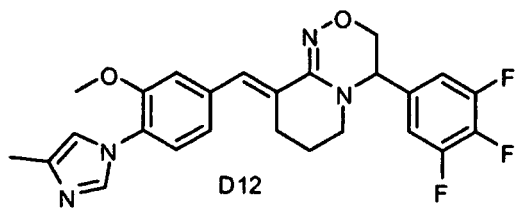
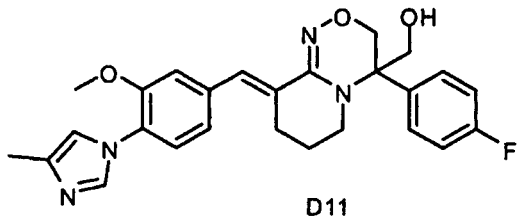


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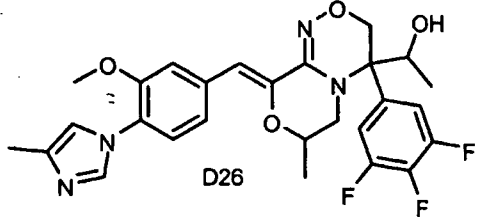
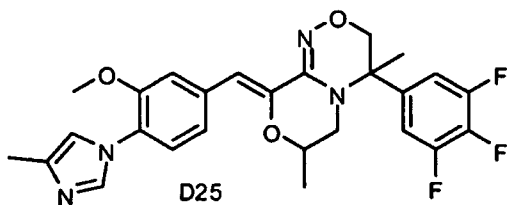
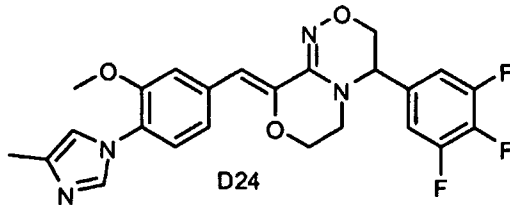
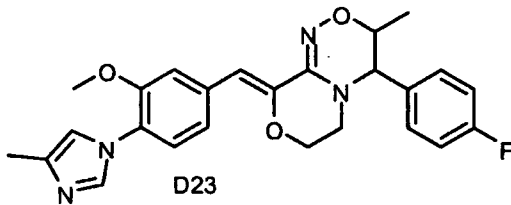
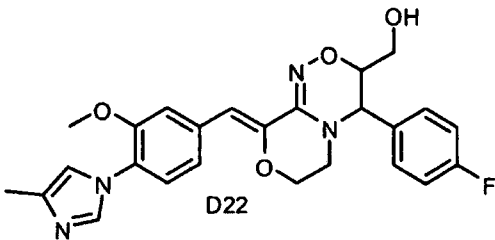
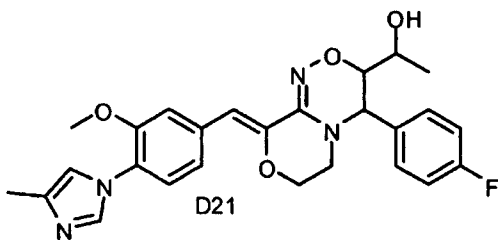


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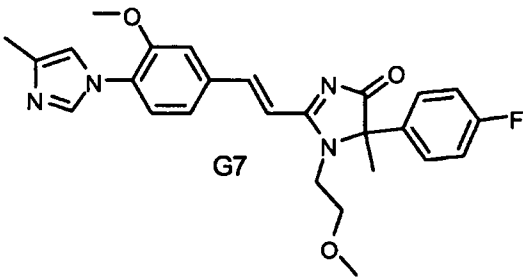
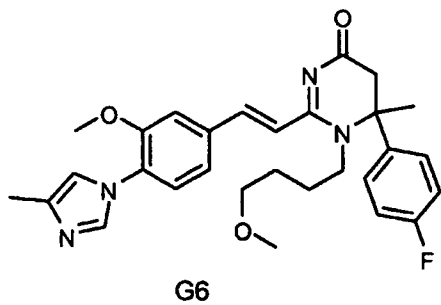
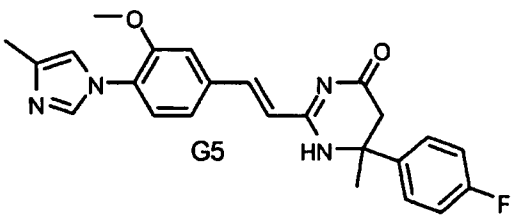
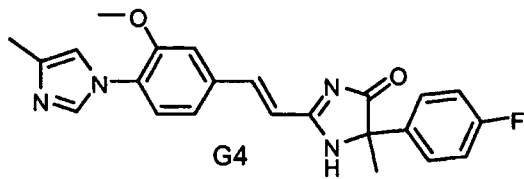


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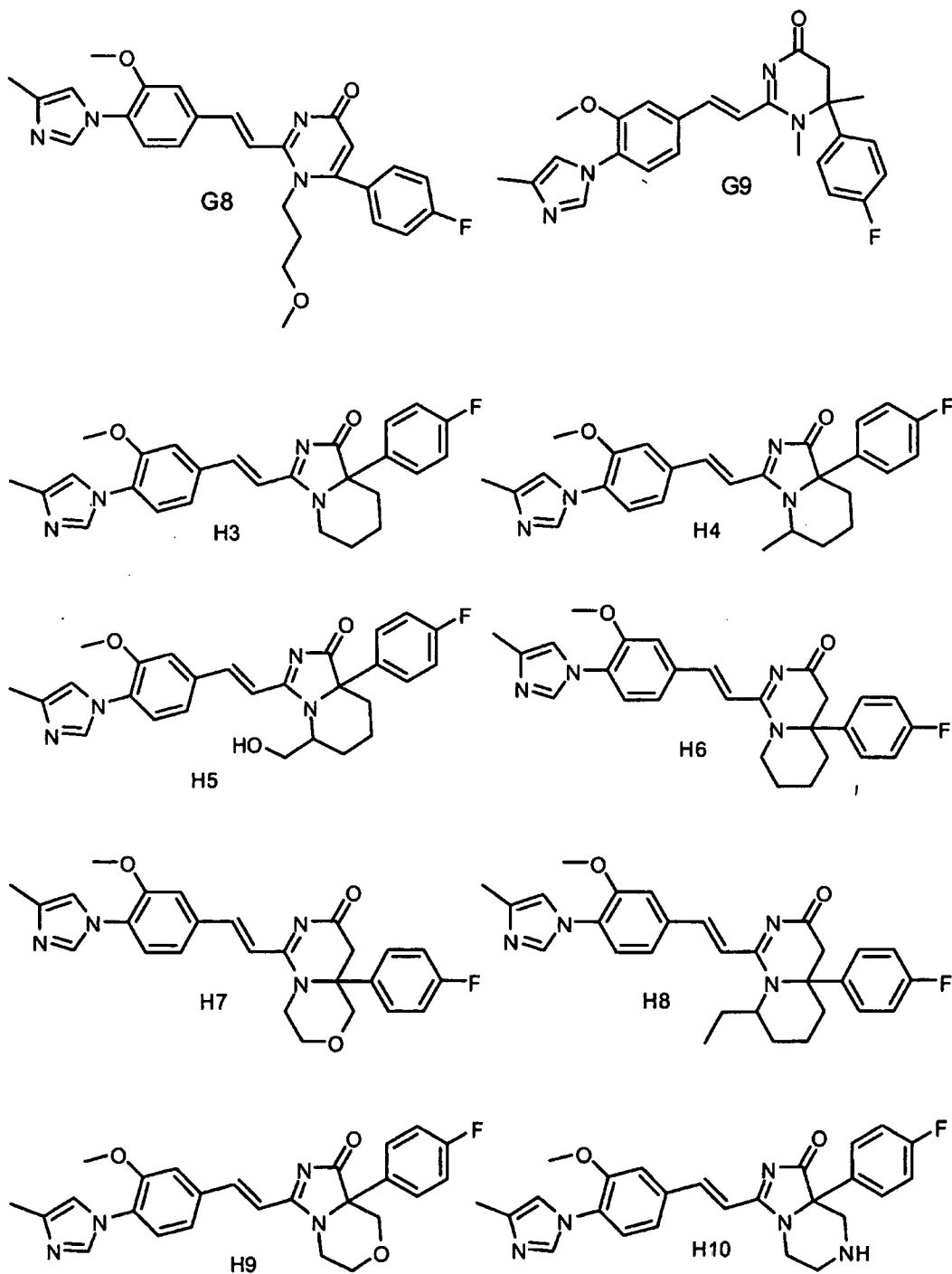
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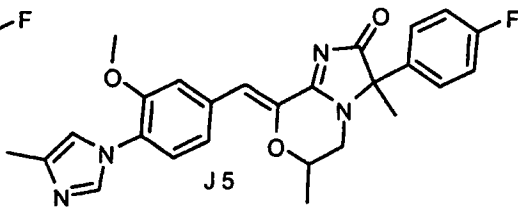
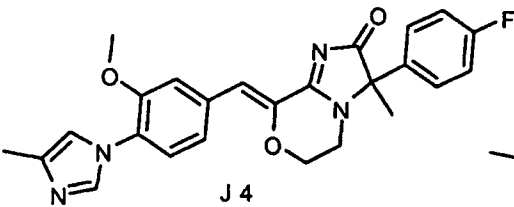
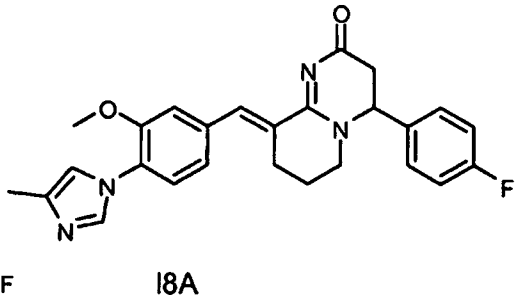
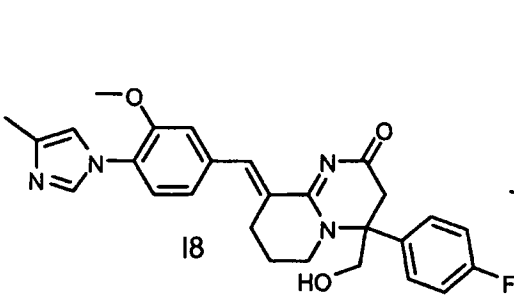
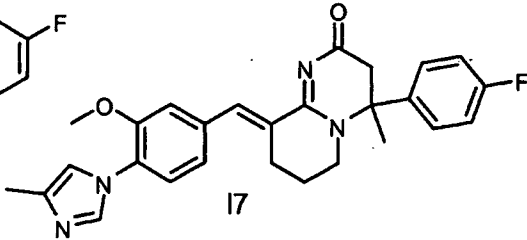
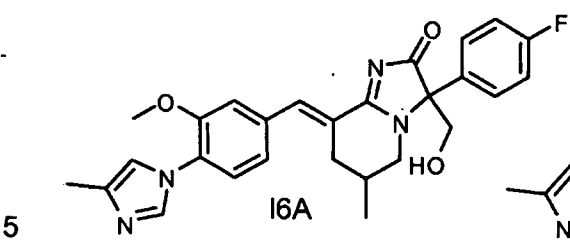
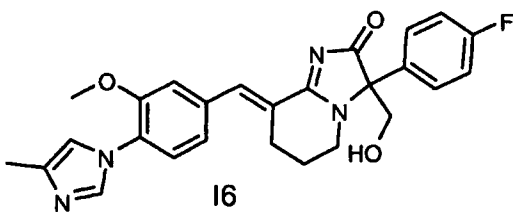
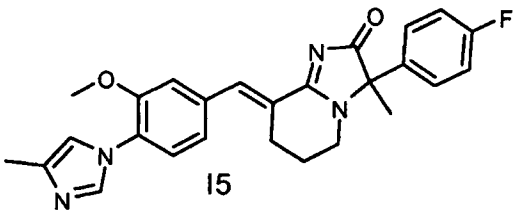
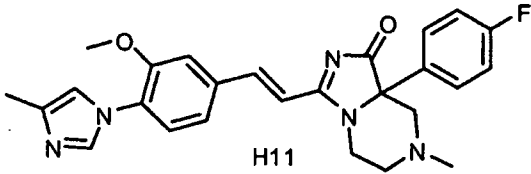


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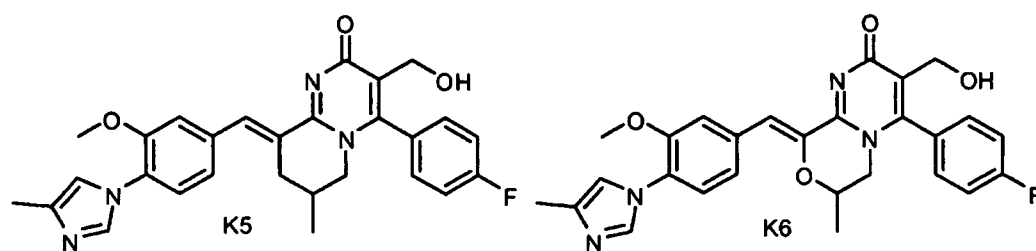
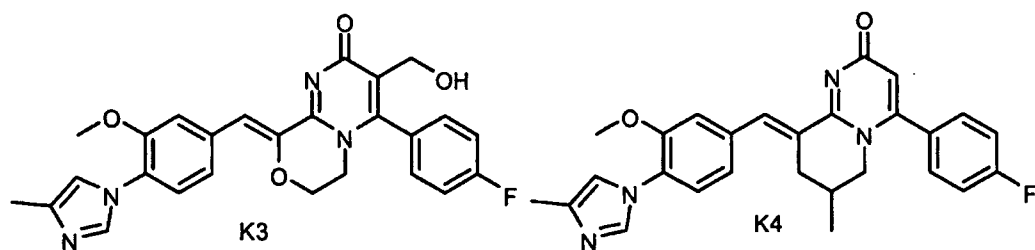
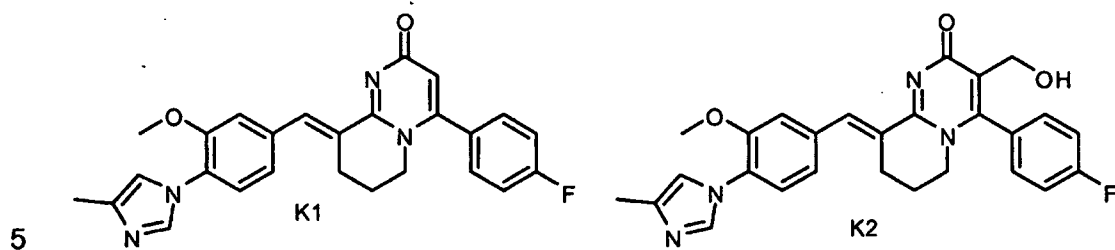
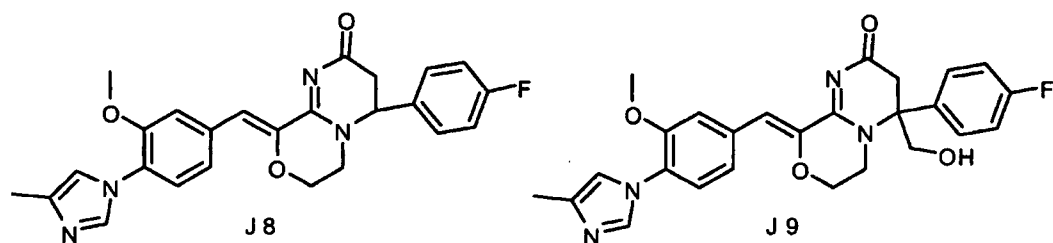
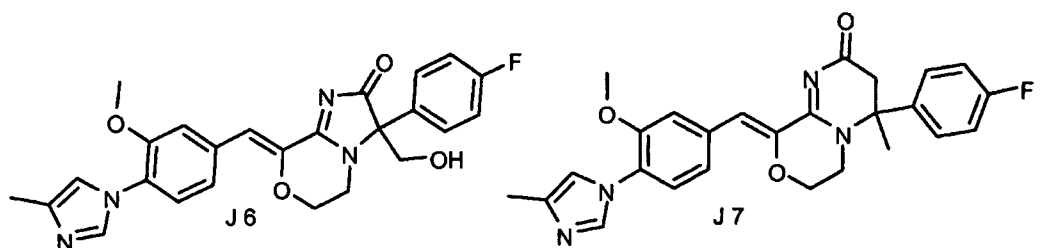


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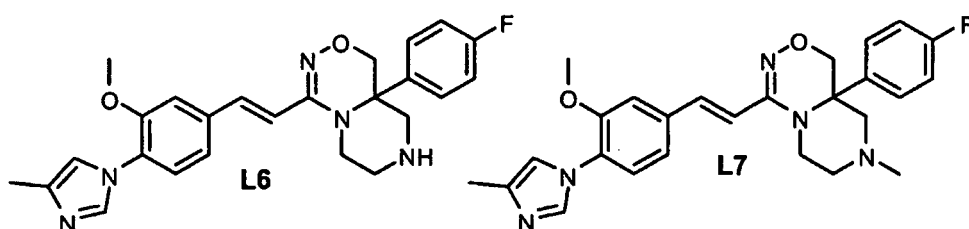
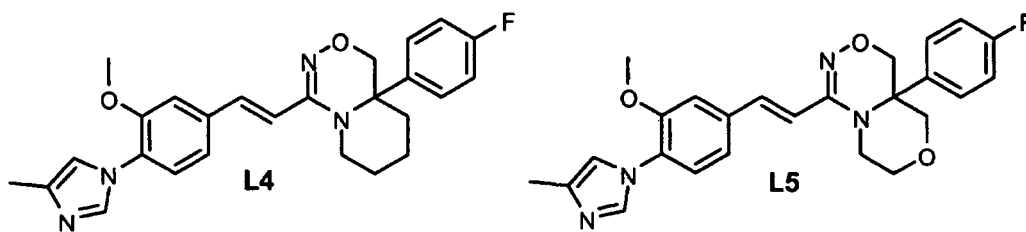
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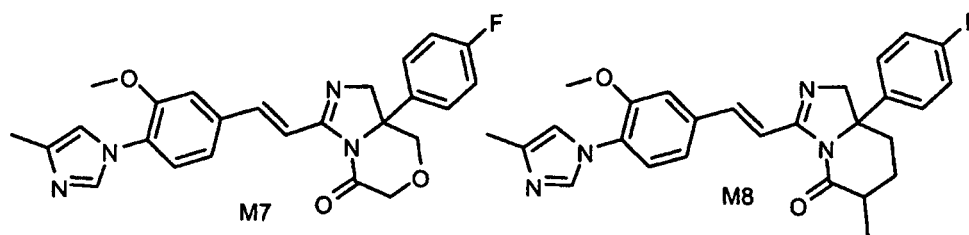
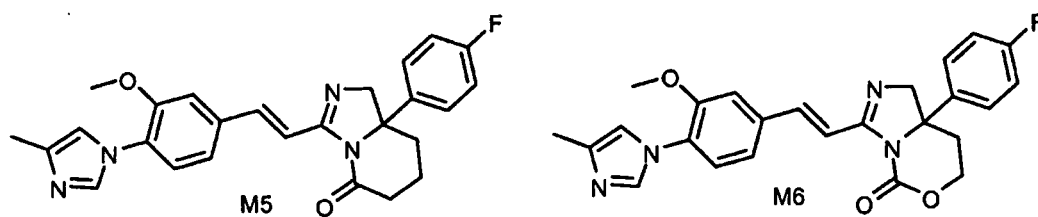
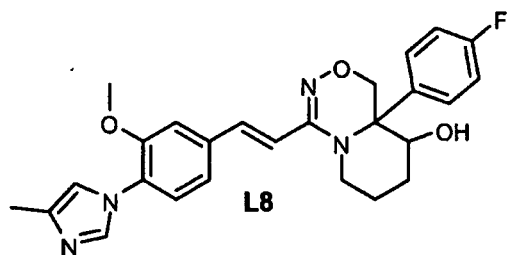


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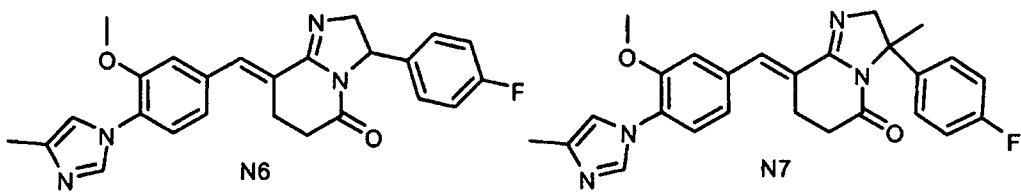
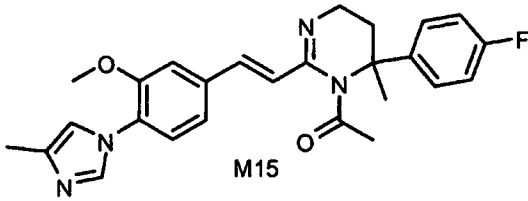
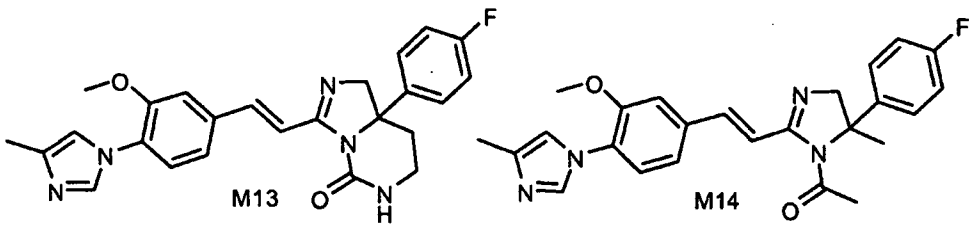
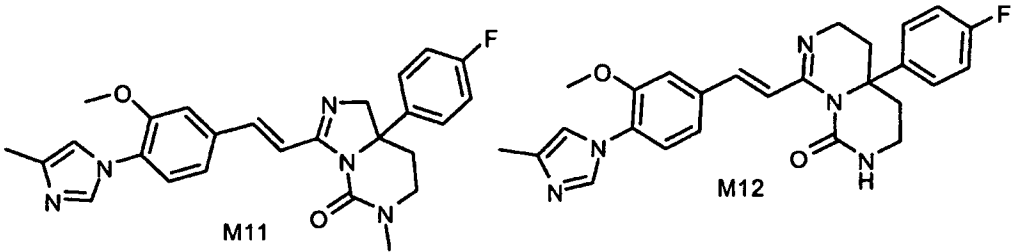
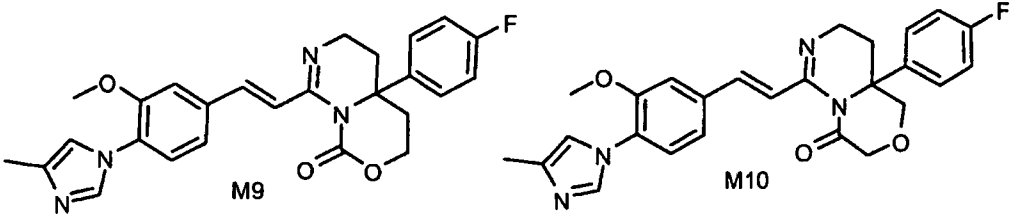


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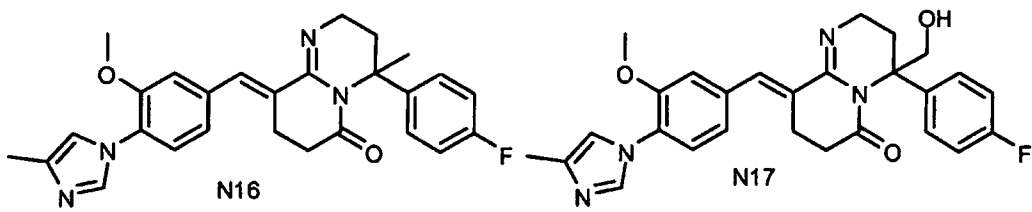
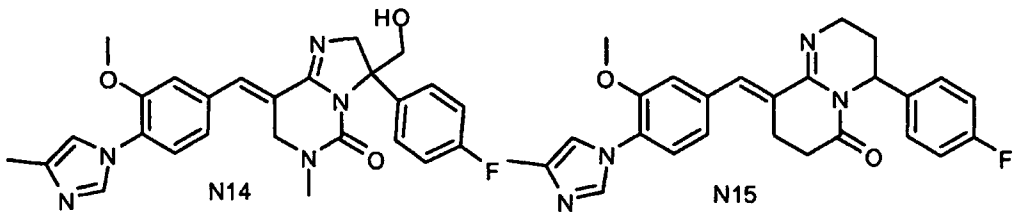
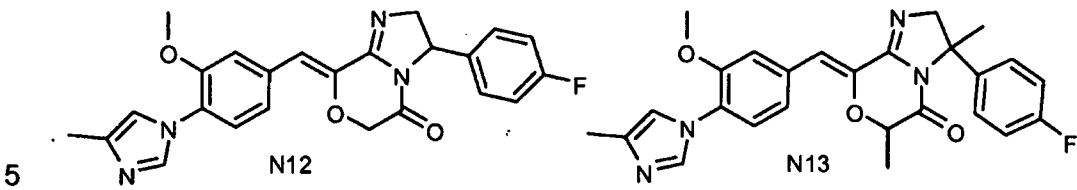
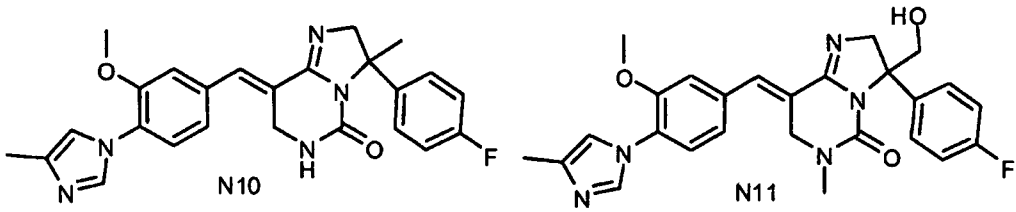
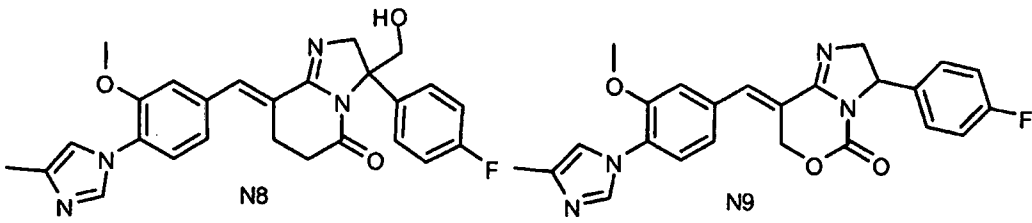


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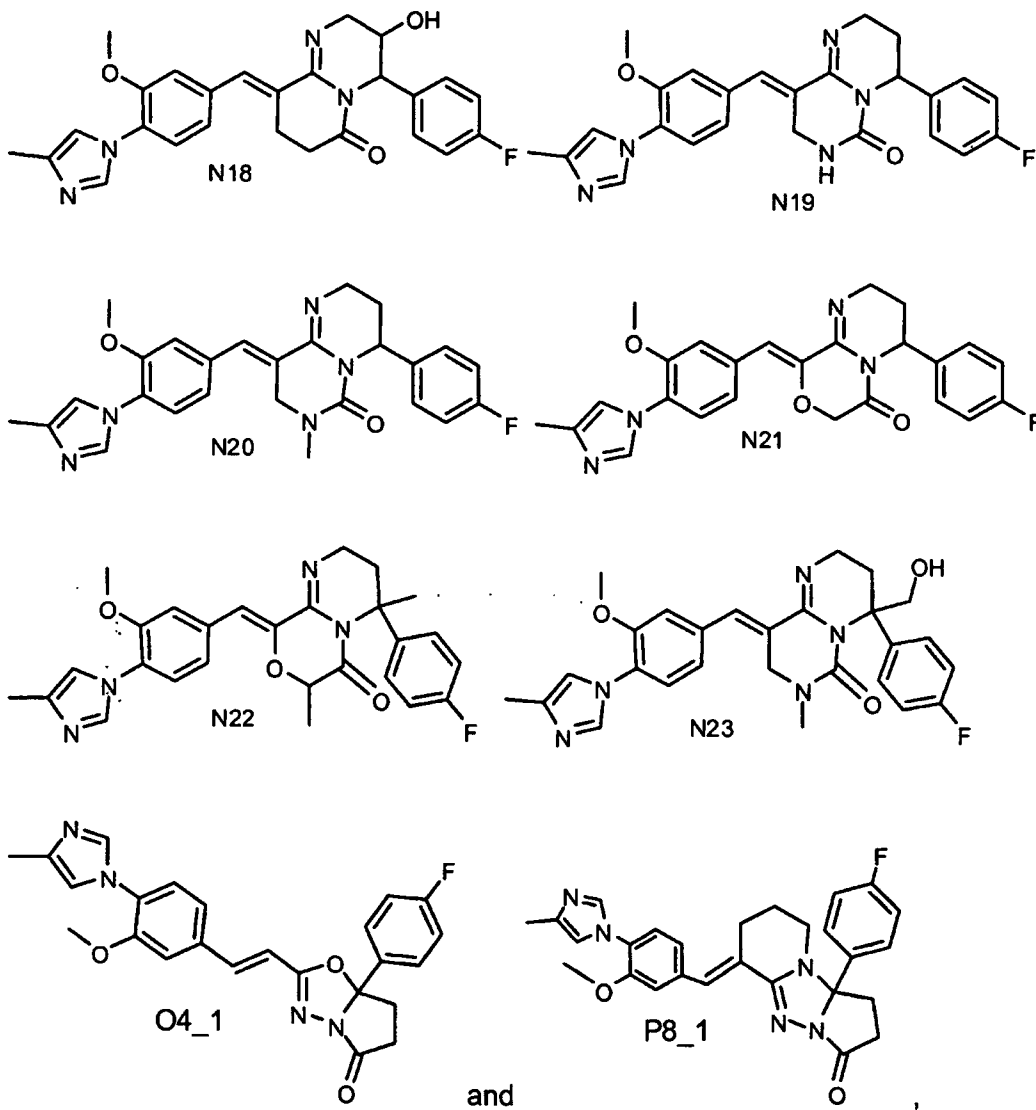
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or a pharmaceutically acceptable salt, solvate, ester or prodrug thereof.

55. The compound of claim 54 wherein said compound is a pharmaceutically acceptable salt of a compound of claim 54.

56. The compound of claim 54 wherein said compound is a solvate of a compound of claim 54.

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57. The compound of claim 54 wherein said compound is an ester of a compound of claim 54.

5 58. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1, and a pharmaceutically acceptable carrier.

59. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 54, and a pharmaceutically acceptable carrier.

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60. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1, and a pharmaceutically acceptable carrier, and an effective amount of one or more other pharmaceutically active drugs selected from the group consisting of: (a) drugs useful for the treatment of  
15 Alzheimer's disease, (b) drugs useful for inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue, (c) drugs useful for treating neurodegenerative diseases, and (d) drugs useful for inhibiting gamma-secretase.

20 61. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 54, and a pharmaceutically acceptable carrier, and an effective amount of one or more other pharmaceutically active drugs selected from the group consisting of: (a) drugs useful for the treatment of  
25 Alzheimer's disease, (b) drugs useful for inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue, (c) drugs useful for treating neurodegenerative diseases, and (d) drugs useful for inhibiting gamma-secretase.

62. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1, and a pharmaceutically acceptable carrier, and an effective amount of one or more BACE inhibitors.

5 63. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 54, and a pharmaceutically acceptable carrier, and an effective amount of one or more BACE inhibitors.

64. A pharmaceutical composition:

- 10 (1) comprising a therapeutically effective amount of at least one compound of claim 1, or a pharmaceutically acceptable salt, solvate, or ester thereof, and at least one pharmaceutically acceptable carrier, or
- (2) comprising a therapeutically effective amount of at least one compound of claim 1, or a pharmaceutically acceptable salt, solvate, or ester  
15 thereof, and at least one pharmaceutically acceptable carrier, and an effective amount of one or more other pharmaceutically active drugs selected from the group consisting of: (a) drugs useful for the treatment of Alzheimer's disease, (b) drugs useful for inhibiting the deposition of amyloid protein (e.g., amyloid beta protein) in, on or around neurological tissue, (c) drugs useful for treating  
20 neurodegenerative diseases, and (d) drugs useful for inhibiting gamma-secretase, or
- (3) comprising a therapeutically effective amount of at least one compound of claim 1, or a pharmaceutically acceptable salt, solvate, or ester thereof, and at least one pharmaceutically acceptable carrier, and an effective  
25 amount of one or more BACE inhibitors,
- (4) comprising a therapeutically effective amount of at least one compound of claim 1, or a pharmaceutically acceptable salt, solvate, or ester thereof, and at least one pharmaceutically acceptable carrier, and effective amount of one or more cholinesterase inhibitors, or

(5) comprising a therapeutically effective amount of at least one compound of claim 1, and at least one pharmaceutically acceptable carrier, and effective amount of one or more cholinesterase inhibitors, or

(6) comprising a therapeutically effective amount of at least one  
5 compound of claim 1, or a pharmaceutically acceptable salt, solvate, or ester thereof, and at least one pharmaceutically acceptable carrier, and effective amount of one or more BACE inhibitors, muscarinic antagonists, cholinesterase inhibitors; gamma secretase inhibitors; gamma secretase modulators; HMG-CoA reductase inhibitors; non-steroidal anti-inflammatory agents; N-methyl-D-aspartate  
10 receptor antagonists; anti-amyloid antibodies; vitamin E; nicotinic acetylcholine receptor agonists; CB1 receptor inverse agonists or CB1 receptor antagonists; an antibiotic; growth hormone secretagogues; histamine H3 antagonists; AMPA agonists; PDE4 inhibitors; GABA<sub>A</sub> inverse agonists; inhibitors of amyloid aggregation; glycogen synthase kinase beta inhibitors; promoters of alpha  
15 secretase activity; PDE-10 inhibitors and cholesterol absorption inhibitors, or

(7) comprising a therapeutically effective amount of at least one compound of claim 1, and at least one pharmaceutically acceptable carrier, and effective amount of one or more BACE inhibitors, muscarinic antagonists, cholinesterase inhibitors; gamma secretase inhibitors; gamma secretase  
20 modulators; HMG-CoA reductase inhibitors; non-steroidal anti-inflammatory agents; N-methyl-D-aspartate receptor antagonists; anti-amyloid antibodies; vitamin E; nicotinic acetylcholine receptor agonists; CB1 receptor inverse agonists or CB1 receptor antagonists; an antibiotic; growth hormone secretagogues; histamine H3 antagonists; AMPA agonists; PDE4 inhibitors; GABA<sub>A</sub> inverse  
25 agonists; inhibitors of amyloid aggregation; glycogen synthase kinase beta inhibitors; promoters of alpha secretase activity; PDE-10 inhibitors and cholesterol absorption inhibitors, or

(8) comprising a therapeutically effective amount of at least one compound of claim 1, or a pharmaceutically acceptable salt, solvate, or ester



thereof, and at least one pharmaceutically acceptable carrier, and an effective amount of donepezil hydrochloride, or

- (9) comprising a therapeutically effective amount of at least one compound of claim 1, and at least one pharmaceutically acceptable carrier, and  
5 an effective amount of donepezil hydrochloride.

65. A method of modulating gamma-secretase comprising administering an effective amount of one or more compounds of claim 1 to a patient in need of such treatment.

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66. A method of treating one or more neurodegenerative diseases, comprising administering an effective amount of one or more compounds of claim 1 to a patient in need of treatment.

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67. A method of inhibiting the deposition of amyloid protein in, on or around neurological tissue, comprising administering an effective amount of one or more compounds of claim 1 to a patient in need of treatment.

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68. A method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1 to a patient in need of treatment.

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69. A method of treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 54 to a patient in need of treatment.

70. A method of treating Alzheimer's disease, comprising administering an effective amount of a compound of claim 1 to a patient in need of treatment.

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71. A method of treating Alzheimer's disease, comprising administering an effective amount of a compound of claim 54 to a patient in need of treatment.

72. A method of (a) modulating gamma-secretase, (b) treating one or more neurodegenerative diseases, (c) inhibiting the deposition of amyloid protein in, on or around neurological tissue, or (d) treating Alzheimer's disease, comprising administering administering:

- (1) an effective amount of a compound of claim 1, and
  - (2) an effective amount of one or more other pharmaceutically active ingredients selected from the group consisting of: BACE inhibitors, muscarinic antagonists, cholinesterase inhibitors; gamma secretase inhibitors; gamma secretase modulators; HMG-CoA reductase inhibitors; non-steroidal anti-inflammatory agents; N-methyl-D-aspartate receptor antagonists; anti-amyloid antibodies; vitamin E; nicotinic acetylcholine receptor agonists; CB1 receptor inverse agonists or CB1 receptor antagonists; an antibiotic; growth hormone secretagogues; histamine H3 antagonists; AMPA agonists; PDE4 inhibitors; GABA<sub>A</sub> inverse agonists; inhibitors of amyloid aggregation; glycogen synthase kinase beta inhibitors; promoters of alpha secretase activity; PDE-10 inhibitors and cholesterol absorption inhibitors,
- to a patient in need of such treatment.

73. A method of treating Alzheimer's disease, comprising administering an effective amount of a compound of claim 1, and an effective amount of one or more compounds selected from the group consisting of A $\beta$  antibody inhibitors, gamma secretase inhibitors and beta secretase inhibitors, to a patient in need of such treatment.

74. A method of treating Alzheimer's disease, comprising administering an effective amount of a compound of claim 1, and an effective amount of one or more BACE inhibitors, to a patient in need of such treatment.

5 75. A method of:

(1) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more cholinesterase, to a patient in need of treatment, or

10 (2) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of donepezil hydrochloride, to a patient in need of treatment, or

(3) treating Alzheimer's disease, comprising administering an effective amount of a compound claim 1, in combination with an effective amount of one or more cholinesterase, to a patient in need of treatment, or

(4) treating Alzheimer's disease, comprising administering an effective amount of a compound of claim 1, in combination with an effective amount of donepezil hydrochloride, to a patient in need of treatment, or

20 (5) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of (rivastigmine, to a patient in need of such treatment, or

(6) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of tacrine, to a patient in need of such treatment, or

25 (7) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of a Tau kinase inhibitor, to a patient in need of such treatment, or

30 (8) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an

effective amount of one or more Tau kinase inhibitors selected from the group consisting of: GSK3beta inhibitors, cdk5 inhibitors, ERK inhibitors, to a patient in need of such treatment, or

5 (9) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one anti-Abeta vaccination, to a patient in need of such treatment, or

10 (10) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more APP ligands, to a patient in need of such treatment, or

15 (11) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more agents that upregulate insulin degrading enzyme and/or neprilysin, to a patient in need of such treatment, or

(12) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more cholesterol lowering agents, to a patient in need of such treatment, or

20 (13) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more cholesterol lowering agents selected from the group consisting of: Atorvastatin, Fluvastatin, Lovastatin, Mevastatin, Pitavastatin, Pravastatin, Rosuvastatin, Simvastatin, and Ezetimibe, to a patient in need of  
25 such treatment, or

(14) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more fibrates, to a patient in need of such treatment, or

30 (15) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an

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effective amount of one or more fibrates selected from the group consisting of, clofibrate, Clofibrade, Etofibrate, Aluminium Clofibrate, to a patient in need of such treatment, or

5 (16) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more LXR agonists, to a patient in need of such treatment, or

10 (17) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more LRP mimics, to a patient in need of such treatment, or

15 (18) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more 5-HT6 receptor antagonists, to a patient in need of such treatment, or

(19) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more nicotinic receptor agonists, to a patient in need of such treatment, or

20 (20) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more H3 receptor antagonists, to a patient in need of such treatment, or

25 (21) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more histone deacetylase inhibitors, to a patient in need of such treatment, or

(22) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an

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effective amount of one or more hsp90 inhibitors, to a patient in need of such treatment, or

(23) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more m1 muscarinic receptor agonists, to a patient in need of such treatment, or

(24) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more 5-HT6 receptor antagonists mGluR1 or mGluR5 positive allosteric modulators or agonists, to a patient in need of such treatment, or

(25) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more mGluR2/3 antagonists, to a patient in need of such treatment, or

(26) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of formula I, in combination with an effective amount of one or more anti-inflammatory agents that can reduce neuroinflammation, to a patient in need of such treatment, or

(27) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more Prostaglandin EP2 receptor antagonists, to a patient in need of such treatment, or

(28) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more PAI-1 inhibitors, to a patient in need of such treatment, or

(29) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an

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effective amount of one or more agents that can induce Abeta efflux, to a patient in need of such treatment, or

(30) treating Alzheimer's disease, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of gelsolin, to a patient in need of such treatment, or

(31) treating Downs syndrome, comprising administering an effective amount of one or more compounds of claim 1 to a patient in need of treatment, or

(32) treating Downs syndrome, comprising administering an effective amount of a compound of claim 1 to a patient in need of treatment, or

(33) treating Downs syndrome, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of one or more cholinesterase inhibitors, to a patient in need of treatment.

(34) treating Downs syndrome, comprising administering an effective amount of one or more compounds of claim 1, in combination with an effective amount of donepezil hydrochloride, to a patient in need of treatment, or

(35) treating Downs syndrome, comprising administering an effective amount of a compound of claim 1, in combination with an effective amount of one or more cholinesterase inhibitors, to a patient in need of treatment.

(37) treating Downs syndrome, comprising administering an effective amount of a compound of claim 1, in combination with an effective amount of donepezil hydrochloride, to a patient in need of treatment, or

(38) treating mild cognitive impairment, comprising administering an effective amount of one or more compounds of claim 1 to a patient in need of treatment, or

(39) treating glaucoma, comprising administering an effective amount of one or more compounds of claim 1 to a patient in need of treatment, or

(40) treating cerebral amyloid angiopathy, comprising administering an effective amount of one or more compounds of claim 1 to a patient in need of treatment, or

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(41) treating stroke, comprising administering an effective amount of one or more compounds of claim 1 to a patient in need of treatment, or

(42) This invention also provides a method of treating dementia, comprising administering an effective amount of one or more compounds of claim 1 to a patient in need of treatment, or

(43) treating microgliosis, comprising administering an effective amount of one or more compounds of claim 1 to a patient in need of treatment, or

(44) treating brain inflammation, comprising administering an effective amount of one or more compounds of claim 1 to a patient in need of treatment, or

(45) treating olfactory function loss, comprising administering an effective amount of one or more compounds of claim 1 to a patient in need of treatment.

76. A kit comprising, in separate containers, in a single package, pharmaceutical compositions for use in combination, wherein one container comprises an effective amount of a compound of claim 1 in a pharmaceutically acceptable carrier, and another container comprises an effective amount of another pharmaceutically active ingredient, the combined quantities of the compound of claim 1 and the other pharmaceutically active ingredient being effective to: (a) treat Alzheimer's disease, or (b) inhibit the deposition of amyloid protein in, on or around neurological tissue, or (c) treat neurodegenerative diseases, or (d) modulate the activity of gamma-secretase.



## **MODULADORES DE LA GAMMA SECRETASA**

### **Referencia con Solicitud Relacionada**

Esta solicitud reivindica el beneficio de la Solicitud Provisional de EE UU No. 60/941405 presentada el 1 de junio de 2007, y de la Solicitud Provisional de EE UU No. 60/984484 presentada el 1 de noviembre de 2007.

### **Campo de la invención**

La presente invención se refiere a ciertos compuestos heterocíclicos útiles como moduladores de la gamma secretasa (incluyendo inhibidores, antagonistas y similares), composiciones farmacéuticas que contienen los compuestos, y métodos de tratamiento usando los compuestos y composiciones para tratar varias enfermedades incluyendo trastornos del sistema nervioso central tales como, por ejemplo, varias enfermedades neurodegenerativas tales como enfermedad de Alzheimer y otras varias enfermedades relacionadas con la deposición de la proteína amiloide. Son especialmente útiles para reducir la producción beta Amiloide (denominada de aquí en adelante A $\beta$ ) que es efectiva en el tratamiento de varias enfermedades causadas por A $\beta$  tales como, por ejemplo, la enfermedad de Alzheimer y el Síndrome de Down.

### **Antecedentes de la invención**

La enfermedad de Alzheimer es una enfermedad caracterizada por degeneración y pérdida de las neuronas y también por la formación de placas seniles y cambio neurofibrilar. Actualmente, el tratamiento de la enfermedad de Alzheimer está limitado a terapias sintomáticas con un agente que mejora los síntomas representado por un inhibidor de la acetilcolinesterasa, y el remedio básico que previene el progreso de la enfermedad no se ha desarrollado. Es necesario desarrollar un método para controlar la causa del inicio de los estados patológicos para la creación del remedio básico de la enfermedad de Alzheimer.

La proteína A $\beta$ , que es un metabolito de la proteína precursora amiloide (de aquí en adelante se menciona como APP por sus siglas en inglés), se considera muy involucrada en la degeneración y pérdida de las neuronas como así también en el comienzo de enfermedades demenciales (por ejemplo, ver Klein W L, et al *Proceeding National Academy of Science USA*, Sep. 2, 2003, 100(18), p. 10417-22, sugieren una base molecular para la pérdida de memoria reversible.

Nitsch R M, y 16 otros, *Antibodies against  $\beta$ -amyloid slow cognitive decline in Alzheimer's disease*, *Neuron*, May 22, 2003, 38(4), p. 547-554) sugieren que los principales componentes de la proteína A $\beta$  son A $\beta$ 40 que consiste en 40 aminoácidos y A $\beta$ 42 que tiene dos aminoácidos adicionales en el extremo terminal C. Las A $\beta$ 40 y A $\beta$ 42 tienden a agregarse (por ejemplo, ver Jarrell J T et al, *The carboxy terminus of the  $\beta$  amyloid protein is critical for the seeding of amyloid formation: implications for the pathogenesis of Alzheimer's disease*, *Biochemistry*, May 11, 1993, 32(18), p. 4693-4697) y constituyen los componentes principales de placas seniles (por ejemplo, (Glenner GG, et al, *Alzheimer's disease: initial report of the purification and characterization of a novel cerebrovascular amyloid protein*, *Biochemical and Biophysical Research Communications*, May 16, 1984, 120(3), p. 885-90. Ver, además, Masters C L, et al, *Amyloid plaque core protein in Alzheimer disease and Down syndrome*, *Proceeding National Academy of Science USA*, June 1985, 82(12), p. 4245-4249.).

Además, se sabe que las mutaciones de APP y genes de presenelina, que se observan en la enfermedad de Alzheimer familiar, aumentan la producción de A $\beta$ 40 y A $\beta$ 42 (por ejemplo, ver Gouras G K, et al, *Intraneuronal A $\beta$ 142 accumulation in human brain*, *American Journal of Pathology*, January 2000, 156(1), p. 15-20. También, ver Scheuner D, et al, *Nature Medicine*, August



1996, 2(8), p. 864-870; y Forman M S, et al, *Differential effects of the Swedish mutant amyloid precursor protein on  $\beta$ -amyloid accumulation and secretion in neurons and nonneuronal cells*, Journal of Biological Chemistry, Dec. 19, 1997, 272(51), p. 32247-32253.). Por consiguiente, se esperan compuestos que reduzcan la producción de A $\beta$ 40 y A $\beta$ 42 como agente para controlar el progreso de la enfermedad de Alzheimer o para la prevención de la enfermedad.

Estas A $\beta$ s se producen cuando se separa la APP por la beta secretasa y posteriormente se adhiere por la gamma secretasa. Como consideración de este hecho, la creación de inhibidores de  $\gamma$  secretasa y  $\beta$  secretasa se ha intentado con la finalidad de reducir la producción de A $\beta$ s. Muchos de estos inhibidores de secretasa son ya péptidos o peptidomiméticos conocidos tales como L-685,458. L-685,458, un imitador antiguo de transición de la aspartil proteasa, es un potente inhibidor de la actividad de  $\gamma$ -secretasa precursora de la proteína  $\beta$  amiloide, Biochemistry, Aug. 1, 2000, 39(30), p. 8698-8704).

Son de interés también en conexión con la presente invención: US 2007/0117798 (Eisai, publicada el 24 de mayo de 2007); US 2007/0117839 (Eisai, publicada el 24 de mayo de 2007); US 2006/0004013 (Eisai, publicada el 5 de enero de 2006); WO 2005/110422 (Boehringer Ingelheim, publicada el 24 de noviembre de 2005); WO 2006/045554 (Cellzone AG, publicada el 4 de mayo de 2006); WO 2004/110350 (Neurogenetics, publicada el 23 de diciembre de 2004); WO 2004/071431 (Myriad Genetics, publicada el 26 de agosto de 2004); US 2005/0042284 (Myriad Genetics, publicada el 23 de febrero de 2005) y WO 2006/001877 (Myriad Genetics, publicada el 5 de enero de 2006).

Existe la necesidad de nuevos compuestos, formulaciones, tratamientos y terapias para tratar enfermedades y trastornos asociados con A $\beta$ . Es, por consiguiente, un objetivo de esta invención proveer compuestos útiles en el

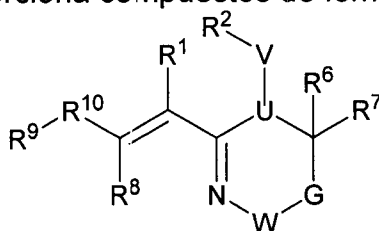
tratamiento o la prevención o el mejoramiento de dichas varias enfermedades y trastornos.

### Síntesis de la invención

En sus muchas realizaciones, la presente invención proporciona una novedosa clase de compuestos heterocíclicos como moduladores de la gamma secretasa (incluyendo inhibidores, antagonistas y similares), métodos para la preparación de dichos compuestos, composiciones farmacéuticas que comprenden uno o más de dichos compuestos, métodos para la preparación de formulaciones farmacéuticas que comprenden uno o más de dichos compuestos, y métodos de tratamiento, prevención, inhibición o mejoramiento de una o más enfermedades asociadas con la A $\beta$  usando dichos compuestos o composiciones farmacéuticas.

Los compuestos de esta invención (Fórmula I) pueden ser útiles como moduladores de la gamma secretasa y pueden ser útiles en el tratamiento y prevención de enfermedades tales como, por ejemplo, enfermedad de Alzheimer, insuficiencia cognitiva leve (ICL), Síndrome de Down, Glaucoma (Guo et. al., Proc. Natl. Acad. Sci. USA 104, 13444-13449 (2007)), Angiopatía amiloide cerebral, infarto o demencia (Frangione et al., Amyloid: J. Protein folding Disord. 8, suppl. 1, 36-42 (2001), Microgliosis e inflamación cerebral (M P Lamber, Proc. Natl. Acad. Sci. USA 95, 6448-53 (1998)), Pérdida de la función olfativa (Getchell, et.al. Neurobiology of Aging, 663-673, 24, 2003).

Esta invención proporciona compuestos de fórmula I:



Fórmula I

En una realización, la presente solicitud presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la Fórmula IA:



Los compuestos de fórmula I pueden ser útiles como moduladores de la gamma secretasa y pueden ser útiles en el tratamiento y prevención de varias enfermedades tales como, por ejemplo, trastornos del sistema nervioso central tales como enfermedad de Alzheimer y Síndrome de Down.

Esta invención provee, además, sales aceptables desde el punto de vista farmacéutico de los compuestos de fórmula I.

Esta invención provee, además, ésteres aceptables desde el punto de vista farmacéutico de los compuestos de fórmula I.

Esta invención provee, además, solvatos aceptables desde el punto de vista farmacéutico de los compuestos de fórmula I.

Esta invención provee, además, compuestos de fórmula I en forma pura y aislada.

Esta invención provee, además, compuestos de fórmula I en forma pura.

Esta invención provee, además, compuestos de fórmula I en forma aislada.

Esta invención provee, además, compuestos 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1..

Esta invención provee, además, compuestos 1 a 20 (es decir, los compuestos que aparecen en la Tabla1).

Esta invención provee, además, compuestos 1 a 20, y 23.

Esta invención provee, además, compuestos 21, 22, y 24.

Esta invención provee, además, composiciones farmacéuticas que comprenden una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I, o una de sus sales, ésteres o solvatos aceptables desde el punto de vista farmacéutico, y un vehículo aceptable desde el punto de vista farmacéutico.

Esta invención provee, además, composiciones farmacéuticas que comprenden una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I, o una de sus sales, ésteres o solvatos aceptables desde el punto de vista farmacéutico, y una cantidad efectiva de uno o más (por ej., uno) ingredientes farmacéuticamente activos distintos (por ej., drogas), y un vehículo aceptable desde el punto de vista farmacéutico.

Esta invención provee, además, un método para modular (incluyendo inhibir, antagonizar y similares) gamma-secretasa, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método para modular (incluyendo inhibir, antagonizar y similares) la gamma-secretasa, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de una o más de varias enfermedades neurodegenerativas, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de una o más de varias enfermedades neurodegenerativas, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de inhibición de la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, sobre o alrededor de un tejido neurológico (por ej., el cerebro), que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de inhibición de la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, sobre o alrededor de un tejido neurológico (por ej., el cerebro), que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de fórmula I a un paciente que necesita de tratamiento.

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Esta invención provee, además, un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más inhibidores de colinesterasa (tales como, por ejemplo, (±)-2,3-dihidro-5,6-dimetoxi-2-[[1-(fenilmetil)-4-piperidinil]metil]-1H-inden-1-ona clorhidrato, es decir, clorhidrato de donepezilo, disponible como la marca Aricept® de clorhidrato de donepezilo), a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más compuestos seleccionados del grupo que consiste en inhibidores del anticuerpo A $\beta$ , inhibidores de la gamma secretasa e inhibidores de la beta secretasa.

Esta invención provee, además, combinaciones que comprenden una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más compuestos seleccionados del grupo que consiste en inhibidores de colinesterasa (tales como, por ejemplo, (±)-2,3-dihidro-5,6-dimetoxi-2-[[1-(fenilmetil)-4-piperidinil]metil]-1H-inden-1-ona clorhidrato, es decir, clorhidrato de donepezilo, disponible como la marca Aricept® de clorhidrato de donepezilo), inhibidores del anticuerpo A $\beta$ , inhibidores de la gamma secretasa e inhibidores de la beta secretasa.

Esta invención provee, además, un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de fórmula I, en combinación



con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) inhibidores de colinesterasa (tales como, por ejemplo,  $(\pm)$ -2,3-dihidro-5,6-dimetoxi-2-[[1-(fenilmetil)-4-piperidinil]metil]-1H-inden-1-ona, clorhidrato, es decir, clorhidrato de donepezilo, disponible como la marca Aricept® de clorhidrato de donepezilo), a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento del síndrome de Down, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento del síndrome de Down, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento del síndrome de Down, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más inhibidores de colinesterasa (tales como, por ejemplo,  $(\pm)$ -2,3-dihidro-5,6-dimetoxi-2-[[1-(fenilmetil)-4-piperidinil]metil]-1H-inden-1-ona, clorhidrato, es decir, clorhidrato de donepezilo, disponible como la marca Aricept® de clorhidrato de donepezilo), a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento del síndrome de Down, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de fórmula I, en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) inhibidores de colinesterasa (tales como, por ejemplo,  $(\pm)$ -2,3-dihidro-5,6-dimetoxi-2-[[1-(fenilmetil)-4-piperidinil]metil]-1H-inden-1-ona,

clorhidrato, es decir, clorhidrato de donepezilo, disponible como la marca Aricept® de clorhidrato de donepezilo), a un paciente que necesita de tratamiento.

Esta invención provee, además, terapias de combinación para (1) modular la gamma-secretasa, o (2) tratar una o más enfermedades neurodegenerativas, o (3) inhibir la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, sobre o alrededor de un tejido neurológico (por ej., el cerebro), o (4) tratar la enfermedad de Alzheimer. Las terapias de combinación se refieren a métodos que comprenden la administración de una cantidad efectiva de uno o más (por ej. uno) compuestos de fórmula I y la administración de una cantidad efectiva de uno o más (por ej., uno) ingredientes activos farmacéuticos distintos (por ej., drogas).

Esta invención provee, además, un método de tratamiento de la insuficiencia cognitiva leve, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento del glaucoma, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de la angiopatía amiloide cerebral, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento del accidente cerebrovascular comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de la demencia, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de la microgliosis, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de la inflamación cerebral, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento la pérdida de la función olfativa, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, composiciones farmacéuticas que comprenden una combinación de una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más compuestos seleccionados del grupo que consiste en inhibidores de colinesterasa, inhibidores del anticuerpo A $\beta$ , inhibidores de la gamma secretasa e inhibidores de la beta secretasa. Las composiciones farmacéuticas comprenden, además, un vehículo aceptable desde el punto de vista farmacéutico.

Esta invención provee, además, un kit que comprende, en recipientes separados, en un envase individual, composiciones farmacéuticas para usar en forma combinada, en el cual un recipiente comprende una cantidad efectiva de un compuesto de fórmula I en un vehículo aceptable desde el punto de vista farmacéutico, y otro recipiente (es decir, un segundo recipiente) comprende una cantidad efectiva de otro principio farmacéuticamente activo, las cantidades combinadas del compuesto de fórmula I y otro principio farmacéuticamente activo efectivo para: (a) tratar la enfermedad de Alzheimer, o (b) inhibir la deposición de la proteína amiloide en, sobre o alrededor de un tejido neurológico (por ej., el

cerebro), o (c) tratar varias enfermedades neurodegenerativas, o (d) modular la actividad de gamma-secretasa.

Esta invención provee, además, un kit que comprende, en recipientes separados, en un envase individual, composiciones farmacéuticas para usar en forma combinada, en el cual un recipiente comprende una cantidad efectiva de un compuesto de fórmula I en un vehículo aceptable desde el punto de vista farmacéutico, y otro recipiente (es decir, un segundo recipiente) comprende una cantidad efectiva de otro principio farmacéuticamente activo (como se describe a continuación), las cantidades combinadas del compuesto de fórmula I y otro principio farmacéuticamente activo efectivo para: (a) tratar la enfermedad de Alzheimer, o (b) inhibir la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, sobre o alrededor de un tejido neurológico (por ej., el cerebro), o (c) tratar varias enfermedades neurodegenerativas, o (d) modular la actividad de gamma-secretasa.

Esta invención provee, además, cualquiera de los métodos divulgados anteriormente y a continuación en los cuales el compuesto se selecciona del grupo que consiste en los compuestos 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Esta invención provee, además, cualquiera de los métodos divulgados anteriormente y a continuación en los cuales el compuesto de fórmula I se selecciona del grupo que consiste en los compuestos 1 a 20, y 23.

Esta invención provee, además, cualquiera de los métodos divulgados anteriormente y a continuación en los cuales el compuesto de fórmula I se selecciona del grupo que consiste en los compuestos 21, 22 y 24.

Esta invención provee, además, cualquiera de los métodos revelados anteriormente y a continuación en los cuales el compuesto de fórmula I se

selecciona del grupo que consiste en los compuestos 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Esta invención provee, además, cualquiera de las composiciones farmacéuticas divulgadas con anterioridad y a continuación en las cuales el compuesto se selecciona del grupo que consiste en los compuestos 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Esta invención provee, además, cualquiera de las composiciones farmacéuticas divulgadas con anterioridad y a continuación en las cuales el compuesto es cualquiera de los compuestos 1 a 20, y 23.

Esta invención provee, además, cualquiera de las composiciones farmacéuticas divulgadas con anterioridad y a continuación en las cuales el compuesto es cualquiera de los compuestos 21, 22 y 24.

Esta invención provee, además, cualquiera de las composiciones farmacéuticas divulgadas con anterioridad y a continuación en las cuales el compuesto es cualquiera de los compuestos 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otras realizaciones de esta invención se refieren a cualquiera de las realizaciones anteriores o posteriores que se refieren a la fórmula I, o el uso de la fórmula I (por ej. las realizaciones referidas a métodos de tratamiento, composiciones farmacéuticas y kits), en las cuales el compuesto es un compuesto de fórmula IA en lugar de la fórmula I. Aquellas personas con experiencia en el arte apreciarán que los compuestos de fórmula I y fórmula IA son isómeros entre sí.

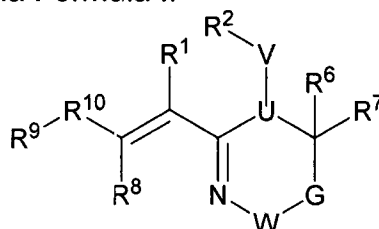
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Esta invención provee, además, cualquiera de los métodos de tratamiento mencionados con anterioridad en los cuales el compuesto de fórmula I se selecciona del grupo que consiste en los compuestos que aparecen en la Tabla 1.

### **Descripción Detallada**

En una realización, la presente invención presenta compuestos que están representados por la Fórmula estructural I, o una de sus sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico, en las cuales los varios restos se describen a continuación.

En una realización, la presente solicitud presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la Fórmula I:



Fórmula I

en la cual:

cualquiera de (i)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (ii)  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma

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independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (iii)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (iv)  $R^6$  y cualquiera de  $R^3$  o  $R^4$  del resto  $-C(R^3)(R^4)-G$ , están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (v)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con dicho resto heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se

selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y

U es  $\begin{cases} \text{---C(R}^5\text{)} \\ \text{N} \end{cases}$ ;

W se selecciona del grupo que consiste en un enlace; -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, y -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G se selecciona del grupo que consiste en -C(R<sup>3</sup>)(R<sup>4</sup>)-, -C(O)- y -N(R<sup>13</sup>)-, con la salvedad de que cuando W es -O- o -S-, G no es -N(R<sup>13</sup>)- o -C(O)-;

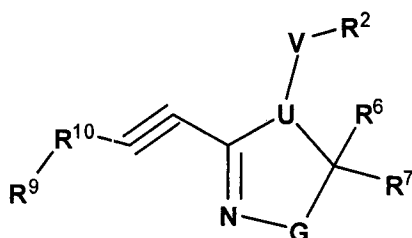
V se selecciona del grupo que consiste en un enlace, -O-, -C(O)-, y -N(R<sup>14</sup>)-;

R<sup>1</sup> (cuando R<sup>1</sup> no está unido a R<sup>2</sup>), R<sup>2</sup> (cuando R<sup>2</sup> no está unido a R<sup>1</sup> o R<sup>6</sup>), R<sup>5</sup>, R<sup>6</sup> (cuando R<sup>6</sup> no está unido a R<sup>2</sup>), y R<sup>7</sup> pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

o, de manera alternativa, R<sup>1</sup> (cuando R<sup>1</sup> no está unido a R<sup>2</sup>) y R<sup>8</sup> se toman juntos para formar un enlace (es decir, hay un enlace triple entre el átomo de carbono al cual R<sup>1</sup> estaba unido y el átomo de carbono al cual R<sup>8</sup> estaba unido, es decir, el compuesto de fórmula I es un compuesto de fórmula II:



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fórmula II

y  $R^2$ ,  $R^5$ ,  $R^6$ , y  $R^7$  son como se los definió con anterioridad, y  $R^3$ ,  $R^4$ ,  $R^{11}$  y  $R^{12}$  son como se los define a continuación);

$R^3$  se selecciona del grupo que consiste en H, halo (y en un ejemplo, F), -OR<sup>15</sup> (y en un ejemplo R<sup>15</sup> es H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o

$R^3$  y  $R^6$  tomados juntos forman un enlace (es decir,  $R^3$  y  $R^6$  forman un enlace entre G y el átomo de carbono al cual  $R^6$  está unido), siempre que cuando  $R^3$  y  $R^6$  forman un enlace: (1) W no es un enlace, (2)  $R^2$  y  $R^6$  no se unen para formar un resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo (como se describió en los puntos (ii) y (iii) anteriores) (3)  $R^6$  y cualquiera de  $R^3$  o  $R^4$  del resto  $-C(R^3)(R^4)-G$  no se unen para formar un resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo (como se describió en el punto (iv) más arriba), y (4)

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$R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G no se unen para formar un resto heterociclilo o heterociclenilo (como se describió en el punto (v) más arriba);

$R^4$ ,  $R^{11}$  y  $R^{12}$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, halo (y en un ejemplo, F),  $-OR^{15}$  (y en un ejemplo  $R^{15}$  es H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alquilo-, alqueno-, alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

siempre que cuando uno de  $R^3$  o  $R^4$  se selecciona del grupo que consiste en:

$-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,



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$R^{13}$  se selecciona en forma independiente del grupo que consiste en H, alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo-, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo, arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-, arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-, arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, heterocicloalquenilarilo-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  y  $-N(R^8)_2$ ; y donde dicho grupos  $R^{13}$  alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo, arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-, arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-, arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, y heterocicloalquenilarilo- están sustituidos en forma opcional con 1 a 5 grupos seleccionados en forma independiente del grupo que consiste en: alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterocicilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo,  $-CN$ ,  $-OR^{15}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-SR^{15}$ ,  $-S(O)N(R^{15})(R^{16})$ , -

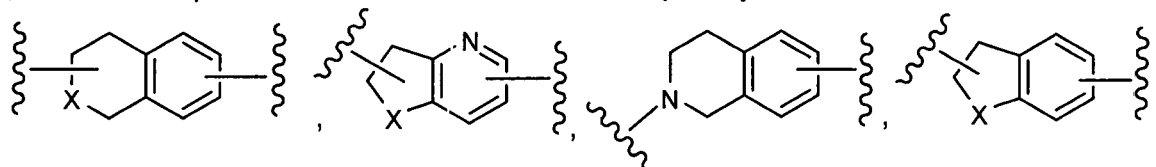
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$\text{CH}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{C}(=\text{NOR}^{15})\text{R}^{16}$ ,  
 $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ,  $-\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{alquil}-\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  
 $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{CH}_2-\text{R}^{15}$ ,  $-\text{CH}_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  
 $-\text{N}(\text{R}^{15})\text{S}(\text{O})\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  
 $-\text{N}(\text{R}^{15})\text{S}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  
 $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{OR}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{OR}^{16}$ ,  $-\text{S}(\text{O})\text{R}^{15}$ ,  $=\text{NOR}^{15}$ ,  $-\text{N}_3$ ,  $-\text{NO}_2$  y  
 $-\text{S}(\text{O})_2\text{R}^{15}$ ;

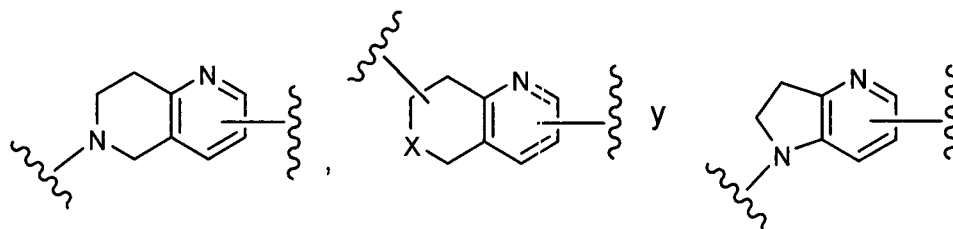
$\text{R}^{14}$  se selecciona del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-,  $-\text{CN}$ ,  $-\text{C}(\text{O})\text{R}^{15}$ ,  $-\text{C}(\text{O})\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{C}(=\text{NOR}^{15})\text{R}^{16}$ , y  $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ;

$\text{R}^8$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, con cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- que no está sustituido o está sustituido en forma independiente y opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

$\text{R}^{10}$  se selecciona del grupo que consiste en un enlace, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo-, heterocicilalquilo- y los restos:



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donde X es O, N(R<sup>14</sup>) o S;

en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- heterociclilalquilo- para R<sup>10</sup> como también los restos mencionados anteriormente para R<sup>10</sup> puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y

R<sup>9</sup> se selecciona del grupo que consiste en alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

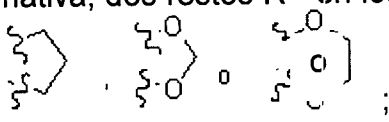
R<sup>15</sup>, R<sup>16</sup> y R<sup>17</sup> se seleccionan en forma independiente del grupo que consiste en H, alquilo, alqueno, alquino, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, arilcicloalquilo-, arilheterociclilo-, R<sup>18</sup>-alquilo, R<sup>18</sup>-cicloalquilo, R<sup>18</sup>-cicloalquilalquilo-, R<sup>18</sup>-heterociclilo, R<sup>18</sup>-heterociclilalquilo-, R<sup>18</sup>-arilo, R<sup>18</sup>-arilalquilo-, R<sup>18</sup>-heteroarilo y R<sup>18</sup>-heteroarilalquilo-;

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$R^{18}$  es de 1-5 sustituyentes seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, arilo, arilalquilo-, arilalquenilo-, arilalquinilo-,  $-\text{NO}_2$ , halo, heteroarilo, HO-alquioxialquilo-,  $-\text{CF}_3$ ,  $-\text{CN}$ , alquil-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alquil})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{heteroarilo})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{NH}(\text{arilo})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterociclilo})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  $-\text{O-heterociclilo}$ ,  $-\text{O-cicloalquilalquilo}$ ,  $-\text{O-heterocicilalquilo}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alquil})_2$ ,  $-\text{N}(\text{arilalquil})_2$ ,  $-\text{N}(\text{arilalquil})(\text{heteroarilalquilo})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{NH}(\text{alquil})$  y  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ;

o, en forma alternativa, dos restos  $R^{18}$  en los carbonos adyacentes pueden ligarse

para formar:



$R^{19}$  es alquilo, cicloalquilo, arilo, arilalquilo- o heteroarilalquilo-;

$R^{20}$  es alquilo, cicloalquilo, arilo, arilo sustituido por halo, arilalquilo-, heteroarilo o heteroarilalquilo-;

donde cada uno de los grupos alquilo, cicloalquilo, cicloalquenilo, cicloalquilalquilo-, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, alquilarilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en  $R^1$ ,  $R^2$ ,  $R^1-R^2$ ,  $R^2-R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  y  $R^{14}$  está no sustituido o sustituido en forma opcional e independiente por 1 a 5 grupos  $R^{21}$  seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo,  $-\text{CN}$ ,  $-\text{OR}^{15}$ ,

$-\text{C}(\text{O})\text{R}^{15}$ ,  $-\text{C}(\text{O})\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{SR}^{15}$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{CH}(\text{R}^{15})(\text{R}^{16})$ ,

$-\text{S(O)}_2\text{N(R}^{15}\text{)(R}^{16}\text{)}$ ,  $-\text{C(=NOR}^{15}\text{)R}^{16}$ ,  $-\text{P(O)(OR}^{15}\text{)(OR}^{16}\text{)}$ ,  $-\text{N(R}^{15}\text{)(R}^{16}\text{)}$ ,  
 $-\text{alquil-N(R}^{15}\text{)(R}^{16}\text{)}$ ,  $-\text{N(R}^{15}\text{)C(O)R}^{16}$ ,  $-\text{CH}_2-\text{N(R}^{15}\text{)C(O)R}^{16}$ ,  
 $-\text{CH}_2-\text{N(R}^{15}\text{)C(O)N(R}^{16}\text{)(R}^{17}\text{)}$ ,  $-\text{CH}_2-\text{R}^{15}$ ;  $-\text{CH}_2\text{N(R}^{15}\text{)(R}^{16}\text{)}$ ,  $-\text{N(R}^{15}\text{)S(O)R}^{16}$ ,  
 $-\text{N(R}^{15}\text{)S(O)}_2\text{R}^{16}$ ,  $-\text{CH}_2-\text{N(R}^{15}\text{)S(O)}_2\text{R}^{16}$ ,  $-\text{N(R}^{15}\text{)S(O)}_2\text{N(R}^{16}\text{)(R}^{17}\text{)}$ ,  
 $-\text{N(R}^{15}\text{)S(O)N(R}^{16}\text{)(R}^{17}\text{)}$ ,  $-\text{N(R}^{15}\text{)C(O)N(R}^{16}\text{)(R}^{17}\text{)}$ ,  $-\text{CH}_2-\text{N(R}^{15}\text{)C(O)N(R}^{16}\text{)(R}^{17}\text{)}$ ,  
 $-\text{N(R}^{15}\text{)C(O)OR}^{16}$ ,  $-\text{CH}_2-\text{N(R}^{15}\text{)C(O)OR}^{16}$ ,  $-\text{S(O)R}^{15}$ ,  $=\text{NOR}^{15}$ ,  $-\text{N}_3$ ,  $-\text{NO}_2$  y  
 $-\text{S(O)}_2\text{R}^{15}$ ;

donde cada uno de los grupos alquilo, cicloalquenilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en  $\text{R}^{21}$  está en forma independiente no sustituido o sustituido por 1 a 5 grupos  $\text{R}^{22}$  seleccionados en forma independiente del grupo que consiste en alquilo, cicloalquilo, cicloalquenilo, heterociclilo, arilo, heteroarilo, halo,  $-\text{CF}_3$ ,  $-\text{CN}$ ,  $-\text{OR}^{15}$ ,  $-\text{C(O)R}^{15}$ ,  $-\text{C(O)OR}^{15}$ ,  $-\text{alquil-C(O)OR}^{15}$ ,  $\text{C(O)N(R}^{15}\text{)(R}^{16}\text{)}$ ,  $-\text{SR}^{15}$ ,  $-\text{S(O)N(R}^{15}\text{)(R}^{16}\text{)}$ ,  $-\text{S(O)}_2\text{N(R}^{15}\text{)(R}^{16}\text{)}$ ,  $-\text{C(=NOR}^{15}\text{)R}^{16}$ ,  $-\text{P(O)(OR}^{15}\text{)(OR}^{16}\text{)}$ ,  $-\text{N(R}^{15}\text{)(R}^{16}\text{)}$ ,  $-\text{alquil-N(R}^{15}\text{)(R}^{16}\text{)}$ ,  $-\text{N(R}^{15}\text{)C(O)R}^{16}$ ,  $-\text{CH}_2-\text{N(R}^{15}\text{)C(O)R}^{16}$ ,  $-\text{N(R}^{15}\text{)S(O)R}^{16}$ ,  $-\text{N(R}^{15}\text{)S(O)}_2\text{R}^{16}$ ,  $-\text{CH}_2-\text{N(R}^{15}\text{)S(O)}_2\text{R}^{16}$ ,  $-\text{N(R}^{15}\text{)S(O)}_2\text{N(R}^{16}\text{)(R}^{17}\text{)}$ ,  $-\text{N(R}^{15}\text{)S(O)N(R}^{16}\text{)(R}^{17}\text{)}$ ,  $-\text{N(R}^{15}\text{)C(O)N(R}^{16}\text{)(R}^{17}\text{)}$ ,  $-\text{CH}_2-\text{N(R}^{15}\text{)C(O)N(R}^{16}\text{)(R}^{17}\text{)}$ ,  $-\text{N(R}^{15}\text{)C(O)OR}^{16}$ ,  $-\text{CH}_2-\text{N(R}^{15}\text{)C(O)OR}^{16}$ ,  $-\text{N}_3$ ,  $=\text{NOR}^{15}$ ,  $-\text{NO}_2$ ,  $-\text{S(O)R}^{15}$  y  $-\text{S(O)}_2\text{R}^{15}$ .

La misma declaración anterior: "cualquiera de (i)  $\text{R}^1$  y  $\text{R}^2$  están unidos para formar un cicloalquilo  $\text{C}_4\text{-C}_8$ , cicloalquenilo  $\text{C}_4\text{-C}_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (ii)  $\text{R}^2$  y  $\text{R}^6$  están unidos para formar un



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cicloalquilo C<sub>4</sub>-C<sub>8</sub>, cicloalquenilo C<sub>4</sub>-C<sub>8</sub>, resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (iii) R<sup>1</sup> y R<sup>2</sup> están unidos para formar un cicloalquilo C<sub>4</sub>-C<sub>8</sub>, cicloalquenilo C<sub>4</sub>-C<sub>8</sub>, resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y R<sup>2</sup> y R<sup>6</sup> están unidos para formar un cicloalquilo C<sub>4</sub>-C<sub>8</sub>, cicloalquenilo C<sub>4</sub>-C<sub>8</sub>, resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (iv) R<sup>6</sup> y cualquiera de R<sup>3</sup> o R<sup>4</sup> del resto -C(R<sup>3</sup>)(R<sup>4</sup>)- G, están unidos para formar un cicloalquilo C<sub>4</sub>-C<sub>8</sub>, cicloalquenilo C<sub>4</sub>-C<sub>8</sub>, resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (v) R<sup>6</sup> y R<sup>13</sup> del resto -N(R<sup>13</sup>)- G, están unidos para formar un cicloalquilo C<sub>4</sub>-C<sub>8</sub>, cicloalquenilo C<sub>4</sub>-C<sub>8</sub>, resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que

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pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; “ significa que cuando ocurren (i), (ii), (iii), (iv) y (v) son mutuamente exclusivas y que sólo uno de (i), (ii), (iii), (iv) y (v) puede estar presente en un momento determinado.

Debe entenderse que cuando  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, cada uno de dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo puede estar adicionalmente y en forma opcional fusionado con un anillo arilo o heteroarilo, donde el resto del anillo que resulta de la fusión puede estar no sustituido o estar sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se mostraron con anterioridad (es decir, cada sustituyente se selecciona en forma independiente del grupo que consiste en los sustituyentes  $R^{21}$ ).

También debe entenderse que cuando  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, cada uno de dichos restos cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo puede estar fusionado en forma opcional e independiente, adicionalmente con un anillo arilo o heteroarilo, donde dicho resto anular que resulta de la fusión puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se mostraron con anterioridad (es decir, cada sustituyente se selecciona en forma independiente del grupo que consiste en los sustituyentes  $R^{21}$ ).

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Debe entenderse que cuando  $R^6$  y cualquiera de  $R^3$  o  $R^4$  del resto  $-C(R^3)(R^4)-G$ , están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, cada uno de dichos restos cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo puede estar fusionado en forma opcional e independiente, adicionalmente con un anillo arilo o heteroarilo, donde dicho resto anular que resulta de la fusión puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se mostraron con anterioridad (es decir, cada sustituyente se selecciona en forma independiente del grupo que consiste en los sustituyentes  $R^{21}$ ).

Debe entenderse que cuando  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, cada uno de dichos restos cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo puede estar fusionado en forma opcional e independiente, adicionalmente con un anillo arilo o heteroarilo, donde dicho resto anular que resulta de la fusión puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se mostraron con anterioridad (es decir, cada sustituyente se selecciona en forma independiente del grupo que consiste en los sustituyentes  $R^{21}$ ).

En una realización, o bien:

(i)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden

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ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se mostraron con anterioridad (es decir, cada sustituyente se selecciona en forma independiente del grupo que consiste en los sustituyentes  $R^{21}$ ); o

(ii)  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se mostraron con anterioridad (es decir, cada sustituyente se selecciona en forma independiente del grupo que consiste en los sustituyentes  $R^{21}$ ); o

(iii)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se mostraron con anterioridad (es decir, cada sustituyente se selecciona en forma independiente del grupo que consiste en los sustituyentes  $R^{21}$ ).

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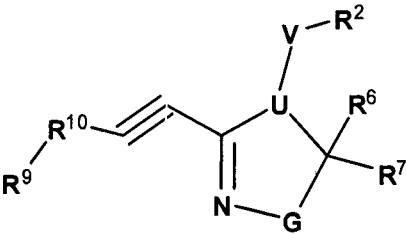
En una realización,  $R^1$  (cuando  $R^1$  no está unido a  $R^2$ ),  $R^2$  (cuando  $R^2$  no está unido a  $R^1$  o  $R^6$ ),  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$  (cuando  $R^6$  no está unido a  $R^2$ ),  $R^7$ ,  $R^{11}$  y  $R^{12}$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alqueno-, alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se mostraron con anterioridad (es decir, cada sustituyente se selecciona en forma independiente del grupo que consiste en los sustituyentes  $R^{21}$ ).

En una realización, cada uno de los grupos alquilo, cicloalquilo, cicloalquilalquilo, heterociclilo, heterocicilalquilo, arilo, arilalquilo, heteroarilo, heteroarilalquilo, alqueno- y alquino- en  $R^1$ ,  $R^2$ ,  $R^1$ - $R^2$ ,  $R^2$ - $R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  y  $R^{14}$  está no sustituido o sustituido en forma opcional e independiente por 1 a 5 grupos  $R^{21}$  seleccionados en forma independiente del grupo que consiste en alquilo, alqueno-, alquino-, cicloalquilo, cicloalquilalquilo, cicloalqueno-, heterociclilo, heterocicilalquilo, arilo, arilalquilo, heteroarilo, heteroarilalquilo, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(C)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>,

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=NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>; y cada uno de los grupos alquilo, cicloalquenoilo, cicloalquilo, cicloalquilalquilo, heterociclilo, heterocicilalquilo, arilo, arilalquilo, heteroarilo, heteroarilalquilo, alquenoilo y alquinilo en R<sup>21</sup> está en forma independiente no sustituido o sustituido por 1 a 5 grupos R<sup>22</sup> seleccionados en forma independiente del grupo que consiste en alquilo, cicloalquilo, cicloalquenoilo, heterociclilo, arilo, heteroarilo, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alquil-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> y -S(O)<sub>2</sub>R<sup>15</sup>.

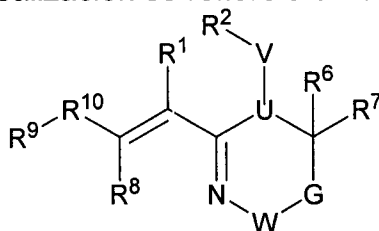
En otra realización, R<sup>1</sup> (cuando R<sup>1</sup> no está unido a R<sup>2</sup>) y R<sup>8</sup> se toman juntos para formar un enlace (es decir, hay un enlace triple entre el átomo de carbono al cual R<sup>1</sup> estaba unido y el átomo de carbono al cual R<sup>8</sup> estaba unido, es decir, el compuesto de fórmula I es un compuesto de fórmula II:



fórmula II

y R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>11</sup> y R<sup>12</sup> son como se los definió con anterioridad).

De este modo, una realización se refiere a un compuesto de fórmula I:



Fórmula I

o una de sus sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico, en la cual:

o bien

(i) R<sup>1</sup> y R<sup>2</sup> están unidos para formar un cicloalquilo C<sub>4</sub>-C<sub>8</sub>, cicloalquenilo C<sub>4</sub>-C<sub>8</sub>, resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes R<sup>21</sup> seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes R<sup>21</sup> seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes R<sup>21</sup> seleccionados en forma independiente; o

(ii) R<sup>2</sup> y R<sup>6</sup> están unidos para formar un cicloalquilo C<sub>4</sub>-C<sub>8</sub>, cicloalquenilo C<sub>4</sub>-C<sub>8</sub>, resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes R<sup>21</sup> seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes R<sup>21</sup> seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido

en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(iii)

(a)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (1) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y

(b)  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (1) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; y

(c) dicho resto  $R^2$  y  $R^6$  cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

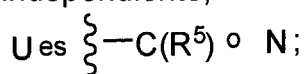
(iv)  $R^6$  y cualquiera de  $R^3$  o  $R^4$  del resto  $-C(R^3)(R^4)-G$ , están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y



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el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(v)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente;



W se selecciona del grupo que consiste en un enlace;  $-O-$ ,  $-C(O)-$ ,  $-S-$ ,  $-S(O)-$ ,  $-S(O_2)-$ , y  $-C(R^{11})(R^{12})-$ ;

G se selecciona del grupo que consiste en  $-C(R^3)(R^4)-$ ,  $-C(O)-$  y

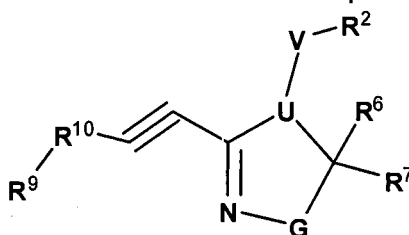
$-N(R^{13})-$ , con la salvedad de que cuando W es  $-O-$  o  $-S-$ , G no es  $-N(R^{13})-$  o  $-C(O)-$ ;

V se selecciona del grupo que consiste en un enlace,  $-O-$ ,  $-C(O)-$  y  $-N(R^{14})-$ ;

$R^1$  (cuando  $R^1$  no está unido a  $R^2$ ),  $R^2$  (cuando  $R^2$  no está unido a  $R^1$  o  $R^6$ ),  $R^5$ ,  $R^6$  (cuando  $R^6$  no está unido a  $R^2$ ), y  $R^7$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e

independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

o, de manera alternativa,  $R^1$  (cuando  $R^1$  no está unido a  $R^2$ ) y  $R^8$  se toman juntos para formar un enlace (es decir, hay un enlace triple entre el átomo de carbono al cual  $R^1$  estaba unido y el átomo de carbono al cual  $R^8$  estaba unido, es decir, el compuesto de fórmula I es un compuesto de fórmula II:



fórmula II

y  $R^2$ ,  $R^5$ ,  $R^6$ , y  $R^7$  son como se los definió con anterioridad, y  $R^3$ ,  $R^4$ ,  $R^{11}$  y  $R^{12}$  son como se los define a continuación);

$R^3$  se selecciona del grupo que consiste en H, halo (y en un ejemplo, F), -OR<sup>15</sup> (y en un ejemplo  $R^{15}$  es H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o

$R^3$  y  $R^6$  tomados juntos forman un enlace (es decir,  $R^3$  y  $R^6$  forman un enlace entre G y el átomo de carbono al cual  $R^6$  está unido), siempre que cuando  $R^3$  y  $R^6$  forman un enlace: (1) W no es un enlace, (2)  $R^2$  y  $R^6$  no se unen para formar un resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo (como se describió en los puntos (ii) y (iii) anteriores) (3)  $R^6$  y cualquiera de  $R^3$  o  $R^4$  del resto  $-C(R^3)(R^4)-$  G no se unen para formar un resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo (como se describió en el punto (iv) más arriba), y (4)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G no se unen para formar un resto heterociclilo o heterociclenilo (como se describió en el punto (v) más arriba);

$R^4$ ,  $R^{11}$  y  $R^{12}$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, halo (y en un ejemplo, F),  $-OR^{15}$  (y en un ejemplo  $R^{15}$  es H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante, y

siempre que cuando uno de  $R^3$  o  $R^4$  se selecciona del grupo que consiste en:

$-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,

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$-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se selecciona del grupo  
 que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  
 $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , y  $-N_3$  (es decir, si uno de  $R^3$  o  $R^4$  es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , o  $-N_3$ , entonces el otro no es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-$   
 $NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  
 $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , o  $-N_3$ ;

siempre que cuando uno de  $R^{11}$  o  $R^{12}$  se selecciona del grupo que consiste  
 en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  
 $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  
 $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se  
 selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , y  $-N_3$  (es decir, si uno de  $R^{11}$  o  $R^{12}$  es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,

$-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , o  $-N_3$ , entonces el otro no es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , o  $-N_3$ ;

$R^{13}$  se selecciona en forma independiente del grupo que consiste en H,  
 alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-,  
 arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-,  
 heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-,  
 heteroarilcicloalquilo-, heterocicloalquilo-, arilheterocicloalquilo-,  
 heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo,  
 arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-,  
 arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-,  
 arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo,  
 cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-,  
 heterocicloalquenilarilo-,  $-OR^{15}$ ,  
 $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  $-C(O)N(R^{11})(R^{12})$ ,  
 $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  y  $-N(R^8)_2$ ; y donde dicho  $R^{13}$   
 de los grupos alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-,  
 heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-,  
 arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo,  
 arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo, arilheterocicloalquilo-,  
 heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo,  
 arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-,  
 arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-,

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arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, y heterocicloalquenilarilo- están sustituidos en forma opcional con 1 a 5 grupos seleccionados en forma independiente del grupo que consiste en: alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(C)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>; -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>;

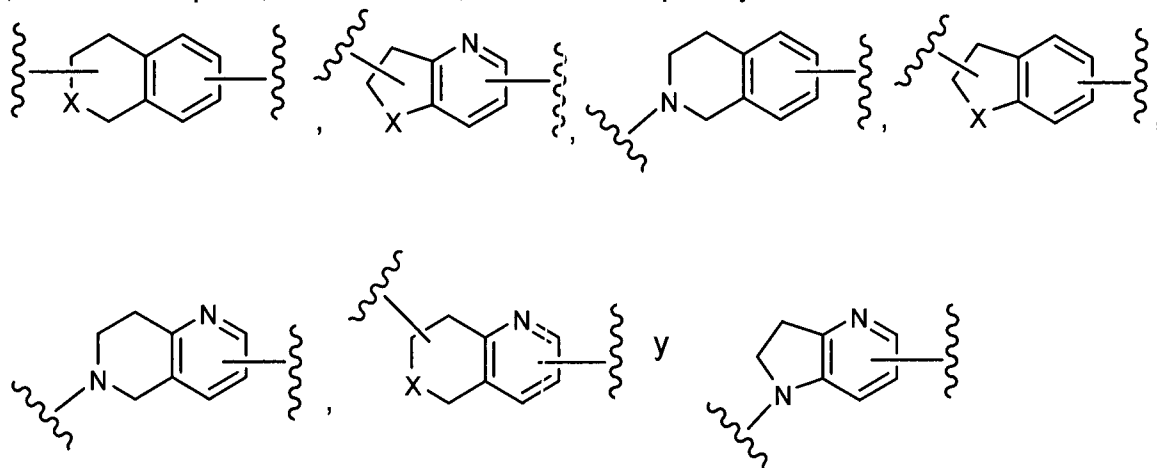
R<sup>8</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-

heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, con cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- está sustituido en forma opcional con 1-3 sustituyentes R<sup>21</sup> seleccionados en forma independiente;

R<sup>9</sup> se selecciona del grupo que consiste en alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, donde cada grupo R<sup>9</sup> está sustituido en forma opcional con 1-3 sustituyentes R<sup>21</sup> seleccionados en forma independiente;

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$R^{10}$  se selecciona del grupo que consiste en un enlace, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo-, heterociclilalquilo- y los restos:



donde X es O,  $N(R^{14})$  o S;

donde cada grupo  $R^{10}$  (a excepción del enlace) está sustituido en forma opcional con 1-3 sustituyentes  $R^{21}$  seleccionados en forma independiente;

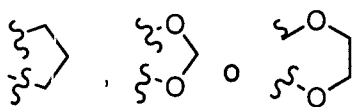
$R^{14}$  se selecciona del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-,  $-CN$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ , y  $-P(O)(OR^{15})(OR^{16})$ , en los cuales cada uno de dicho alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, y heteroarilalquilo- está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente;

$R^{15}$ ,  $R^{16}$  y  $R^{17}$  se seleccionan de manera independiente del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, arilcicloalquilo-, arilheterociclilo-,  $(R^{18})_r$ -alquilo,  $(R^{18})_r$ -cicloalquilo,  $(R^{18})_r$ -cicloalquilalquilo-,  $(R^{18})_r$ -heterociclilo,  $(R^{18})_r$ -heterociclilalquilo-,  $(R^{18})_r$ -arilo,  $(R^{18})_r$ -arilalquilo-,  $(R^{18})_r$ -heteroarilo y  $(R^{18})_r$ -heteroarilalquilo-; en la cual R es de 1-5;

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Cada  $R^{18}$  se selecciona en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, arilo, arilalquilo-, arilalquenilo-, arilalquinilo-,  $-\text{NO}_2$ , halo, heteroarilo, HO-alquioxialquilo-,  $-\text{CF}_3$ ,  $-\text{CN}$ , alquil-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alquil})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{heteroarilo})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{NH}(\text{arilo})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterociclilo})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  $-\text{O-heterociclilo}$ ,  $-\text{O-cicloalquilalquilo}$ ,  $-\text{O-heterociclilalquilo}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alquil})_2$ ,  $-\text{N}(\text{arilalquil})_2$ ,  $-\text{N}(\text{arilalquil})-(\text{heteroarilalquilo})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{NH}(\text{alquil})$  y  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ;

o, en forma alternativa, dos restos  $R^{18}$  en los carbonos adyacentes pueden ligarse para formar:



$R^{19}$  se selecciona del grupo que consiste en: alquilo, cicloalquilo, arilo, arilalquilo- y heteroarilalquilo-;

$R^{20}$  se selecciona del grupo que consiste en: alquilo, cicloalquilo, arilo, arilo sustituido por halo, arilalquilo-, heteroarilo y heteroarilalquilo-;

Cada grupo  $R^{21}$  se selecciona en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo,  $-\text{CN}$ ,  $-\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{R}^{15}$ ,  $-\text{C}(\text{O})\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{SR}^{15}$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{CH}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{C}(=\text{NOR}^{15})\text{R}^{16}$ ,  $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ,  $-\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{alquil-N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,

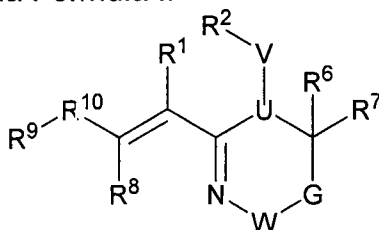


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-CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>; -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y  
 -S(O)<sub>2</sub>R<sup>15</sup>; y donde cada uno de los grupos alquilo, cicloalquenilo, cicloalquilo,  
 cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo,  
 heteroarilalquilo-, alquenilo y alquinilo de R<sup>21</sup> está sustituido en forma opcional con  
 1 a 5 grupos R<sup>22</sup> seleccionados en forma independiente; y

Cada R<sup>22</sup> se selecciona en forma independiente del grupo que consiste en:  
 alquilo, cicloalquilo, cicloalquenilo, heterociclilo, arilo, heteroarilo, halo, -CF<sub>3</sub>, -CN,  
 -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alquil-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -  
 S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -  
 N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -  
 N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> y  
 -S(O)<sub>2</sub>R<sup>15</sup>.

En otra realización, la presente solicitud presenta un compuesto, o las  
 sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista  
 farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura  
 general que se muestra en la Fórmula I:



Fórmula I

en la cual:

$R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

U es  $\begin{cases} -C(R^5) & \text{o} & N; \end{cases}$

W se selecciona del grupo que consiste en un enlace, -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, y -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G se selecciona del grupo que consiste en -C(R<sup>3</sup>)(R<sup>4</sup>)-, -C(O)- y -N(R<sup>13</sup>)-; con la salvedad de que cuando W es -O- o -S-; G no es -N(R<sup>13</sup>)- o -C(O)-;

V se selecciona del grupo que consiste en un enlace, -O-, -C(O)-, y -N(R<sup>14</sup>)-;

$R^5$ ,  $R^6$ , y  $R^7$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

$R^3$  se selecciona del grupo que consiste en H, halo (y en un ejemplo, F), -OR<sup>15</sup> (y en un ejemplo  $R^{15}$  es H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>,

-C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o

R<sup>3</sup> y R<sup>6</sup> tomados juntos forman un enlace (es decir, R<sup>3</sup> y R<sup>6</sup> forman un enlace entre G y el átomo de carbono al cual R<sup>6</sup> está unido), siempre que cuando R<sup>3</sup> y R<sup>6</sup> forman un enlace W no es un enlace;

R<sup>4</sup>, R<sup>11</sup> y R<sup>12</sup> pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, halo (y en un ejemplo, F), -OR<sup>15</sup> (y en un ejemplo R<sup>15</sup> es H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada

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sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

siempre que cuando uno de  $R^3$  o  $R^4$  se selecciona del grupo que consiste en:

$-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  
 $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se selecciona del grupo  
que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  
 $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , y  $-N_3$  (es decir, si uno de  $R^3$  o  $R^4$  es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , o  $-N_3$ , entonces el otro no es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  
 $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , o  $-N_3$ );

siempre que cuando uno de  $R^{11}$  o  $R^{12}$  se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  
 $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  
 $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se  
selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,

$-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , y  $-N_3$  (es decir, si uno de  $R^{11}$  o  $R^{12}$  es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , o  $-N_3$ , entonces el otro no es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , o  $-N_3$ );

$R^{13}$  se selecciona en forma independiente del grupo que consiste en H,  
 alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-,  
 arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-,  
 heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-,  
 heteroarilcicloalquilo-, heterocicloalquilo-, arilheterocicloalquilo-,  
 heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo,  
 arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-,  
 arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-,  
 arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo,  
 cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-,  
 heterocicloalquenilarilo-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  
 $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  y  $-N(R^8)_2$ ;  
 y donde dicho  $R^{13}$  alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-,  
 heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-,  
 arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo,

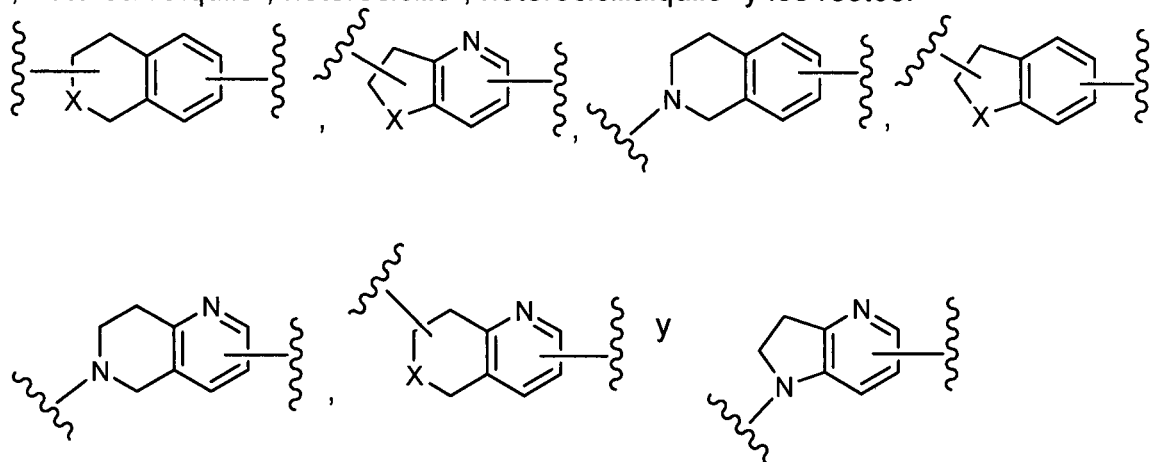
arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo-, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo, arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-, arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-, arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, y heterocicloalquenilarilo- están sustituidos en forma opcional con 1 a 5 grupos seleccionados en forma independiente del grupo que consiste en: alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>;

R<sup>14</sup> se selecciona del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, y -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);

R<sup>8</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, con cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-,

cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- que no está sustituido o está sustituido en forma independiente y opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

$R^{10}$  se selecciona del grupo que consiste en un enlace, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo-, heterociclilalquilo- y los restos:



donde X es O,  $N(R^{14})$  o S;

en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- heterociclilalquilo- para  $R^{10}$  como también los restos mencionados anteriormente para  $R^{10}$  puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y

$R^9$  se selecciona del grupo que consiste en alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-,

cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

$R^{15}$ ,  $R^{16}$  y  $R^{17}$  se seleccionan de manera independiente del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, arilcicloalquilo-, arilheterociclilo,  $R^{18}$ -alquilo,  $R^{18}$ -cicloalquilo,  $R^{18}$ -cicloalquilalquilo-,  $R^{18}$ -heterociclilo,  $R^{18}$ -heterocicilalquilo-,  $R^{18}$ -arilo,  $R^{18}$ -arilalquilo-,  $R^{18}$ -heteroarilo y  $R^{18}$ -heteroarilalquilo-;

$R^{18}$  es de 1-5 sustituyentes seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, arilo, arilalquilo-, arilalquenilo-, arilalquinilo-,  $-NO_2$ , halo, heteroarilo, HO-alquioxialquilo,  $-CF_3$ ,  $-CN$ , alquil-CN,  $-C(O)R^{19}$ ,  $-C(O)OH$ ,  $-C(O)OR^{19}$ ,  $-C(O)NHR^{20}$ ,  $-C(O)NH_2$ ,  $-C(O)NH_2-C(O)N(alquil)_2$ ,  $-C(O)N(alquil)(arilo)$ ,  $-C(O)N(alquil)(heteroarilo)$ ,  $-SR^{19}$ ,  $-S(O)_2R^{20}$ ,  $-S(O)NH_2$ ,  $-S(O)NH(alquilo)$ ,  $-S(O)N(alquil)(alquilo)$ ,  $-S(O)NH(arilo)$ ,  $-S(O)_2NH_2$ ,  $-S(O)_2NHR^{19}$ ,  $-S(O)_2NH(heterociclilo)$ ,  $-S(O)_2N(alquil)_2$ ,  $-S(O)_2N(alquil)(arilo)$ ,  $-OCF_3$ ,  $-OH$ ,  $-OR^{20}$ ,  $-O-heterociclilo$ ,  $-O-cicloalquilalquilo$ ,  $-O-heterocicilalquilo$ ,  $-NH_2$ ,  $-NHR^{20}$ ,  $-N(alquil)_2$ ,  $-N(arilalquil)_2$ ,  $-N(arilalquil)-(heteroarilalquilo)$ ,  $-NHC(O)R^{20}$ ,  $-NHC(O)NH_2$ ,  $-NHC(O)NH(alquilo)$ ,  $-NHC(O)N(alquil)(alquilo)$ ,  $-N(alquil)C(O)NH(alquilo)$ ,  $-N(alquil)C(O)N(alquil)(alquilo)$ ,  $-NHS(O)_2R^{20}$ ,  $-NHS(O)_2NH(alquilo)$ ,  $-NHS(O)_2N(alquil)(alquilo)$ ,  $-N(alquil)S(O)_2NH(alquil)$  y  $-N(alquil)S(O)_2N(alquil)(alquilo)$ ;

o, en forma alternativa, dos restos  $R^{18}$  en los carbonos adyacentes pueden

ligarse para formar:

$R^{19}$  es alquilo, cicloalquilo, arilo, arilalquilo- o heteroarilalquilo-;





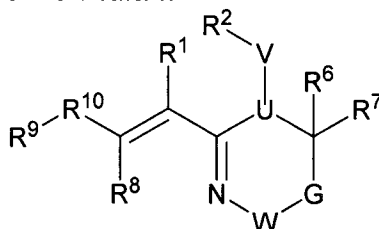
$R^{20}$  es alquilo, cicloalquilo, arilo, arilo sustituido por halo, arilalquilo-, heteroarilo o heteroarilalquilo-;

donde cada uno de los grupos alquilo, cicloalquilo, cicloalquenilo, cicloalquilalquilo-, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, alquilarilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en  $R^1$ - $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  y  $R^{14}$  está no sustituido o sustituido en forma opcional e independiente por 1 a 5 grupos  $R^{21}$  seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo, cicloalquenilo, heterociclilo, heterocicilalquilo, arilo, arilalquilo, heteroarilo, heteroarilalquilo, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>; -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>;

donde cada uno de los grupos alquilo, cicloalquenilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en  $R^{21}$  está en forma independiente no sustituido o sustituido por 1 a 5 grupos  $R^{22}$  seleccionados en forma independiente del grupo que consiste en alquilo, cicloalquilo, cicloalquenilo, heterociclilo, arilo, heteroarilo, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alquil-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-

$N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-CH_2-N(R^{15})C(O)OR^{16}$ ,  $-N_3$ ,  $=NOR^{15}$ ,  $-NO_2$ ,  $-S(O)R^{15}$  y  $-S(O)_2R^{15}$ .

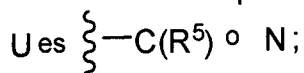
En otra realización, la presente solicitud presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la Fórmula I:



### Fórmula I

en la cual:

R<sup>2</sup> y R<sup>6</sup> están unidos para formar un cicloalquilo C<sub>4</sub>-C<sub>8</sub>, cicloalqueno C<sub>4</sub>-C<sub>8</sub>, resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;



W se selecciona del grupo que consiste en un enlace, -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, y -C(R<sup>11</sup>)(R<sup>12</sup>)-;

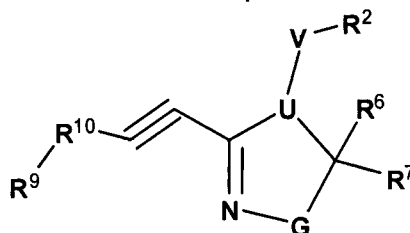
G es  $-C(R^3)(R^4)-$ ,  $-C(O)-$  y  $-N(R^{13})-$ ; con la salvedad de que cuando W es  $-O-$  o  $-S-$ , G no es  $-N(R^{13})-$  o  $-C(O)-$ ;

V se selecciona del grupo que consiste en un enlace, -O-, -C(O)-, y -N(R<sup>14</sup>)-;

R<sup>1</sup> (cuando R<sup>1</sup> no está unido a R<sup>2</sup>), R<sup>5</sup>, R<sup>6</sup> (cuando R<sup>6</sup> no está unido a R<sup>2</sup>), y R<sup>7</sup> pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-,

heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

o, de manera alternativa,  $R^1$  (cuando  $R^1$  no está unido a  $R^2$ ) y  $R^8$  se toman juntos para formar un enlace (es decir, hay un enlace triple entre el átomo de carbono al cual  $R^1$  estaba unido y el átomo de carbono al cual  $R^8$  estaba unido, es decir, el compuesto de fórmula I es un compuesto de fórmula II:



fórmula II

y  $R^2$ ,  $R^5$ ,  $R^6$ , y  $R^7$  son como se los definió con anterioridad, y  $R^3$ ,  $R^4$ ,  $R^{11}$  y  $R^{12}$  son como se los define a continuación);

$R^3$  se selecciona del grupo que consiste en H, halo (y en un ejemplo, F), -OR<sup>15</sup> (y en un ejemplo  $R^{15}$  es H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-

puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o

$R^4$ ,  $R^{11}$  y  $R^{12}$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, halo (y en un ejemplo, F),  $-OR^{15}$  (y en un ejemplo  $R^{15}$  es H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alquilo-, alqueno-, alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

siempre que cuando uno de  $R^3$  o  $R^4$  se selecciona del grupo que consiste en:

$-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,

$-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , y  $-N_3$  (es decir, si uno de  $R^3$  o  $R^4$  es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , o  $-N_3$ , entonces el otro no es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-$   
 $NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  
 $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , o  $-N_3$ ;

siempre que cuando uno de  $R^{11}$  o  $R^{12}$  se selecciona del grupo que consiste  
 en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  
 $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  
 $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se  
 selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , y  $-N_3$  (es decir, si uno de  $R^{11}$  o  $R^{12}$  es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , o  $-N_3$ , entonces el otro no es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,

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$-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , o  $-N_3$ ;

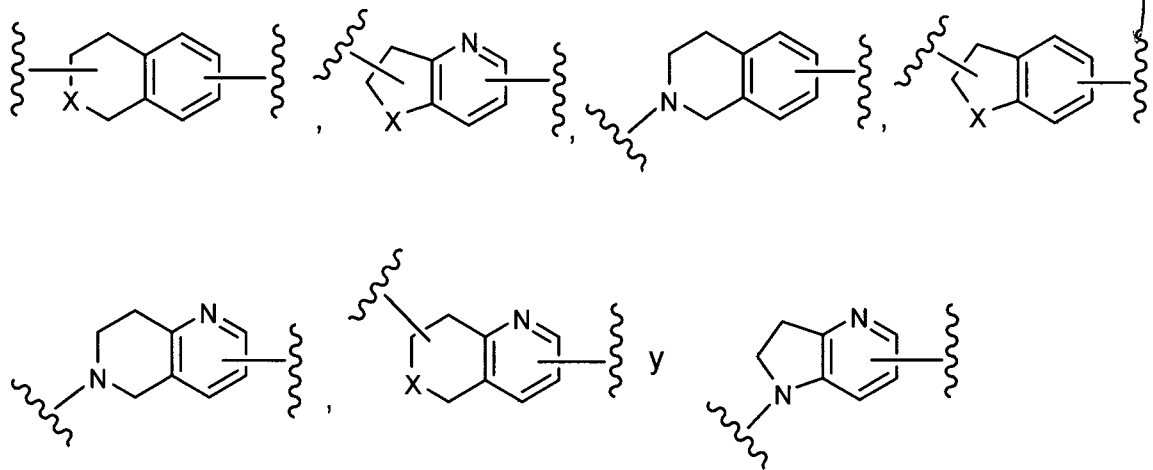
$R^{13}$  se selecciona en forma independiente del grupo que consiste en H, alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo-, arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo-, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo, arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-, arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-, arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, heterocicloalquenilarilo-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  y  $-N(R^8)_2$ ; y donde dicho  $R^{13}$  alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo, cicloalquenilo, arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo, arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-, arilo, cicloalquilarilo, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, y heterocicloalquenilarilo- están sustituidos en forma opcional con 1 a 5 grupos seleccionados en forma independiente del grupo que consiste en: alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterocicilo,

heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>; -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>;

R<sup>14</sup> se selecciona del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, y -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);

R<sup>8</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, con cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- que no está sustituido o está sustituido en forma independiente y opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

R<sup>10</sup> se selecciona del grupo que consiste en un enlace, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo-, heterociclilalquilo- y los restos:



donde X es O, N(R<sup>14</sup>) o S;

en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- heterociclilalquilo- para R<sup>10</sup> como también los restos mencionados anteriormente para R<sup>10</sup> puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

R<sup>9</sup> se selecciona del grupo que consiste en alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

R<sup>15</sup>, R<sup>16</sup> y R<sup>17</sup> se seleccionan de manera independiente del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-,



arilcicloalquilo- arilheterociclilo-,  $R^{18}$ -alquilo,  $R^{18}$ -cicloalquilo,  $R^{18}$ -cicloalquilalquilo-,  $R^{18}$ -heterociclilo,  $R^{18}$ -heterociclilalquilo-,  $R^{18}$ -arilo,  $R^{18}$ -arilalquilo-,  $R^{18}$ -heteroarilo y  $R^{18}$ -heteroarilalquilo-;

$R^{18}$  es de 1-5 sustituyentes seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, arilo, arilalquilo-, arilalquenilo-, arilalquinilo-,  $-\text{NO}_2$ , halo, heteroarilo, HO-alquioxialquilo,  $-\text{CF}_3$ ,  $-\text{CN}$ , alquil-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alquil})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{heteroarilo})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{NH}(\text{arilo})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterociclilo})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  $-\text{O-heterociclilo}$ ,  $-\text{O-cicloalquilalquilo}$ ,  $-\text{O-heterociclilalquilo}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alquil})_2$ ,  $-\text{N}(\text{arilalquil})_2$ ,  $-\text{N}(\text{arilalquil})-(\text{heteroarilalquilo})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{NH}(\text{alquil})$  y  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ;

o, en forma alternativa, dos restos  $R^{18}$  en los carbonos adyacentes pueden

ligarse para formar:

$R^{19}$  es alquilo, cicloalquilo, arilo, arilalquilo- o heteroarilalquilo-;

$R^{20}$  es alquilo, cicloalquilo, arilo, arilo sustituido por halo, arilalquilo-, heteroarilo o heteroarilalquilo-;

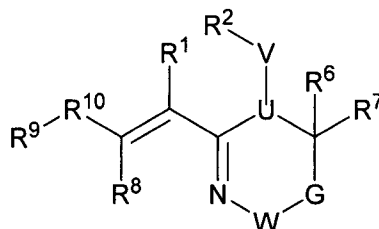
donde cada uno de los grupos alquilo, cicloalquilo, cicloalquenilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, alquilarilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en  $R^1$ ,  $R^2$ - $R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  y  $R^{14}$  está no sustituido o sustituido en forma opcional e independiente por 1 a 5 grupos  $R^{21}$  seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-,

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cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo, heteroarilo, heteroarilalquilo-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>; donde cada uno de los grupos alquilo, cicloalquenilo-, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en R<sup>21</sup> está en forma independiente no sustituido o sustituido por 1 a 5 grupos R<sup>22</sup> seleccionados en forma independiente del grupo que consiste en alquilo, cicloalquilo, cicloalquenilo-, heterociclilo, arilo, heteroarilo, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alquil-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> y -S(O)<sub>2</sub>R<sup>15</sup>.

En otra realización, la presente solicitud presenta un compuesto, o las sales, solvatos, ésteres o prodrugas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la Fórmula I:

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Fórmula I

en la cual:

$R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalqueno  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalqueno  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

U es  $\begin{matrix} \diagup \\ \diagdown \end{matrix} -C(R^5) \text{ o } N$ ;

W se selecciona del grupo que consiste en un enlace, -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, y -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G es -C(R<sup>3</sup>)(R<sup>4</sup>)-, -C(O)- y -N(R<sup>13</sup>)-; con la salvedad de que cuando W es -O- o -S-, G no es -N(R<sup>13</sup>)- o -C(O)-;

V se selecciona del grupo que consiste en un enlace, -O-, -C(O)- y -N(R<sup>14</sup>)-;

$R^5$ ,  $R^6$ , y  $R^7$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alqueno-, alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-,

heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

$R^3$  se selecciona del grupo que consiste en H, halo (y en un ejemplo, F),  $-OR^{15}$  (y en un ejemplo  $R^{15}$  es H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o

$R^4$ ,  $R^{11}$  y  $R^{12}$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, halo (y en un ejemplo, F),  $-OR^{15}$  (y en un ejemplo  $R^{15}$  es H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,



$-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , o  $-N_3$ ;

siempre que cuando uno de  $R^{11}$  o  $R^{12}$  se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  
 $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  
 $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se  
selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , y  $-N_3$  (es decir, si uno de  $R^{11}$  o  $R^{12}$  es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , o  $-N_3$ , entonces el otro no es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , o  $-N_3$ ;

$R^{13}$  se selecciona en forma independiente del grupo que consiste en H,  
alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-,  
arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-,  
heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-,  
heteroarilcicloalquilo-, heterocicloalquilo-, arilheterocicloalquilo-,  
heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo,  
arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo,

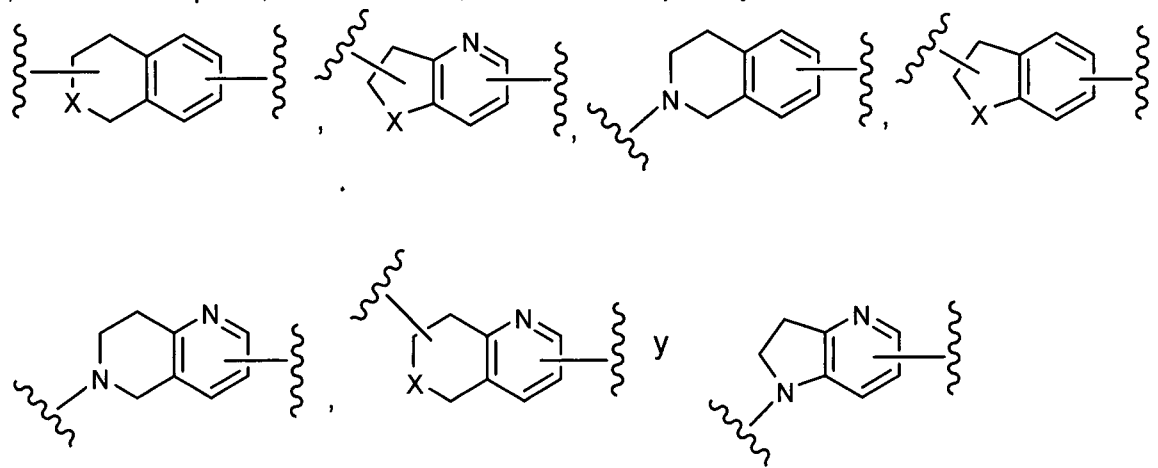
arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-,  
 arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo,  
 cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-,  
 heterocicloalquenilarilo-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  
 $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  y  
 $-N(R^8)_2$ ; y donde dicho  $R^{13}$  alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-,  
 heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-,  
 arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo,  
 arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo-, arilheterocicloalquilo-,  
 heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo,  
 arilcicloalquenilo, heteroarilcicloalquenilo-, heterocicloalquenilo-,  
 arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-,  
 arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo,  
 cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, y  
 heterocicloalquenilarilo- están sustituidos en forma opcional con 1 a 5 grupos  
 seleccionados en forma independiente del grupo que consiste en: alquilo,  
 alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterocicilo,  
 heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo,  $-CN$ ,  $-$   
 $OR^{15}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-SR^{15}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-$   
 $CH(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $-N(R^{15})(R^{16})$ ,  $-alquil-N(R^{15})(R^{16})$ ,  $-N(R^{15})C(O)R^{16}$ ,  
 $-CH_2-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-R^{15}$ ,  $-CH_2N(R^{15})(R^{16})$ ,  
 $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-CH_2-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)OR^{16}$ ,  $-CH_2-N(R^{15})C(O)OR^{16}$ ,  $-S(O)R^{15}$ ,  $=NOR^{15}$ ,  $-N_3$ ,  $-NO_2$  y  
 $-S(O)_2R^{15}$ ;

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$R^{14}$  se selecciona del grupo que consiste en H, alquilo, alqueno, alquino, cicloalquilo, cicloalquilalquilo-, cicloalqueno, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, -CN, -C(O) $R^{15}$ , -C(O)OR $^{15}$ , -C(O)N( $R^{15}$ )( $R^{16}$ ), -S(O)N( $R^{15}$ )( $R^{16}$ ), -S(O) $_2$ N( $R^{15}$ )( $R^{16}$ ), -C(=NOR $^{15}$ ) $R^{16}$ , y -P(O)(OR $^{15}$ )(OR $^{16}$ );

$R^8$  se selecciona del grupo que consiste en H, alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, con cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- que no está sustituido o está sustituido en forma independiente y opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

$R^{10}$  se selecciona del grupo que consiste en un enlace, alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo-, heterocicilalquilo- y los restos:



donde X es O, N( $R^{14}$ ) o S;

en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-,



heterociclilo- heterocicilalquilo- para  $R^{10}$  como también los restos mencionados anteriormente para  $R^{10}$  puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y

$R^9$  se selecciona del grupo que consiste en alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

$R^{15}$ ,  $R^{16}$  y  $R^{17}$  se seleccionan de manera independiente del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, arilcicloalquilo-, arilheterociclilo-,  $R^{18}$ -alquilo,  $R^{18}$ -cicloalquilo,  $R^{18}$ -cicloalquilalquilo-,  $R^{18}$ -heterociclilo,  $R^{18}$ -heterocicilalquilo-,  $R^{18}$ -arilo,  $R^{18}$ -arilalquilo-,  $R^{18}$ -heteroarilo y  $R^{18}$ -heteroarilalquilo-;

$R^{18}$  es de 1-5 sustituyentes seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, arilo, arilalquilo-, arilalquenilo-, arilalquinilo-,  $-\text{NO}_2$ , halo, heteroarilo,  $\text{HO}$ -alquioxialquilo,  $-\text{CF}_3$ ,  $-\text{CN}$ , alquil-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alquil})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{heteroarilo})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{NH}(\text{arilo})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterociclilo})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,

-O-heterociclilo, -O-cicloalquilalquilo, -O-heterociclilalquilo,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alquil})_2$ ,  $-\text{N}(\text{arilalquil})_2$ ,  $-\text{N}(\text{arilalquil})-(\text{heteroarilalquilo})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{NH}(\text{alquil})$  y  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ;

o, en forma alternativa, dos restos  $\text{R}^{18}$  en los carbonos adyacentes pueden

ligarse para formar:

$\text{R}^{19}$  es alquilo, cicloalquilo, arilo, arilalquilo- o heteroarilalquilo-;

$\text{R}^{20}$  es alquilo, cicloalquilo, arilo, arilo sustituido por halo, arilalquilo-, heteroarilo o heteroarilalquilo-;

donde cada uno de los grupos alquilo, cicloalquilo, cicloalquenilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, alquilarilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en  $\text{R}^1$ - $\text{R}^2$ ,  $\text{R}^2$ - $\text{R}^6$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^7$ ,  $\text{R}^8$ ,  $\text{R}^9$ ,  $\text{R}^{10}$ ,  $\text{R}^{11}$ ,  $\text{R}^{12}$  y  $\text{R}^{14}$  está no sustituido o sustituido en forma opcional e independiente por 1 a 5 grupos  $\text{R}^{21}$  seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo,  $-\text{CN}$ ,  $-\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{R}^{15}$ ,  $-\text{C}(\text{O})\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{SR}^{15}$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{CH}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{C}(=\text{NOR}^{15})\text{R}^{16}$ ,  $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ,  $-\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{alquil}-\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{CH}_2-\text{R}^{15}$ ,  $-\text{CH}_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{OR}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{OR}^{16}$ ,  $-\text{S}(\text{O})\text{R}^{15}$ ,  $=\text{NOR}^{15}$ ,  $-\text{N}_3$ ,  $-\text{NO}_2$  y  $-\text{S}(\text{O})_2\text{R}^{15}$ ;

donde cada uno de los grupos alquilo, cicloalqueno, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, alqueno y alquino en  $R^{21}$  está en forma independiente no sustituido o sustituido por 1 a 5 grupos  $R^{22}$  seleccionados en forma independiente del grupo que consiste en alquilo, cicloalquilo, cicloalqueno, heterociclilo, arilo, heteroarilo, halo,  $-CF_3$ ,  $-CN$ ,  $-OR^{15}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-alquil-C(O)OR^{15}$ ,  $C(O)N(R^{15})(R^{16})$ ,  $-SR^{15}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $-N(R^{15})(R^{16})$ ,  $-alquil-N(R^{15})(R^{16})$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-CH_2-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-CH_2-N(R^{15})C(O)OR^{16}$ ,  $-N_3$ ,  $=NOR^{15}$ ,  $-NO_2$ ,  $-S(O)R^{15}$  y  $-S(O)_2R^{15}$ .

En otra realización, U es  $C(R^5)$ .

En otra realización, U es N.

En otra realización,  $R^2$  es H.

En otra realización,  $R^2$  es alquilo.

En otra realización,  $R^2$  es metilo.

En otra realización,  $R^2$  es alcoxilalquilo-.

En otra realización,  $R^2$  es 3-metoxipropilo-.

En otra realización, U es N y  $R^2$  es 3-metoxipropilo-.

En otra realización, W es un enlace.

En otra realización, W es  $-O-$ .

En otra realización, W es  $-C(O)-$ .

En otra realización, W es  $-S-$ .

En otra realización, W es  $-S(O)-$ .

En otra realización, W es  $-S(O_2)-$ .

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En otra realización, W es  $-C(R^{11})(R^{12})-$ .

En otra realización,  $=N-W-G-$  es  $=N-C(R^{11}R^{12})-C(O)-$ .

En otra realización, G es  $-C(R^3)(R^4)-$ .

En otra realización, G es  $-C(O)-$ .

En otra realización, G es  $-N(R^{13})-$ .

En otra realización, V es un enlace.

En otra realización, V es  $-O-$ .

En otra realización, V es  $-C(O)-$ .

En otra realización, V es  $-N(R^{14})-$ .

En otra realización,  $R^2$  es arilalquilo-.

En otra realización,  $R^2$  es fenilmetilo-.

En otra realización,  $R^2$  es (4-alkoxi)fenilmetilo-.

En otra realización,  $R^2$  es (4-metoxi)fenilmetilo-.

En otra realización,  $R^1$  es H.

En otra realización,  $R^1$  es alquilo.

En otra realización,  $R^1$  es metilo.

En otra realización,  $R^1$  y  $R^2$  están unidos para formar un anillo ciclopentilo, que no está sustituido.

En otra realización,  $R^1$  y  $R^2$  están unidos para formar un anillo ciclopentilo, que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo,  $-CN$ ,  $-NH_2$ ,  $-NH(\text{alquilo})$ ,  $-N(\text{alquil})_2$ , hidroxilo y alcoxi.

En otra realización,  $R^1$  y  $R^2$  están unidos para formar un anillo ciclohexilo, que no está sustituido.

En otra realización,  $R^1$  y  $R^2$  están unidos para formar un anillo ciclohexilo, que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes,

cada uno se selecciona en forma independiente del grupo que consiste en alcoxi halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y grupos.

En otra realización, U es N, y R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo piperidinilo incluyendo el N de U como el nitrógeno de dicho anillo piperidinilo, que no está sustituido.

En otra realización, U es N, y R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo piperidinilo incluyendo el N de U como el nitrógeno de dicho anillo piperidinilo, donde dicho anillo piperidinilo está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

En otra realización, U es N, y R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo pirrolidinilo incluyendo el N de U como el nitrógeno de dicho anillo pirrolidinilo, que no está sustituido.

En otra realización, U es N, y R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo pirrolidinilo incluyendo el N de U como el nitrógeno de dicho anillo pirrolidinilo, donde dicho anillo pirrolidinilo está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

En otra realización, U es N, y R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo piperazinilo incluyendo el N de U como el nitrógeno de dicho anillo piperazinilo, que no está sustituido.

En otra realización, U es N, y R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo piperazinilo incluyendo el N de U como el nitrógeno de dicho anillo piperazinilo, donde dicho anillo piperazinilo está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo

que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

En otra realización R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo sustituido en forma opcional con 1 a 5 sustituyentes R<sup>21</sup> seleccionados en forma independiente, y dicho anillo está fusionado con un anillo arilo o heteroarilo, y dicho anillo fusionado resultante está sustituido en forma opcional con 1 a 5 sustituyentes R<sup>21</sup> seleccionados en forma independiente.

En otra realización R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo sustituido con 1 a 5 sustituyentes R<sup>21</sup> seleccionados en forma independiente, y dicho anillo está fusionado con un anillo arilo o heteroarilo, y dicho anillo fusionado resultante está sustituido en forma opcional con 1 a 5 sustituyentes R<sup>21</sup> seleccionados en forma independiente.

En otra realización R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo sustituido en forma opcional con 1 a 5 sustituyentes R<sup>21</sup> seleccionados en forma independiente.

En otra realización R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo.

En otra realización R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo heterociclilo sustituido en forma opcional con 1 a 5 sustituyentes R<sup>21</sup> seleccionados en forma independiente.

En otra realización R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo heterociclilo sustituido con 1 a 5 sustituyentes R<sup>21</sup> seleccionados en forma independiente.

En otra realización U es N, y R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo heterociclilo sustituido en forma opcional con 1 a 5 sustituyentes R<sup>21</sup> seleccionados en forma independiente.

En otra realización U es N, y R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo heterociclilo sustituido con 1 a 5 sustituyentes R<sup>21</sup> seleccionados en forma independiente.

En otra realización  $R^1$  y  $R^2$  están unidos para formar un anillo, y dicho anillo está fusionado con un anillo arilo o heteroarilo, y dicho anillo fusionado resultante está sustituido en forma opcional con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^1$  y  $R^2$  están unidos para formar un anillo heterociclilo.

En otra realización U es N, y  $R^1$  y  $R^2$  están unidos para formar un anillo heterociclilo.

En otra realización  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido en forma opcional con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización U es N, y  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido en forma opcional con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización U es N, y  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido en forma opcional con un resto =O.

En otra realización U es N, y  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido en forma opcional con un resto =O.

En otra realización  $R^1$  y  $R^2$  están unidos para formar un piperidinilo.

En otra realización U es N, y  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo.

En otra realización  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido con un resto =O.

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En otra realización U es N, y  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido con un resto =O.

En otra realización  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización:

(a)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (1) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y

(b)  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (1) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; y

(c) dicho resto  $R^2$  y  $R^6$  cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y



el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y cualquiera de  $R^3$  o  $R^4$  del resto  $-C(R^3)(R^4)-G$ , están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (b) dicho resto heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, donde dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, donde dicho resto heterociclilo is sustituido con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

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En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto heterociclilo está sustituido en forma opcional con un  $=O$ , y (b) dicho resto heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, donde dicho resto heterociclilo está sustituido en forma opcional con  $a = O$ .

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, donde dicho resto heterociclilo heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto heterociclilo está sustituido con un  $=O$ , y (b) dicho resto heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, donde dicho resto heterociclilo está sustituido con  $a=O$ .

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5 miembros, en la cual: (a) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (b) dicho resto heterociclilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5 miembros, donde dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5 miembros, en la cual: (a) dicho resto heterociclilo está sustituido en forma opcional con un  $=O$ , y (b) dicho resto heterociclilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5 miembros, donde dicho resto heterociclilo está sustituido en forma opcional con  $a=O$ .

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5 miembros, donde dicho resto heterociclilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que

resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5 miembros.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5 miembros, en la cual: (a) dicho resto heterociclilo está sustituido con un  $=O$ , y (b) dicho resto heterociclilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5 miembros, donde dicho resto heterociclilo está sustituido con a  $=O$ .

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un anillo pirrolidinilo, en la cual: (a) dicho anillo pirrolidinilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (b) dicho anillo pirrolidinilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un 5 anillo pirrolidinilo, donde dicho anillo pirrolidinilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un anillo pirrolidinilo, en la cual: (a) dicho anillo pirrolidinilo está sustituido en forma opcional con un  $=O$ , y (b) dicho anillo pirrolidinilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión

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está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un anillo pirrolidinilo, donde dicho anillo pirrolidinilo está sustituido en forma opcional con  $a=O$ .

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un anillo pirrolidinilo, donde dicho anillo pirrolidinilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un anillo pirrolidinilo.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un anillo pirrolidinilo, en la cual: (a) dicho anillo pirrolidinilo está sustituido con un  $=O$ , y (b) dicho anillo pirrolidinilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un anillo pirrolidinilo, donde dicho anillo pirrolidinilo está sustituido con  $a=O$ .

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5 miembros, en la cual: (a) dicho resto heterociclilo está sustituido con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (b) dicho resto heterociclilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5 miembros, donde dicho resto heterociclilo está sustituido con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un anillo pirrolidinilo, en la cual: (a) dicho anillo pirrolidinilo está sustituido con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (b) dicho anillo pirrolidinilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un 5 anillo pirrolidinilo, donde dicho anillo pirrolidinilo está sustituido con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

En otra realización,  $R^6$  es H.

En otra realización,  $R^6$  es alquilo.

En otra realización,  $R^6$  es metilo.

En otra realización,  $R^7$  es arilo.

En otra realización,  $R^7$  es un fenilo no sustituido.

En otra realización,  $R^7$  es un fenilo que está sustituido con 1-4 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en heteroarilo halo, alquilo,  $-CN$ ,  $-NH_2$ ,  $-NH(\text{alquilo})$ ,  $-N(\text{alquil})_2$ , hidroxilo, alcoxi, arilo y grupos.

En otra realización,  $R^7$  es un naftilo no sustituido.

En otra realización,  $R^7$  es naftilo que está sustituido con 1-4 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo,  $-CN$ ,  $-NH_2$ ,  $-NH(\text{alquilo})$ ,  $-N(\text{alquil})_2$ , hidroxilo, alcoxi, arilo y heteroarilo.

En otra realización,  $R^7$  es bifenilo no sustituido.

PATENTE DE INVENCION

09-137086

Tono: 3/3

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En otra realización,  $R^7$  es bifenilo que está sustituido con 1-4 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxilo y alcoxi.

En otra realización,  $R^7$  es 3-(1,1'-bifenil)-ilo.

En otra realización,  $R^7$  es 4-(1,1'-bifenil)-ilo.

En otra realización,  $R^6$  es H y  $R^7$  es un bifenilo que puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-4 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxilo y alcoxi.

En otra realización,  $R^6$  es metilo, y  $R^7$  es un bifenilo que puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-4 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxilo y alcoxi.

En otra realización,  $R^6$  es H, y  $R^7$  es un fenilo que puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-4 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxilo y alcoxi.

En otra realización,  $R^6$  es metilo, y  $R^7$  es un bifenilo que puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-4 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxilo y alcoxi.

En otra realización,  $R^2$  y  $R^6$  están unidos para formar un anillo ciclopentilo.

TOMA 3/E



En otra realización,  $R^2$  y  $R^6$  están unidos para formar un anillo ciclopentilo, que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

En otra realización,  $R^2$  y  $R^6$  están unidos para formar un anillo ciclohexilo.

En otra realización,  $R^2$  y  $R^6$  están unidos para formar un anillo ciclohexilo, que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

En otra realización, U es N, y  $R^2$  y  $R^6$  están unidos para formar un anillo piperidinilo incluyendo el N de U como el nitrógeno de dicho anillo piperidinilo, que no está sustituido.

En otra realización, U es N, y  $R^2$  y  $R^6$  están unidos para formar un anillo piperidinilo incluyendo el N de U como el nitrógeno de dicho anillo piperidinilo, donde dicho anillo piperidinilo está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

En otra realización, U es N, y  $R^2$  y  $R^6$  están unidos para formar un anillo pirrolidinilo incluyendo el N de U como el nitrógeno de dicho anillo pirrolidinilo, que no está sustituido.

En otra realización, U es N, y  $R^2$  y  $R^6$  están unidos para formar un anillo pirrolidinilo incluyendo el N de U como el nitrógeno de dicho anillo pirrolidinilo, donde dicho anillo pirrolidinilo está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

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En otra realización, U es N, y  $R^2$  y  $R^6$  están unidos para formar un anillo piperazinilo incluyendo el N de U como el nitrógeno de dicho anillo piperazinilo, que no está sustituido.

En otra realización, U es N, y  $R^2$  y  $R^6$  están unidos para formar un anillo piperazinilo incluyendo el N de U como el nitrógeno de dicho anillo piperazinilo, donde dicho anillo piperazinilo está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

En otra realización,  $R^2$  y  $R^6$  están unidos para formar un anillo morfolinilo que no está sustituido.

En otra realización,  $R^2$  y  $R^6$  están unidos para formar un anillo morfolinilo, que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

En otra realización,  $R^2$  y  $R^6$  están unidos para formar un anillo piranilo que no está sustituido.

En otra realización,  $R^2$  y  $R^6$  están unidos para formar un anillo piranilo, que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

En otra realización,  $R^2$  y  $R^6$  están unidos para formar un anillo pirrolidinilo que no está sustituido.

En otra realización,  $R^2$  y  $R^6$  están unidos para formar un anillo pirrolidinilo, que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

No

En otra realización, ambos ( $R^1$  y  $R^2$ ) y ( $R^2$  y  $R^6$ ) se unen para formar anillos cicloalquilo independientes.

En otra realización, ambos ( $R^1$  y  $R^2$ ) y ( $R^2$  y  $R^6$ ) se unen para formar anillos cicloalquilo independientes, cada uno de los cuales en forma independiente está sustituido en forma opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxilo y alcoxi.

En otra realización, ambos ( $R^1$  y  $R^2$ ) y ( $R^2$  y  $R^6$ ) se unen para formar anillos heterociclilo independientes.

En otra realización, ambos ( $R^1$  y  $R^2$ ) y ( $R^2$  y  $R^6$ ) se unen para formar anillos heterociclilo independientes, cada uno de los cuales en forma independiente está sustituido en forma opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxilo y alcoxi.

En otra realización, ambos ( $R^1$  y  $R^2$ ) y ( $R^2$  y  $R^6$ ) se unen para formar anillos cicloalquilo independientes.

En otra realización, ambos  $R^1$  y  $R^2$  están unidos para formar un anillo cicloalquilo, y  $R^2$  y  $R^6$  están unidos para formar un anillo heterociclilo, cada uno de los cuales en forma independiente está sustituido en forma opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxilo y alcoxi.

En otra realización, ambos  $R^1$  y  $R^2$  están unidos para formar un anillo heterociclilo, y  $R^2$  y  $R^6$  están unidos para formar un anillo cicloalquilo, cada uno de los cuales en forma independiente está sustituido en forma opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en

yes

forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

En otra realización, R<sup>7</sup> es arilo.

En otra realización, R<sup>7</sup> es un fenilo no sustituido.

En otra realización, R<sup>7</sup> es un fenilo que está sustituido con 1-4 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí, alcoxi, arilo y heteroarilo.

En otra realización, R<sup>7</sup> es 4-fluorofenilo.

En otra realización, R<sup>7</sup> es un naftilo no sustituido.

En otra realización, R<sup>7</sup> es naftilo que está sustituido con 1-4 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí, alcoxi, arilo y heteroarilo.

En otra realización, R<sup>7</sup> es bifenilo no sustituido.

En otra realización, R<sup>7</sup> es bifenilo que está sustituido con 1-4 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

En otra realización, R<sup>7</sup> es 3-(1,1'-bifenil)-ilo.

En otra realización, R<sup>7</sup> es 4-(1,1'-bifenil)-ilo.

En otra realización, R<sup>8</sup> es H.

En otra realización, R<sup>8</sup> es alquilo.

En otra realización, R<sup>8</sup> es metilo.

En otra realización, R<sup>10</sup> es arilo.

En otra realización, R<sup>10</sup> es fenilo.

En otra realización R<sup>10</sup> es arilo sustituido con 1 halo.

En otra realización  $R^{10}$  es arilo sustituido con 1 halo, y dicho halo es F.

En otra realización  $R^{10}$  es arilo sustituido con 1 a 3 restos  $R^{21}$  seleccionados en forma independiente.

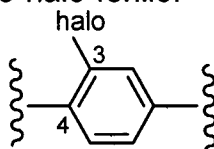
En otra realización  $R^{10}$  es arilo sustituido con 1 a 3 restos  $R^{21}$ , donde cada resto  $R^{21}$  es el mismo grupo  $-OR^{15}$  o uno diferente.

En otra realización  $R^{10}$  es arilo sustituido con 1 resto  $R^{21}$ .

En otra realización  $R^{10}$  es fenilo sustituido con 1 halo.

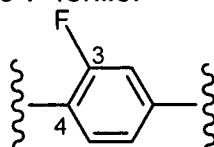
En otra realización  $R^{10}$  es fenilo sustituido con 1 halo, y dicho halo es F.

En otra realización  $R^{10}$  es 3-halo-fenilo:



(donde el enlace del carbono marcado como 4 es para el resto  $R^9$ ).

En otra realización  $R^{10}$  es 3-F-fenilo:



(donde el enlace del carbono marcado como 4 es para el resto  $R^9$ ).

En otra realización  $R^{10}$  es arilo sustituido con un grupo  $-OR^{15}$ .

En otra realización  $R^{10}$  es arilo sustituido con un grupo  $-OR^{15}$ , y dicho  $R^{15}$  es alquilo (por ej., metilo).

En otra realización  $R^{10}$  es fenilo sustituido con 1 a 3 restos  $R^{21}$  seleccionados en forma independiente.

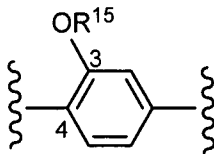
En otra realización  $R^{10}$  es fenilo sustituido con 1 a 3 restos  $R^{21}$ , donde cada resto  $R^{21}$  es el mismo grupo  $-OR^{15}$  o uno diferente.

En otra realización  $R^{10}$  es fenilo sustituido con 1 resto  $R^{21}$ .

En otra realización  $R^{10}$  es fenilo sustituido con un grupo  $-OR^{15}$ .

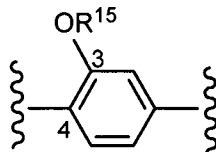
En otra realización  $R^{10}$  es fenilo sustituido con un grupo  $-OR^{15}$ , y dicho  $R^{15}$  es alquilo (por ej., metilo).

En otra realización  $R^{10}$  es 3-OR<sup>15</sup>-fenilo:



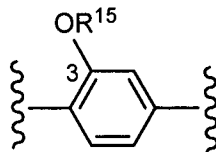
(donde el enlace del carbono marcado como 4 es para el resto R<sup>9</sup>).

En otra realización  $R^{10}$  es 3-OR<sup>15</sup>-fenilo:



en la cual R<sup>15</sup> es alquilo (donde el enlace del carbono marcado como 4 es para el resto R<sup>9</sup>).

En otra realización  $R^{10}$  es 3-OR<sup>15</sup>-fenilo:



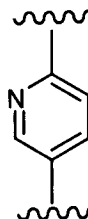
en la cual R<sup>15</sup> es metilo (es decir, R<sup>10</sup> is 3-metoxi-fenilo).

En otra realización, R<sup>10</sup> es heteroarilo.

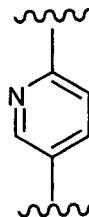
En otra realización, R<sup>10</sup> es heteroarilo no sustituido.

En otra realización R<sup>10</sup> es heteroarilo no sustituido donde dicho heteroarilo es piridilo.

En otra realización R<sup>10</sup> es:

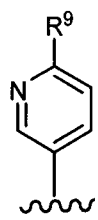


En otra realización R<sup>10</sup> es:



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donde el resto -R<sup>10</sup>-R<sup>9</sup> es:



En otra realización R<sup>10</sup> es arilo sustituido con 1 a 3 restos R<sup>21</sup>, donde cada resto R<sup>21</sup> es el mismo halo o uno diferente.

En otra realización R<sup>10</sup> es arilo sustituido con 1 a 3 restos R<sup>21</sup>, donde cada resto R<sup>21</sup> es F.

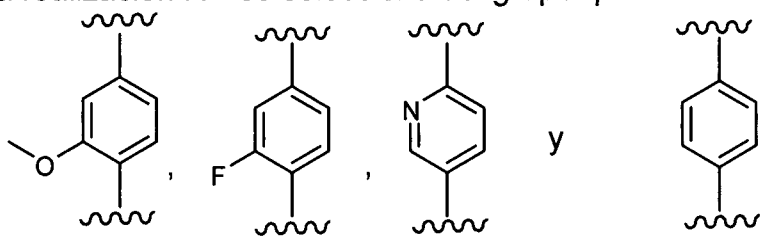
En otra realización R<sup>10</sup> es arilo sustituido con un resto R<sup>21</sup>, y dicho resto R<sup>21</sup> es halo.

En otra realización R<sup>10</sup> es arilo sustituido con un resto R<sup>21</sup>, dicho resto R<sup>21</sup> es -halo, y dicho halo es F.

En otra realización R<sup>10</sup> es fenilo sustituido con 1 a 3 restos R<sup>21</sup>, donde cada resto R<sup>21</sup> es el mismo halo o uno diferente.

En otra realización R<sup>10</sup> es fenilo sustituido con 1 a 3 restos R<sup>21</sup>, donde cada resto R<sup>21</sup> es F.

En otra realización R<sup>10</sup> se selecciona del grupo que consiste en:



En otra realización de esta invención R<sup>9</sup> se selecciona del grupo que consiste en heteroarilo y heteroarilo sustituido con 1-3 grupos R<sup>21</sup>, y donde cada R<sup>21</sup> se selecciona en forma independiente.

En otra realización, R<sup>9</sup> es heteroarilo no sustituido.

En otra realización, R<sup>9</sup> es heteroarilo que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se

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selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, CN, NH<sub>2</sub>, NH(alquilo), N(alquil)<sub>2</sub>, hidroxí y alcoxi.

En otra realización, R<sup>9</sup> es heteroarilo sustituido con 1 a 3 grupos alquilo seleccionados en forma independiente.

En otra realización, R<sup>9</sup> es heteroarilo sustituido con un grupo alquilo (por ej., metilo).

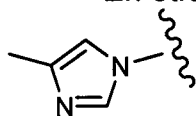
En otra realización de esta invención R<sup>9</sup> se selecciona del grupo que consiste en imidazolilo y imidazolilo sustituido con 1-3 grupos R<sup>21</sup>, y donde cada R<sup>21</sup> se selecciona en forma independiente.

En otra realización de esta invención R<sup>9</sup> es imidazolilo sustituido con 1-3 grupos R<sup>21</sup>, y donde cada R<sup>21</sup> se selecciona en forma independiente.

En otra realización, R<sup>9</sup> es imidazolilo sustituido con 1-3 sustituyentes seleccionados en forma independiente del grupo que consiste en grupos halo, alquilo, CN, NH<sub>2</sub>, NH(alquilo), N(alquil)<sub>2</sub>, hidroxí y alcoxi.

En otra realización, R<sup>9</sup> es imidazol-1-ilo.

En otra realización, R<sup>9</sup> es 4-metil-imidazol-1-ilo:



En otra realización, R<sup>9</sup> es 5-cloro-4-metilo-imidazol-1-ilo.

En otra realización R<sup>10</sup> se selecciona del grupo que consiste en arilo y arilo sustituido con uno o más grupos R<sup>21</sup>, y R<sup>9</sup> se selecciona del grupo que consiste en heteroarilo y heteroarilo sustituido con uno o más grupos R<sup>21</sup>, y donde cada R<sup>21</sup> se selecciona en forma independiente.

En otra realización R<sup>10</sup> se selecciona del grupo que consiste en fenilo y fenil sustituido con 1-3 grupos R<sup>21</sup> sustituidos en forma independiente, y R<sup>9</sup> se selecciona del grupo que consiste en imidazolilo y imidazolilo sustituido con 1-3 grupos R<sup>21</sup> sustituidos en forma independiente.



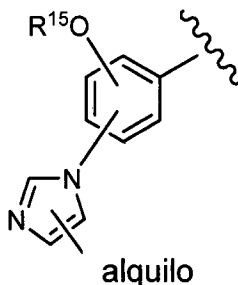
En otra realización  $R^{10}$  es fenilo sustituido con 1-3 grupos  $R^{21}$  sustituidos en forma independiente, y  $R^9$  se selecciona del grupo que consiste en imidazolilo y imidazolilo sustituido con 1-3 grupos  $R^{21}$  sustituidos en forma independiente.

En otra realización  $R^{10}$  se selecciona del grupo que consiste en heteroarilo y heteroarilo sustituido con 1-3 grupos  $R^{21}$ , y el grupo  $R^9$  se selecciona del grupo que consiste en heteroarilo y heteroarilo sustituido con 1-3 grupos  $R^{21}$ , y donde cada  $R^{21}$  se selecciona en forma independiente.

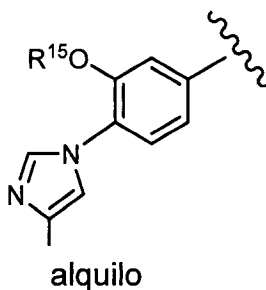
En otra realización  $R^{10}$  se selecciona del grupo que consiste en piridilo y piridilo sustituido con 1-3 grupos  $R^{21}$ , y el grupo  $R^9$  se selecciona del grupo que consiste en imidazolilo y imidazolilo sustituido con 1-3 grupos  $R^{21}$ , y donde cada  $R^{21}$  se selecciona en forma independiente.

En otra realización  $R^{10}$  es piridilo, y el grupo  $R^9$  es imidazolilo sustituido con 1-3 grupos  $R^{21}$ , y donde cada  $R^{21}$  se selecciona en forma independiente.

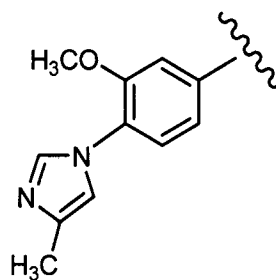
En otra realización el resto  $R^9-R^{10}$  es:



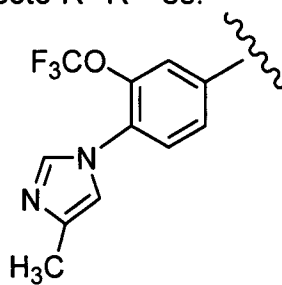
En otra realización el resto  $R^9-R^{10}$  es:



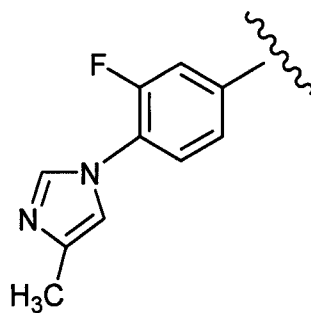
En otra realización el resto  $R^9-R^{10}$  es:



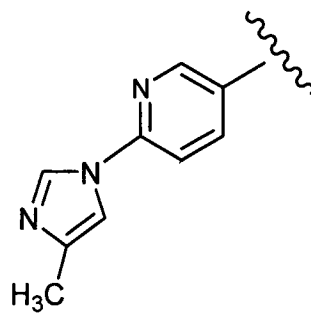
En otra realización el resto  $\text{R}^9\text{-R}^{10}$  es:



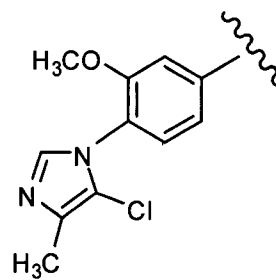
En otra realización el resto  $\text{R}^9\text{-R}^{10}$  es:



En otra realización el resto  $\text{R}^9\text{-R}^{10}$  es:

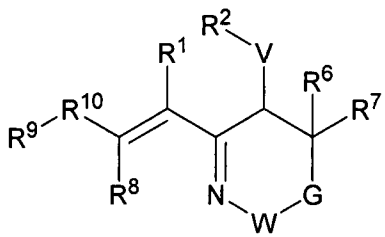


En otra realización el resto  $\text{R}^9\text{-R}^{10}$  es:



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En otra realización, la presente solicitud presenta un compuesto de fórmula I, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general de Fórmula IB:



Fórmula IB

en la cual:

cualquiera de (i) R<sup>1</sup> y R<sup>2</sup> están unidos para formar un cicloalquilo C<sub>4</sub>-C<sub>8</sub>, cicloalquenilo C<sub>4</sub>-C<sub>8</sub>, resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (ii) R<sup>2</sup> y R<sup>6</sup> están unidos para formar un cicloalquilo C<sub>4</sub>-C<sub>8</sub>, cicloalquenilo C<sub>4</sub>-C<sub>8</sub>, resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (iii) R<sup>1</sup> y R<sup>2</sup> están unidos para formar un cicloalquilo C<sub>4</sub>-C<sub>8</sub>, cicloalquenilo C<sub>4</sub>-C<sub>8</sub>, resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5

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sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

y

W se selecciona del grupo que consiste en un enlace; -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, y -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G se selecciona del grupo que consiste en -C(R<sup>3</sup>)(R<sup>4</sup>)-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, -C(O)-O-, y -N(R<sup>13</sup>)-;

V se selecciona del grupo que consiste en un enlace, -O-, y -N(R<sup>14</sup>)-;

$R^1$  (cuando  $R^1$  no está unido a  $R^2$ ),  $R^2$  (cuando  $R^2$  no está unido a  $R^1$  o  $R^6$ ),  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$  (cuando  $R^6$  no está unido a  $R^2$ ),  $R^7$ ,  $R^{11}$  y  $R^{12}$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

$R^{13}$  se selecciona en forma independiente del grupo que consiste en H, alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo-, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo, arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-, arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-, arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, heterocicloalquenilarilo-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  y  $-N(R^8)_2$ ; y donde dicho  $R^{13}$  alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo, arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-, arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-, arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, y heterocicloalquenilarilo- están sustituidos en forma opcional con 1 a 5 grupos seleccionados en forma independiente del grupo que consiste en: alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterocicilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo,  $-CN$ ,  $-OR^{15}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-SR^{15}$ ,  $-S(O)N(R^{15})(R^{16})$ , -

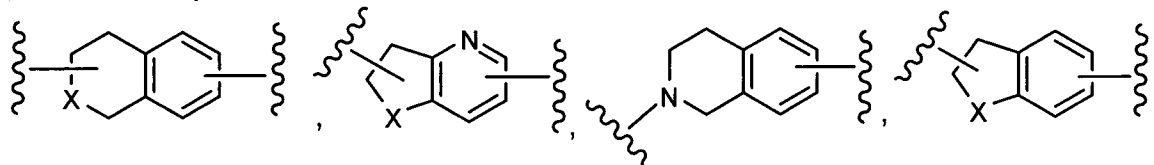
V15

$\text{CH}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{C}(=\text{NOR}^{15})\text{R}^{16}$ ,  
 $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ,  $-\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{alquil-N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  
 $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{CH}_2-\text{R}^{15}$ ;  $-\text{CH}_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  
 $-\text{N}(\text{R}^{15})\text{S}(\text{O})\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  
 $-\text{N}(\text{R}^{15})\text{S}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  
 $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{OR}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{OR}^{16}$ ,  $-\text{S}(\text{O})\text{R}^{15}$ ,  $=\text{NOR}^{15}$ ,  $-\text{N}_3$ ,  $-\text{NO}_2$  y  
 $-\text{S}(\text{O})_2\text{R}^{15}$ ;

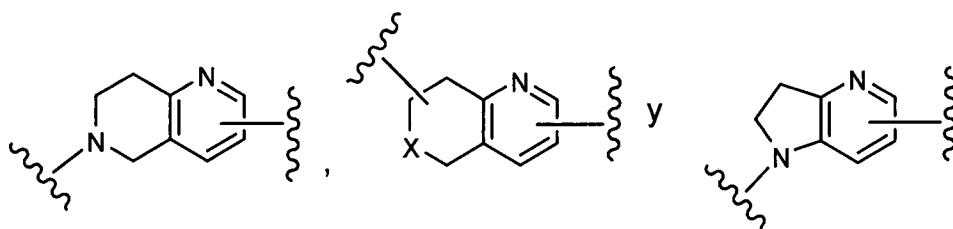
$\text{R}^{14}$  se selecciona del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-,  $-\text{CN}$ ,  $-\text{C}(\text{O})\text{R}^{15}$ ,  $-\text{C}(\text{O})\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{C}(=\text{NOR}^{15})\text{R}^{16}$ , y  $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ;

$\text{R}^8$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, con cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- que no está sustituido o está sustituido en forma independiente y opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

$\text{R}^{10}$  se selecciona del grupo que consiste en un enlace, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo-, heterocicilalquilo- y los restos:



H/b



donde X es O, N(R<sup>14</sup>) o S;

en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- heterociclilalquilo- para R<sup>10</sup> como también los restos mencionados anteriormente para R<sup>10</sup> puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y

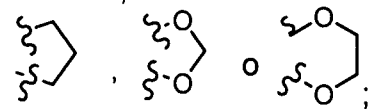
R<sup>9</sup> se selecciona del grupo que consiste en alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

R<sup>15</sup>, R<sup>16</sup> y R<sup>17</sup> se seleccionan de manera independiente del grupo que consiste en H, alquilo, alqueno, alquino, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo, heteroarilo, heteroarilalquilo-, arilcicloalquilo-, arilheterociclilo-, R<sup>18</sup>-alquilo, R<sup>18</sup>-cicloalquilo, R<sup>18</sup>-cicloalquilalquilo-, R<sup>18</sup>-heterociclilo, R<sup>18</sup>-heterociclilalquilo-, R<sup>18</sup>-arilo, R<sup>18</sup>-arilalquilo, R<sup>18</sup>-heteroarilo y R<sup>18</sup>-heteroarilalquilo-;

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$R^{18}$  es de 1-5 sustituyentes seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, arilo, arilalquilo-, arilalquenilo-, arilalquinilo-,  $-NO_2$ , halo, heteroarilo, HO-alquioxialquilo,  $-CF_3$ ,  $-CN$ , alquil-CN,  $-C(O)R^{19}$ ,  $-C(O)OH$ ,  $-C(O)OR^{19}$ ,  $-C(O)NHR^{20}$ ,  $-C(O)NH_2$ ,  $-C(O)NH_2-C(O)N(alquil)_2$ ,  $-C(O)N(alquil)(arilo)$ ,  $-C(O)N(alquil)(heteroarilo)$ ,  $-SR^{19}$ ,  $-S(O)_2R^{20}$ ,  $-S(O)NH_2$ ,  $-S(O)NH(alquilo)$ ,  $-S(O)N(alquil)(alquilo)$ ,  $-S(O)NH(arilo)$ ,  $-S(O)_2NH_2$ ,  $-S(O)_2NHR^{19}$ ,  $-S(O)_2NH(heterociclilo)$ ,  $-S(O)_2N(alquil)_2$ ,  $-S(O)_2N(alquil)(arilo)$ ,  $-OCF_3$ ,  $-OH$ ,  $-OR^{20}$ ,  $-O-heterociclilo$ ,  $-O-cicloalquilalquilo$ ,  $-O-heterocicilalquilo$ ,  $-NH_2$ ,  $-NHR^{20}$ ,  $-N(alquil)_2$ ,  $-N(arilalquil)_2$ ,  $-N(arilalquil)-(heteroarilalquilo)$ ,  $-NHC(O)R^{20}$ ,  $-NHC(O)NH_2$ ,  $-NHC(O)NH(alquilo)$ ,  $-NHC(O)N(alquil)(alquilo)$ ,  $-N(alquil)C(O)NH(alquilo)$ ,  $-N(alquil)C(O)N(alquil)(alquilo)$ ,  $-NHS(O)_2R^{20}$ ,  $-NHS(O)_2NH(alquilo)$ ,  $-NHS(O)_2N(alquil)(alquilo)$ ,  $-N(alquil)S(O)_2NH(alquil)$  y  $-N(alquil)S(O)_2N(alquil)(alquilo)$ ;

o, en forma alternativa, dos restos  $R^{18}$  en los carbonos adyacentes pueden

ligarse para formar: ;

$R^{19}$  es alquilo, cicloalquilo, arilo, arilalquilo o heteroarilalquilo;

$R^{20}$  es alquilo, cicloalquilo, arilo, arilo sustituido por halo, arilalquilo, heteroarilo o heteroarilalquilo;

donde cada uno de dichos grupos alquilo, cicloalquilo, cicloalquenilo, cicloalquilalquilo, heterociclilo, heterocicilalquilo, arilo, arilalquilo, alquilarilo, heteroarilo, heteroarilalquilo, alquenilo y alquinilo en  $R^1$ ,  $R^2$ ,  $R^1-R^2$ ,  $R^2-R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  y  $R^{14}$  está no sustituido o sustituido en forma opcional e independiente por 1 a 5 grupos  $R^{21}$  seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-,

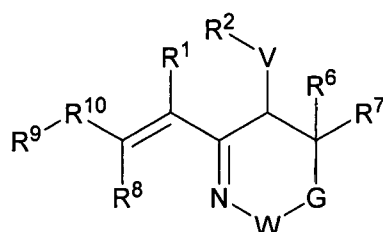


heteroarilo, heteroarilalquilo-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>;

donde cada uno de los grupos alquilo, cicloalquenilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en R<sup>21</sup> está en forma independiente no sustituido o sustituido por 1 a 5 grupos R<sup>22</sup> seleccionados en forma independiente del grupo que consiste en alquilo, cicloalquilo, cicloalquenilo, heterociclilo, arilo, heteroarilo, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alquil-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> y -S(O)<sub>2</sub>R<sup>15</sup>.

En otra realización, la presente solicitud presenta un compuesto de fórmula I, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general de Fórmula IB:

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Fórmula IB

en la cual:

o bien

(i)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(ii)  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(iii)

no

(a)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (1) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y

(b)  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (1) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; y

(c) dicho resto  $R^2$  y  $R^6$  cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(iv)  $R^6$  y cualquiera de  $R^3$  o  $R^4$  del resto  $-C(R^3)(R^4)-G$ , están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(v)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; y

W se selecciona del grupo que consiste en un enlace,  $-O-$ ,  $-C(O)-$ ,  $-S-$ ,  $-S(O)-$ ,  $-S(O_2)-$ , y  $-C(R^{11})(R^{12})-$ ;

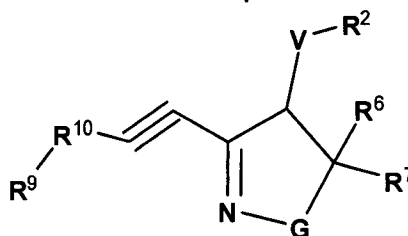
G se selecciona del grupo que consiste en  $-C(R^3)(R^4)-$ ,  $-C(O)-$ ,  $-S-$ ,  $-S(O)-$ ,  $-S(O_2)-$ ,  $-C(O)-O-$ , y  $-N(R^{13})-$  ;

V se selecciona del grupo que consiste en un enlace,  $-O-$ ,  $-C(O)-$  y  $-N(R^{14})-$ ;

$R^1$  (cuando  $R^1$  no está unido a  $R^2$ ),  $R^2$  (cuando  $R^2$  no está unido a  $R^1$  o  $R^6$ ),  $R^5$ ,  $R^6$  (cuando  $R^6$  no está unido a  $R^2$ ), y  $R^7$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

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o, de manera alternativa,  $R^1$  (cuando  $R^1$  no está unido a  $R^2$ ) y  $R^8$  se toman juntos para formar un enlace (es decir, hay un enlace triple entre el átomo de carbono al cual  $R^1$  estaba unido y el átomo de carbono al cual  $R^8$  estaba unido, es decir, el compuesto de fórmula I es un compuesto de fórmula IIA:



fórmula IIA

y  $R^2$ ,  $R^5$ ,  $R^6$ , y  $R^7$  son como se los definió con anterioridad, y  $R^3$ ,  $R^4$ ,  $R^{11}$  y  $R^{12}$  son como se los define a continuación);

$R^3$  se selecciona del grupo que consiste en H, halo (y en un ejemplo, F), -OR<sup>15</sup> (y en un ejemplo  $R^{15}$  es H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o

$R^3$  y  $R^6$  tomados juntos forman un enlace (es decir,  $R^3$  y  $R^6$  forman un enlace entre G y el átomo de carbono al cual  $R^6$  está unido), siempre que cuando  $R^3$  y  $R^6$  forman un enlace: (1) W no es un enlace, (2)  $R^2$  y  $R^6$  no se unen para

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formar un resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo (como se describió en los puntos (ii) y (iii) anteriores) (3)  $R^6$  y cualquiera de  $R^3$  o  $R^4$  del resto  $-C(R^3)(R^4)-$  G no se unen para formar un resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo (como se describió en el punto (iv) más arriba), y (4)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G no se unen para formar un resto heterociclilo o heterociclenilo (como se describió en el punto (v) más arriba);

$R^4$ ,  $R^{11}$  y  $R^{12}$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, halo (y en un ejemplo, F),  $-OR^{15}$  (y en un ejemplo  $R^{15}$  es H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

siempre que cuando uno de  $R^3$  o  $R^4$  se selecciona del grupo que consiste en:

$-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se selecciona del grupo

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que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$  (es decir, si uno de  $R^3$  o  $R^4$  es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , o  $-N_3$ , entonces el otro no es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , o  $-N_3$ );

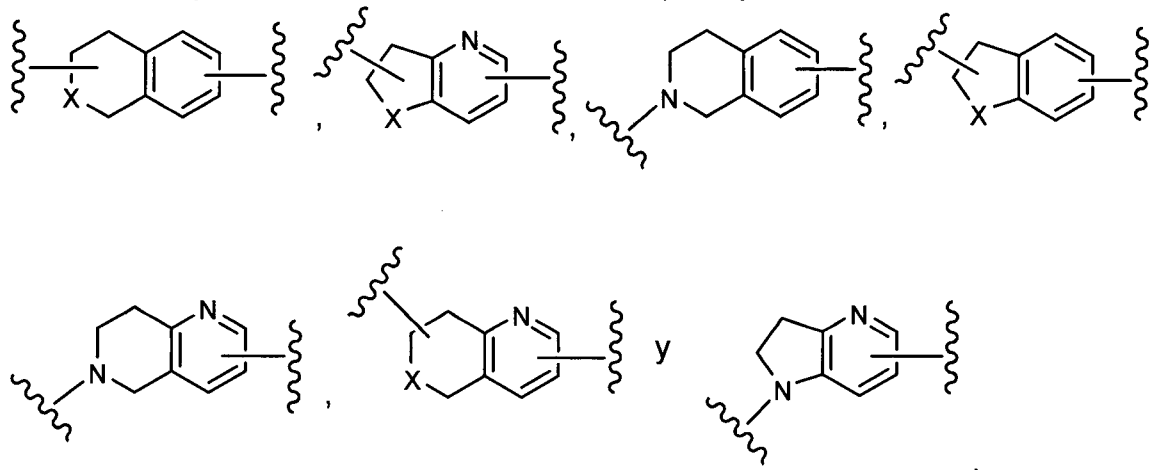
siempre que cuando uno de  $R^{11}$  o  $R^{12}$  se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$  (es decir, si uno de  $R^{11}$  o  $R^{12}$  es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , o  $-N_3$ , entonces el otro no es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,

$-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , o  $-N_3$ ;

$R^8$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, con cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- están sustituidos en forma opcional con 1-3 sustituyentes  $R^{21}$  seleccionados en forma independiente;

$R^9$  se selecciona del grupo que consiste en alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, donde cada grupo  $R^9$  está sustituido en forma opcional con 1-3 sustituyentes  $R^{21}$  seleccionados en forma independiente;

$R^{10}$  se selecciona del grupo que consiste en un enlace, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo-, heterociclilalquilo- y los restos:



donde X es O,  $N(R^{14})$  o S;



donde cada grupo  $R^{10}$  (a excepción del enlace) está sustituido en forma opcional con 1-3 sustituyentes  $R^{21}$  seleccionados en forma independiente;

$R^{13}$  se selecciona en forma independiente del grupo que consiste en H, alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo-, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo, arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-, arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-, arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, heterocicloalquenilarilo-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  y  $-N(R^8)_2$ ; y donde dicho  $R^{13}$  alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo, arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-, arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-, arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, y heterocicloalquenilarilo- están sustituidos en forma opcional con 1 a 5 grupos seleccionados en forma independiente del grupo que consiste en: alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterocicilo,

heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>; -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>;

R<sup>14</sup> se selecciona del grupo que consiste en H, alquilo, alquenoilo, alquinoilo, cicloalquilo, cicloalquilalquilo-, cicloalquenoilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, y -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), en los cuales cada uno de dicho alquilo, alquenoilo, alquinoilo, cicloalquilo, cicloalquilalquilo-, cicloalquenoilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, y heteroarilalquilo- está sustituido en forma opcional con 1-5 sustituyentes R<sup>21</sup> seleccionados en forma independiente;

R<sup>15</sup>, R<sup>16</sup> y R<sup>17</sup> se seleccionan de manera independiente del grupo que consiste en H, alquilo, alquenoilo, alquinoilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo, heteroarilo, heteroarilalquilo-, arilcicloalquilo-, arilheterociclilo-, R<sup>18</sup>)<sub>r</sub> -alquilo, R<sup>18</sup>)<sub>r</sub> -cicloalquilo, R<sup>18</sup>)<sub>r</sub> -cicloalquilalquilo-, R<sup>18</sup>)<sub>r</sub> -heterociclilo, R<sup>18</sup>)<sub>r</sub> -heterociclilalquilo-, R<sup>18</sup>)<sub>r</sub> -arilo, R<sup>18</sup>)<sub>r</sub> -arilalquilo, R<sup>18</sup>)<sub>r</sub> -heteroarilo y R<sup>18</sup>)<sub>r</sub> -heteroarilalquilo-, en la cual R es de 1-5;

Cada R<sup>18</sup> se selecciona en forma independiente del grupo que consiste en alquilo, alquenoilo, alquinoilo, arilo, arilalquilo-, arilalquenoilo-, arilalquinoilo-, -NO<sub>2</sub>, halo, heteroarilo, HO-alquioxialquilo, -CF<sub>3</sub>, -CN, alquil-CN, -C(O)R<sup>19</sup>, -C(O)OH, -C(O)OR<sup>19</sup>,

$-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alquil})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{arilo})$ ,  
 $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{heteroarilo})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alquilo})$ ,  
 $-\text{S}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{NH}(\text{arilo})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  
 $-\text{S}(\text{O})_2\text{NH}(\text{heterociclilo})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  
 $-\text{O-heterociclilo}$ ,  $-\text{O-cicloalquilalquilo}$ ,  $-\text{O-heterociclilalquilo}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alquil})_2$ ,  
 $-\text{N}(\text{arilalquil})_2$ ,  $-\text{N}(\text{arilalquil})-(\text{heteroarilalquilo})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  
 $-\text{NHC}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{NH}(\text{alquilo})$ ,  
 $-\text{N}(\text{alquil})\text{C}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alquilo})$ ,  
 $-\text{NHS}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{NH}(\text{alquil})$  y  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ;

o, en forma alternativa, dos restos  $\text{R}^{18}$  en los carbonos adyacentes pueden

ligarse para formar:

$\text{R}^{19}$  se selecciona del grupo que consiste en alquilo, cicloalquilo, arilo, arilalquilo- y heteroarilalquilo-;

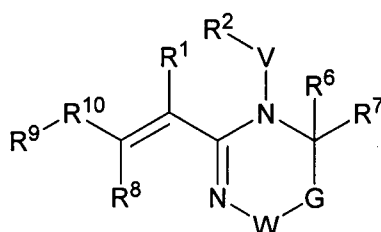
$\text{R}^{20}$  se selecciona del grupo que consiste en alquilo, cicloalquilo, arilo, arilo sustituido por halo, arilalquilo-, heteroarilo o heteroarilalquilo-;

Cada grupo  $\text{R}^{21}$  se selecciona en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo,  $-\text{CN}$ ,  $-\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{R}^{15}$ ,  $-\text{C}(\text{O})\text{OR}^{15}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{SR}^{15}$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{CH}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{C}(=\text{NOR}^{15})\text{R}^{16}$ ,  $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ,  $-\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{alquil}-\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{CH}_2-\text{R}^{15}$ ,  $-\text{CH}_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{R}^{16}$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{CH}_2-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,

$-N(R^{15})C(O)OR^{16}$ ,  $-CH_2-N(R^{15})C(O)OR^{16}$ ,  $-S(O)R^{15}$ ,  $=NOR^{15}$ ,  $-N_3$ ,  $-NO_2$  y  $-S(O)_2R^{15}$ ; y donde cada uno de los grupos alquilo, cicloalqueno, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, alqueno y alquino de  $R^{21}$  está sustituido en forma opcional con 1 a 5 grupos  $R^{22}$  seleccionados en forma independiente; y

Cada  $R^{22}$  se selecciona en forma independiente del grupo que consiste en alquilo, cicloalquilo, cicloalqueno, heterociclilo, arilo, heteroarilo, halo,  $-CF_3$ ,  $-CN$ ,  $-OR^{15}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-alquil-C(O)OR^{15}$ ,  $C(O)N(R^{15})(R^{16})$ ,  $-SR^{15}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $-N(R^{15})(R^{16})$ ,  $-alquil-N(R^{15})(R^{16})$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-CH_2-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-CH_2-N(R^{15})C(O)OR^{16}$ ,  $-N_3$ ,  $=NOR^{15}$ ,  $-NO_2$ ,  $-S(O)R^{15}$  y  $-S(O)_2R^{15}$ .

En otra realización, esta invención presenta un compuesto de fórmula I, o las sales, solvatos, ésteres o prodrugs aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general de fórmula IC:



Fórmula IC

en la cual:

cualquiera de (i)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalqueno  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional

VBO

con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (ii)  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (iii)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

y

W se selecciona del grupo que consiste en un enlace, -O-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, y -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G se selecciona del grupo que consiste en -C(R<sup>3</sup>)(R<sup>4</sup>)-, -C(O)-, -S-, -S(O)-, -S(O<sub>2</sub>)-, -C(O)-O-, y -N(R<sup>13</sup>)-;

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V es seleccionados del grupo que consiste en un enlace, -O-, y -N(R<sup>14</sup>)-;

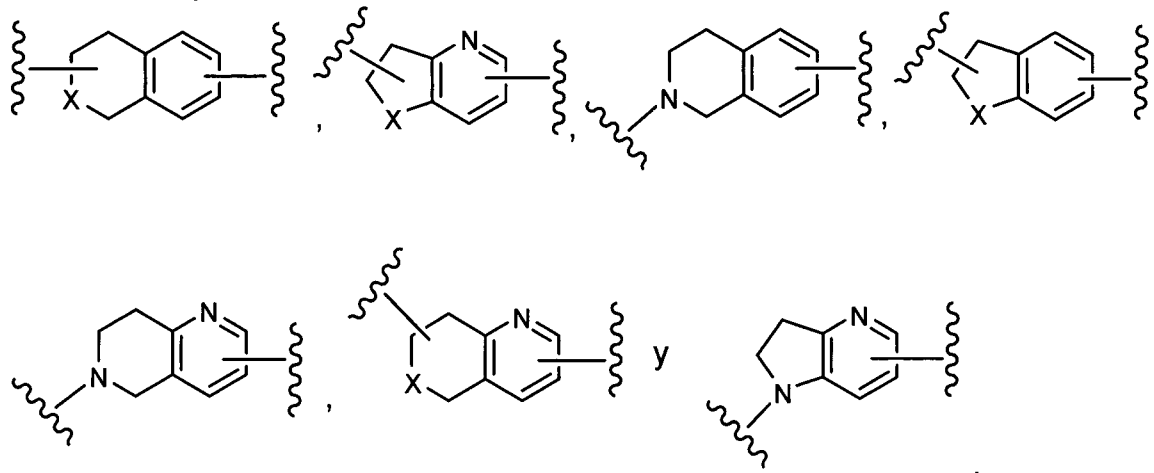
R<sup>1</sup> (cuando R<sup>1</sup> no está unido a R<sup>2</sup>), R<sup>2</sup> (cuando R<sup>2</sup> no está unido a R<sup>1</sup> o R<sup>6</sup>), R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> (cuando R<sup>6</sup> no está unido a R<sup>2</sup>), R<sup>7</sup>, R<sup>11</sup> y R<sup>12</sup> pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

R<sup>14</sup> se selecciona del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo, cicloalquenilo, heterociclilo, heterociclilalquilo, arilo, arilalquilo, heteroarilo, heteroarilalquilo, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, y -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);

R<sup>8</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, con cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- que no está sustituido o está sustituido en forma independiente y opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

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$R^{10}$  se selecciona del grupo que consiste en un enlace, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo-, heterociclilalquilo- y los restos:



donde X es O,  $N(R^{14})$  o S;

en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- heterociclilalquilo- para  $R^{10}$  como también los restos mencionados anteriormente para  $R^{10}$  puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y

$R^9$  se selecciona del grupo que consiste en alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquil- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

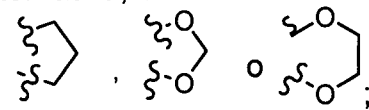
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$R^{15}$ ,  $R^{16}$  y  $R^{17}$  se seleccionan de manera independiente del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, arilcicloalquilo-, arilheterociclilo-,  $R^{18}$ -alquilo,  $R^{18}$ -cicloalquilo,  $R^{18}$ -cicloalquilalquilo,  $R^{18}$ -heterociclilo,  $R^{18}$ -heterociclilalquilo,  $R^{18}$ -arilo,  $R^{18}$ -arilalquilo,  $R^{18}$ -heteroarilo y  $R^{18}$ -heteroarilalquilo;

$R^{18}$  es de 1-5 sustituyentes seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, arilo, arilalquilo-, arilalquenilo-, arilalquinilo-,  $-\text{NO}_2$ , halo, heteroarilo, HO-alquioxialquilo,  $-\text{CF}_3$ ,  $-\text{CN}$ , alquil-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alquil})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{heteroarilo})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{NH}(\text{arilo})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterociclilo})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  $-\text{O-heterociclilo}$ ,  $-\text{O-cicloalquilalquilo}$ ,  $-\text{O-heterociclilalquilo}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alquil})_2$ ,  $-\text{N}(\text{arilalquil})_2$ ,  $-\text{N}(\text{arilalquil})-(\text{heteroarilalquilo})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{NH}(\text{alquil})$  y  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ;

o, en forma alternativa, dos restos  $R^{18}$  en los carbonos adyacentes pueden

ligarse para formar:



$R^{19}$  es alquilo, cicloalquilo, arilo, arilalquilo o heteroarilalquilo;

$R^{20}$  es alquilo, cicloalquilo, arilo, arilo sustituido por halo, arilalquilo, heteroarilo o heteroarilalquilo;



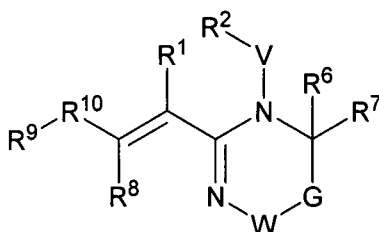
donde cada uno de los grupos alquilo, cicloalquilo, cicloalquenilo, cicloalquilalquilo, heterociclilo, heterociclilalquilo, arilo, arilalquilo, alquilarilo-, heteroarilo, heteroarilalquilo, alquenilo y alquinilo en  $R^1$ ,  $R^2$ ,  $R^1-R^2$ ,  $R^2-R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  y  $R^{14}$  está no sustituido o sustituido en forma opcional e independiente por 1 a 5 grupos  $R^{21}$  seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>;

donde cada uno de los grupos alquilo, cicloalquenilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en  $R^{21}$  está en forma independiente no sustituido o sustituido por 1 a 5 grupos  $R^{22}$  seleccionados en forma independiente del grupo que consiste en alquilo, cicloalquilo, cicloalquenilo, heterociclilo, arilo, heteroarilo, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alquil-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),

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$-N(R^{15})C(O)OR^{16}$ ,  $-CH_2-N(R^{15})C(O)OR^{16}$ ,  $-N_3$ ,  $=NOR^{15}$ ,  $-NO_2$ ,  $-S(O)R^{15}$  y  $-S(O)_2R^{15}$ .

En otra realización, esta invención presenta un compuesto de fórmula I, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general de fórmula IC:



Fórmula IC

en la cual:

cualquiera de

(i)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalqueno  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalqueno, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(ii)  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalqueno  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes

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$R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(iii)

(a)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (1) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y

(b)  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (1) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; y

(c) dicho resto  $R^2$  y  $R^6$  cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(iv)  $R^6$  y cualquiera de  $R^3$  o  $R^4$  del resto  $-C(R^3)(R^4)-G$ , están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido

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en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(v)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; y

W se selecciona del grupo que consiste en un enlace,  $-O-$ ,  $-C(O)-$ ,  $-S-$ ,  $-S(O)-$ ,  $-S(O_2)-$ , y  $-C(R^{11})(R^{12})-$ ;

G se selecciona del grupo que consiste en  $-C(R^3)(R^4)-$ ,  $-C(O)-$ ,  $-S-$ ,  $-S(O)-$ ,  $-S(O_2)-$ ,  $-C(O)-O-$ , y  $-N(R^{13})-$  ;

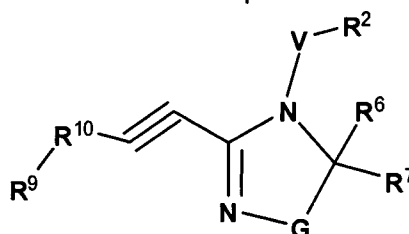
V se selecciona del grupo que consiste en un enlace,  $-O-$ ,  $-C(O)-$  y  $-N(R^{14})-$ ;

$R^1$  (cuando  $R^1$  no está unido a  $R^2$ ),  $R^2$  (cuando  $R^2$  no está unido a  $R^1$  o  $R^6$ ),  $R^5$ ,  $R^6$  (cuando  $R^6$  no está unido a  $R^2$ ), y  $R^7$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y

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heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

o, de manera alternativa,  $R^1$  (cuando  $R^1$  no está unido a  $R^2$ ) y  $R^8$  se toman juntos para formar un enlace (es decir, hay un enlace triple entre el átomo de carbono al cual  $R^1$  estaba unido y el átomo de carbono al cual  $R^8$  estaba unido, es decir, el compuesto de fórmula I es un compuesto de fórmula II:



fórmula IIB

y  $R^2$ ,  $R^5$ ,  $R^6$ , y  $R^7$  son como se los definió con anterioridad, y  $R^3$ ,  $R^4$ ,  $R^{11}$  y  $R^{12}$  son como se los define a continuación);

$R^3$  se selecciona del grupo que consiste en H, halo (y en un ejemplo, F), -OR<sup>15</sup> (y en un ejemplo  $R^{15}$  es H), -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se

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selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o

$R^3$  y  $R^6$  tomados juntos forman un enlace (es decir,  $R^3$  y  $R^6$  forman un enlace entre G y el átomo de carbono al cual  $R^6$  está unido), siempre que cuando  $R^3$  y  $R^6$  forman un enlace: (1) W no es un enlace, (2)  $R^2$  y  $R^6$  no se unen para formar un resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo (como se describió en los puntos (ii) y (iii) anteriores) (3)  $R^6$  y cualquiera de  $R^3$  o  $R^4$  del resto  $-C(R^3)(R^4)-G$  no se unen para formar un resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo (como se describió en el punto (iv) más arriba), y (4)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$  no se unen para formar un resto heterociclilo o heterociclenilo (como se describió en el punto (v) más arriba);

$R^4$ ,  $R^{11}$  y  $R^{12}$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, halo (y en un ejemplo, F),  $-OR^{15}$  (y en un ejemplo  $R^{15}$  es H),  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

siempre que cuando uno de  $R^3$  o  $R^4$  se selecciona del grupo que consiste en:

$-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$  (es decir, si uno de  $R^3$  o  $R^4$  es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , o  $-N_3$ , entonces el otro no es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , o  $-N_3$ );

siempre que cuando uno de  $R^{11}$  o  $R^{12}$  se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,

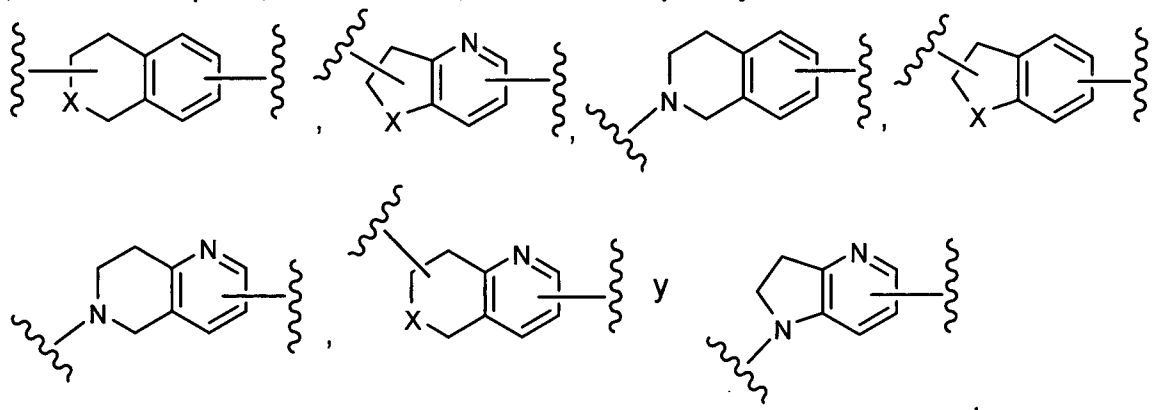
$-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , y  $-N_3$  (es decir, si uno de  $R^{11}$  o  $R^{12}$  es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , o  $-N_3$ , entonces el otro no es  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , o  $-N_3$ );

$R^8$  se selecciona del grupo que consiste en H, alquilo-, alqueno- y alquino-,  
 arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-,  
 heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, con cada uno de dicho  
 alquilo-, alqueno-, alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-,  
 cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-  
 están sustituidos en forma opcional con 1-3 sustituyentes  $R^{21}$  seleccionados en  
 forma independiente;

$R^9$  se selecciona del grupo que consiste en alquilo-, alqueno- y alquino-,  
 arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-,  
 heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de  
 dicho alquilo-, alqueno-, alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-,  
 cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-  
 está sustituido en forma opcional con 1-3 sustituyentes  $R^{21}$  seleccionados en  
 forma independiente que pueden ser iguales o diferentes, cada sustituyente se  
 selecciona en forma independiente del grupo que consiste en los restos que se  
 muestran más adelante,



$R^{10}$  se selecciona del grupo que consiste en un enlace, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo-, heterociclilalquilo- y los restos:



donde X es O,  $N(R^{14})$  o S;

en los cuales cada uno de dicho  $R^{10}$  restos (excepto el enlace) está sustituido en forma opcional con 1-3 sustituyentes  $R^{21}$  seleccionados en forma independiente que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y

$R^{14}$  se selecciona del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo, cicloalquenilo, heterociclilo, heterociclilalquilo, arilo, arilalquilo, heteroarilo, heteroarilalquilo, -CN,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ , y  $-P(O)(OR^{15})(OR^{16})$ , en los cuales cada uno de dicho alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo, cicloalquenilo, heterociclilo, heterociclilalquilo, arilo, arilalquilo, heteroarilo, heteroarilalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente;

$R^{15}$ ,  $R^{16}$  y  $R^{17}$  se seleccionan de manera independiente del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, arilcicloalquilo-, arilheterociclilo-,  $(R^{18})_r$  -alquilo,  $(R^{18})_r$  -cicloalquilo,  $(R^{18})_r$  -

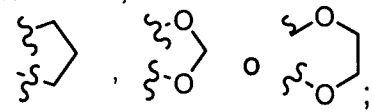
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cicloalquilalquilo,  $(R^{18})_r$ -heterociclilo,  $(R^{18})_r$ -heterociclilalquilo,  $(R^{18})_r$ -arilo,  $(R^{18})_r$ -arilalquilo,  $(R^{18})_r$ -heteroarilo y  $(R^{18})_r$ -heteroarilalquilo, en la cual R es de 1-5;

Cada  $R^{18}$  se selecciona en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, arilo, arilalquilo-, arilalquenilo-, arilalquinilo-,  $-NO_2$ , halo, heteroarilo, HO-alquioxialquilo,  $-CF_3$ ,  $-CN$ , alquil-CN,  $-C(O)R^{19}$ ,  $-C(O)OH$ ,  $-C(O)OR^{19}$ ,  $-C(O)NHR^{20}$ ,  $-C(O)NH_2$ ,  $-C(O)NH_2-C(O)N(alquil)_2$ ,  $-C(O)N(alquil)(arilo)$ ,  $-C(O)N(alquil)(heteroarilo)$ ,  $-SR^{19}$ ,  $-S(O)_2R^{20}$ ,  $-S(O)NH_2$ ,  $-S(O)NH(alquilo)$ ,  $-S(O)N(alquil)(alquilo)$ ,  $-S(O)NH(arilo)$ ,  $-S(O)_2NH_2$ ,  $-S(O)_2NHR^{19}$ ,  $-S(O)_2NH(heterociclilo)$ ,  $-S(O)_2N(alquil)_2$ ,  $-S(O)_2N(alquil)(arilo)$ ,  $-OCF_3$ ,  $-OH$ ,  $-OR^{20}$ ,  $-O$ -heterociclilo,  $-O$ -cicloalquilalquilo,  $-O$ -heterociclilalquilo,  $-NH_2$ ,  $-NHR^{20}$ ,  $-N(alquil)_2$ ,  $-N(arilalquil)_2$ ,  $-N(arilalquil)-(heteroarilalquilo)$ ,  $-NHC(O)R^{20}$ ,  $-NHC(O)NH_2$ ,  $-NHC(O)NH(alquilo)$ ,  $-NHC(O)N(alquil)(alquilo)$ ,  $-N(alquil)C(O)NH(alquilo)$ ,  $-N(alquil)C(O)N(alquil)(alquilo)$ ,  $-NHS(O)_2R^{20}$ ,  $-NHS(O)_2NH(alquilo)$ ,  $-NHS(O)_2N(alquil)(alquilo)$ ,  $-N(alquil)S(O)_2NH(alquil)$  y  $-N(alquil)S(O)_2N(alquil)(alquilo)$ ;

o, en forma alternativa, dos restos  $R^{18}$  en los carbonos adyacentes pueden

ligarse para formar:



$R^{19}$  se selecciona del grupo que consiste en alquilo, cicloalquilo, arilo, arilalquilo- y heteroarilalquilo-;

$R^{20}$  se selecciona del grupo que consiste en alquilo, cicloalquilo, arilo, arilo sustituido por halo, arilalquilo-, heteroarilo y heteroarilalquilo-;

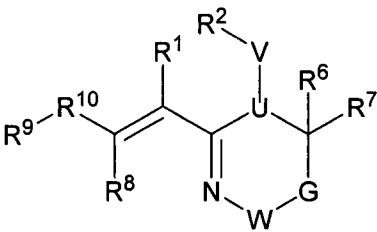
Cada grupo  $R^{21}$  se selecciona en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo,  $-CN$ ,  $-OR^{15}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-SR^{15}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-CH(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $-N(R^{15})(R^{16})$ ,

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-alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>,  
-CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y  
-S(O)<sub>2</sub>R<sup>15</sup>; y donde cada uno de los grupos alquilo, cicloalquenilo, cicloalquilo,  
cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo,  
heteroarilalquilo-, alquenilo y alquinilo de R<sup>21</sup> está sustituido en forma opcional con  
1 a 5 grupos R<sup>22</sup> seleccionados en forma independiente; y

Cada R<sup>22</sup> se selecciona en forma independiente del grupo que consiste en  
alquilo, cicloalquilo, cicloalquenilo, heterociclilo, arilo, heteroarilo, halo, -CF<sub>3</sub>, -CN,  
-OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -alquil-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -  
S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -  
N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -  
N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> y  
-S(O)<sub>2</sub>R<sup>15</sup>.

En otra realización, esta invención presenta un compuesto, o las sales,  
solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de  
dicho compuesto, donde dicho compuesto tiene la estructura general que se  
muestra en la fórmula I:



Fórmula I

donde U es C(R<sup>5</sup>);

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$R^1$  es H;

$R^2$  y  $R^6$  están conectados para formar un anillo cicloalquilo de 4-7 miembros;

$R^7$  es 3-(1,1'-bifenil)-ilo;

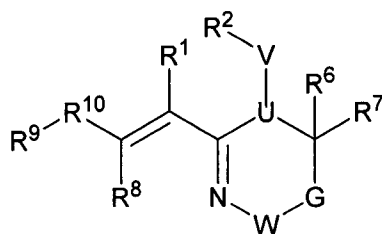
$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  es fenilo; y

$R^9$  es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ );

$R^6$  es H;

1146

R<sup>1</sup> y R<sup>2</sup> están conectados para formar un anillo cicloalquilo de 4-7 miembros;

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

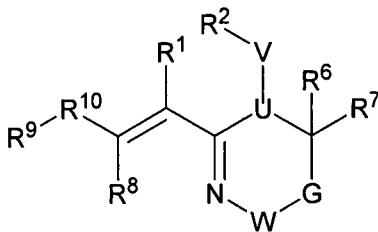
R<sup>8</sup> es H;

R<sup>5</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

R<sup>10</sup> es fenilo; y

R<sup>9</sup> es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C(R<sup>5</sup>) o N;

R<sup>1</sup> es H;

R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo heterociclilo de 5-8 miembros;

$R^7$  es 3-(1,1'-bifenil)-ilo;

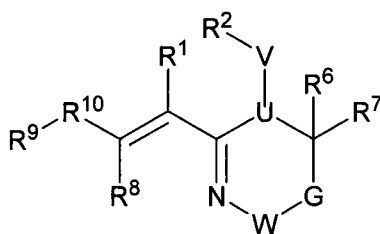
$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  es fenilo; y

$R^9$  es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ );

$R^6$  es H;

$R^1$  y  $R^2$  están conectados para formar un anillo heterociclilo de 5-8 miembros;

$R^7$  es 3-(1,1'-bifenil)-ilo;

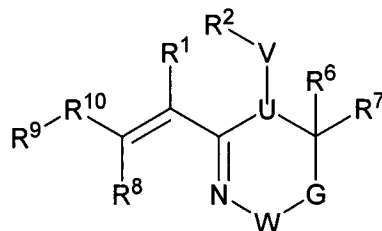
$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  es fenilo; y

$R^9$  es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ ) o N;

$R^1$  y  $R^2$  están conectados para formar un anillo heterociclilo de 5-8 miembros;

$R^2$  y  $R^6$  están conectados para formar un anillo heterociclilo de 5-8 miembros;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

 $R^8$  es  $H$ ;



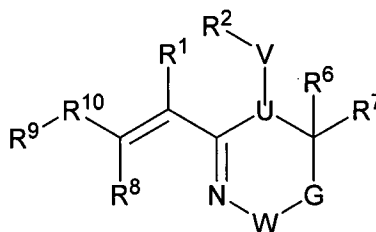
450

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  es fenilo; y

$R^9$  es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ ) o N;

$R^1$  y  $R^2$  están conectados para formar un anillo piperidinilo;

$R^2$  y  $R^6$  están conectados para formar un anillo piperidinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de

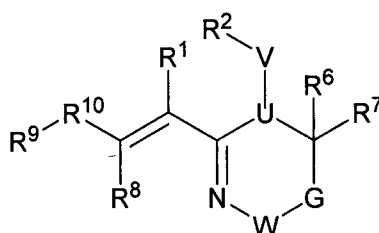
451

dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  es fenilo; y

$R^9$  es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es N;

$R^1$  y  $R^2$  están conectados para formar un anillo piperazinilo;

$R^2$  y  $R^6$  están conectados para formar un anillo piperazinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con

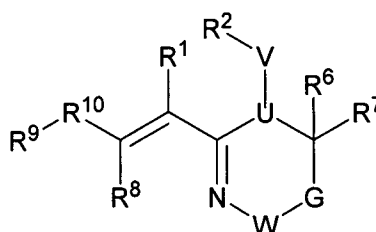
US2

1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  es fenilo; y

$R^9$  es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es  $C(R^5)$  o N;

$R^1$  y  $R^2$  están conectados para formar un anillo piperidinilo;

$R^2$  y  $R^6$  están conectados para formar un anillo piperazinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

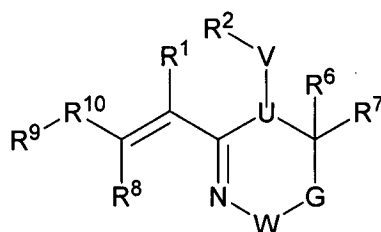
$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  es fenilo; y

$R^9$  es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ ) o N;

$R^1$  y  $R^2$  están conectados para formar un anillo piperazinilo;

$R^2$  y  $R^6$  están conectados para formar un anillo piperidinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  es fenilo; y

$R^9$  es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

R9R10C(R8)=C(R1)N=C(R2)U(R6)G(R7)W

donde  $U$  es  $C(\mathbb{R}^5)$ ;

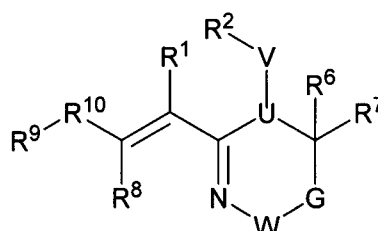
**R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo piperidinilo;**

 $R^8$  es  $H$ ;

$R^{10}$  es fenilo; y

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de

dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C(R<sup>5</sup>);

R<sup>1</sup> y R<sup>2</sup> están conectados para formar un anillo ciclohexilo;

R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo piperazinilo;

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

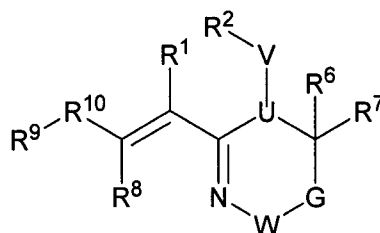
R<sup>8</sup> es H;

R<sup>5</sup> se selecciona del grupo que consiste en H, alquilo-, alquenoilo- y alquinoilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenoilo- y alquinoilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

R<sup>10</sup> es fenilo; y

R<sup>9</sup> es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C(R<sup>5</sup>);

R<sup>1</sup> y R<sup>2</sup> están conectados para formar un anillo piperidinilo;

R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo ciclohexilo;

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

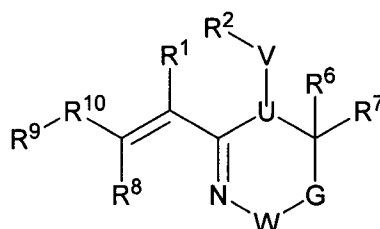
R<sup>8</sup> es H;

R<sup>5</sup> se selecciona del grupo que consiste en H, alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

R<sup>10</sup> es fenilo; y

R<sup>9</sup> es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



### Fórmula I

donde  $U$  es  $C(\mathbb{R}^5)$ ;

**R<sup>1</sup> y R<sup>2</sup> están conectados para formar un anillo piperazinilo;**

**R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo ciclohexilo;**

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

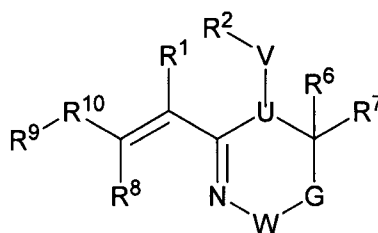
 $R^8$  es  $H$ ;

R<sup>5</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

**R<sup>10</sup> es fenilo; y**

R<sup>9</sup> es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



### Fórmula I

donde  $U$  es  $C(\mathbb{R}^5)$  o  $\mathbb{N}$ ;



VSB

$R^6$  es H;

$R^1$  y  $R^2$  están conectados para formar un anillo piperidinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

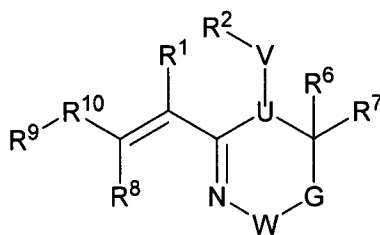
$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  es fenilo; y

$R^9$  es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrugas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ ) o N;

$R^6$  es H;

$R^1$  y  $R^2$  están conectados para formar un anillo piperazinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

USA

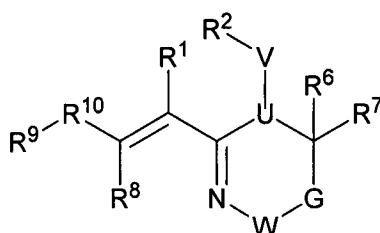
$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  es fenilo; y

$R^9$  es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ ) o N;

$R^1$  es H;

$R^6$  y  $R^2$  están conectados para formar un anillo piperidinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

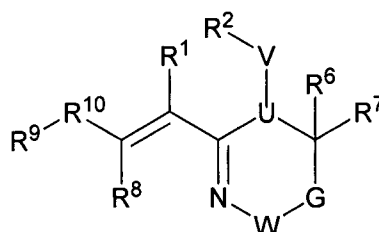
$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  es fenilo; y

$R^9$  es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ ) o N;

$R^1$  es H;

$R^6$  y  $R^2$  están conectados para formar un anillo piperazinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de

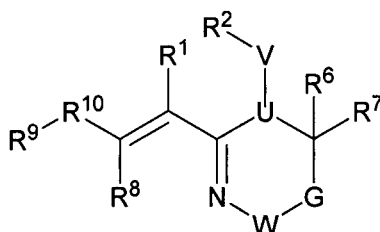
461

dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  es fenilo; y

$R^9$  es imidazol-1-ilo, y los otros restos como se definió con anterioridad.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrugs aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es  $C(R^5)$ ;

$R^1$  es H;

$R^2$  y  $R^6$  están conectados para formar un anillo cicloalquilo de 4-7 miembros;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-

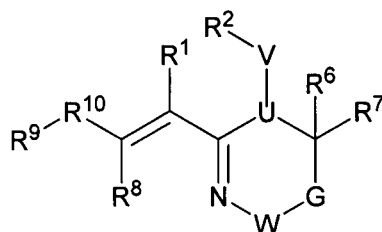
1162

puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenil (y en un ejemplo  $R^{10}$  es 3-metoxi-fenilo, y en otro ejemplo  $R^{10}$  es 3-F-fenilo);

$R^9$  es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ );

$R^6$  es H;

$R^1$  y  $R^2$  están conectados para formar un anillo cicloalquilo de 4-7 miembros;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

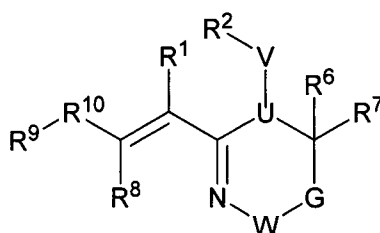
$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con

1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenil (y en un ejemplo  $R^{10}$  es 3-metoxi-fenilo, y en otro ejemplo  $R^{10}$  es 3-F-fenilo);

$R^9$  es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ ) o N;

$R^1$  es H;

$R^2$  y  $R^6$  están conectados para formar un anillo heterociclilo de 5-8 miembros;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se

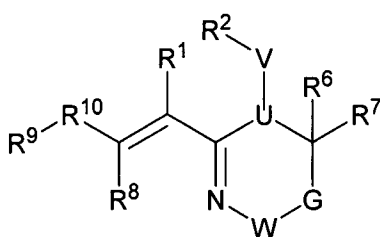
464

selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenil (y en un ejemplo  $R^{10}$  es 3-metoxi-fenilo, y en otro ejemplo  $R^{10}$  es 3-F-fenilo);

$R^9$  es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ );

$R^6$  es H;

$R^1$  y  $R^2$  están conectados para formar un anillo heterociclilo de 5-8 miembros;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

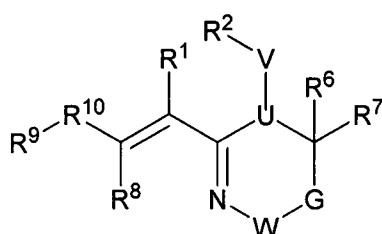
$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se

selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo  $R^{10}$  es 3-metoxi-fenilo, y en otro ejemplo  $R^{10}$  es 3-F-fenilo);

$R^9$  es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ ) o N;

$R^1$  y  $R^2$  están conectados para formar un anillo heterociclilo de 5-8 miembros;

$R^2$  y  $R^6$  están conectados para formar un anillo heterociclilo de 5-8 miembros;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se



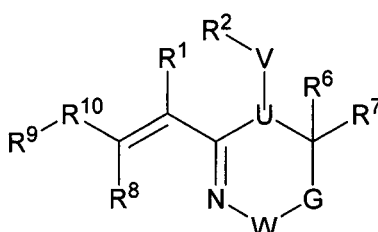
Vb6

selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo  $R^{10}$  es 3-metoxi-fenilo, y en otro ejemplo  $R^{10}$  es 3-F-fenilo);

$R^9$  es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es  $C(R^5)$ ;

$R^2$  y  $R^6$  están conectados para formar un anillo cicloalquilo de 4-7 miembros;

$R^1$  y  $R^2$  están conectados para formar un anillo cicloalquilo de 4-7 miembros;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con

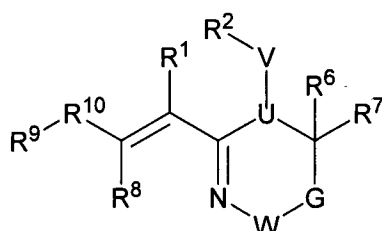
Hb7

1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo  $R^{10}$  es 3-metoxi-fenilo, y en otro ejemplo  $R^{10}$  es 3-F-fenilo);

$R^9$  es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es  $C(R^5)$  o N;

$R^1$  y  $R^2$  están conectados para formar un anillo piperidinilo;

$R^2$  y  $R^6$  están conectados para formar un anillo piperidinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se

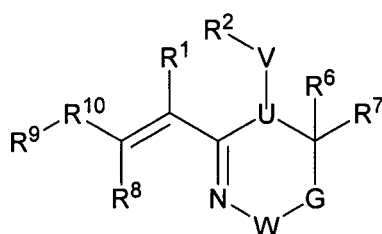
H68

selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo  $R^{10}$  es 3-metoxi-fenilo, y en otro ejemplo  $R^{10}$  es 3-F-fenilo);

$R^9$  es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es N;

$R^1$  y  $R^2$  están conectados para formar un anillo piperazinilo;

$R^2$  y  $R^6$  están conectados para formar un anillo piperazinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

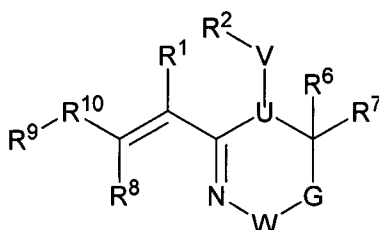
$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo  $R^{10}$  es 3-metoxi-fenilo, y en otro ejemplo  $R^{10}$  es 3-F-fenilo);

$R^9$  es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrugas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ ) o N;

$R^1$  y  $R^2$  están conectados para formar un anillo piperidinilo;

$R^2$  y  $R^6$  están conectados para formar un anillo piperazinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

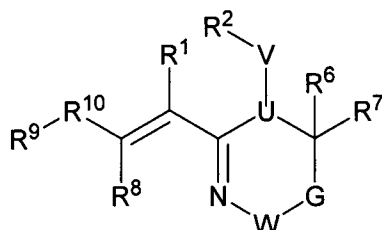
$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo  $R^{10}$  es 3-metoxi-fenilo, y en otro ejemplo  $R^{10}$  es 3-F-fenilo);

$R^9$  es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C( $R^5$ ) o N;

$R^1$  y  $R^2$  están conectados para formar un anillo piperazinilo;

$R^2$  y  $R^6$  están conectados para formar un anillo piperidinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

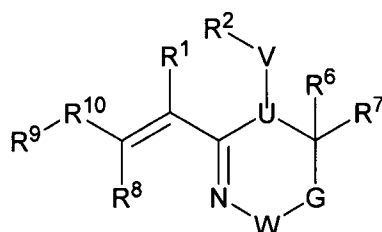
$R^8$  es H;

$R^5$  se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo  $R^{10}$  es 3-metoxi-fenilo, y en otro ejemplo  $R^{10}$  es 3-F-fenilo);

$R^9$  es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C(R<sup>5</sup>);

R<sup>1</sup> y R<sup>2</sup> están conectados para formar un anillo ciclohexilo;

R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo piperidinilo;

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

R<sup>8</sup> es H;

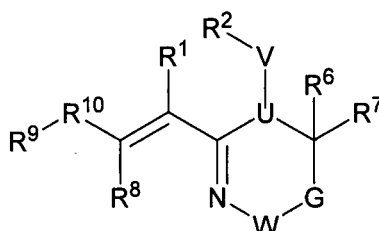
R<sup>5</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

R<sup>10</sup> se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo R<sup>10</sup> es 3-metoxi-fenilo, y en otro ejemplo R<sup>10</sup> es 3-F-fenilo);

R<sup>9</sup> es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de

dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C(R<sup>5</sup>);

R<sup>1</sup> y R<sup>2</sup> están conectados para formar un anillo ciclohexilo;

R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo piperazinilo;

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

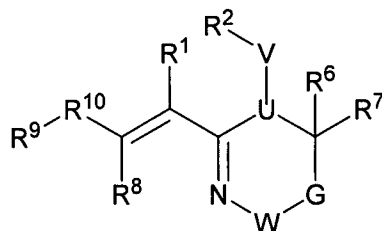
R<sup>8</sup> es H;

R<sup>5</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

R<sup>10</sup> se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo R<sup>10</sup> es 3-metoxi-fenilo, y en otro ejemplo R<sup>10</sup> es 3-F-fenilo);

R<sup>9</sup> es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrugas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



### Fórmula I

donde  $U$  es  $C(\mathbb{R}^5)$ ;

**R<sup>1</sup> y R<sup>2</sup> están conectados para formar un anillo piperidinilo;**

**R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo ciclohexilo;**

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

 $R^8$  es  $H$ ;

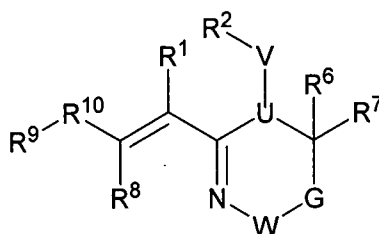
R<sup>5</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad:

R<sup>10</sup> se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo R<sup>10</sup> es 3-metoxi-fenilo, y en otro ejemplo R<sup>10</sup> es 3-F-fenilo);

**R<sup>9</sup> es 4-metil-imidazolilo-1-ilo.**

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:





Fórmula I

donde U es C(R<sup>5</sup>);

R<sup>1</sup> y R<sup>2</sup> están conectados para formar un anillo piperazinilo;

R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo ciclohexilo;

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

R<sup>8</sup> es H;

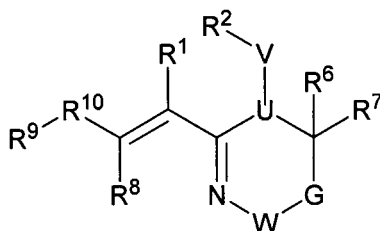
R<sup>5</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

R<sup>10</sup> se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo R<sup>10</sup> es 3-metoxi-fenilo, y en otro ejemplo R<sup>10</sup> es 3-F-fenilo);

R<sup>9</sup> es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:

H2S



Fórmula I

donde U es C(R<sup>5</sup>) o N;

R<sup>6</sup> es H;

R<sup>1</sup> y R<sup>2</sup> están conectados para formar un anillo piperidinilo;

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

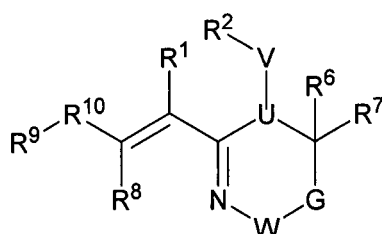
R<sup>8</sup> es H;

R<sup>5</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

R<sup>10</sup> se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo R<sup>10</sup> es 3-metoxi-fenilo, y en otro ejemplo R<sup>10</sup> es 3-F-fenilo);

R<sup>9</sup> es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C(R<sup>5</sup>) o N;

R<sup>6</sup> es H;

R<sup>1</sup> y R<sup>2</sup> están conectados para formar un anillo piperazinilo;

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

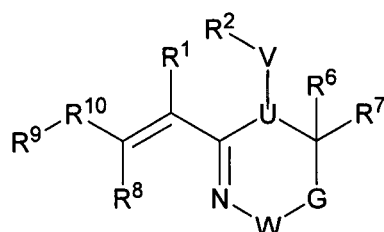
R<sup>8</sup> es H;

R<sup>5</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

R<sup>10</sup> se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo R<sup>10</sup> es 3-metoxi-fenilo, y en otro ejemplo R<sup>10</sup> es 3-F-fenilo);

R<sup>9</sup> es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:



Fórmula I

donde U es C(R<sup>5</sup>) o N;

R<sup>1</sup> es H;

R<sup>6</sup> y R<sup>2</sup> están conectados para formar un anillo piperidinilo;

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

R<sup>8</sup> es H;

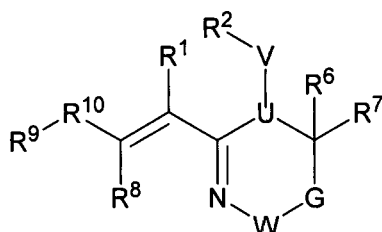
R<sup>5</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

R<sup>10</sup> se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo R<sup>10</sup> es 3-metoxi-fenilo, y en otro ejemplo R<sup>10</sup> es 3-F-fenilo);

R<sup>9</sup> es 4-metil-imidazolilo-1-ilo.

En otra realización, esta invención presenta un compuesto, o las sales, solvatos, ésteres o prodrugas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula I:

WAB



Fórmula I

donde U es C(R<sup>5</sup>) o N;

R<sup>1</sup> es H;

R<sup>6</sup> y R<sup>2</sup> están conectados para formar un anillo piperazinilo;

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

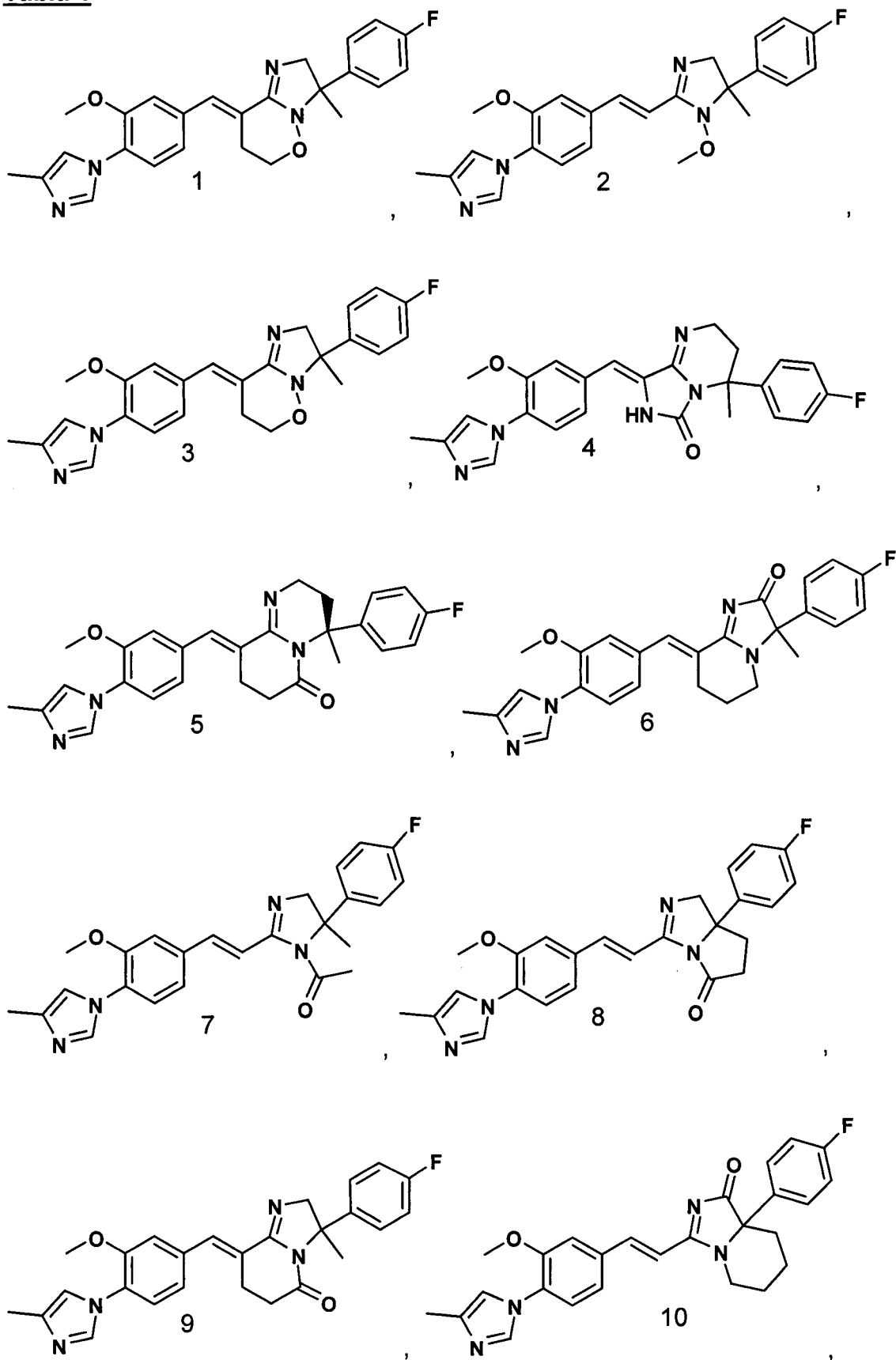
R<sup>8</sup> es H;

R<sup>5</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos descritos con anterioridad;

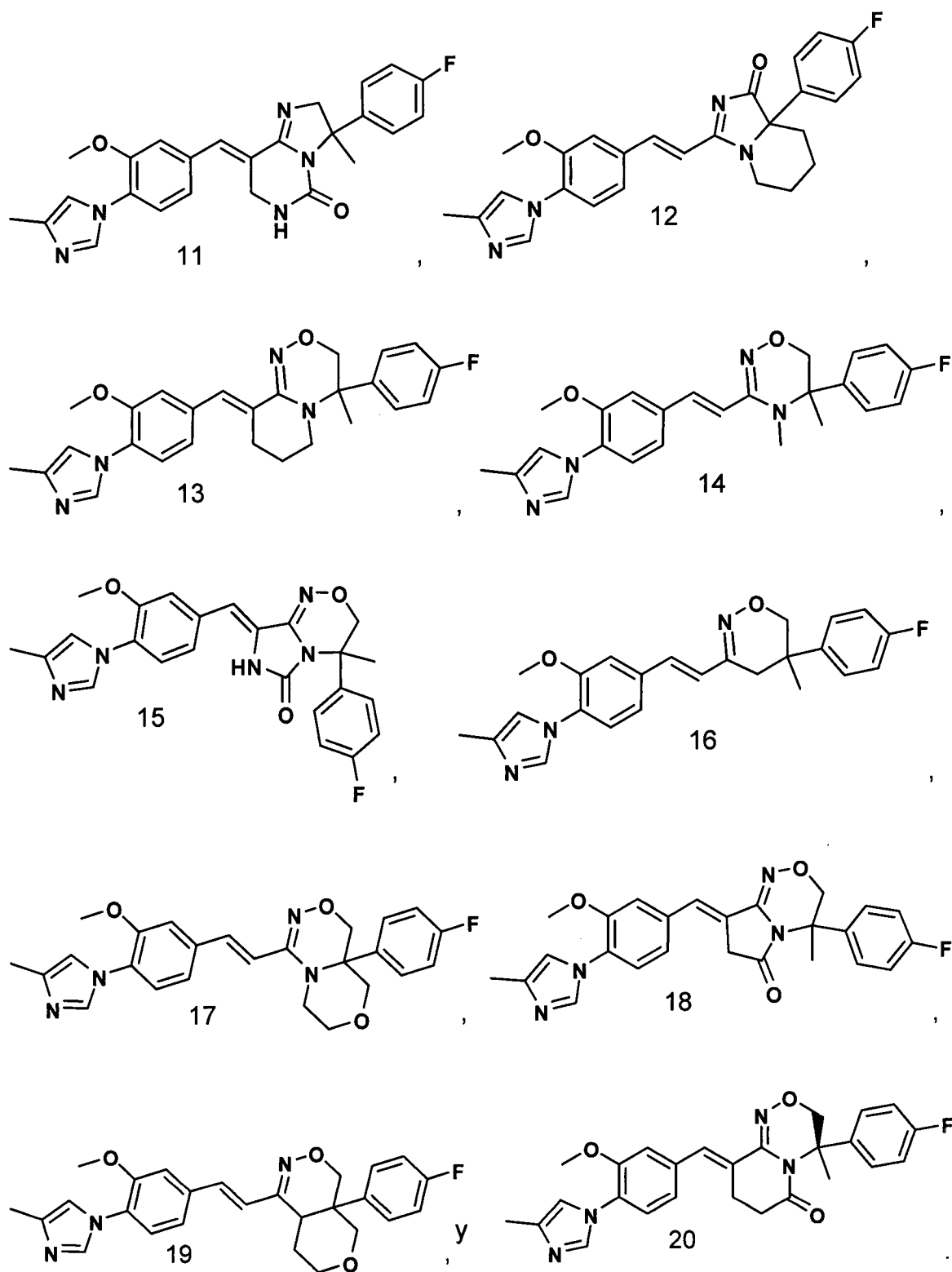
R<sup>10</sup> se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo (y en un ejemplo R<sup>10</sup> es 3-metoxi-fenilo, y en otro ejemplo R<sup>10</sup> es 3-F-fenilo);

R<sup>9</sup> es 4-metil-imidazolilo-1-ilo.

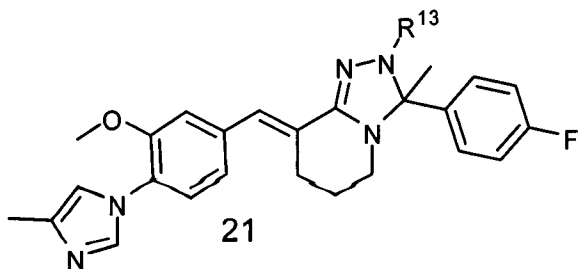
Un grupo ilustrativo de compuestos de la invención se muestran y aparecen en la **Tabla 1**.

**Tabla 1**

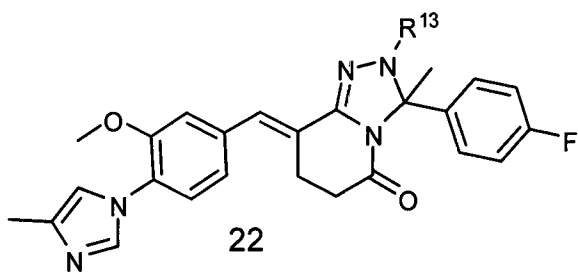
480



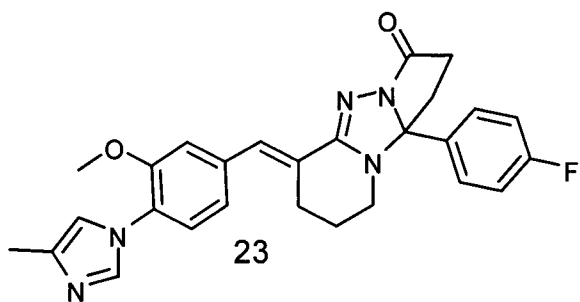
Los compuestos representativos de esta invención también incluyen:



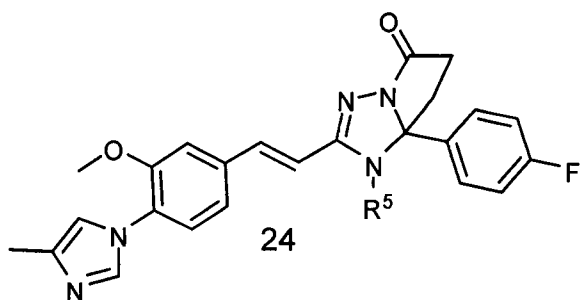
en la cual  $R^{13}$  en el compuesto 21 es como se lo definió para la fórmula I (y en un ejemplo  $R^{13}$  es H),



en la cual  $R^{13}$  en el compuesto 22 es como se lo definió para la fórmula I (y en un ejemplo  $R^{13}$  es H),



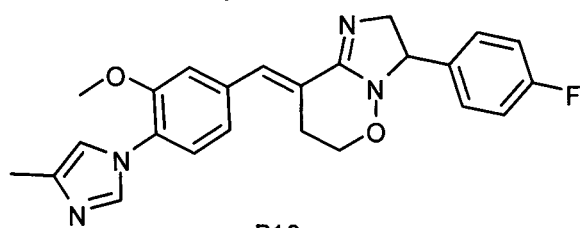
, y



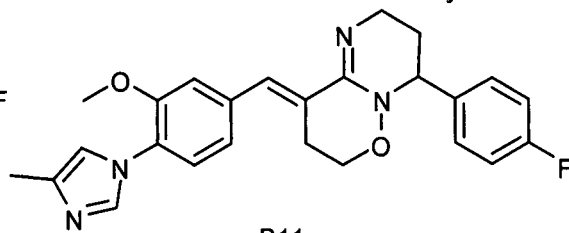
en la cual  $R^5$  en el compuesto 22 es como se lo definió para la fórmula I (y en un ejemplo  $R^5$  es H).



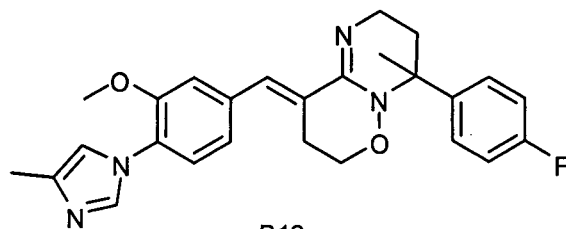
Los compuestos representativos de esta invención también incluyen:



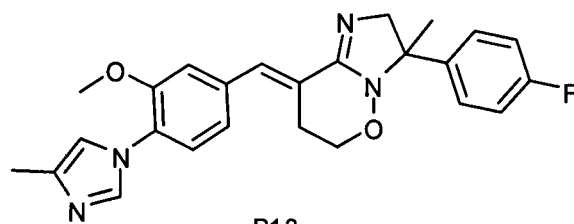
B10



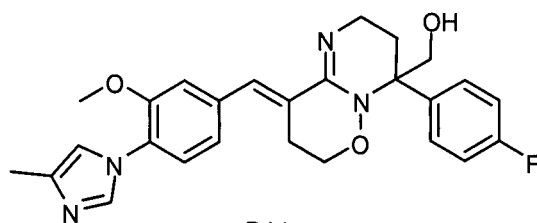
B11



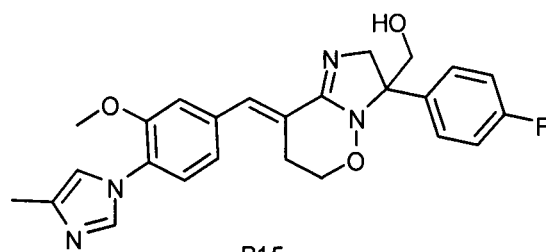
B12



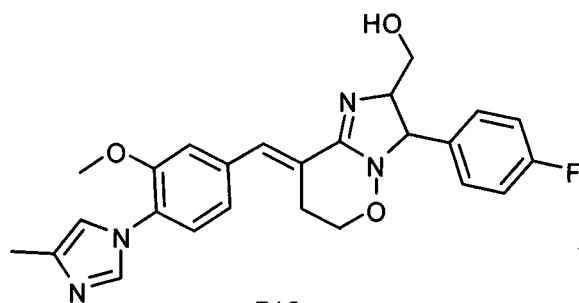
B13



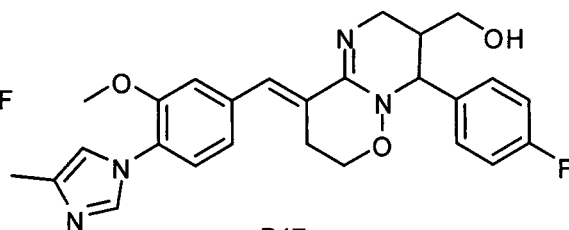
B14



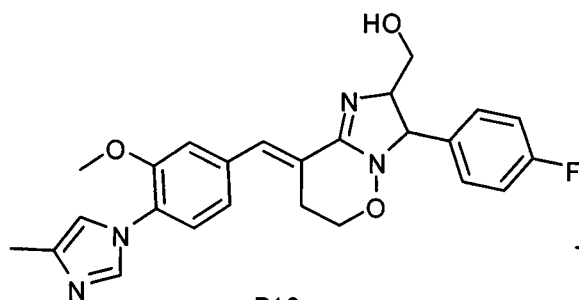
B15



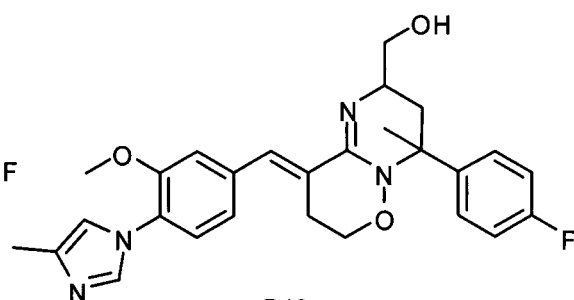
B16



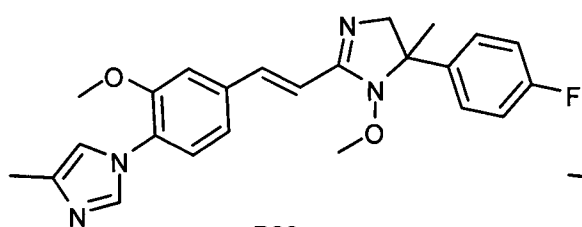
B17



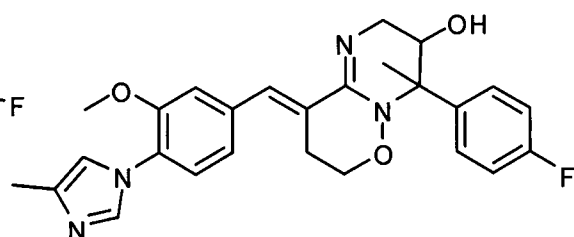
B18



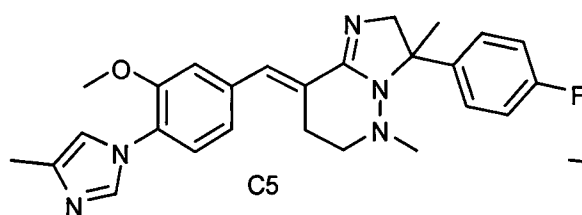
B19



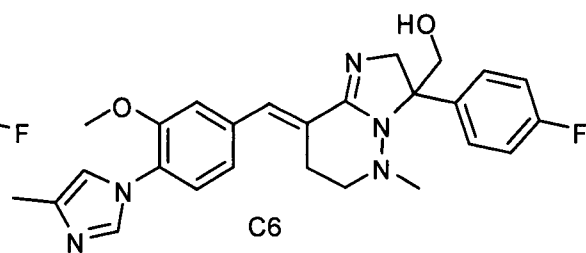
B20



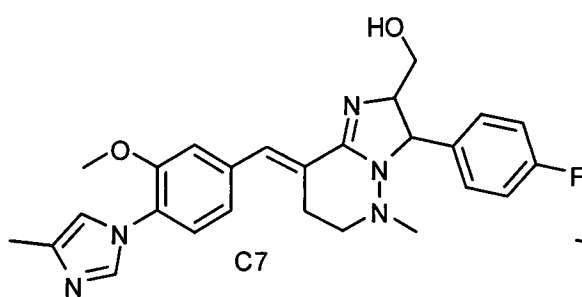
B21



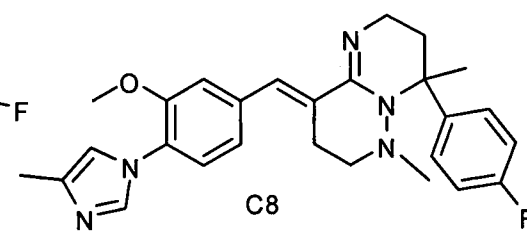
C5



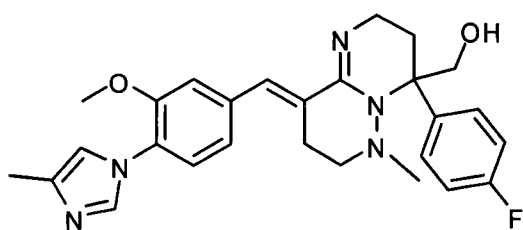
C6



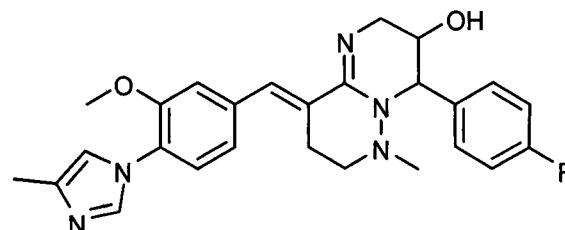
C7



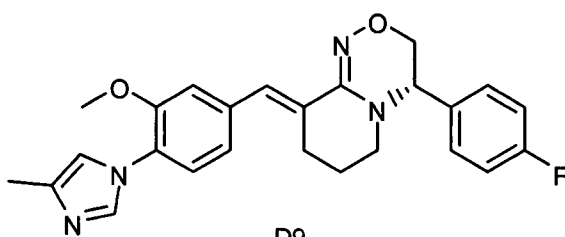
C8



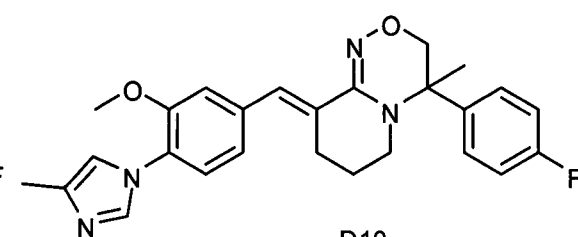
C9



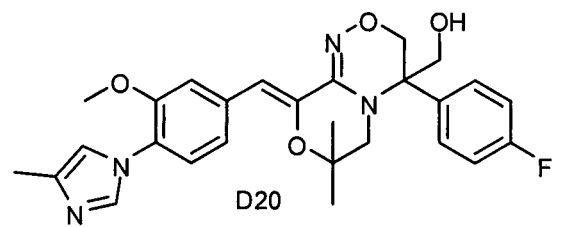
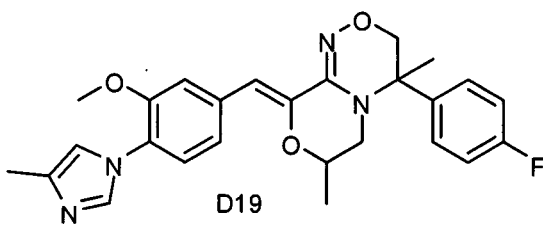
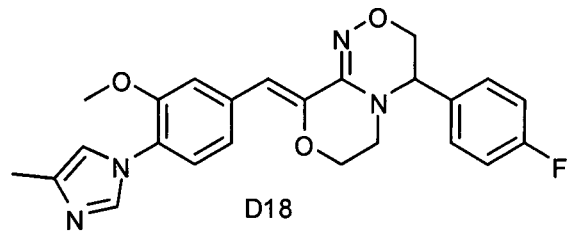
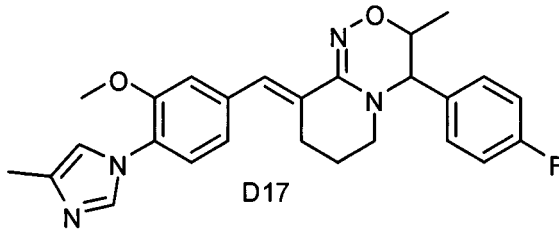
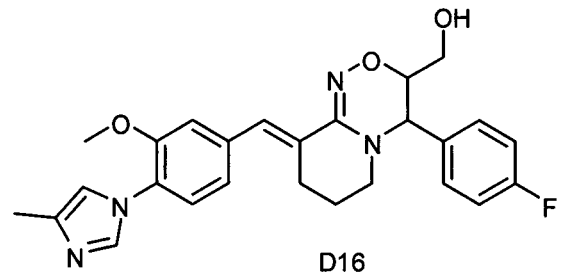
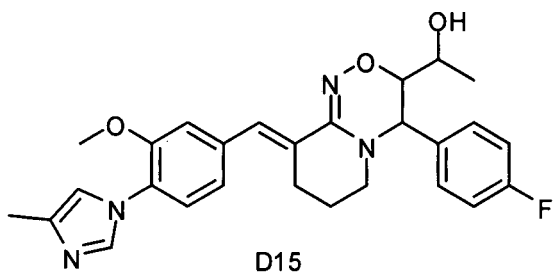
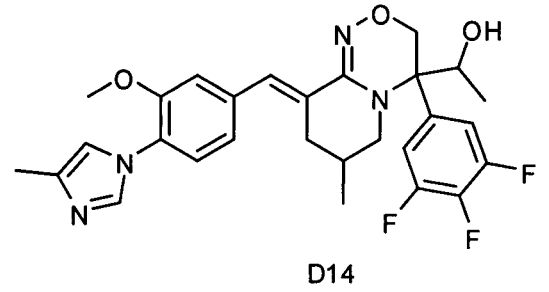
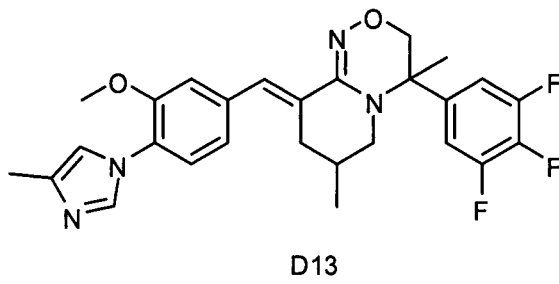
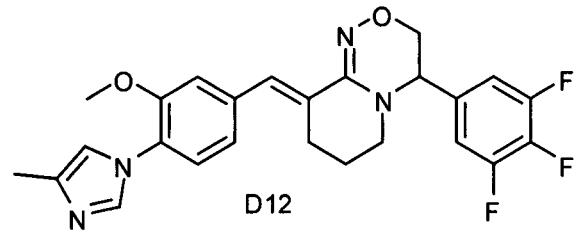
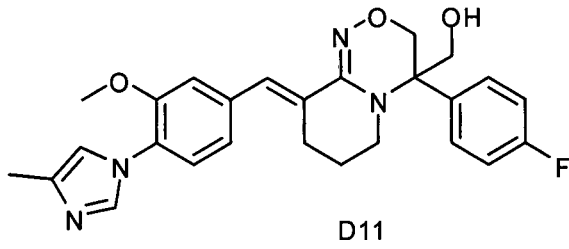
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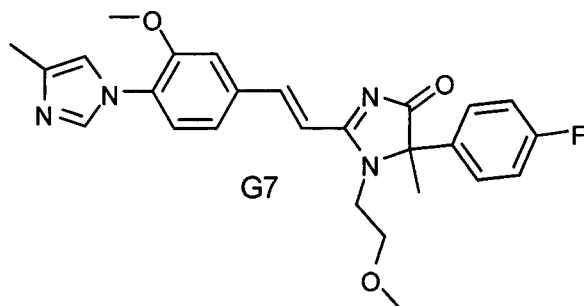
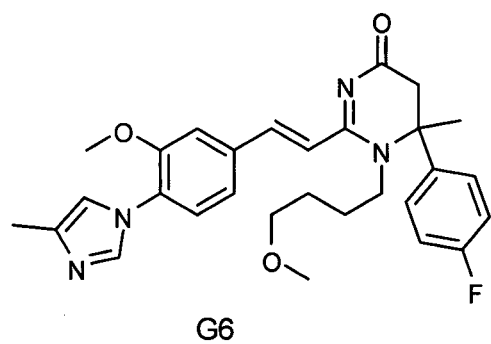
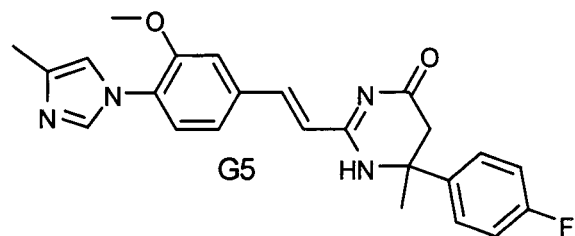
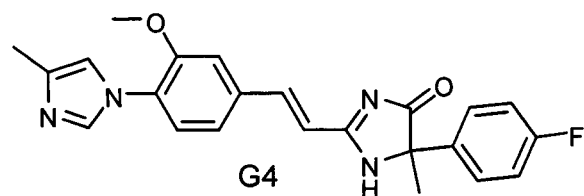
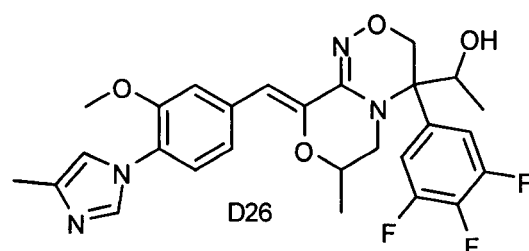
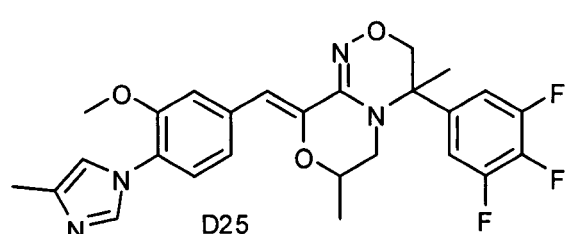
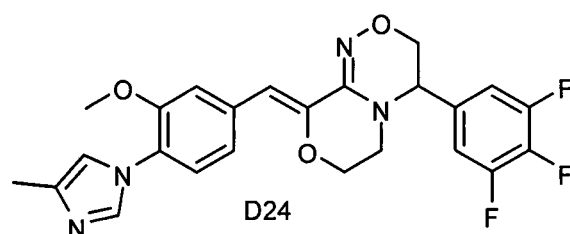
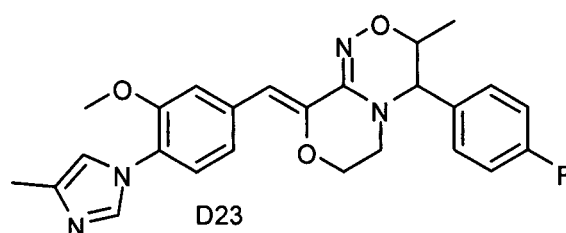
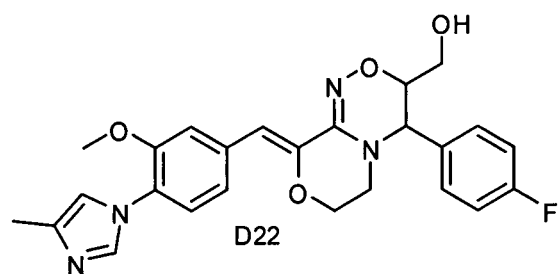
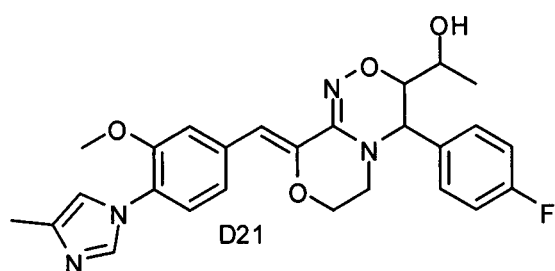
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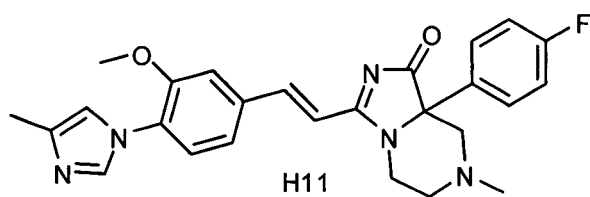
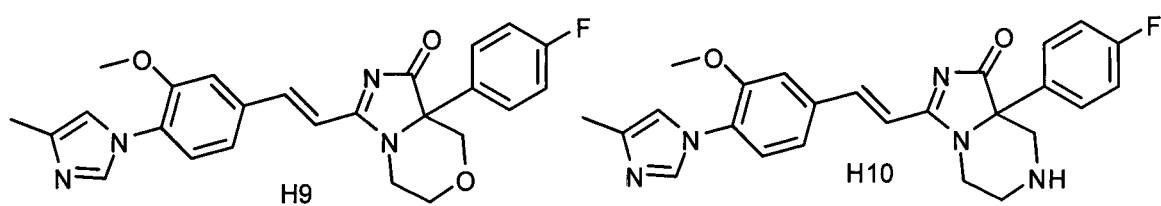
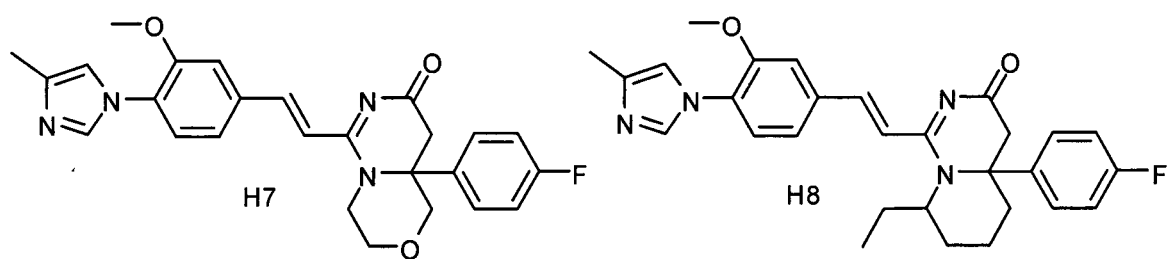
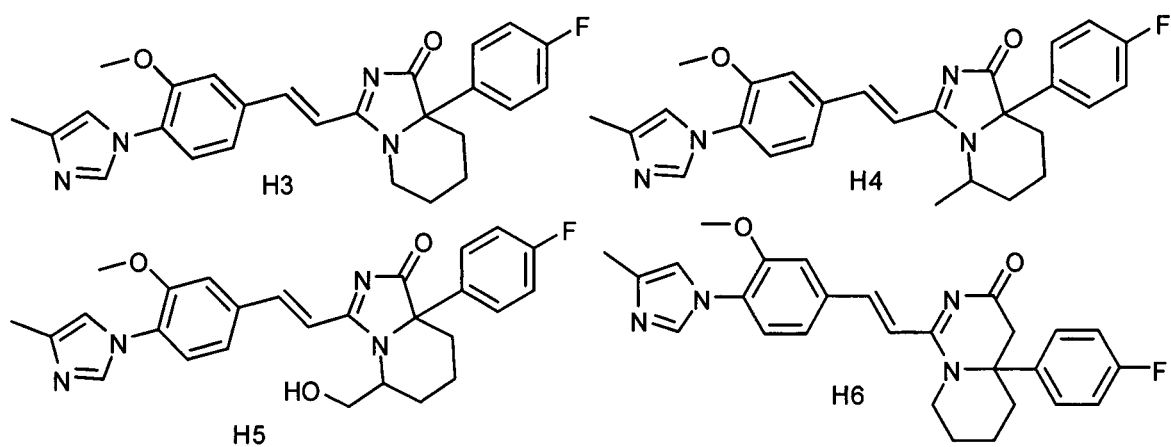
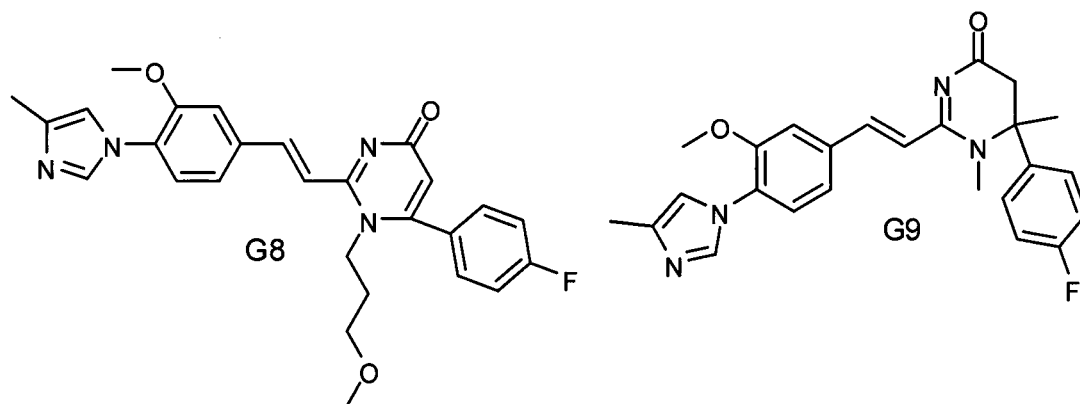


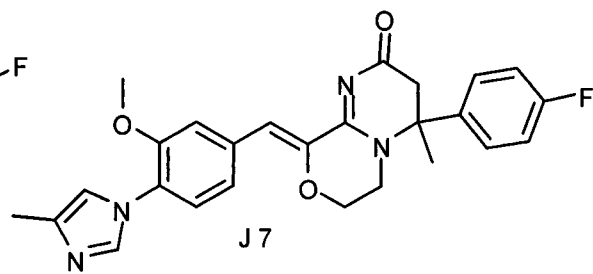
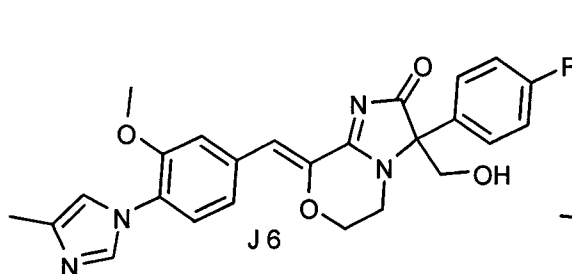
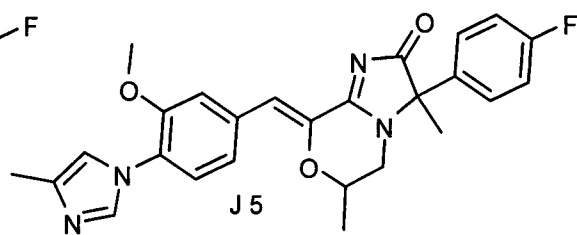
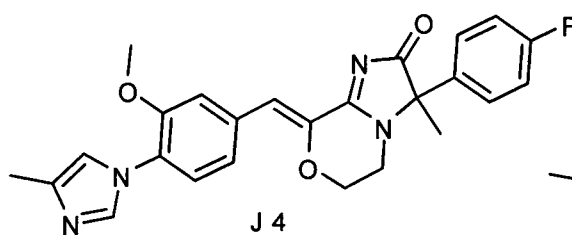
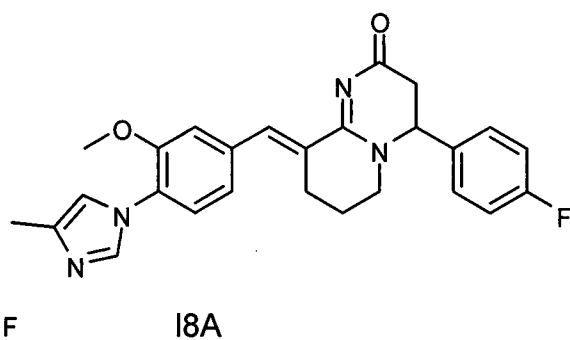
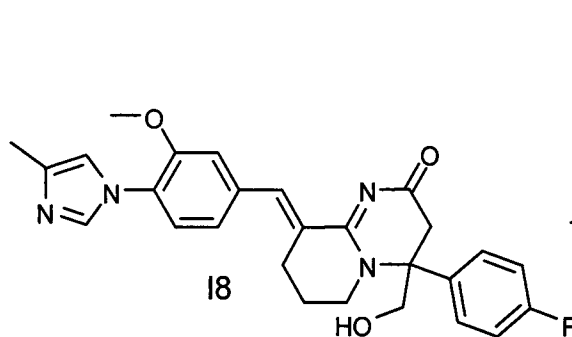
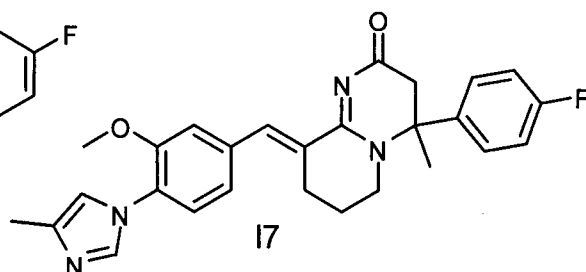
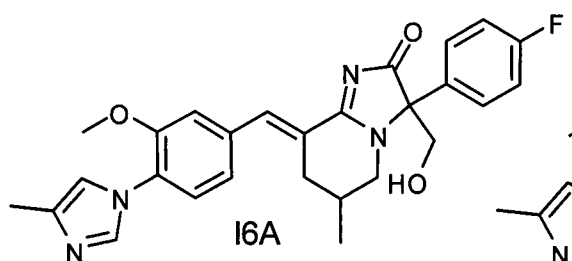
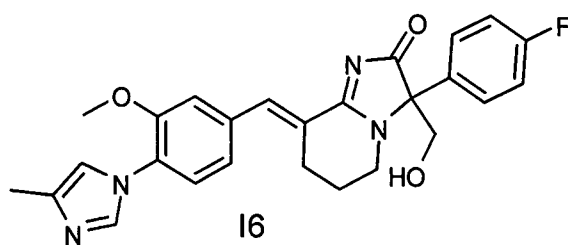
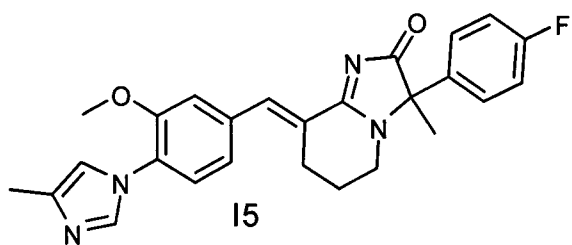
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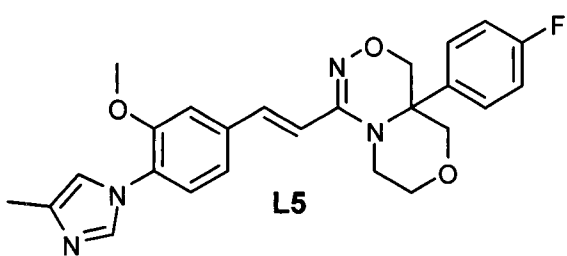
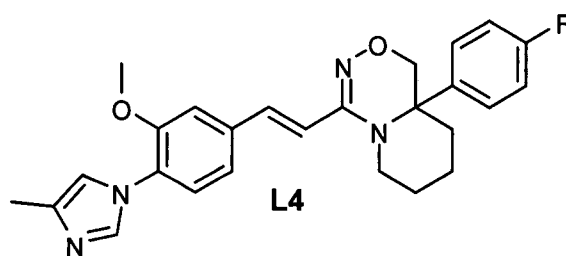
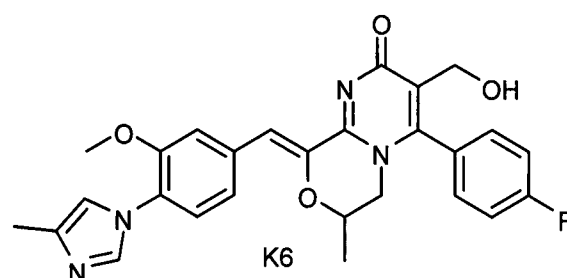
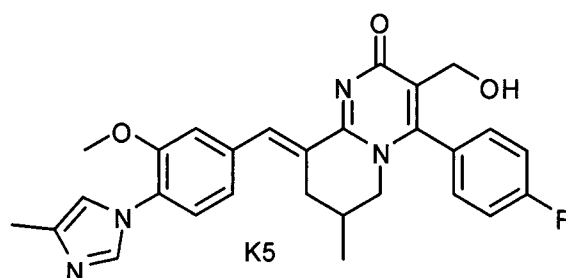
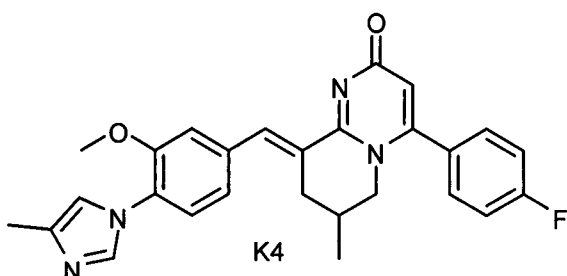
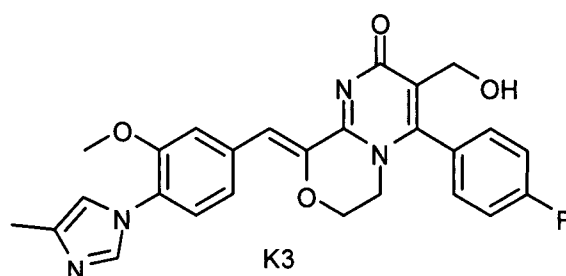
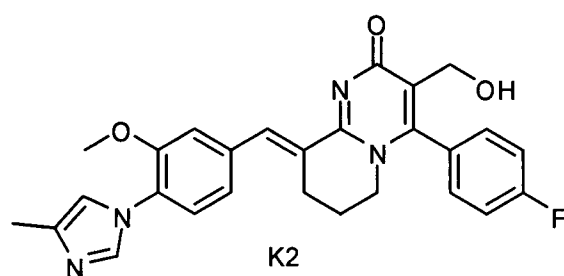
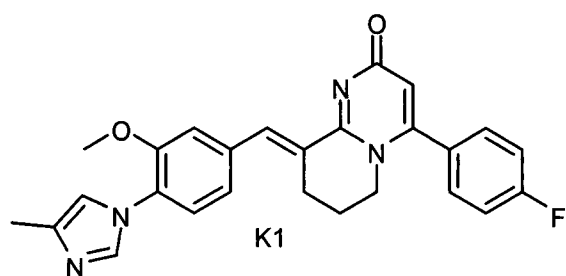
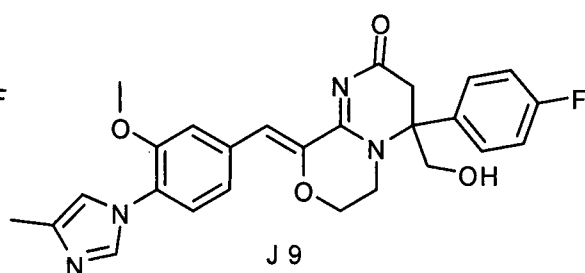
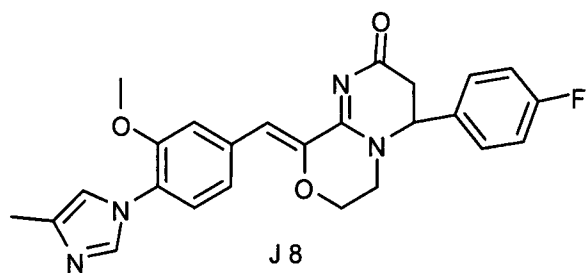
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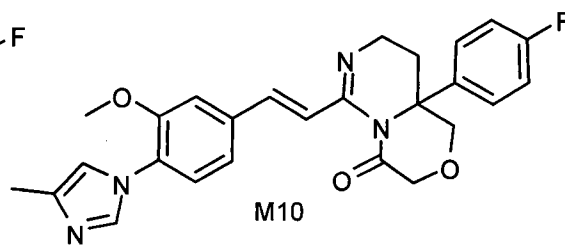
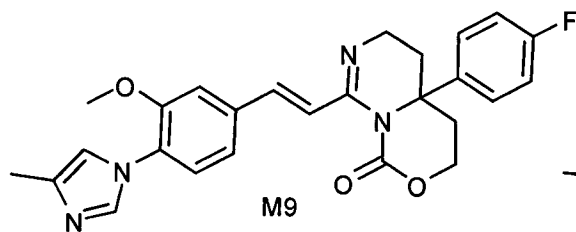
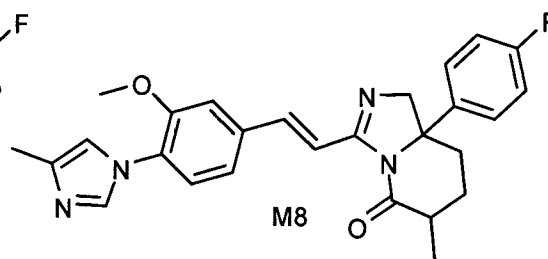
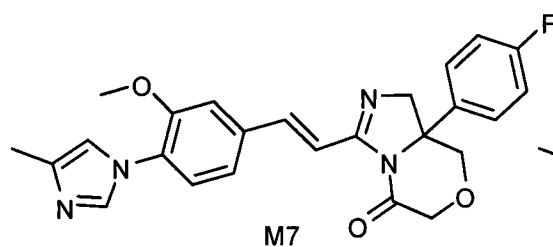
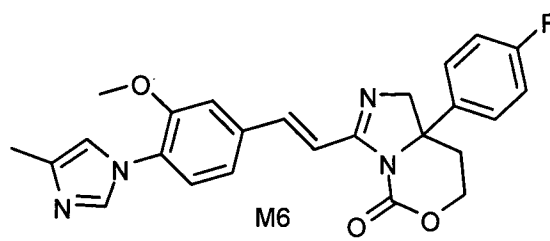
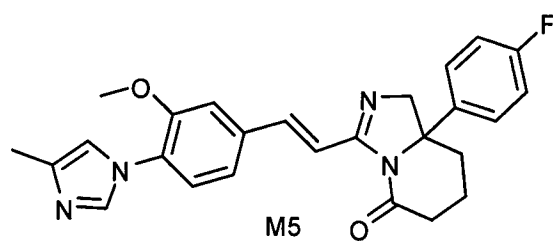
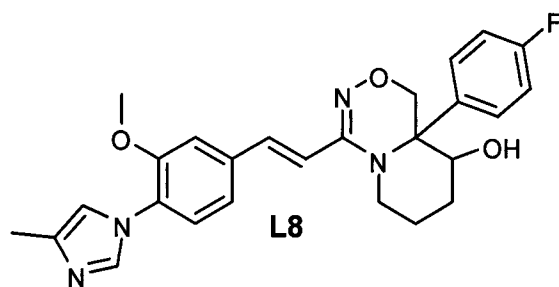
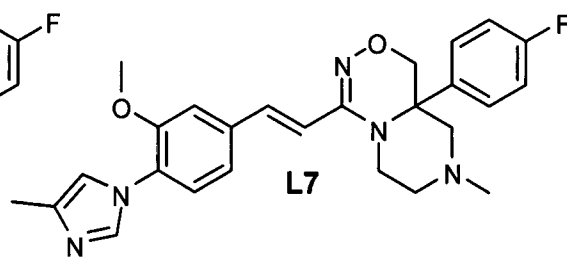
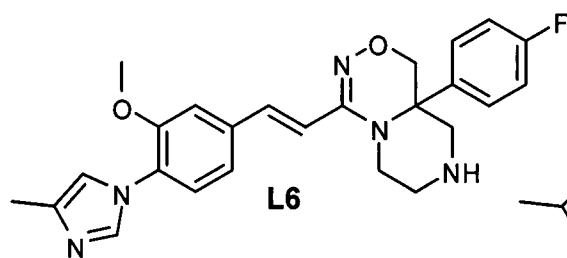




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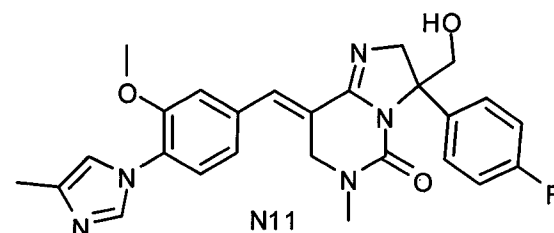
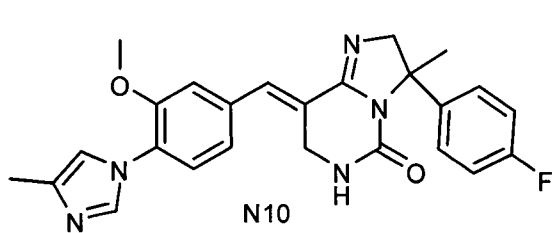
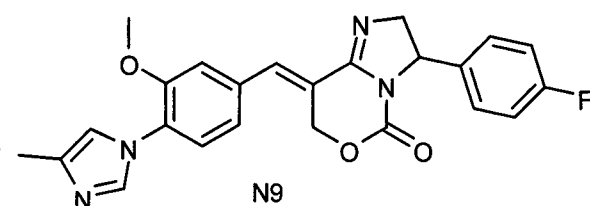
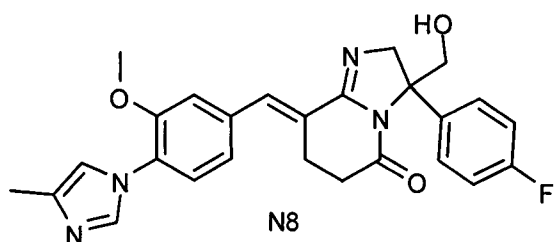
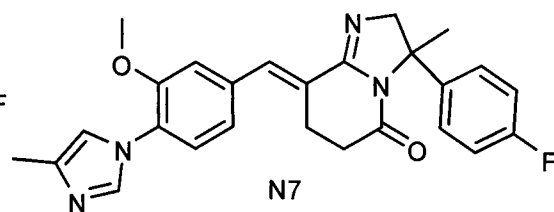
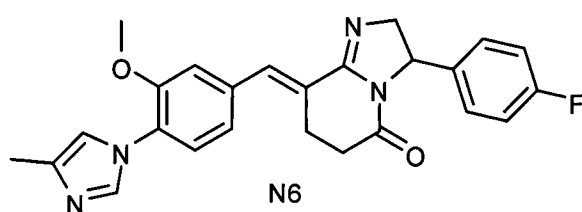
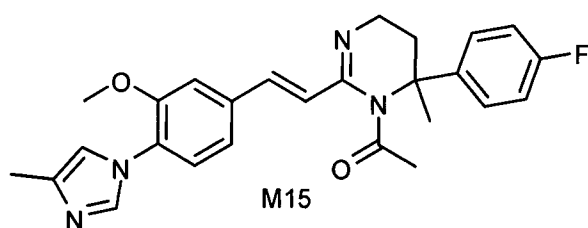
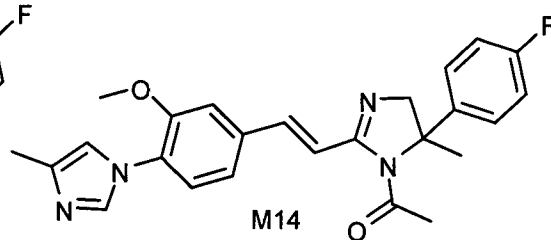
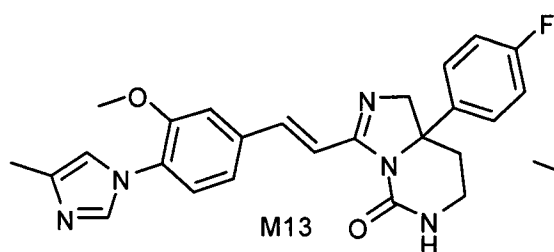
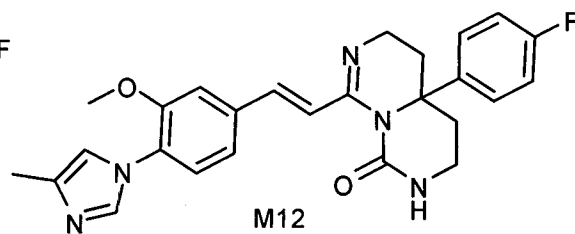
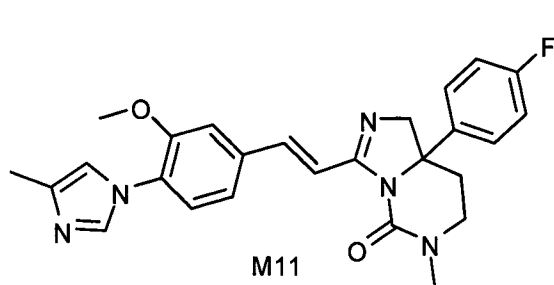


JFA

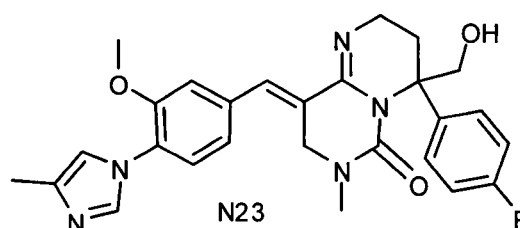
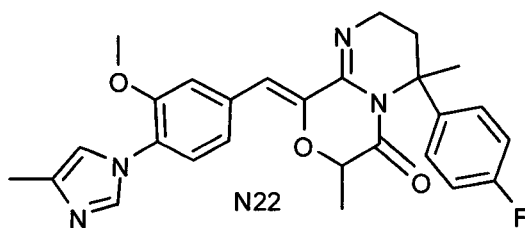
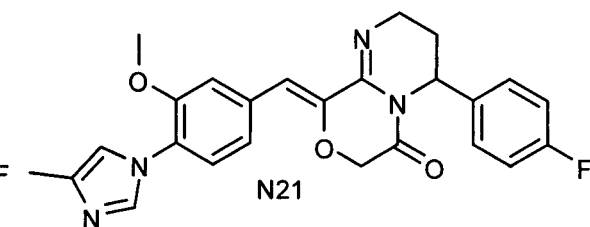
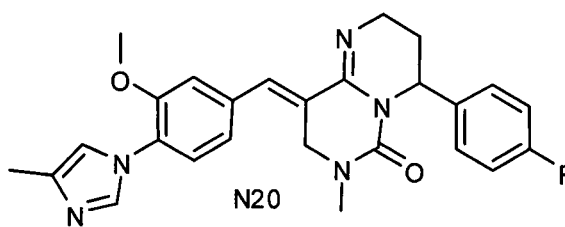
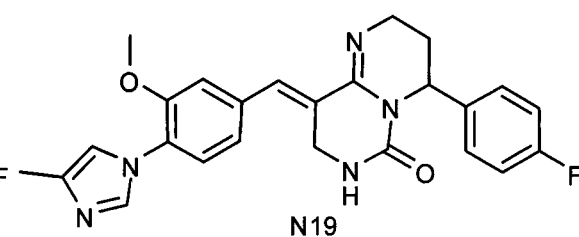
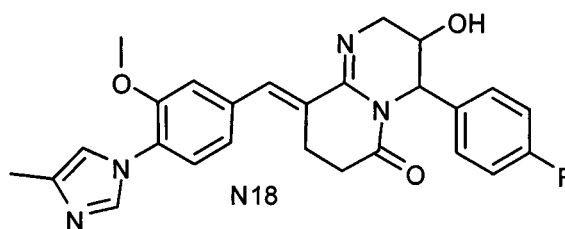
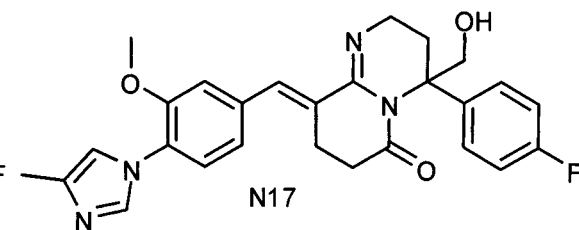
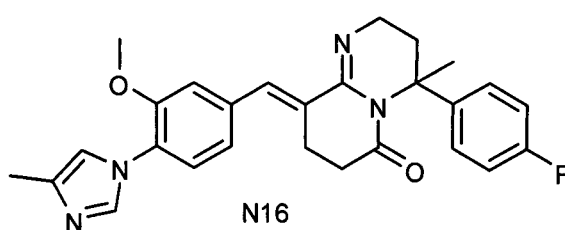
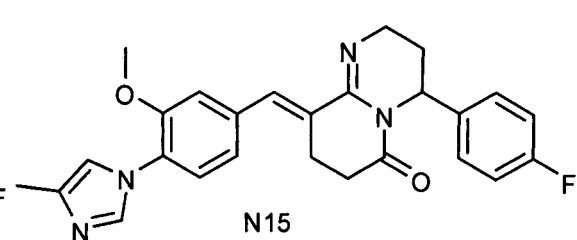
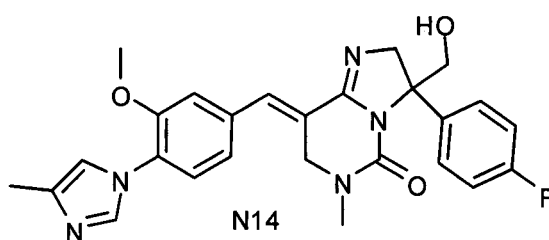
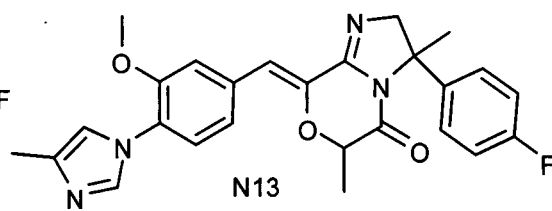
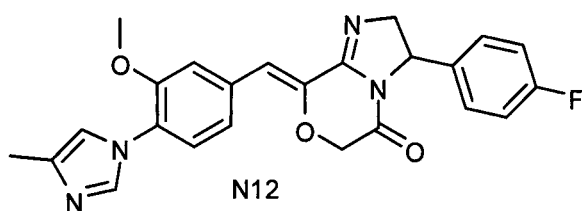




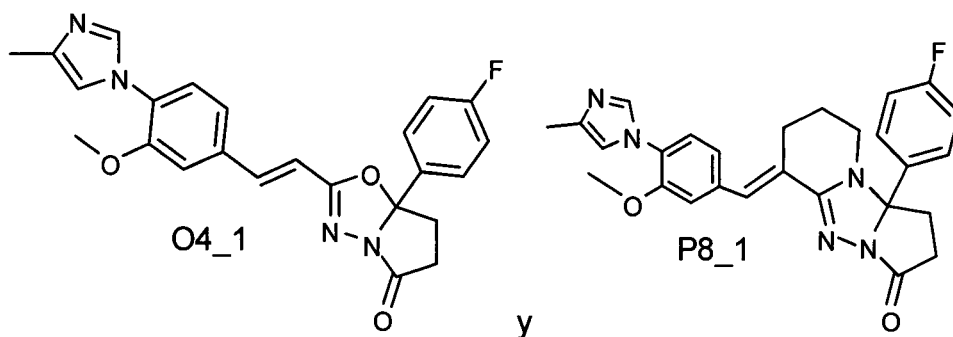
490



val



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- Una realización de esta invención se refiere al compuesto 1.
- Otra realización de esta invención se refiere al compuesto 2.
- Otra realización de esta invención se refiere al compuesto 3.
- Otra realización de esta invención se refiere al compuesto 4.
- Otra realización de esta invención se refiere al compuesto 5.
- Otra realización de esta invención se refiere al compuesto 6.
- Otra realización de esta invención se refiere al compuesto 7.
- Otra realización de esta invención se refiere al compuesto 8.
- Otra realización de esta invención se refiere al compuesto 9.
- Otra realización de esta invención se refiere al compuesto 10.
- Otra realización de esta invención se refiere al compuesto 11.
- Otra realización de esta invención se refiere al compuesto 12.
- Otra realización de esta invención se refiere al compuesto 13.
- Otra realización de esta invención se refiere al compuesto 14.
- Otra realización de esta invención se refiere al compuesto 15.
- Otra realización de esta invención se refiere al compuesto 16.
- Otra realización de esta invención se refiere al compuesto 17.
- Otra realización de esta invención se refiere al compuesto 18.
- Otra realización de esta invención se refiere al compuesto 19.
- Otra realización de esta invención se refiere al compuesto 20.
- Otra realización de esta invención se refiere al compuesto 21.

HAB

Otra realización de esta invención se refiere al compuesto 22.  
Otra realización de esta invención se refiere al compuesto 23.  
Otra realización de esta invención se refiere al compuesto 24.  
Otra realización de esta invención se refiere al compuesto B10.  
Otra realización de esta invención se refiere al compuesto B11.  
Otra realización de esta invención se refiere al compuesto B12.  
Otra realización de esta invención se refiere al compuesto B13.  
Otra realización de esta invención se refiere al compuesto B14.  
Otra realización de esta invención se refiere al compuesto B15.  
Otra realización de esta invención se refiere al compuesto B16.  
Otra realización de esta invención se refiere al compuesto B17.  
Otra realización de esta invención se refiere al compuesto B18.  
Otra realización de esta invención se refiere al compuesto B19.  
Otra realización de esta invención se refiere al compuesto B20.  
Otra realización de esta invención se refiere al compuesto B21.  
Otra realización de esta invención se refiere al compuesto C5.  
Otra realización de esta invención se refiere al compuesto C6.  
Otra realización de esta invención se refiere al compuesto C7.  
Otra realización de esta invención se refiere al compuesto C8.  
Otra realización de esta invención se refiere al compuesto C9.  
Otra realización de esta invención se refiere al compuesto C10.  
Otra realización de esta invención se refiere al compuesto D9.  
Otra realización de esta invención se refiere al compuesto D10.  
Otra realización de esta invención se refiere al compuesto D11.  
Otra realización de esta invención se refiere al compuesto D12.  
Otra realización de esta invención se refiere al compuesto D13.  
Otra realización de esta invención se refiere al compuesto D14.

Otra realización de esta invención se refiere al compuesto D15.  
Otra realización de esta invención se refiere al compuesto D16.  
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Otra realización de esta invención se refiere al compuesto D23.  
Otra realización de esta invención se refiere al compuesto D24.  
Otra realización de esta invención se refiere al compuesto D25.  
Otra realización de esta invención se refiere al compuesto D26.  
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Otra realización de esta invención se refiere al compuesto G6.  
Otra realización de esta invención se refiere al compuesto G7.  
Otra realización de esta invención se refiere al compuesto G8.  
Otra realización de esta invención se refiere al compuesto G9.  
Otra realización de esta invención se refiere al compuesto H3.  
Otra realización de esta invención se refiere al compuesto H4.  
Otra realización de esta invención se refiere al compuesto H5.  
Otra realización de esta invención se refiere al compuesto H6.  
Otra realización de esta invención se refiere al compuesto H7.  
Otra realización de esta invención se refiere al compuesto H8.  
Otra realización de esta invención se refiere al compuesto H9.  
Otra realización de esta invención se refiere al compuesto H10.  
Otra realización de esta invención se refiere al compuesto H11.

WAS

Otra realización de esta invención se refiere al compuesto I5.  
Otra realización de esta invención se refiere al compuesto I6.  
Otra realización de esta invención se refiere al compuesto I6A.  
Otra realización de esta invención se refiere al compuesto I7.  
Otra realización de esta invención se refiere al compuesto I8.  
Otra realización de esta invención se refiere al compuesto I8A.  
Otra realización de esta invención se refiere al compuesto J4.  
Otra realización de esta invención se refiere al compuesto J5.  
Otra realización de esta invención se refiere al compuesto J6.  
Otra realización de esta invención se refiere al compuesto J7.  
Otra realización de esta invención se refiere al compuesto J8.  
Otra realización de esta invención se refiere al compuesto J9.  
Otra realización de esta invención se refiere al compuesto K1.  
Otra realización de esta invención se refiere al compuesto K2.  
Otra realización de esta invención se refiere al compuesto K3.  
Otra realización de esta invención se refiere al compuesto K4.  
Otra realización de esta invención se refiere al compuesto K5.  
Otra realización de esta invención se refiere al compuesto K6.  
Otra realización de esta invención se refiere al compuesto L4.  
Otra realización de esta invención se refiere al compuesto L5.  
Otra realización de esta invención se refiere al compuesto L6.  
Otra realización de esta invención se refiere al compuesto L7.  
Otra realización de esta invención se refiere al compuesto L8.  
Otra realización de esta invención se refiere al compuesto M5.  
Otra realización de esta invención se refiere al compuesto M6.  
Otra realización de esta invención se refiere al compuesto M7.  
Otra realización de esta invención se refiere al compuesto M8.

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Otra realización de esta invención se refiere al compuesto M9.  
Otra realización de esta invención se refiere al compuesto M10.  
Otra realización de esta invención se refiere al compuesto M11.  
Otra realización de esta invención se refiere al compuesto M12.  
Otra realización de esta invención se refiere al compuesto M13.  
Otra realización de esta invención se refiere al compuesto M14.  
Otra realización de esta invención se refiere al compuesto M15.  
Otra realización de esta invención se refiere al compuesto N6.  
Otra realización de esta invención se refiere al compuesto N7.  
Otra realización de esta invención se refiere al compuesto N8.  
Otra realización de esta invención se refiere al compuesto N9.  
Otra realización de esta invención se refiere al compuesto N10.  
Otra realización de esta invención se refiere al compuesto N11.  
Otra realización de esta invención se refiere al compuesto N12.  
Otra realización de esta invención se refiere al compuesto N13.  
Otra realización de esta invención se refiere al compuesto N14.  
Otra realización de esta invención se refiere al compuesto N15.  
Otra realización de esta invención se refiere al compuesto N16.  
Otra realización de esta invención se refiere al compuesto N17.  
Otra realización de esta invención se refiere al compuesto N18.  
Otra realización de esta invención se refiere al compuesto N19.  
Otra realización de esta invención se refiere al compuesto N20.  
Otra realización de esta invención se refiere al compuesto N21.  
Otra realización de esta invención se refiere al compuesto N22.  
Otra realización de esta invención se refiere al compuesto N23.  
Otra realización de esta invención se refiere al compuesto O4\_1.  
Otra realización de esta invención se refiere al compuesto P8\_1.

Como se usó con anterioridad y en toda esta memoria descriptiva, los siguientes términos, salvo que se indique de otro modo, tendrán los siguientes significados:

"ADDP" significa 1,1'-(azodicarbonil)dipiperidina.

"AIBN" significa 2,2'-azobis(2-metilpropionitrilo).

"CAN" significa nitrato de amonio y cerio (IV).

"DCC" significa N, N'-diciclohexilcarbodiimida.

"DCM" significa diclorometano.

"DMF" significa dimetilformamida.

"HOBT" significa 1-hidroxilbenzotriazol.

"LDA" significa diisopropilamida de litio.

"TBAF" significa fluoruro de tetra-N-butilamonio.

"TBSO" significa ter-butildimetilsililoxi.

"TfO" significa trifluorometilsulfoniloxi.

"Por lo menos uno" significa uno o más de uno, por ejemplo, 1, 2 o 3, o en otro ejemplo, 1 o 2, o en otro ejemplo 1.

"Uno o más" con referencia al uso de los compuestos de esta invención significa que se usa uno o más de un compuesto, por ejemplo, 1, 2 o 3, o en otro ejemplo, 1 o 2, o en otro ejemplo 1.

"Paciente" incluye ambos humanos y animales.

"Mamíferos" significa humanos y otros animales mamíferos.

Se observa que los carbonos de fórmula I y otras fórmulas de la invención pueden reemplazarse con 1 a 3 átomos de silicio en tanto se cumplan los requerimientos de valencia.

"Alquilo" significa un grupo hidrocarbonado alifático que puede ser recto o ramificado y que comprende aproximadamente 1 hasta aproximadamente 20



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átomos de carbono en la cadena. Los grupos alquilo preferidos contienen aproximadamente 1 hasta aproximadamente 12 átomos de carbono en la cadena. Los grupos alquilo más preferidos contienen aproximadamente 1 hasta aproximadamente 6 átomos de carbono en la cadena. Ramificado significa que uno o más grupos alquilo inferior tales como metilo, etilo o propilo, se unen a una cadena alquilo lineal. "Alquilo inferior" significa un grupo que tiene aproximadamente 1 hasta aproximadamente 6 átomos de carbono en la cadena que puede ser recto o ramificado. El "Alquilo" puede no estar sustituido o estar sustituido en forma opcional por uno o más sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en halo, alquilo, arilo, cicloalquilo, ciano, hidroxilo, alcoxi, alquiltio, amino, oxima (por ej.,  $=N-OH$ ),  $-NH(\text{alquilo})$ ,  $-NH(\text{cicloalquilo})$ ,  $-N(\text{alquil})_2$ ,  $-O-C(O)-\text{alquilo}$ ,  $-O-C(O)-\text{arilo}$ ,  $-O-C(O)-\text{cicloalquilo}$ , carboxi y  $-C(O)O-\text{alquilo}$ . Ejemplos no limitativos de grupos alquilo apropiados incluyen metilo, etilo, n-propilo, isopropilo y t-butilo.

"Alquenilo" significa un grupo hidrocarbonado alifático que contiene por lo menos uno doble enlace carbono-Carbono y que puede ser recto o ramificado y que comprende aproximadamente 2 hasta aproximadamente 15 átomos de carbono en la cadena. Los grupos alquenilo preferidos tienen aproximadamente 2 hasta aproximadamente 12 átomos de carbono en la cadena; y con mayor preferencia aproximadamente 2 hasta aproximadamente 6 átomos de carbono en la cadena. Ramificado significa que uno o más grupos alquilo inferior tales como metilo, etilo o propilo, se unen a una cadena alquilo lineal. "Alquenilo inferior" significa aproximadamente 2 hasta aproximadamente 6 átomos de carbono en la cadena que puede ser recto o ramificado. El "alquenilo" puede no estar sustituido o estar sustituido en forma opcional por uno o más sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del

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grupo que consiste en halo, alquilo, arilo, cicloalquilo, ciano, alcoxi y  $-S(\text{alquilo})$ . Ejemplos no limitativos de grupos alquenilo apropiados incluyen etenilo, propenilo, n-butenilo, 3-metilobut-2-enilo, n-pentenilo, octenilo y decenilo.

"Alquilenilo" significa un grupo di-funcional obtenido por eliminación del átomo de hidrógeno de un grupo alquilo que se definió con anterioridad. Ejemplos no limitativos de alquilenilo incluyen metileno, etileno y propileno.

"Alquinilo" significa un grupo hidrocarbonado alifático que contiene por lo menos un enlace triple carbono carbono y que puede ser recto o ramificado y que comprende aproximadamente 2 hasta aproximadamente 15 átomos de carbono en la cadena. Los grupos alquinilo preferidos tienen aproximadamente 2 hasta aproximadamente 12 átomos de carbono en la cadena; y con mayor preferencia aproximadamente 2 hasta aproximadamente 4 átomos de carbono en la cadena. Ramificado significa que uno o más grupos alquilo inferior tales como metilo, etilo o propilo, se unen a una cadena alquinilo lineal. "Alquinilo inferior" significa aproximadamente 2 hasta aproximadamente 6 átomos de carbono en la cadena que puede ser recto o ramificado. Ejemplos no limitativos de grupos alquinilo apropiados incluyen etinilo, propinilo, 2-butinilo y 3-metilbutinilo. El "alquinilo" puede no estar sustituido o estar sustituido en forma opcional por uno o más sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en alquilo, arilo y cicloalquilo.

"Arilo" significa un sistema anular monocíclico o multicíclico aromático que comprende aproximadamente 6 hasta aproximadamente 14 átomos de carbono, con preferencia aproximadamente 6 hasta aproximadamente 10 átomos de carbono. El grupo arilo puede estar sustituido en forma opcional con uno o más "sustituyentes del sistema anular" que pueden ser iguales o diferentes, y son



como se los define aquí. Ejemplos no limitativos de grupos arilo incluyen fenilo y naftilo.

"Heteroarilo" significa un sistema anular monocíclico o multicíclico aromático que comprende aproximadamente 5 hasta aproximadamente 14 átomos en el anillo, con preferencia aproximadamente 5 hasta aproximadamente 10 átomos en el anillo, en los cuales uno o más de los átomos en el anillo es un elemento distinto de carbono, por ejemplo nitrógeno, oxígeno o azufre, sólo o combinado. Los heteroarilos preferidos contienen aproximadamente 5 hasta aproximadamente 6 átomos en el anillo. El "heteroarilo" puede estar sustituido en forma opcional por uno o más "sustituyentes del sistema anular" que pueden ser iguales o diferentes, y son como se los define aquí. El prefijo aza, oxa o tia antes del nombre de raíz heteroarilo significa que por lo menos un átomo de nitrógeno, oxígeno o azufre respectivamente, está presente como átomo del anillo. Un átomo de nitrógeno de un heteroarilo puede oxidarse en forma opcional al correspondiente N-óxido. "Heteroarilo" también puede incluir un heteroarilo como se definió con anterioridad fusionado a un arilo como se definió con anterioridad. Ejemplos no limitativos de heteroarilos apropiados incluyen piridilo, pirazinilo, furanilo, tienilo, pirimidinilo, piridona (incluyendo piridonas N-sustituidas), isoxazolilo, isotiazolilo, oxazolilo, tiazolilo, pirazolilo, furazanilo, pirrolilo, pirazolilo, triazolilo, 1,2,4-tiadiazolilo, pirazinilo, piridazinilo, quinoxalinilo, ftalazinilo, oxindolilo, imidazo[1,2-a]piridinilo, imidazo[2,1-b]tiazolilo, benzofurazanilo, indolilo, azaindolilo, benzimidazolilo, benzotienilo, quinolinilo, imidazolilo, tienopiridilo, quinazolinilo, tienopirimidilo, pirrolopiridilo, imidazopiridilo, isoquinolinilo, benzoazaindolilo, 1,2,4-triazinilo, benzotiazolilo y similares. El término "heteroarilo" se refiere, además, a restos heteroarilo parcialmente saturados tales como, por ejemplo, tetrahidroisoquinolilo, tetrahydroquinolilo y similares.

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"Aralquilo" o "arilalquilo" significa un grupo aril-alquilo- en el cual el arilo y el alquilo son como se los describió con anterioridad. Los aralquilos preferidos comprenden un grupo alquilo inferior. Ejemplos no limitativos de grupos aralquilo apropiados incluyen bencilo, 2-fenetilo y naftalenilmetilo. El enlace al resto principal es a través del alquilo.

"Alquilarilo" significa un grupo alquil-arilo- en el cual el alquilo y el arilo son como se los describió con anterioridad. Los alquilarilos comprenden un grupo alquilo inferior. Un ejemplo no limitativo de un grupo alquilarilo apropiado es tolilo. El enlace al resto principal es a través del arilo.

"Cicloalquilo" significa un sistema anular no aromático, mono- o multicíclico que comprende aproximadamente 3 hasta aproximadamente 10 átomos de carbono, con preferencia aproximadamente 5 hasta aproximadamente 10 átomos de carbono. Los anillos cicloalquilo contienen aproximadamente 5 hasta aproximadamente 7 átomos en el anillo. El cicloalquilo puede estar sustituido en forma opcional con uno o más "sustituyentes del sistema anular" que pueden ser iguales o diferentes, y son como se los definió con anterioridad. Ejemplos no limitativos de cicloalquilos monocíclicos apropiados incluyen ciclopropilo, ciclopentilo, ciclohexilo, cicloheptilo y similares. Ejemplos no limitativos de cicloalquilos multicíclicos apropiados incluyen 1-decalinilo, norbornilo, adamantilo y similares.

"Cicloalquilalquilo" significa un resto cicloalquilo como se definió con anterioridad ligado a través de un resto alquilo (definido con anterioridad) a un núcleo original. Ejemplos no limitativos de cicloalquilalquilos apropiados incluyen ciclohexilmetilo, adamantilmetilo y similares.

"Cicloalquenilo" significa un sistema anular no aromático mono o multicíclico que comprende aproximadamente 3 hasta aproximadamente 10 átomos de carbono, con preferencia aproximadamente 5 hasta aproximadamente

10 átomos de carbono que contiene por lo menos uno doble enlace carbono-carbono. Los anillos cicloalquenilo preferidos contienen aproximadamente 5 hasta aproximadamente 7 átomos en el anillo. El cicloalquenilo puede estar sustituido en forma opcional con uno o más "sustituyentes del sistema anular" que pueden ser iguales o diferentes, y son como se los definió con anterioridad. Ejemplos no limitativos de cicloalquenilos monocíclicos apropiados incluyen ciclopentenilo, ciclohexenilo, ciclohepta-1,3-dienilo, y similares. Un ejemplo no limitativo de un cicloalquenilo multicíclico apropiado es norbornilenilo.

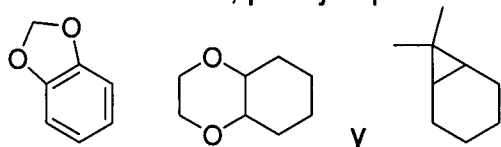
"Cicloalquenilalquilo" significa un resto cicloalquenilo como se definió con anterioridad ligado a través de un resto alquilo (definido con anterioridad) a un núcleo principal. Ejemplos no limitativos de cicloalquenilalquilos apropiados incluyen ciclopentenilmetilo, ciclohexenilmetilo y similares.

"Halógeno" significa flúor, cloro, bromo, o yodo. Se prefieren el flúor, cloro y bromo. "Halo" se refiere a fluoro, cloro, bromo o yodo.

"Sustituyente del sistema anular" significa un sustituyente unido a un sistema anular aromático o no aromático que, por ejemplo, reemplaza un hidrógeno disponible en el sistema anular. Los sustituyentes del sistema anular pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, arilo, heteroarilo, aralquilo, alquilarilo, heteroaralquilo, heteroarilalquenilo, heteroarilalquinilo, alquilheteroarilo, hidroxilo, hidroxialquilo, alcoxi, ariloxi, aralcoxi, acilo, aroilo, halo, nitro, ciano, carboxi, alcoxycarbonilo, ariloxycarbonilo, aralcoxycarbonilo, alquilosulfonilo, arilsulfonilo, heteroarilsulfonilo, alquiltio, ariltio, heteroariltio, aralquiltio, heteroaralquiltio, cicloalquilo, heterociclilo, -O-C(O)-alquilo, -O-C(O)-arilo, -O-C(O)-cicloalquilo, -C(=N-CN)-NH<sub>2</sub>, -C(=NH)-NH<sub>2</sub>, -C(=NH)-NH(alquilo), oxima (por ej., =N-OH), Y<sub>1</sub>Y<sub>2</sub>N-, Y<sub>1</sub>Y<sub>2</sub>N-alquilo-, Y<sub>1</sub>Y<sub>2</sub>NC(O)-, Y<sub>1</sub>Y<sub>2</sub>NSO<sub>2</sub>- y -SO<sub>2</sub>NY<sub>1</sub>Y<sub>2</sub>, donde Y<sub>1</sub> y Y<sub>2</sub> pueden ser iguales o diferentes y se seleccionan de manera



independiente del grupo que consiste en hidrógeno, alquilo, arilo, cicloalquilo, y aralquilo. "Sustituyente del sistema anular" también puede significar un resto simple que reemplaza en forma simultánea dos hidrógenos disponibles en dos átomos de carbono adyacentes (un H en cada carbono) en un sistema anular. Algunos ejemplos de dicho resto son metilen dioxi, etilendioxi,  $-\text{C}(\text{CH}_3)_2-$  y similares que forman restos tales como, por ejemplo:

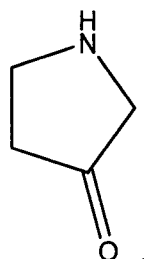


"Heteroarilalquilo" significa un resto heteroarilo como se definió con anterioridad ligado a través de un resto alquilo (definido con anterioridad) a un núcleo principal. Ejemplos no limitativos de heteroarilos apropiados incluyen 2-piridinilmetilo, quinolinilmetilo y similares.

"Heterociclilo" significa un sistema no aromático monocíclico o multicíclico saturado que comprende aproximadamente 3 hasta aproximadamente 10 átomos en el anillo, con preferencia aproximadamente 5 hasta aproximadamente 10 átomos en el anillo, en el cual uno o más de los átomos en el sistema anular es un elemento distinto de carbono, por ejemplo nitrógeno, oxígeno o azufre, sólo o combinado. No hay átomos de oxígeno y/o azufre presentes en el sistema anular. Los heterociclilos preferidos contienen aproximadamente 5 hasta aproximadamente 6 átomos en el anillo. El prefijo aza, oxa o tia antes del nombre de raíz heterociclilo significa que por lo menos un átomo de nitrógeno, oxígeno o azufre respectivamente está presente como átomo del anillo. Cualquier  $-\text{NH}$  en un anillo heterociclilo puede existir protegido tales como, por ejemplo, como un grupo  $-\text{N}(\text{Boc})$ ,  $-\text{N}(\text{CBz})$ ,  $-\text{N}(\text{Tos})$  y similares; dichas protecciones se consideran parte de esta invención. El heterociclilo puede estar sustituido en forma opcional por uno o más "sustituyentes del sistema anular" que pueden ser iguales o diferentes, y son como se los define aquí. El átomo de nitrógeno o azufre del

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heterociclilo puede oxidarse en forma opcional al correspondiente N-óxido, S-óxido o S,S-dióxido. Ejemplos no limitativos de anillos heterociclilo monocíclicos apropiados incluyen piperidilo, pirrolidinilo, piperazinilo, morfolinilo, tiomorfolinilo, tiazolidinilo, 1,4-dioxanilo, tetrahidrofuranilo, tetrahidrotiofenilo, lactama, lactona, y similares. "Heterociclilo" también puede significar un anillo heterociclilo en el cual un resto simple (por ej., =O) reemplaza en forma simultánea dos hidrógenos disponibles en el mismo átomo de carbono en un sistema anular. Un ejemplo de dicho resto es pirrolidona:

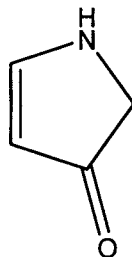


"Heterociclilalquilo" significa un resto heterociclilo como se definió con anterioridad ligado a través de un resto alquilo (definido con anterioridad) a un núcleo principal. Ejemplos no limitativos de heterociclilalquilos apropiados incluyen piperidinilmetilo, piperazinilmetilo y similares.

"Heterociclenilo" significa un sistema anular no aromático monocíclico o multicíclico que comprende aproximadamente 3 hasta aproximadamente 10 átomos en el anillo, con preferencia aproximadamente 5 hasta aproximadamente 10 átomos en el anillo, en el cual uno o más de los átomos en el sistema anular es un elemento distinto de carbono, por ejemplo átomo de nitrógeno, oxígeno o azufre, sólo o combinado, y que contiene por lo menos un doble enlace carbono-carbono o enlace doble carbono-nitrógeno. No hay átomos de oxígeno y/o azufre adyacentes presentes en el sistema anular. Los anillos heterociclenilo preferidos contienen aproximadamente 5 hasta aproximadamente 6 átomos en el anillo. El prefijo aza, oxa o tia antes del nombre de raíz heterociclenilo significa que por lo menos un átomo de nitrógeno, oxígeno o azufre respectivamente está presente

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como átomo del anillo. El heterociclenilo puede estar sustituido en forma opcional por uno o más sustituyentes del sistema anular, donde el "sustituyente del sistema anular" es como se definió con anterioridad. El átomo de nitrógeno o azufre del heterociclenilo puede estar oxidado en forma opcional al correspondiente N-óxido, S-óxido o S,S-dióxido. Ejemplos no limitativos de grupos heterociclenilo apropiados incluyen 1,2,3,4- tetrahidropiridinilo, 1,2-dihidropiridinilo, 1,4-dihidropiridinilo, 1,2,3,6-tetrahidropiridinilo, 1,4,5,6-tetrahidropirimidinilo, 2-pirrolinilo, 3-pirrolinilo, 2-imidazolinilo, 2-pirazolinilo, dihidroimidazolilo, dihidrooxazolilo, dihidrooxadiazolilo, dihidrotiazolilo, 3,4-dihidro-2H-piranilo, dihidrofuranilo, fluorodihidrofuranilo, 7-oxabicyclo[2.2.1]heptenilo, dihidrotiofenilo, dihidrotiopiranilo, y similares. "Heterociclenilo" también puede significar un resto simple (por ej., carbonilo) que reemplaza en forma simultánea dos hidrógenos disponibles en el mismo átomo de carbono en un sistema anular. Un ejemplo de dicho resto es pirrolidinona:

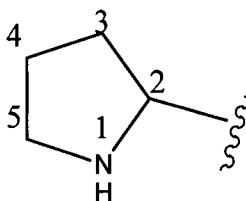


"Heterociclenilalquilo" significa un resto heterociclenilo como se definió con anterioridad ligado a través de un resto alquilo (definido con anterioridad) a un núcleo principal.

Debe observarse que en el heteroátomo que contiene los sistemas anulares de esta invención, no hay grupos hidroxilo en los átomos de carbono adyacentes a un N, O, o S, como tampoco hay grupos N o S en el carbono adyacente a otro heteroátomo. De este modo, por ejemplo, en el anillo:

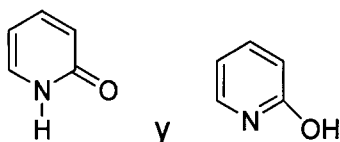


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no hay -OH unido directamente a los carbonos marcados 2 y 5.

También debe observarse que las formas tautoméricas tales como, por ejemplo, los restos:



se consideran equivalentes en determinadas realizaciones de esta invención.

"Alquinilalquilo" significa un grupo alquinil-alquilo- en el cual el alquinilo y alquilo son como se los describió con anterioridad. Los alquinilalquilos preferidos contienen un grupo alquinilo inferior y un grupo alquilo inferior. El enlace al resto principal es a través del alquilo. Ejemplos no limitativos de grupos alquinilalquilo apropiados incluyen propargilmetilo.

"Heteroarylalquilo" significa un grupo heteroaryl-alquilo- en el cual el heteroaryl y alquilo son como se los describió con anterioridad. Los heteroarylalquilos preferidos contienen un grupo alquilo inferior. Ejemplos no limitativos de grupos aralquilo apropiados incluyen piridilmetilo, y quinolin-3-ilmetilo. El enlace al resto principal es a través del alquilo.

"Hidroxialquilo" significa un grupo HO-alquilo- en el cual el alquilo es como se definió con anterioridad. Los hidroxialquilos preferidos contienen alquilo inferior. Ejemplos no limitativos de grupos hidroxialquilo apropiados incluyen hidroximetilo y 2-hidroxietilo.

"Acilo" significa un grupo H-C(O)-, alquil-C(O)- o cicloalquil-C(O)-, en el cual los varios grupos son como se los describió con anterioridad. El enlace al resto principal es a través del carbonilo. Los acilos preferidos contienen un alquilo

inferior. Ejemplos no limitativos de grupos acilo apropiados incluyen formilo, acetilo y propanoilo.

"Aroilo" significa un grupo aril-C(O)- en el cual el grupo arilo es como se lo describió con anterioridad. El enlace al resto principal es a través del carbonilo. Ejemplos no limitativos de grupos apropiados incluyen benzoilo y 1- naftoilo.

"Alcoxi" significa un grupo alquil-O- en el cual el grupo alquilo es como se lo describió con anterioridad. Ejemplos no limitativos de grupos alcoxi apropiados incluyen metoxi, etoxi, n-propoxi, isopropoxi y n-butoxi. El enlace al resto principal es a través del oxígeno del éter.

"Ariloxi" significa un grupo aril-O- en el cual el grupo arilo es como se lo describió con anterioridad. Ejemplos no limitativos de grupos ariloxi apropiados incluyen fenoxi y naftoxi. El enlace al resto principal es a través del oxígeno del éter.

"Aralquilo" significa un grupo aralquil-O- en el cual el grupo aralquilo es como se lo describió con anterioridad. Ejemplos no limitativos de grupos aralquilo apropiados incluyen benciloxi y 1- o 2-naftalenmetoxi. El enlace al resto principal es a través del oxígeno del éter.

"Alquiltio" significa un grupo alquil-S- en el cual el grupo alquilo es como se lo describió con anterioridad. Ejemplos no limitativos de grupos alquiltio apropiados incluyen metiltio y etiltio. El enlace al resto principal es a través del azufre.

"Arltio" significa un grupo aril-S- en el cual el grupo arilo es como se lo describió con anterioridad. Ejemplos no limitativos de grupos arltio apropiados incluyen feniltio y naftiltio. El enlace al resto principal es a través del azufre.

"Aralquiltio" significa un grupo aralquil-S- en el cual el grupo aralquilo es como se lo describió con anterioridad. Un ejemplo no limitativo de un grupo

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aralquiltio apropiado es benciltio. El enlace al resto principal es a través del azufre.

"Alcoxicarbonilo" significa un grupo  $\text{alquil-O-CO-}$ . Ejemplos no limitativos de grupos alcoxicarbonilo apropiados incluyen metoxycarbonilo y etoxycarbonilo. El enlace al resto principal es a través del carbonilo.

"Ariloxycarbonilo" significa un grupo  $\text{aril-O-C(O)-}$ . Ejemplos no limitativos de grupos ariloxycarbonilo apropiados incluyen fenoxycarbonilo y naftoxycarbonilo. El enlace al resto principal es a través del carbonilo.

"Aralcoxicarbonilo" significa un grupo  $\text{aralquil-O-C(O)-}$ . Un ejemplo no limitativo de un grupo aralcoxicarbonilo apropiado es benciloxycarbonilo. El enlace al resto principal es a través del carbonilo.

"Alquilosulfonilo" significa un grupo  $\text{alquil-S(O}_2\text{)-}$ . Los grupos preferidos son aquellos en los cuales el grupo alquilo es alquilo inferior. El enlace al resto principal es a través del sulfonilo.

"Arlsulfonilo" significa un grupo  $\text{aril-S(O}_2\text{)-}$ . El enlace al resto principal es a través del sulfonilo.

El término "sustituido" significa que uno o más hidrógenos en el átomo designado está reemplazado con una selección del grupo indicado, siempre que la valencia del átomo designado en circunstancias de existencia normales no se exceda, y que la sustitución genere un compuesto estable. Se permiten combinaciones de sustituyentes y/o variables sólo si dichas combinaciones producen compuestos estables. Por "compuesto estable" o "estructura estable" se entiende un compuesto que es lo suficientemente robusto para sobrevivir el aislamiento hasta un grado útil de pureza a partir de una mezcla de reacción, y la formulación en un agente terapéutico eficaz.

El término "sustituido en forma opcional" significa la sustitución opcional con los grupos, radicales o restos específicos.

El término "purificado", "en forma purificada " o "en forma aislada y pura" para un compuesto se refiere al estado físico de dicho compuesto luego de ser aislado a partir de un proceso de síntesis (por ej., a partir de una mezcla de reacción), o fuente natural o combinación de los anteriores. De este modo, el término "purificado", "en forma purificada " o "en forma aislada y purificada" para un compuesto se refiere al estado físico de dicho compuesto luego de obtenerse a partir de un proceso de purificación o de procesos descritos aquí o conocidos por los expertos en el arte (por ej., cromatografía, recristalización y similares), en pureza suficiente para ser caracterizable por técnicas analíticas estándar descritas aquí o conocidas por los expertos en el arte.

También debe observarse que cualquier carbono, como también cualquier heteroátomo con valencias no satisfechas en el texto, esquemas, ejemplos y Tablas de la invención tiene el número suficiente de átomo(s) de hidrógeno para satisfacer las valencias.

Cuando un grupo funcional en un compuesto se denomina "protegido", esto significa que el grupo está en forma modificada para evitar cualquier reacción no deseada en el sitio protegido cuando el compuesto se somete a una reacción. Los grupos protectores apropiados serán reconocidos por personas con experiencia en el arte con referencia a libros de texto estándar tales como, por ejemplo, T. W. Greene *et al*, *Protective Grupos in organic Synthesis* (1991), Wiley, New York.

Cuando cualquier variable (por ej., arilo, heterociclo,  $R^2$ , etc.) ocurre más de una vez en cualquier constituyente o en la Fórmula I, su definición en cada caso es independiente de su definición en cualquier otro caso.

Como se usa aquí, el término "composición" pretende abarcar un producto que comprende los componentes específicos en las cantidades específicas, como también cualquier producto que se genera, directamente o indirectamente, a partir de la combinación de los componentes específicos en las cantidades específicas.

Las prodrogas y los solvatos de los compuestos de la invención también se contemplan aquí. Una discusión sobre prodrogas se provee en T. Higuchi and V. Stella, *Pro-drugs as Novel Delivery Systems* (1987) 14 of the A.C.S. Symposium Series, y en *Bioreversible Carriers in Drug Design*, (1987) Edward B. Roche, ed., American Pharmaceutical Association and Pergamon Press. El término "prodroga" significa un compuesto (por ej., un precursor farmacológico) que se transforma *in vivo* para producir un compuesto de Fórmula (I) o una sal, un hidrato o un solvato aceptables desde el punto de vista farmacéutico del compuesto. La transformación puede ocurrir a través de varios mecanismos (por ej., por procesos químicos o metabólicos), tales como, por ejemplo, a través de hidrólisis en sangre. Una discusión sobre el uso de prodrogas se provee en T. Higuchi and W. Stella, "Pro-drugs as Novel Delivery Systems," Vol. 14 of the A.C.S. Symposium Series, y en *Bioreversible Carriers in Drug Design*, ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987.

Por ejemplo, si un compuesto de Fórmula (I) o una sal, un hidrato o un solvato aceptables desde el punto de vista farmacéutico del compuesto contiene un grupo funcional ácido carboxílico, una prodroga puede comprender un éster formado por el reemplazo de un átomo de hidrógeno del grupo ácido con un grupo tal como, por ejemplo, alquilo ( $C_1-C_8$ ), alcanoiloximetilo ( $C_2-C_{12}$ ), 1—(alcanoiloxi)etilo que tiene desde 4 hasta 9 átomos de carbono, 1—metil—1—(alcanoiloxi)—etilo que tiene desde 5 hasta 10 átomos de carbono, alcóxicarboniloximetilo que tiene desde 3 hasta 6 átomos de carbono, 1—(alcóxicarboniloxi)etilo que tiene desde 4 hasta 7 átomos de carbono, 1—metil—1—(alcóxicarboniloxi)etilo que tiene desde 5 hasta 8 átomos de carbono, N—(alcóxicarbonil)aminometilo que tiene desde 3 hasta 9 átomos de carbono, 1—(N—(alcóxicarbonil)amino)etilo que tiene desde 4 hasta 10 átomos de carbono, 3—phthalidilo, 4-Crotonolactonilo, gamma—butirolacton—4—ilo, di—N,N—

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alquilamino ( $C_1-C_2$ ) alquilo ( $C_2-C_3$ ) (tales como  $\beta$ -dimetilaminoetilo), carbamoil—alquilo ( $C_1-C_2$ ), N,N—di alquilcarbamoil ( $C_1-C_2$ )—alquilo ( $C_1-C_2$ ) y piperidino—, pirrolidino— o morfolino( $C_2-C_3$ )alquilo, y similares.

En forma similar, si un compuesto de Fórmula (I) contiene un grupo funcional alcohólico, una prodroga puede formarse por el reemplazo del átomo de hidrógeno del grupo alcohólico con un grupo tal como, por ejemplo, alcanoiloximetilo ( $C_1-C_6$ ), 1—(alcanoiloxi ( $C_1-C_6$ ))etilo, 1—metil—1—(alcanoiloxi ( $C_1-C_6$ ))etilo, alcoxicarboniloximetilo ( $C_1-C_6$ ), N—alcoxicarbonilaminometilo ( $C_1-C_6$ ), succinoilo, alcanoilo ( $C_1-C_6$ ),  $\alpha$ —amino( $C_1-C_4$ )alcanilo, arilacilo y  $\alpha$ —aminoacilo, o  $\alpha$ —aminoacil— $\alpha$ —aminoacilo, donde cada grupo  $\alpha$ —aminoacilo se selecciona en forma independiente de los L-aminoácidos naturales,  $P(O)(OH)_2$ , — $P(O)(O(C_1-C_6)alquil)_2$  o glicosilo (el radical que se obtiene a partir de la eliminación de un grupo hidroxilo de la forma semiacetal del carbohidrato), y similares.

Si un compuesto de Fórmula (I) incorpora un grupo funcional amina, una prodroga puede formarse por el reemplazo de un átomo de hidrógeno en el grupo amina con un grupo tal como, por ejemplo, R-Carbonilo, RO-Carbonilo, NRR'-Carbonilo donde R y R' son cada uno en forma independiente alquilo ( $C_1-C_{10}$ ), cicloalquilo ( $C_3-C_7$ ), bencilo, o R-Carbonilo es un  $\alpha$ —aminoacilo natural o  $\alpha$ —aminoacilo natural,  $-C(OH)C(O)OY^1$  donde  $Y^1$  es H, alquilo ( $C_1-C_6$ ) o bencilo,  $-C(OY^2)Y^3$  donde  $Y^2$  es alquilo ( $C_1-C_4$ ) y  $Y^3$  es alquilo ( $C_1-C_6$ ), carboxi alquilo ( $C_1-C_6$ ), amino alquilo ( $C_1-C_4$ ) o mono—N— o di—N,N— alquil aminoalquilo ( $C_1-C_6$ ),  $-C(Y^4)Y^5$  donde  $Y^4$  es H o metilo y  $Y^5$  es mono—N— o di—N,N— alquilamino ( $C_1-C_6$ ) morfolino, piperidin—1—ilo o pirrolidin—1—ilo, y similares.

Uno o más compuestos de la invención pueden existir en forma solvatada como no solvatada con solventes aceptables desde el punto de vista farmacéutico tales como agua, etanol, y similares, y se pretende que la invención abarque tanto

las formas solvatadas como no solvatadas. "Solvato" significa una asociación física de un compuesto de esta invención con una o más moléculas de solvente. Esta asociación física incluye grados variables de enlace iónico y covalente, incluyendo unión por hidrógeno. En determinados casos, el solvato será capaz de aislarse, por ejemplo cuando una o más moléculas de solvente se incorporan en el retículo de cristal del sólido cristalino. "Solvato" abarca tanto solvatos de fase en solución o susceptibles de aislarse. Ejemplos no limitativos de solvatos apropiados incluyen etanolatos, metanolatos, y similares. "Hidrato" es un solvato en el cual la molécula de solvente es H<sub>2</sub>O.

Uno o más compuestos de la invención pueden convertirse en forma opcional en un solvato. La preparación de solvatos se conoce en sentido general. De este modo, por ejemplo, M. Caira *et al*, *J. Pharmaceutical Sci.*, 93(3), 601-611 (2004) describe la preparación de los solvatos de cluconazol antifúngico en acetato de etilo como también a partir de agua. Preparaciones similares de solvatos, semi-solvatos, hidratos y similares se describen en el texto escrito por E. C. van Tonder *et al*, *AAPS PharmSciTech.*, 5(1), article 12 (2004); y A. L. Bingham *et al*, *Chem. Commun.*, 603-604 (2001). Un proceso típico, no limitativo, implica disolución del compuesto de la invención en las cantidades deseadas del solvente deseado (orgánico o agua o sus mezclas) a una temperatura superior que la temperatura ambiente, y enfriamiento de la solución a una velocidad suficiente para formar cristales que luego se aíslan por métodos estándar. Las técnicas de análisis tales como, por ejemplo espectroscopía por I. R., muestran la presencia del solvente (o agua) en los cristales como solvato (o hidrato).

"Cantidad efectiva" o "cantidad efectiva para uso terapéutico" pretende describir una cantidad de compuesto o una composición de la presente invención efectiva para inhibir las varias enfermedades mencionadas con anterioridad y de este modo producir el efecto terapéutico, de alivio, inhibidor o preventivo deseado.

Los compuestos de fórmula I pueden formar sales que también se encuentran dentro del alcance de esta invención. La referencia a un compuesto de fórmula I aquí pretende incluir referencia a sus sales, salvo que se indique de otro modo. El término "sal(es)", como se emplea aquí, denota sales ácidas formadas con ácidos inorgánicos y/u orgánicos, como también sales alcalinas formadas con bases orgánicas y/o inorgánicas. Además, cuando un compuesto de fórmula I contiene ambos un resto alcalino, tales como, sin carácter limitativo una piridina o imidazol, y un resto ácido, tales como, sin carácter limitativo un ácido carboxílico, pueden formarse zwitteriones ("sales internas") y se incluyen dentro del término "sal(es)" como se usa aquí. Las sales aceptables desde el punto de vista farmacéutico (es decir, no tóxicas, fisiológicamente aceptables) son las que se prefieren, aunque también son útiles otras sales. Las sales de los compuestos de la Fórmula I pueden formarse, por ejemplo, haciendo reaccionar un compuesto de fórmula I con una cantidad de ácido o base, tal como una cantidad equivalente, en un medio tal como aquel en el cual la sal se precipita o en un medio acuoso seguido de liofilización.

Las sales de adición con ácido ejemplificativas incluyen acetatos, ascorbatos, benzoatos, bencensulfonatos, bisulfatos, boratos, butiratos, citratos, alcanforatos, alcanforsulfonatos, fumaratos, clorhidratos, bromhidratos, yodhidratos, lactatos, maleatos, metansulfonatos, naftalensulfonatos, nitratos, oxalatos, fosfatos, propionatos, salicilatos, succinatos, sulfatos, tartaratos, tiocianatos, toluensulfonatos (conocidos también como tosilatos,) y similares. Adicionalmente, los ácidos que se consideran generalmente apropiados para la formación de sales farmacéuticamente útiles a partir de compuestos farmacéuticos se discuten, por ejemplo, en P. Stahl *et al*, Camille G. (eds.) *Handbook of Pharmaceutical Salts. Properties, Selection and Use*. (2002) Zurich: Wiley-VCH; S. Berge *et al*, *Journal of Pharmaceutical Sciences* (1977) 66(1) 1-19;



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P. Gould, *International J. of Pharmaceutics* (1986) 33 201-217; yerson *et al*, *The Practice of Medicinal Chemistry* (1996), Academic Press, New York; y in *The Orange Book* (Food & Drug Administration, Washington, D.C. en su sitio en internet). Estas descripciones se incorporan aquí a modo de referencia.

Las sales alcalinas ejemplificativas incluyen sales de amonio, sales de metales alcalinos tales como sodio, litio y potasio, sales de metales alcalino térreos tales como sales de calcio y magnesio, sales con bases orgánicas (por ejemplo, aminas orgánicas) tales como dicitclohexilaminas, t-butil aminas, y sales con aminoácidos tales como arginina, lisina y similares. Los grupos alcalinos que contienen nitrógeno pueden cuaternizarse con agentes tales como haluros de alquilo inferior (por ej. cloruros, bromuros y yoduros de metilo, etilo, y butilo), dialquil sulfatos (por ej. dimetil, dietil, y dibutil sulfatos), haluros de cadena larga (por ej. cloruros, bromuros y yoduros de decilo, laurilo, y estearilo), haluros de aralquilo (por ej. bromuros de bencilo y fenetilo), y otros.

Todas dichas sales ácidas y sales alcalinas pretender ser sales aceptables desde el punto de vista farmacéutico dentro del alcance de la invención y todas las sales ácidas y alcalinas se consideran equivalentes a las formas libres de los correspondientes compuestos para los fines de la invención.

Los ésteres aceptables desde el punto de vista farmacéutico de los presentes compuestos incluyen los siguientes grupos: (1) ésteres de ácido carboxílico obtenidos por esterificación de los grupos hidroxilo, en los cuales el resto no carbonilo de la porción ácido carboxílico de la agrupación éster se selecciona de alquilo de cadena recta o ramificada (por ejemplo, acetilo, n-propilo, t-butilo, o n-butilo), alcoxialquilo (por ejemplo, metoximetilo), aralquilo (por ejemplo, bencilo), ariloxialquilo (por ejemplo, fenoximetilo), arilo (por ejemplo, fenilo sustituido en forma opcional con, por ejemplo, halógeno, alquilo C<sub>1-4</sub>, o alcoxi C<sub>1-4</sub> o amino); (2) ésteres de sulfonato, tales como alquil- o aralquilsulfonilo

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(por ejemplo, metansulfonilo); (3) ésteres de aminoácidos (por ejemplo, L-valilo o L-isoleucilo); (4) ésteres de fosfonato y (5) ésteres de mono-, di- o trifosfato. Los ésteres de fosfato pueden esterificarse además por, por ejemplo, un alcohol  $C_{1-20}$  o su derivado reactivo, o por un 2,3-di acilo ( $C_{6-24}$ ) glicerol.

Los compuestos de fórmula I, y sus sales, solvatos, ésteres y prodrogas, pueden existir en su forma tautomérica (por ejemplo, como amida, enol, ceto o éter de imino). Todas dichas formas tautoméricas se contemplan aquí como parte la presente invención.

Los compuestos de fórmula (I) pueden contener centros asimétricos o quirales, y, por consiguiente, existir en diferentes formas estereoisoméricas. Se pretende que todas las formas estereoisoméricas de los compuestos de fórmula (I) como también sus mezclas, incluyendo mezclas racémicas, formen parte de la presente invención. Además, la presente invención abarca todos los isómeros geométricos y de posición. Por ejemplo, si un compuesto de Fórmula (I) incorpora un enlace doble o un anillo fusionado, tanto las formas cis- como trans-, como también sus mezclas, están abarcados dentro de la invención.

Las mezclas diasteroméricas pueden separarse en sus diasterómeros individuales en base a sus diferencias físico- químicas por métodos muy conocidos para aquellas personas con experiencia en el arte, tales como, por ejemplo, por cromatografía y/o cristalización fraccional. Los enantiómeros pueden separarse por conversión de la mezcla enantiomérica en una mezcla diasteromérica por reacción con un compuesto ópticamente activo apropiado (por ej., auxiliar quiral tales como un alcohol quiral o cloruro ácido de Mosher), separando los diasterómeros y convirtiendo (por ej., hidrolizando) los diasterómeros individuales en los correspondiente enantiómeros puros. Además, algunos de los compuestos de fórmula (I) pueden ser atropisómeros (por ej.,

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biarilos sustituidos) y se consideran parte de esta invención. Los enantiómeros pueden separarse por el uso de columna de HPLC quiral.

También es posible que los compuestos de fórmula (I) puedan existir en diferentes formas tautoméricas, y todas dichas formas se abarcan dentro del alcance de la invención. Además, por ejemplo, todas las formas ceto-enólicas y de imina-enamina de los compuestos se incluyen en la invención.

Todos los estereoisómeros (por ejemplo, isómeros geométricos, isómeros ópticos y similares) de los presentes compuestos (incluyendo aquellos de las sales, los solvatos, los ésteres y las prodrogas de los compuestos como también las sales, los solvatos y los ésteres de las prodrogas), tales como aquellos que pueden existir debido a los carbonos asimétricos en varios sustituyentes, incluyendo las formas enantioméricas (que pueden existir incluso en ausencia de carbonos asimétricos), formas rotaméricas, atropisómeros, y formas diasteroméricas, se contemplan dentro del alcance de esta invención, como lo son los isómeros de posición (tales como, por ejemplo, 4-piridilo y 3-piridilo). (Por ejemplo, si un compuesto de Fórmula (I) incorpora un enlace doble o un anillo fusionado, tanto las formas cis- y trans-, como también sus mezclas, se abarcan dentro del alcance de la invención. Además, por ejemplo, todas las formas ceto-enólicas e imina-enamina de los compuestos se incluyen en la invención.) Los estereoisómeros individuales de los compuestos de la invención, por ejemplo, pueden ser sustancialmente libres de otros isómeros, o pueden mezclarse, por ejemplo, como racematos o con todos los demás estereoisómeros, u otros seleccionados. Los centros quirales de la presente invención pueden tener la configuración S o R según lo definen las Recomendaciones de IUPAC de 1974. El uso de los términos "sal", "solvato", "éster", "prodroga" y similares, pretende igualmente aplicarse a la sal, el solvato, el éster y la prodroga de enantiómeros,

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estereoisómeros, rotámeros, tautómeros, isómeros de posición, racematos o prodrogas de los compuestos de la invención.

La presente invención también abarca compuestos isotópicamente rotulados de la presente invención que son idénticos a los que se menciona aquí, aunque por el hecho de que uno o más átomos están reemplazados por n átomo que tiene una masa atómica o número de masa diferente de la masa atómica o número de masa que usualmente se encuentra en la naturaleza. Algunos ejemplos de isótopos que pueden incorporarse en los compuestos de la invención incluyen isótopos de hidrógeno, carbono, nitrógeno, oxígeno, fósforo, flúor y cloro, tales como  $^2\text{H}$ ,  $^3\text{H}$ ,  $^{13}\text{C}$ ,  $^{14}\text{C}$ ,  $^{15}\text{N}$ ,  $^{18}\text{O}$ ,  $^{17}\text{O}$ ,  $^{31}\text{P}$ ,  $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^{18}\text{F}$ , y  $^{36}\text{Cl}$ , respectivamente.

Ciertos compuestos isotópicamente rotulados de fórmula (I) (por ej., aquellos rotulados con  $^3\text{H}$  y  $^{14}\text{C}$ ) son útiles en los ensayos de distribución en tejidos de compuesto y/o sustrato. Los isótopos titulados (es decir,  $^3\text{H}$ ) y carbono-14 (es decir,  $^{14}\text{C}$ ) se prefieren particularmente por su facilidad de preparación y posibilidad de detección. Además, la sustitución con isótopos más pesados como deuterio (es decir,  $^2\text{H}$ ) pueden producir ciertas ventajas terapéuticas como resultado de una mayor estabilidad metabólica (por ej., aumento de los requerimientos de vida media in vivo o reducción de la dosis) y por consiguiente pueden resultar preferibles en ciertas circunstancias. Los compuestos isotópicamente rotulados de fórmula (I) pueden prepararse generalmente siguiendo procedimientos análogos a los que se revelan en los Esquemas y/o en los Ejemplos que siguen a continuación, sustituyendo un reactivo apropiado isotópicamente rotulado en lugar de un reactivo no rotulado en forma isotópica.

Las formas polimórficas de los compuestos de fórmula I, y de las sales, solvatos, ésteres y prodrogas de los compuestos de fórmula I, pretenden estar incluidos en la presente invención.

Los compuestos de acuerdo con la invención pueden tener propiedades farmacológicas; en particular, los compuestos de fórmula I pueden ser moduladores de la gamma secretasa (incluyendo inhibidores, antagonistas y similares).

Más específicamente, los compuestos de fórmula I pueden ser útiles en el tratamiento de una variedad de trastornos del sistema nervioso central incluyendo, por ejemplo, incluyendo, sin carácter limitativo, enfermedad de Alzheimer, demencia relacionada con el SIDA, enfermedad de Parkinson, esclerosis amiotrófica lateral, retinitis pigmentosa, atrofia muscular espinal y degeneración cerebelar y similares.

Otro aspecto de esta invención es un método de tratamiento de un mamífero (*por ej.*, humano) que tiene una enfermedad o afección del sistema nervioso central mediante la administración de una cantidad efectiva para uso terapéutico de por lo menos un compuesto de fórmula I, o una sal, un solvato, un éster o una prodroga aceptables desde el punto de vista farmacéutico de dicho compuesto a los mamíferos.

Una dosis preferida es de aproximadamente 0,001 a 500 mg/kg de peso corporal/día del compuesto de fórmula I. Una dosificación especialmente preferida es de aproximadamente 0,01 a 25 mg/kg de peso corporal/día de un compuesto de fórmula I, o una sal o un solvato aceptables desde el punto de vista farmacéutico de dicho compuesto.

Los compuestos de esta invención también pueden ser útiles en combinación (administrados juntos o en forma consecutiva) con uno o más agentes adicionales enumerados con anterioridad.

Los compuestos de esta invención también pueden ser útiles en combinación (administrados juntos o en forma consecutiva) con uno o más



compuestos de fórmula I, y cantidad efectiva de uno o más inhibidores de colinesterasa (por ej., acetilo- y/o butirilcolinesterasa inhibidores), y un vehículo aceptable desde el punto de vista farmacéutico.

Los compuestos de fórmula I pueden ser útiles como moduladores de la gamma secretasa y pueden ser útiles en el tratamiento y prevención de varias enfermedades tales como, por ejemplo, trastornos del sistema nervioso central tales como la enfermedad de Alzheimer y Síndrome de Down.

De este modo, otra realización de esta invención se refiere a un método para modular (incluyendo inhibir, antagonizar y similares) gamma-secretasa que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de dicho tratamiento.

Otra realización de esta invención se refiere a un método para modular (incluyendo inhibir, antagonizar y similares) gamma-secretasa, que comprende administrar una cantidad efectiva de un compuesto de fórmula I a un paciente que necesita de tratamiento.

Otra realización de esta invención se refiere a un método de tratamiento de una o más de varias enfermedades neurodegenerativas, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Otra realización de esta invención se refiere a un método de tratamiento de una o más de varias enfermedades neurodegenerativas, que comprende administrar una cantidad efectiva de un compuesto de fórmula I a un paciente que necesita de tratamiento.

Otra realización de esta invención se refiere a un método de inhibición de la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico (por ej., el cerebro), que comprende administrar

una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Otra realización de esta invención se refiere a un método de inhibición de la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico (por ej., el cerebro), que comprende administrar una cantidad efectiva de un compuesto de fórmula I a un paciente que necesita de tratamiento.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de un compuesto de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, terapias de combinación para (1) modular la gamma-secretasa, o (2) tratar una o más de varias enfermedades neurodegenerativas, o (3) inhibir la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico (por ej., el cerebro), o (4) tratar la enfermedad de Alzheimer. Las terapias de combinación se refieren a métodos que comprenden la administración de una cantidad efectiva de uno o más (por ej. uno) compuestos de fórmula I y la administración de una cantidad efectiva de uno o más (por ej., uno) principios activos farmacéuticos distintos (por ej., drogas). Los compuestos de fórmula I y las otras drogas pueden administrarse en forma separada (es decir, cada una en su propia forma de dosificación propia), o los compuestos de fórmula I pueden combinarse con las otras drogas en la misma forma de dosificación.



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De este modo, otras realizaciones de esta invención se refieren a cualquiera de los métodos de tratamiento, o métodos de inhibición, como se describe aquí, en los cuales una cantidad efectiva de el compuesto de fórmula I se usa en combinación con una cantidad efectiva de uno o más principios farmacéuticamente activos distintos seleccionados del grupo que consiste en: inhibidores de BACE (beta secretasa inhibidores), antagonistas muscarínicos (por ej., agonistas de  $m_1$  o antagonistas de  $m_2$ ), inhibidores de colinesterasa (por ej., inhibidores de acetil- y/o butirilcolinesterasa); inhibidores de la gamma secretasa; moduladores de la gamma secretasa; inhibidores de la HMG-CoA reductasa; agentes anti-inflamatorios no esteroideos; antagonistas del receptor de N-metil-D-aspartato; anticuerpos anti-amiloides; vitamina E; agonistas del receptor nicotínico de acetilcolina; agonistas inversos del receptor de CB1 o antagonistas del receptor de CB1; un antibiótico, secretagogos de la hormona del crecimiento; antagonistas de histamina H3; agonistas de AMPA; inhibidores de PDE4; agonistas inversos de GABA<sub>A</sub>; inhibidores de agregación amiloide; inhibidores de glucógeno sintasa quinasa beta; promotores de la actividad de alfa secretasa; inhibidores de PDE-10 e inhibidores de la absorción del colesterol (por ej., ezetimibe).

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I, en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más inhibidores de colinesterasa (tales como, por ejemplo, (±)—2,3—dihidro—5,6—dimetoxi—2—[[1—(fenilmetil)—4—piperidinil]metil]—1H—inden—1—ona, clorhidrato, es decir, clorhidrato de donepezilo, provisto al mercado como la marca Aricept® de clorhidrato de donepezilo), a un paciente que necesita de tratamiento.

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Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de un compuesto de fórmula I, en combinación con una cantidad efectiva de uno o más (por ej., uno) inhibidores de colinesterasa (tales como, por ejemplo, (±)—2,3—dihidro—5,6—dimetoxi—2—[[1—(fenilmetil)—4—piperidinil]metil]—1H—inden—1—ona, clorhidrato, es decir, clorhidrato de donepezilo, provisto al mercado como la marca Aricept® de clorhidrato de donepezilo), a un paciente que necesita de tratamiento.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más compuestos seleccionados del grupo que consiste en inhibidores del anticuerpo A $\beta$ , inhibidores de la gamma secretasa e inhibidores de la beta secretasa.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más inhibidores de BACE.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de Exelon (rivastigmina).

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de Cognex (tacrina).

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de un inhibidor de quinasas Tau.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más inhibidores de quinasas Tau (por ej., inhibidor de GSK3 $\beta$ , inhibidor de cdk5, inhibidor de ERK).

Esta invención provee, además, un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de una vacunación anti-Abeta (inmunización activa).

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más ligandos de APP.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más agentes que regulan en sentido ascendente la enzima degradante de insulina y/o neprilisina.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más agentes reductores del colesterol (por ejemplo, estatinas tales como Atorvastatina, Fluvastatina, Lovastatina, Mevastatina, Pitavastatina, Pravastatina,

Rosuvastatina, Simvastatina, e inhibidores de absorción del colesterol tales como Ezetimibe).

Esta invención provee, además, un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más fibratos (por ejemplo, clofibrato, Clofibride, Etofibrate, Clofibrato de aluminio).

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más agonistas de LXR.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más imitadores de LRP.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más antagonistas del receptor 5-HT<sub>6</sub>.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más agonistas del receptor nicotínico.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más antagonistas del receptor H<sub>3</sub>.

Esta invención provee, además, un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más inhibidores de histona desacetilasa.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más inhibidores de hsp90.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más agonistas del receptor muscarínico m1.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más moduladores o agonistas alostéricos positivos de antagonistas del receptor 5-HT6 mGluR1 o mGluR5.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más antagonistas de mGluR2/3.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más agentes anti-inflamatorios que pueden reducir la neuroinflamación.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de

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uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más antagonistas del receptor de Prostaglandina EP2.

Esta invención provee, además, un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más inhibidores de PAI-1.

Esta invención provee, además, un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más agentes que pueden inducir el eflujo Abeta tales como gelsolin.

Esta invención provee, además, un método de tratamiento del síndrome de Down, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento del síndrome de Down, que comprende administrar una cantidad efectiva de un compuesto de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento del síndrome de Down, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más inhibidores de colinesterasa (tales como, por ejemplo,  $(\pm)$ -2,3-dihidro-5,6-dimetoxi-2-[[1-(fenilmetil)-4-piperidinil]metil]-1H-inden-1-ona, clorhidrato, es decir, clorhidrato de donepezilo, provisto al mercado como la marca Aricept® de clorhidrato de donepezilo), a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento del síndrome de Down, que comprende administrar una cantidad efectiva de un compuesto de fórmula I, en combinación con una cantidad efectiva de uno o más (por ej., uno) inhibidores de colinesterasa (tales como, por ejemplo,  $(\pm)$ -2,3-dihidro-5,6-

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dimetoxi—2—[[1—(fenilmetil)—4—piperidinil]metil]—1H—inden—1—ona, clorhidrato, es decir, clorhidrato de donepezilo, provisto al mercado como la marca Aricept® de clorhidrato de donepezilo), a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de la insuficiencia cognitiva leve, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento del glaucoma, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de la angiopatía amiloide cerebral, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento del infarto, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de demencia, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de microgliosis, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, un método de tratamiento de la inflamación cerebral, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

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Esta invención provee, además, un método de tratamiento la pérdida de la función olfativa, que comprende administrar una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I a un paciente que necesita de tratamiento.

Esta invención provee, además, combinaciones (es decir, composiciones farmacéuticas) que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más compuestos seleccionados del grupo que consiste en inhibidores de colinesterasa (tales como, por ejemplo,  $(\pm)$ -2,3-dihidro-5,6-dimetoxi-2-[[1-(fenilmetil)-4-piperidinil]metil]-1H-inden-1-ona, clorhidrato, es decir, clorhidrato de donepezilo, provisto al mercado como la marca Aricept® de clorhidrato de donepezilo), inhibidores del anticuerpo A $\beta$ , inhibidores de la gamma secretasa e inhibidores de la beta secretasa. Las composiciones farmacéuticas comprenden, además, un vehículo aceptable desde el punto de vista farmacéutico.

Esta invención provee, además, un kit que comprende, en envases separados, en un envase individual, composiciones farmacéuticas para usar en forma combinada, en el cual un envase comprende una cantidad efectiva de un compuesto de fórmula I en un vehículo aceptable desde el punto de vista farmacéutico, y otro envase (es decir, un segundo envase) comprende una cantidad efectiva de otro principio farmacéuticamente activo (como se describió con anterioridad), las cantidades combinadas del compuesto de fórmula I y otro principio farmacéuticamente activo efectivo para: (a) tratar la enfermedad de Alzheimer, o (b) inhibir la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico (por ej., el cerebro), o (c) tratar varias enfermedades neurodegenerativas, o (d) modular la actividad de gamma-secretasa.

Otra realización de esta invención se refiere a una sal aceptable desde el punto de vista farmacéutico de un compuesto de Fórmula (I), dicho compuesto de



Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un éster aceptable desde el punto de vista farmacéutico de un compuesto de Fórmula (I), dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un solvato de un compuesto de Fórmula (I), dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un compuesto de Fórmula (I) en forma aislada, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un compuesto de Fórmula (I) en forma pura, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un compuesto de Fórmula (I) en forma pura y aislada, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

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Otra realización se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula (I) y un vehículo aceptable desde el punto de vista farmacéutico, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización se refiere a una composición farmacéutica que comprende una cantidad efectiva de una sal aceptable desde el punto de vista farmacéutico of uno o más (por ej., uno) compuestos de fórmula (I) y un vehículo aceptable desde el punto de vista farmacéutico, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización se refiere a una composición farmacéutica que comprende una cantidad efectiva de un éster aceptable desde el punto de vista farmacéutico of uno o más (por ej., uno) compuestos de fórmula (I) y un vehículo aceptable desde el punto de vista farmacéutico, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización se refiere a una composición farmacéutica que comprende una cantidad efectiva de un solvato of uno o más (por ej., uno) compuestos de fórmula (I) y un vehículo aceptable desde el punto de vista farmacéutico, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-

B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula (I), y una cantidad efectiva de uno o más (por ej., uno) principios farmacéuticamente activos distintos (por ej., drogas), y un vehículo aceptable desde el punto de vista farmacéutico. Ejemplos de los principios farmacéuticamente activos distintos incluyen, sin carácter limitativo drogas seleccionadas del grupo que consiste en: (a) drogas útiles para el tratamiento de la enfermedad de Alzheimer, (b) drogas útiles para inhibir la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico (por ej., el cerebro), (c) drogas útiles para tratar varias enfermedades neurodegenerativas, y (d) drogas útiles para inhibir la gamma-secretasa, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula (I), y cantidad efectiva de uno o más inhibidores de BACE, y un vehículo aceptable desde el punto de vista farmacéutico, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno)

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compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y una cantidad efectiva de uno o más inhibidores de colinesterasa (por ej., inhibidores de acetil- y/o butirilcolinesterasa), y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más antagonistas muscarínicos (por ej., agonistas de  $m_1$  o antagonistas de  $m_2$ ), y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de Exelon (rivastigmina), y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de Cognex (tacrina), y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10,

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D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de un inhibidor de quinasa Tau, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más inhibidor de quinasa Tau (por ej., inhibidor de GSK3beta, inhibidor de cdk5, inhibidor de ERK), y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de una vacuna anti-Abeta (inmunización activa), y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más ligandos de APP, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más agentes que regulan en



sentido ascendente la enzima degradante de insulina y/o neprilisina, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más agentes reductores del colesterol (por ejemplo, estatinas tales como Atorvastatina, Fluvastatina, Lovastatina, Mevastatina, Pitavastatina, Pravastatina, Rosuvastatina, Simvastatina, e inhibidores de absorción del colesterol tales como Ezetimibe), y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más fibratos (por ejemplo, clofibrato, Clofibrade, Etofibrate, Clofibrato de aluminio), y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más agonistas de LXR, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10,

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D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más imitadores de LRP, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más antagonistas del receptor 5-HT6, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más agonistas del receptor nicotínico, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más antagonistas del receptor H3, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más inhibidores de histona desacetilasa, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más inhibidores de hsp90, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más agonistas del receptor muscarínico m1, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más moduladores o agonistas alostéricos positivos de antagonistas del receptor 5-HT6 mGluR1 o mGluR5, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más antagonistas de mGluR2/3, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno)



compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más agentes anti-inflamatorios que pueden reducir la neuroinflamación, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más antagonistas del receptor de Prostaglandina EP2, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más inhibidores de PAI-1, y un vehículo aceptable desde el punto de vista farmacéutico.

Otra realización de esta invención se refiere a una composición farmacéutica que comprende una cantidad efectiva de uno o más (por ej., uno) compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y cantidad efectiva de uno o más agentes que pueden inducir el flujo Abeta tales como gelsolin, y un vehículo aceptable desde el punto de vista farmacéutico.

Los compuestos de fórmula I seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-

K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1 pueden ser útiles como moduladores de la gamma secretasa y pueden ser útiles en el tratamiento y prevención de varias enfermedades tales como, por ejemplo, trastornos del sistema nervioso central (tales como enfermedad de Alzheimer y Síndrome de Down), y tratar la insuficiencia cognitiva leve, glaucoma, angiopatía amiloide cerebral, infarto, demencia, microgliosis, inflamación cerebral, y pérdida de la función olfativa.

De este modo, otra realización de esta invención se refiere a un método para modular (incluyendo inhibir, antagonizar y similares) gamma-secretasa que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) compuestos de fórmula (I) a un paciente que necesita de dicho tratamiento, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un método para modular (incluyendo inhibir, antagonizar y similares) gamma-secretasa, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de Fórmula (I) a un paciente que necesita de tratamiento, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un método de tratamiento de una o más de varias enfermedades neurodegenerativas, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) compuestos de fórmula (I) a un paciente que necesita de tratamiento, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un método de tratamiento de una o más de varias enfermedades neurodegenerativas, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de Fórmula (I) a un paciente que necesita de tratamiento, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un método de inhibición de la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico (por ej., el cerebro), que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) compuestos de fórmula (I) a un paciente que necesita de tratamiento, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un método de inhibición de la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico (por ej., el cerebro), que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de Fórmula (I) a un paciente que necesita de tratamiento, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) compuestos de fórmula (I) a un paciente que necesita de tratamiento, dicho compuesto de

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Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de Fórmula (I) a un paciente que necesita de tratamiento, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un método de tratamiento de la insuficiencia cognitiva leve, glaucoma, angiopatía amiloide cerebral, infarto, demencia, microgliosis, inflamación cerebral, o pérdida de la función olfativa, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) compuestos de fórmula (I) a un paciente que necesita de tratamiento, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Otra realización de esta invención se refiere a un método de tratamiento de la insuficiencia cognitiva leve, glaucoma, angiopatía amiloide cerebral, infarto, demencia, microgliosis, inflamación cerebral, o pérdida de la función olfativa, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de Fórmula (I) a un paciente que necesita de tratamiento, dicho compuesto de Fórmula (I) se selecciona del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

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Esta invención provee, además, terapias de combinación para (1) modular la gamma-secretasa, o (2) tratar una o más de varias enfermedades neurodegenerativas, o (3) inhibir la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico (por ej., el cerebro), o (4) tratar la enfermedad de Alzheimer. Las terapias de combinación se refieren a métodos que comprenden la administración de uno o más (por ej. uno) compuestos de fórmula (I), y la administración de uno o más (por ej., uno) principios activos farmacéuticos distintos (por ej., drogas). Los compuestos de fórmula (I), y las otras drogas pueden administrarse en forma separada (es decir, cada una en su propia forma de dosificación propia), o los compuestos de fórmula (I) pueden combinarse con las otras drogas en la misma forma de dosificación.

De este modo, otras realizaciones de esta invención se refieren a cualquiera de los métodos de tratamiento, o métodos de inhibición, como se describe aquí, en los cuales los compuestos de fórmula (I) se usan en combinación con una cantidad efectiva de uno o más principios farmacéuticamente activos distintos seleccionados del grupo que consiste en: inhibidores de BACE (beta secretasa inhibidores); antagonistas muscarínicos (por ej., agonistas de  $m_1$  o antagonistas de  $m_2$ ); inhibidores de colinesterasa (por ej., inhibidores de acetil- y/o butirilcolinesterasa); inhibidores de la gamma secretasa; moduladores de la gamma secretasa; inhibidores de la HMG-CoA reductasa; agentes anti-inflamatorios no esteroideos; antagonistas del receptor de N-metil-D-aspartato; anticuerpos anti-amiloides; vitamina E; agonistas del receptor nicotínico de acetilcolina; agonistas inversos del receptor de CB1 o antagonistas del receptor de CB1; un antibiótico, secretagogos de la hormona del crecimiento; antagonistas de histamina H3; agonistas de AMPA; inhibidores de PDE4; agonistas inversos de GABA<sub>A</sub>; inhibidores de agregación amiloide; inhibidores de glucógeno sintasa quinasa beta; promotores de la actividad de alfa secretasa;

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PDE-10 inhibidores; Exelon (rivastigmina); Cognex (tacrina); inhibidores de quinasa Tau (por ej., inhibidores de GSK3beta, inhibidores de cdk5, o inhibidores de ERK); vacuna anti-Abeta; ligandos de APP; agentes que regulan en sentido ascendente la insulina, agentes reductores del colesterol (por ejemplo, estatinas tales como Atorvastatina, Fluvastatina, Lovastatina, Mevastatina, Pitavastatina, Pravastatina, Rosuvastatina, Simvastatin); inhibidores de la absorción del colesterol (tales como Ezetimibe); fibratos (tales como, por ejemplo, por ejemplo, clofibrato, Clofibrade, Etofibrate, y Clofibrato de aluminio); agonistas de LXR; imitadores de LRP; agonistas del receptor nicotínico; antagonistas del receptor H3; inhibidores de histona desacetilasa; inhibidores de hsp90; agonistas del receptor muscarínico m1; antagonistas del receptor 5-HT6; mGluR1; mGluR5; moduladores o agonistas alostéricos positivos; antagonistas de mGluR2/3; agentes anti-inflamatorios que pueden reducir la neuroinflamación; antagonistas del receptor de Prostaglandina EP2; inhibidores de PAI-1; y agentes que pueden inducir el eflujo Abeta tales como gelsolin.

Esta invención provee, además, terapias de combinación para (1) modular la gamma-secretasa, o (2) tratar una o más de varias enfermedades neurodegenerativas, o (3) inhibir la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico (por ej., el cerebro), o (4) tratar la enfermedad de Alzheimer. Las terapias de combinación se refieren a métodos que comprenden la administración de uno o más (por ej. uno) compuestos de fórmula (I) seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y la administración de uno o más (por ej., uno) principios activos farmacéuticos distintos (por ej., drogas). Los compuestos de fórmula 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, y las otras drogas

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pueden administrarse en forma separada (es decir, cada una en su propia forma de dosificación propia), o los compuestos de fórmula 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1 pueden combinarse con las otras drogas en la misma forma de dosificación.

De este modo, otras realizaciones de esta invención se refieren a cualquiera de los métodos de tratamiento, o métodos de inhibición, como se describe aquí, en los cuales los compuestos de fórmula (I), seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1 se usan en combinación con una cantidad efectiva de uno o más principios farmacéuticamente activos distintos seleccionados del grupo que consiste en: inhibidores de BACE (beta secretasa inhibidores), antagonistas muscarínicos (por ej., agonistas de  $m_1$  o antagonistas de  $m_2$ ), inhibidores de colinesterasa (por ej., inhibidores de acetil- y/o butirilcolinesterasa); inhibidores de la gamma secretasa; moduladores de la gamma secretasa; inhibidores de la HMG-CoA reductasa; agentes anti-inflamatorios no esteroideos; antagonistas del receptor de N-metil-D-aspartato; anticuerpos anti-amiloides; vitamina E; agonistas del receptor nicotínico de acetilcolina; agonistas inversos del receptor de CB1 o antagonistas del receptor de CB1; un antibiótico, secretagogos de la hormona del crecimiento; antagonistas de histamina H3; agonistas de AMPA; inhibidores de PDE4; agonistas inversos de GABA<sub>A</sub>; inhibidores de agregación amiloide; inhibidores de glucógeno sintasa quinasa beta; promotores de la actividad de alfa secretasa; PDE-10 inhibidores; Exelon (rivastigmina); Cognex (tacrina); inhibidores de quinasa Tau (por ej., inhibidores de GSK3beta, inhibidores de cdk5, o inhibidores de ERK); vacuna anti-Abeta; ligandos de APP; agentes que regulan en sentido ascendente la insulina, agentes reductores del colesterol (por ejemplo, estatinas

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tales como Atorvastatina, Fluvastatina, Lovastatina, Mevastatina, Pitavastatina, Pravastatina, Rosuvastatina, Simvastatin); inhibidores de la absorción del colesterol (tales como Ezetimibe); fibratos (tales como, por ejemplo, por ejemplo, clofibrato, Clofibrade, Etofibrate, y Clofibrato de aluminio); agonistas de LXR; imitadores de LRP; agonistas del receptor nicotínico; antagonistas del receptor H3; inhibidores de histona desacetilasa; inhibidores de hsp90; agonistas del receptor muscarínico m1; antagonistas del receptor 5-HT6; mGluR1; mGluR5; moduladores o agonistas alostéricos positivos; antagonistas de mGluR2/3; agentes anti-inflamatorios que pueden reducir la neuroinflamación; antagonistas del receptor de Prostaglandina EP2; inhibidores de PAI-1; y agentes que pueden inducir el eflujo Abeta tales como gelsolin.

Otras realizaciones de esta invención se refieren a cualquiera de los métodos de tratamiento, o métodos de inhibición, como se describe aquí, en los cuales los compuestos de fórmula (I), seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1 se usan en combinación con una cantidad efectiva de uno o más principios farmacéuticamente activos distintos seleccionados del grupo que consiste en: inhibidores de BACE (beta secretasa inhibidores), antagonistas muscarínicos (por ej., agonistas de m<sub>1</sub> o antagonistas de m<sub>2</sub>), inhibidores de colinesterasa (por ej., inhibidores de acetil- y/o butirilcolinesterasa); inhibidores de la gamma secretasa; moduladores de la gamma secretasa; inhibidores de la HMG-CoA reductasa; agentes anti-inflamatorios no esteroides; antagonistas del receptor de N-metil-D-aspartato; anticuerpos anti-amiloides; vitamina E; agonistas del receptor nicotínico de acetilcolina; agonistas inversos del receptor de CB1 o antagonistas del receptor de CB1; un antibiótico, secretagogos de la hormona del crecimiento; antagonistas de histamina H3; agonistas de AMPA; inhibidores de PDE4; agonistas inversos de



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GABA<sub>A</sub>; inhibidores de agregación amiloide; inhibidores de glucógeno sintasa quinasa beta; promotores de la actividad de alfa secretasa; PDE-10 inhibidores; y inhibidores de la absorción del colesterol (por ej., ezetimibe).

Otras realizaciones de esta invención se refieren a cualquiera de los métodos de tratamiento, o métodos de inhibición, como se describe aquí, en los cuales los compuestos de fórmula (I), seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1 se usan en combinación con una cantidad efectiva de uno o más principios farmacéuticamente activos distintos seleccionados del grupo que consiste en: Exelon (rivastigmina); Cognex (tacrina); inhibidores de quinasa Tau (por ej., inhibidores de GSK3beta, inhibidores de cdk5, o inhibidores de ERK); vacuna anti-Abeta; ligandos de APP; agentes que regulan en sentido ascendente la insulina, agentes reductores del colesterol (por ejemplo, estatinas tales como Atorvastatina, Fluvastatina, Lovastatina, Mevastatina, Pitavastatina, Pravastatina, Rosuvastatina, Simvastatin); inhibidores de la absorción del colesterol (tales como Ezetimibe); fibratos (tales como, por ejemplo, por ejemplo, clofibrato, Clofibrade, Etofibrate, y Clofibrato de aluminio); agonistas de LXR; imitadores de LRP; agonistas del receptor nicotínico; antagonistas del receptor H3; inhibidores de histona desacetilasa; inhibidores de hsp90; agonistas del receptor muscarínico m1; antagonistas del receptor 5-HT6; mGluR1; mGluR5; moduladores o agonistas alostéricos positivos; antagonistas de mGluR2/3; agentes anti-inflamatorios que pueden reducir la neuroinflamación; antagonistas del receptor de Prostaglandina EP2; inhibidores de PAI-1; y agentes que pueden inducir el eflujo Abeta tales como gelsolin.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) compuestos de

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fórmula (I) seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más inhibidores de colinesterasa (tales como, por ejemplo,  $(\pm)$ -2,3-dihidro-5,6-dimetoxi-2-[[1-(fenilmetil)-4-piperidinil]metil]-1H-inden-1-ona, clorhidrato, es decir, clorhidrato de donepezilo, provisto al mercado como la marca Aricept® de clorhidrato de donepezilo), a un paciente que necesita de tratamiento.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de Fórmula (I) seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) inhibidores de colinesterasa (tales como, por ejemplo,  $(\pm)$ -2,3-dihidro-5,6-dimetoxi-2-[[1-(fenilmetil)-4-piperidinil]metil]-1H-inden-1-ona, clorhidrato, es decir, clorhidrato de donepezilo, provisto al mercado como la marca Aricept® de clorhidrato de donepezilo), a un paciente que necesita de tratamiento.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) compuestos de fórmula (I) seleccionados del grupo que consiste en: en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más compuestos seleccionados del grupo que consiste en inhibidores del anticuerpo A $\beta$ , inhibidores de la gamma secretasa e inhibidores de la beta secretasa.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) compuestos de fórmula (I) seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más inhibidores de BACE.

Otra realización de esta invención se refiere a un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de Fórmula (I) seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más inhibidores de BACE.

Otra realización de esta invención se refiere a un método de tratamiento del síndrome de Down, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) compuestos de fórmula (I) seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1 a un paciente que necesita de tratamiento.

Otra realización de esta invención se refiere a un método de tratamiento del síndrome de Down, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de Fórmula (I) seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, a un paciente que necesita de tratamiento.

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Otra realización de esta invención se refiere a un método de tratamiento del síndrome de Down, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) compuestos de fórmula (I) seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más inhibidores de colinesterasa (tales como, por ejemplo,  $(\pm)$ -2,3-dihidro-5,6-dimetoxi-2-[[1-(fenilmetil)-4-piperidinil]metil]-1H-inden-1-ona, clorhidrato, es decir, clorhidrato de donepezilo, provisto al mercado como la marca Aricept® de clorhidrato de donepezilo), a un paciente que necesita de tratamiento.

Otra realización de esta invención se refiere a un método de tratamiento del síndrome de Down, que comprende administrar una cantidad efectiva (es decir, terapéuticamente efectiva) de un compuesto de Fórmula (I) seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1, en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) inhibidores de colinesterasa (tales como, por ejemplo,  $(\pm)$ -2,3-dihidro-5,6-dimetoxi-2-[[1-(fenilmetil)-4-piperidinil]metil]-1H-inden-1-ona, clorhidrato, es decir, clorhidrato de donepezilo, provisto al mercado como la marca Aricept® de clorhidrato de donepezilo), a un paciente que necesita de tratamiento.

Otra realización de esta invención se refiere a combinaciones (es decir, composiciones farmacéuticas) que comprende una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más (por ej., uno) compuestos de fórmula (I) seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1,

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y P8\_1 en combinación con una cantidad efectiva (es decir, terapéuticamente efectiva) de uno o más compuestos seleccionados del grupo que consiste en inhibidores de colinesterasa (tales como, por ejemplo,  $(\pm)$ -2,3-dihidro-5,6-dimetoxi-2-[[1-(fenilmetil)-4-piperidinil]metil]-1H-inden-1-ona, clorhidrato, es decir, clorhidrato de donepezilo, provisto al mercado como la marca Aricept® de clorhidrato de donepezilo), inhibidores del anticuerpo A $\beta$ , inhibidores de la gamma secretasa e inhibidores de la beta secretasa. Las composiciones farmacéuticas comprenden, además, un vehículo aceptable desde el punto de vista farmacéutico.

Esta invención provee, además, un kit que comprende, en envases separados, en un envase individual, composiciones farmacéuticas para usar en forma combinada, en el cual un envase comprende una cantidad efectiva de uno o más (por ej., uno) compuestos de fórmula (I) (por ej., compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1 en un vehículo aceptable desde el punto de vista farmacéutico, y otro envase (es decir, un segundo envase) comprende una cantidad efectiva de otro principio farmacéuticamente activo (como se describió con anterioridad), las cantidades combinadas de los compuestos de fórmula (I) y otro principio farmacéuticamente activo efectivo para: (a) tratar la enfermedad de Alzheimer, o (b) inhibir la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico (por ej., el cerebro), o (c) tratar varias enfermedades neurodegenerativas, o (d) modular la actividad de gamma-secretasa.

Esta invención provee, además, un kit que comprende, en envases separados, en un envase individual, composiciones farmacéuticas para usar en forma combinada, en el cual un envase comprende una cantidad efectiva de un compuesto seleccionados del grupo que consiste en los compuestos de fórmulas



(I) (por ej. los compuestos seleccionados del grupo que consiste en: 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1) en un vehículo aceptable desde el punto de vista farmacéutico, y otro envase (es decir, un segundo envase) comprende una cantidad efectiva de otro principio farmacéuticamente activo (como se describió con anterioridad), las cantidades combinadas del compuesto de formulas (I) y otro principio farmacéuticamente activo efectivo para: (a) tratar la enfermedad de Alzheimer, o (b) inhibir la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico (por ej., el cerebro), o (c) tratar varias enfermedades neurodegenerativas, o (d) modular la actividad de gamma-secretasa.

Otras realizaciones de esta invención se refieren a cualquiera de los métodos de tratamiento, composiciones farmacéuticas, o kits en los cuales el compuesto de fórmula I es cualquiera de los compuestos 1 a 24, B10-B21, C5-C10, D9-D26, G4-G9, H3-H11, I5, I6, I6A, I7, I8, I8A, J4-J9, K1-K6, L4-L8, M5-M15, N6-N23, O4\_1, y P8\_1.

Algunos ejemplos de inhibidores de colinesterasa son tacrina, donepezilo, rivastigmina, galantamina, piridostigmina y neostigmina, prefiriéndose la tacrina, donepezilo, rivastigmina y galantamina.

Algunos ejemplos de agonistas de  $m_1$  agonists se conocen en el arte. Algunos ejemplos de antagonistas de  $m_2$  también se conocen en el arte; en particular, los antagonistas de  $m_2$  se describen en las patentes de EE UU 5.883.096; 6.037.352; 5.889.006; 6.043.255; 5.952.349; 5.935.958; 6.066.636; 5.977.138; 6.294.554; 6.043.255; y 6.458.812; y en la WO 03/031412, todas las cuales se incorporan aquí a modo de referencia.

Algunos ejemplos de inhibidores de BACE incluyen aquellos descritos en: US2005/0119227 publicada el 02/06/2005 (ver, además, la WO2005/016876

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publicada el 24/02/2005), US2005/0043290 publicada el 24/02/2005 (ver, además, la WO2005/014540 publicada el 17/02/2005), WO2005/058311 publicada el 30/06/2005 (ver, además, US2007/0072852 publicada el 29/03/2007), US2006/0111370 publicada el 25/05/2006 (ver, además, la WO2006/065277 publicada el 22/06/2006), Solicitud de EE UU con Número de Serie 11/710582 presentada el 23/02/2007, US2006/0040994 publicada el 23/02/2006 (ver, además, la WO2006/014762 publicada el 09/02/2006), WO2006/014944 publicada el 09/02/2006 (ver, además, US2006/0040948 publicada el 23/02/2006), WO2006/138266 publicada el 28/12/2006 (ver, además, US2007/0010667 publicada el 11/01/2007), WO2006/138265 publicada el 28/12/2006, WO2006/138230 publicada el 28/12/2006, WO2006/138195 publicada el 28/12/2006 (ver, además, US2006/0281729 publicada el 14/12/2006), WO2006/138264 publicada el 28/12/2006 (ver, además, US2007/0060575 publicada el 15/03/2007), WO2006/138192 publicada el 28/12/2006 (ver, además, US2006/0281730 publicada el 14/12/2006), WO2006/138217 publicada el 28/12/2006 (ver, además, US2006/0287294 publicada el 21/12/2006), US2007/0099898 publicada el 03/05/200 (ver, además, la WO2007/050721 publicada el 03/05/2007), WO2007/053506 publicada el 10/05/2007 (ver, además, US2007/099875 publicada el 03/05/2007), Solicitud de EE UU con Número de Serie 11/759336 presentada el 07/06/2007, Solicitud de EE UU con Número de Serie 60/874362 presentada el 12/12/2006, y Solicitud de EE UU con Número de Serie 60/874419 presentada el 12/12/2006, cuyas menciones se incorporan aquí a modo de referencia a las mismas.

Para preparar las composiciones farmacéuticas a partir de los compuestos descritos por esta invención, los vehículos inertes, aceptables desde el punto de vista farmacéutico pueden ser tanto sólidos como líquidos. Las preparaciones en forma sólida incluyen polvos, comprimidos, gránulos dispersables, cápsulas,

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cachés y supositorios. Los polvos y los comprimidos pueden estar formados por desde aproximadamente 5 hasta aproximadamente 95 por ciento de principio activo. Los vehículos sólidos apropiados se conocen en el arte, por ej., carbonato de magnesio, estearato de magnesio, talco, azúcar o lactosa. Los comprimidos, polvos, cachés y cápsulas pueden usarse como formas de dosificación sólidas apropiadas para administración oral. Algunos ejemplos de vehículos aceptables desde el punto de vista farmacéutico y métodos de fabricación de varias composiciones pueden encontrarse en A. Gennaro (ed.), *Remington's Pharmaceutical Sciences*, 18<sup>th</sup> Edition, (1990), Mack Publishing Co., Easton, Pennsylvania.

Las preparaciones de forma líquida incluyen soluciones, suspensiones y emulsiones. Como ejemplo pueden mencionarse soluciones en agua o agua-propilenglicol para inyección parenteral o el agregado de edulcorantes y opacantes para soluciones, suspensiones y emulsiones orales. Las preparaciones de forma líquida también pueden incluir soluciones para administración intranasal.

Las preparaciones en aerosol para inhalación pueden incluir soluciones y sólidos en forma de polvo, que pueden combinarse con un vehículo aceptable desde el punto de vista farmacéutico, tal como un gas comprimido inerte, por ej. nitrógeno.

También se incluyen las preparaciones de forma sólida que pretenden convertirse, inmediatamente antes de usar, en preparaciones de forma líquida para administración tanto oral como parenteral. Dichas formas líquidas incluyen soluciones, suspensiones y emulsiones.

Los compuestos de la invención también pueden administrarse por vía transdérmica. Las composiciones transdérmicas pueden tomar la forma de cremas, lociones, aerosoles y/o emulsiones y pueden incluirse en un parche



transdérmico del tipo de matriz o reservorio con los que son convencionales en el arte para este fin.

Los compuestos de esta invención también pueden administrarse por vía subcutánea.

Con preferencia el compuesto se administra por vía oral.

Con preferencia, la preparación farmacéutica se encuentra en forma de dosificación unitaria. En dicha forma, la preparación se subdivide en dosis unitarias de tamaño apropiado que contiene las cantidades apropiadas de principio activo, por ej., una cantidad efectiva para lograr la finalidad deseada.

La cantidad de compuesto activo en una dosis unitaria de preparación puede variarse o ajustarse desde aproximadamente 1 mg hasta aproximadamente 100 mg, con preferencia desde aproximadamente 1 mg hasta aproximadamente 50 mg, con mayor preferencia desde aproximadamente 1 mg hasta aproximadamente 25 mg, de acuerdo con la aplicación particular.

La dosificación real empleada puede variarse dependiendo de los requerimientos del paciente, y de la severidad de la afección sometida a tratamiento. La determinación del régimen de dosificación apropiado para una situación particular se encuentra dentro de la experiencia en el arte. Por conveniencia, la dosificación diaria total puede dividirse y administrarse en porciones durante el día según el requerimiento.

La cantidad y la frecuencia de administración de los compuestos de la invención y/o sus sales aceptables desde el punto de vista farmacéutico se regularán de acuerdo con el criterio del médico a cargo del tratamiento considerando factores tales como la edad, la condición, y el tamaño del paciente como también la severidad de los síntomas sometidos a tratamiento. Un régimen de dosificación diaria típica recomendada para administración oral puede variar

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desde aproximadamente 1 mg/día hasta aproximadamente 500 mg/día, con preferencia 1 mg/día hasta 200 mg/día, en dos a cuatro dosis divididas.

Otro aspecto de esta invención es un kit que comprende a cantidad efectiva para uso terapéutico de por lo menos un compuesto de fórmula I, o una sal, un solvato, un éster o una prodroga aceptables desde el punto de vista farmacéutico de dicho compuesto y un vehículo, portador o diluyente aceptables desde el punto de vista farmacéutico.

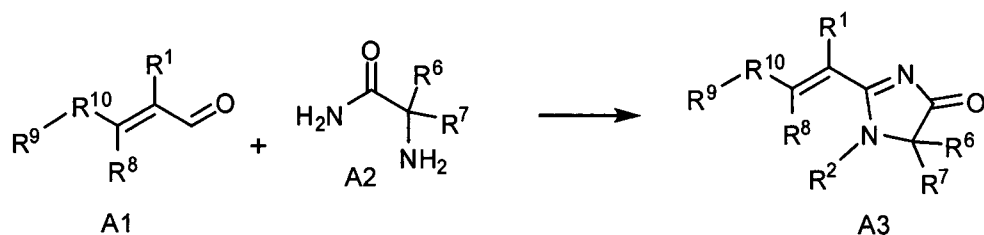
Incluso otro aspecto de esta invención es un kit que comprende una cantidad de por lo menos un compuesto de fórmula I, o una sal, un solvato, un éster o una prodroga aceptables desde el punto de vista farmacéutico de dicho compuesto y una cantidad de por lo menos un agente adicional enumerado con anterioridad en el cual las cantidades de los dos o más principios producen el efecto terapéutico deseado.

La invención revelada aquí se ejemplifica con los siguientes ejemplos ilustrativos que no deben construirse como limitación del alcance de la presentación. Las vías mecánicas y estructuras análogas alternativas resultarán obvias para aquellas personas con experiencia en el arte.

Donde se presentan datos de RMN, los espectros de  $^1\text{H}$  se obtuvieron en cualquiera de Varian VXR-200 (200 MHz,  $^1\text{H}$ ), Varian Gemini-300 (300 MHz) o XL-400 (400 MHz) y se informan como ppm descendente de  $\text{Me}_4\text{Si}$  con número de protones, multiplicidades y constantes de acoplamiento en Hertz indicados entre paréntesis. Donde se presentan los datos de CL/EM, los análisis se realizaron usando un espectrómetro de masa Applied Biosystems API-100 y columna Shimadzu SCL-10A LC: Altech platinum C18, 3 micrones, 33mm x 7mm ID; flujo de gradiente: 0 min – 10%  $\text{CH}_3\text{CN}$ , 5 min – 95%  $\text{CH}_3\text{CN}$ , 7 min – 95%  $\text{CH}_3\text{CN}$ , 7,5 min – 10%  $\text{CH}_3\text{CN}$ , 9 min – detener. Se da el ion principal observado.

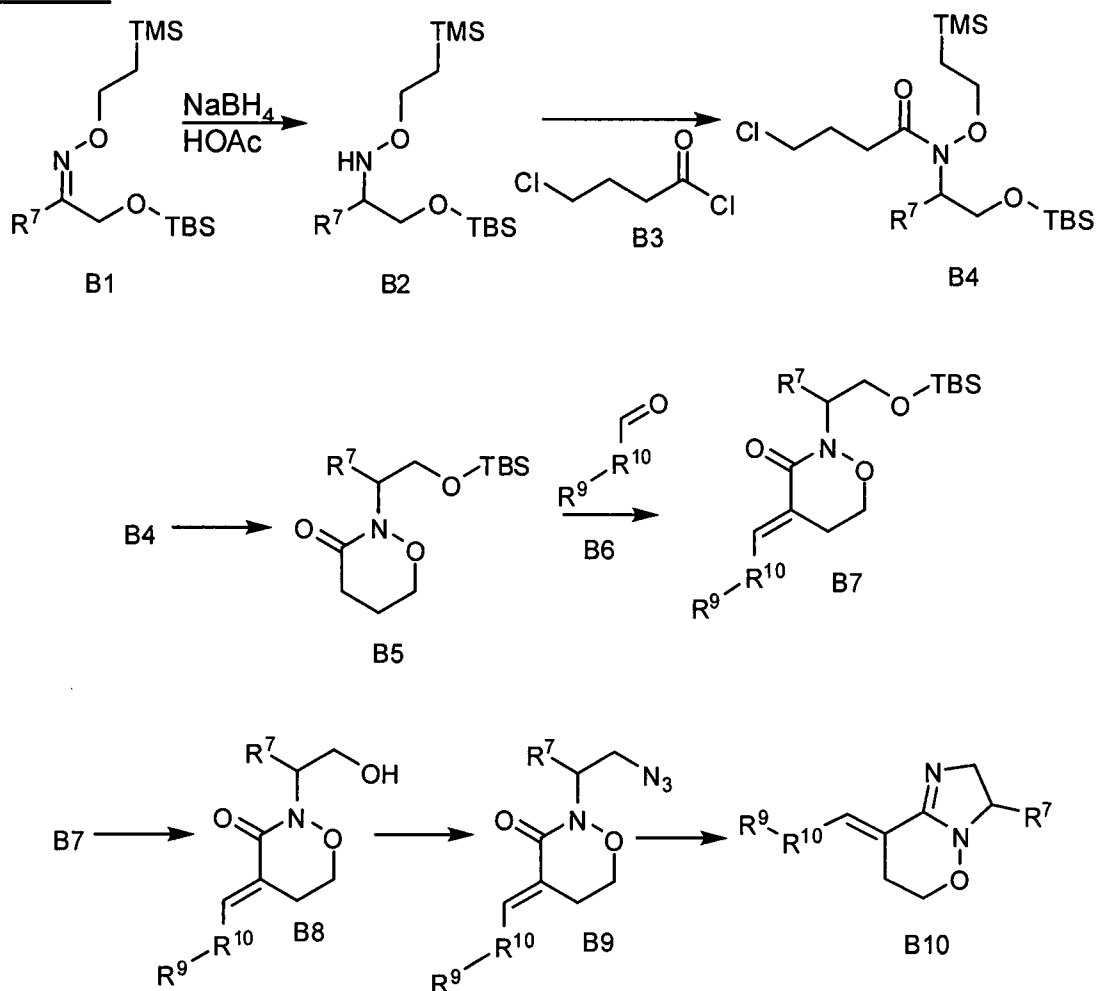
#### **Método A**

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A una solución en diclorometano de **A1** ( $R^1 = \text{H}$ ,  $R^8 = \text{H}$ ,  $R^{10} = 3$ -(metoxi)fenilo,  $R^9 = 4$ -(4-Me-imidazol-ilo) y **A2** ( $R^6 = \text{Me}$ ,  $R^7 = 4$ -fluorofenilo) se agrega N-clorosuccinimida y la mezcla de reacción se agita hasta la mañana siguiente y luego se procesa para dar el compuesto **A3** ( $R^2 = \text{H}$ ,  $R^8 = \text{H}$ ,  $R^{10} = 3$ -(metoxi)fenilo,  $R^9 = 4$ -(4-Me-imidazol-ilo),  $R^6 = \text{Me}$ ,  $R^7 = 4$ -fluorofenilo).

### Método B



### **Método B, Paso 1;**

El Compuesto **B1** ( $R^7 = p\text{-F-Ph}$ ), que se obtiene a partir de la correspondiente cetona y oxima, se reduce a hidroxilamina usando  $\text{NaBH}_4$  y  $\text{HOAc}$  como solvente para dar el compuesto **B2** ( $R^7 = p\text{-F-Ph}$ ).

**Método B, Paso 2;**

El Compuesto **B2** ( $R^7 = p\text{-F-Ph}$ ) se convierte en **B4** ( $R^7 = p\text{-F-Ph}$ ) usando condiciones estándar para la formación de amida.

**Método B, Paso 3;**

El Compuesto **B4** ( $R^7 = p\text{-F-Ph}$ ) se trata con 1,5 eq. de TBAF para generar el Compuesto **B5** ( $R^7 = p\text{-F-Ph}$ ) a través de la desprotección selectiva del grupo trimetilsililetilo a lo que le sigue ciclación.

**Método B, Paso 4**

El Compuesto **B5** ( $R^7 = p\text{-F-Ph}$ ) se trata con LDA seguido del Compuesto **B6** ( $R^9 = 4\text{-(4'-metilimidazol-1-ilo)}$  y  $R^{10} = 3\text{-MeOFenilo}$ ) para dar el Compuesto **B7** ( $R^7 = p\text{-F-Ph}$ ,  $R^9 = 4\text{-(4-metilimidazol-1-ilo)}$  y  $R^{10} = 3\text{-MeOFenilo}$ ).

**Método B, Paso 5**

El Compuesto **B7** ( $R^7 = p\text{-F-Ph}$ ,  $R^9 = 4\text{-(4-metilimidazol-1-ilo)}$  y  $R^{10} = 3\text{-MeOFenilo}$ ) se trata con TFA para dar el Compuesto **B8** ( $R^7 = p\text{-F-Ph}$ ,  $R^9 = 4\text{-(4-metilimidazol-1-ilo)}$  y  $R^{10} = 3\text{-MeOFenilo}$ ).

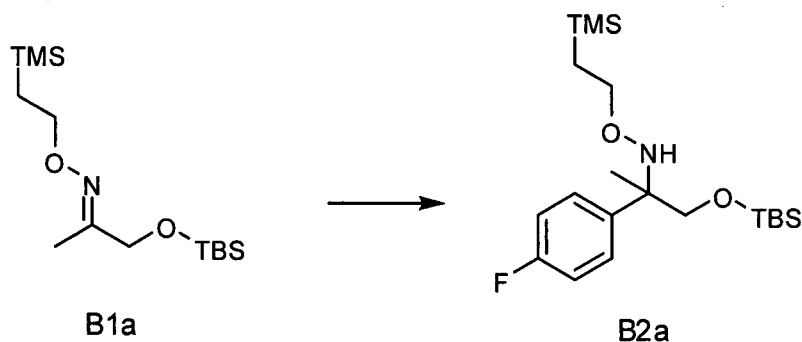
**Método B, Paso 6**

El Compuesto **B8** ( $R^7 = p\text{-F-Ph}$ ,  $4\text{-(4-metilimidazol-1-ilo)}$  y  $R^{10} = 3\text{-MeOFenilo}$ ) se trata con DPPA para dar el Compuesto **B9** ( $R^7 = p\text{-F-Ph}$ ,  $R^9 = 4\text{-(4'-metilimidazol-1-ilo)}$  y  $R^{10} = 3\text{-MeOFenilo}$ ).

**Método B, Paso 7**

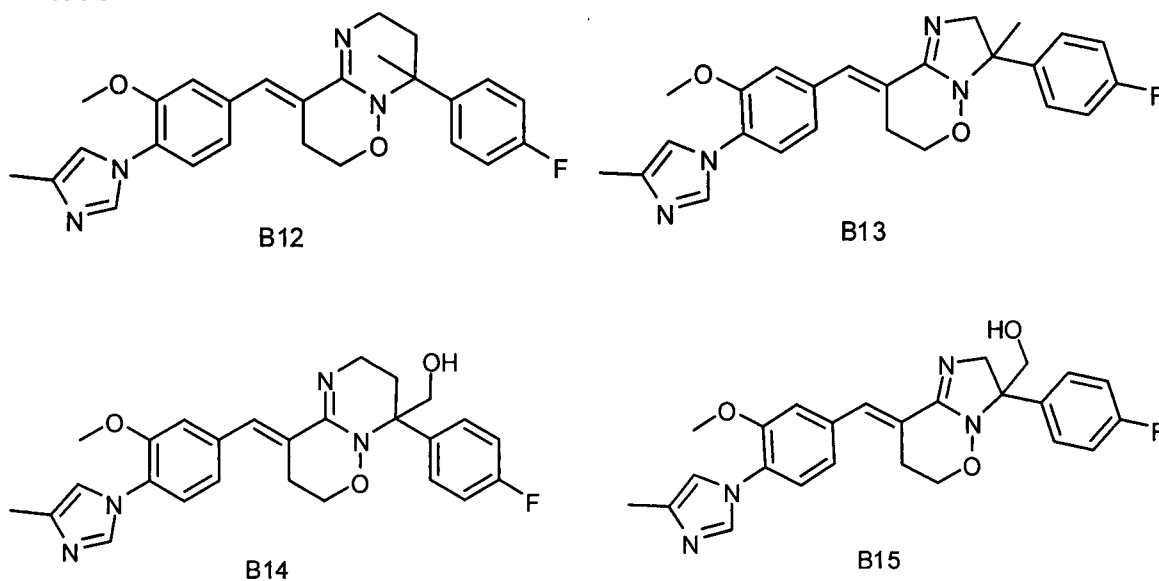
El Compuesto **B9** ( $R^7 = p\text{-F-Ph}$ ,  $R^9 = 4\text{-(4'-metilimidazol-1-ilo)}$  y  $R^{10} = 3\text{-MeOFenilo}$ ) se trata con tributilfosfina en tolueno a reflujo para dar el Compuesto **B10A** ( $R^7 = p\text{-F-Ph}$ ,  $R^9 = 4\text{-(4'-metilimidazol-1-ilo)}$  y  $R^{10} = 3\text{-MeOFenilo}$ ).

En forma alternativa, Los análogos de **B2** pueden generarse usando un método similar al que sigue: *Diastereoselective additions of organolithium reagents to the C=N bond of protected erythrulose oxime ethers. Synthesis of enantiopure  $\alpha$ -disubstituted  $\alpha$ -amino acids* Marco, J. Alberto; Carda, Miguel; Murga, Juan; Gonzalez, Florenci; Falomir, Eva. *Tetrahedron Letters* (1997), **38**(10), 1841-1844.

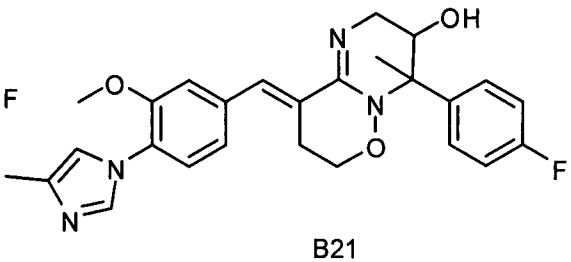
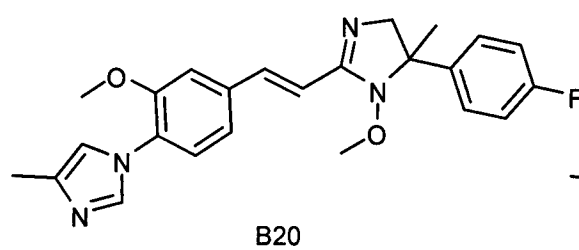
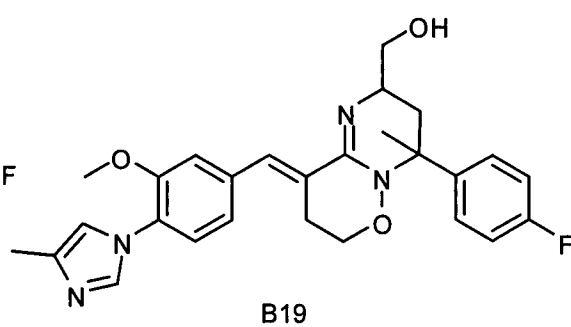
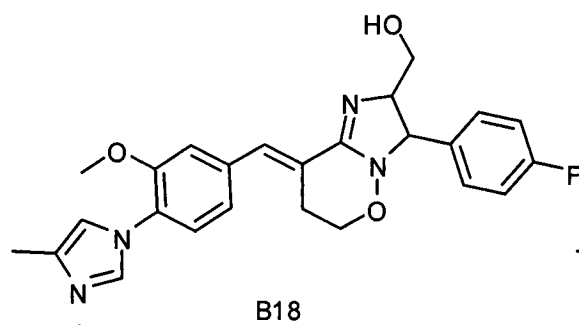
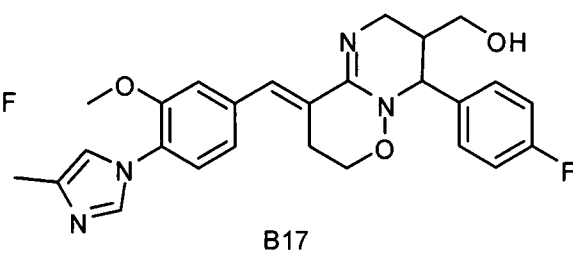
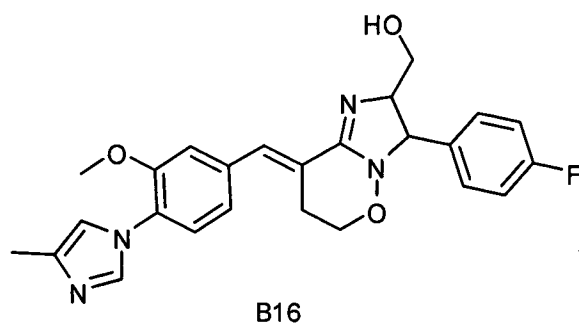
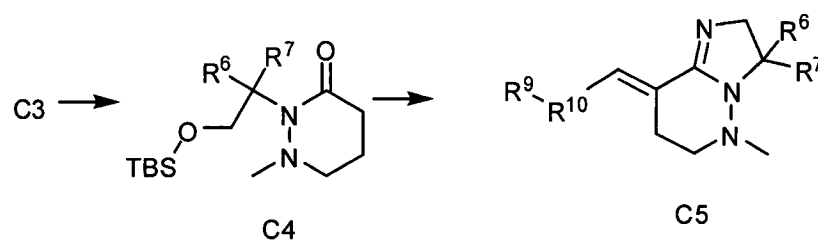
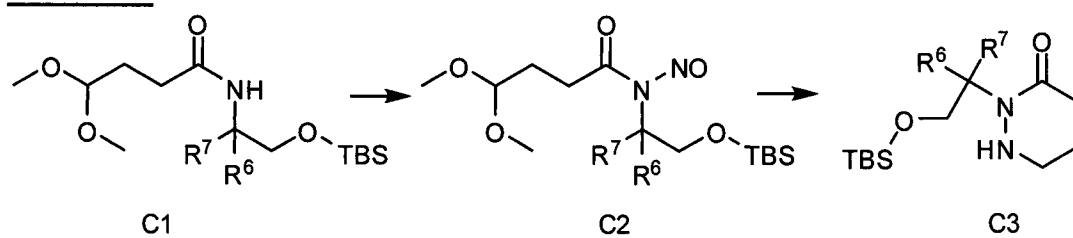


A una solución en éter de **B1a** se agrega fenil litio para dar el Compuesto **B2a** que se aplica al resto de la vía de síntesis en el Método B.

Los siguientes compuestos se sintetizan usando un método similar al Método B.



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**Método C****Método C, Paso 1**

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El Compuesto **C1** ( $R^6=Me$ ,  $R^7 = p\text{-F-fenilo}$ ), que se obtiene usando el correspondiente ácido y amina a través de química de acoplamiento de amida, se convierte en el producto N-nitroso **C2** ( $R^6=Me$ ,  $R^7 = p\text{-F-fenilo}$ ) usando condiciones similares a la siguiente bibliografía: *Enantioselective syntheses of carbocyclic ribavirin and its analogs: linear versus convergent approaches*. Kuang, R.; Ganguly, A. K.; Chan, T.-M.; Pramanik, B. N.; Blythin, D. J.; McPhailo, A. T.; Saksena, A. K. *Tetrahedron Letters* (2000), **41**(49), 9575-9579.

### Método C, Paso 2

**C2** ( $R^6=Me$ ,  $R^7=p\text{-F-fenilo}$ ) se trata con  $Zn/HOAc/H_2O$  para dar el compuesto **C3** ( $R^6=Me$ ,  $R^7=p\text{-F-fenilo}$ ).

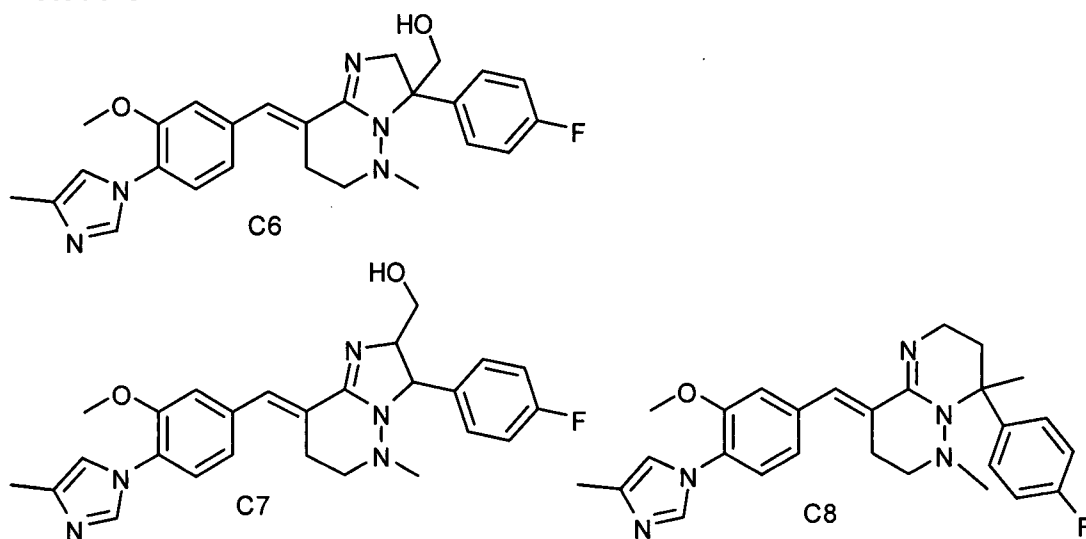
### Método C, Paso 3

El Compuesto **C3** ( $R^6=Me$ ,  $R^7=p\text{-F-fenilo}$ ) se trata con  $NaH$  a lo que le sigue  $MeI$  para dar el compuesto **C4** ( $R^6=Me$ ,  $R^7 = p\text{-F-fenilo}$ ).

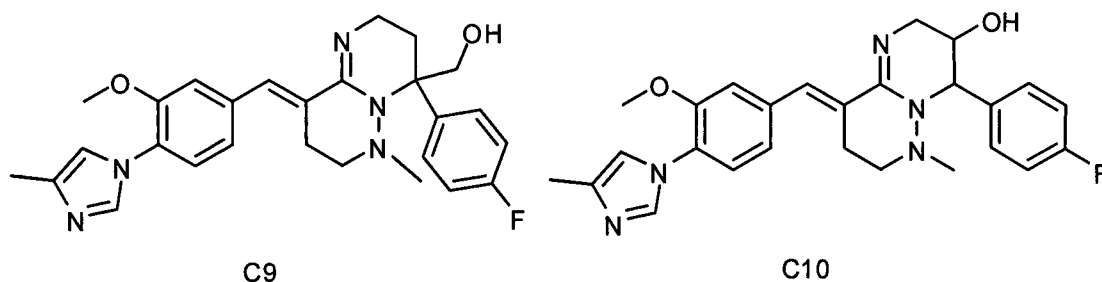
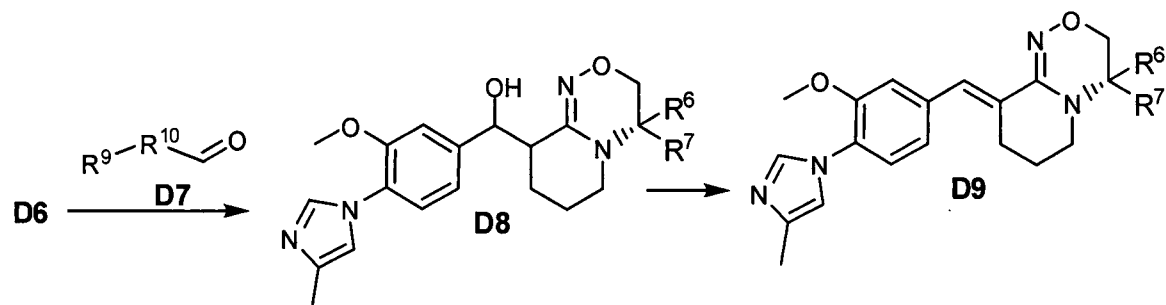
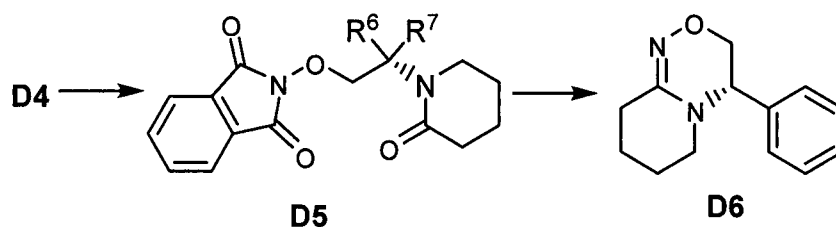
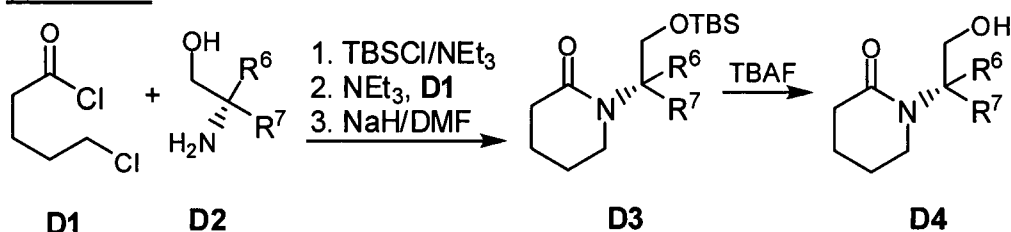
### Método C, Paso 4

El Compuesto **C4** ( $R^6=Me$ ,  $R^7 = p\text{-F-fenilo}$ ) se convierte en compuesto **C5** ( $R^6=Me$ ,  $R^7 = p\text{-F-fenilo}$ ,  $R^9=4\text{-(4-metilimidazol-1-ilo)}$ ,  $R^{10} = 3\text{-MeOfenilo}$ ) usando un procedimiento similar al Método B Pasos 4, 5, 6 y 7.

Los siguientes compuestos se obtienen usando métodos similares al Método C:



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**Método D****Método D, PASO 1:**

TBSCl (5,6 g, 37,2 mmol) en  $\text{CH}_2\text{Cl}_2$  (10 mL) se agregó gota a gota a una solución de **D2** ((S),  $\text{R}^6 = \text{H}$ ,  $\text{R}^7 = \text{Ph}$ ) (5,1 g, 37,2 mmol),  $\text{NEt}_3$  (10,4 mL, 74,4 mmol) y DMAP (20 mg) en  $\text{CH}_2\text{Cl}_2$  (20) a temperatura ambiente. La mezcla se agitó luego hasta la mañana siguiente. La mezcla se diluyó con  $\text{CH}_2\text{Cl}_2$  (200 ml) y solución de  $\text{NH}_4\text{Cl}$  (30 ml). La fase orgánica se lavó con agua, salmuera, se secó sobre  $\text{MgSO}_4$ , y se concentró para dar el producto en bruto (6,0 g) se absorbió en



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$\text{CH}_2\text{Cl}_2$  (50 ml) y se trató con  $\text{NEt}_3$  (3,8 ml, 27,45 mmol). El Compuesto **D1** se agregó gota a gota a la mezcla a  $0^\circ\text{C}$ . La mezcla de reacción resultante se agitó a temperatura ambiente hasta la mañana siguiente. La mezcla se diluyó con EtOAc (200 ml) y solución  $\text{NaHCO}_3$  (40 ml). La fase orgánica se lavó con agua, salmuera, se secó sobre  $\text{MgSO}_4$ , y se concentró para dar el producto en bruto. El residuo en bruto se disolvió en DMF (50 ml) y se trató con NaH (1,25 g, 28,6 mmol, 60% en parafina) a temperatura ambiente. La mezcla resultante luego se calentó a  $60^\circ\text{C}$  hasta la mañana siguiente. La mezcla se diluyó con EtOAc (200 ml) y solución acuosa de  $\text{NH}_4\text{Cl}$  (40 ml). La fase orgánica se lavó con agua (3x), salmuera, se secó sobre  $\text{MgSO}_4$ , y se concentró para dar el producto en bruto que se purificó por cromatografía en columna eluyendo con EtOAc/hexanos para producir el compuesto **D3** ((S),  $\text{R}^6 = \text{H}$ ,  $\text{R}^7 = \text{Ph}$ ; 5,0 g).

**Método D, PASO 2:**

Se agregó TBAF (3,15 ml, 3,15 mmol, 1,0 M en THF) gota a gota a una solución de compuesto **D3** ((S),  $\text{R}^6 = \text{H}$ ,  $\text{R}^7 = \text{Ph}$ ; 0,7 g, 2,1 mmol) en THF (10 ml). La mezcla se agitó durante 2 horas antes de diluirse con EtOAc (100 ml) y solución de HCl (20 ml, 0,5 M). La fase orgánica se lavó con agua, salmuera, se secó sobre  $\text{MgSO}_4$ , y se concentró para dar el producto en bruto que se purificó por cromatografía en columna eluyendo con EtOAc/hexanos para producir el compuesto hidroxilo **D4** ((S),  $\text{R}^6 = \text{H}$ ,  $\text{R}^7 = \text{Ph}$ ; 0,44 g).

**Método D, PASO 3:**

Se agregó  $\text{PBU}_3$  (0,2 ml, 0,82 mmol) a una solución de compuesto **D4** ((S),  $\text{R}^6 = \text{H}$ ,  $\text{R}^7 = \text{Ph}$ ; 0,1 g, 0,457 mmol), ADDP (0,2 g, 0,82 mmol) y ftalimida (0,12 g, 0,685 mmol) en THF (5 ml) a temperatura ambiente. La mezcla resultante luego se calentó a  $80^\circ\text{C}$  durante 2 horas. La mezcla se diluyó con EtOAc (100 ml) y solución de  $\text{NaHCO}_3$  (20 ml). La fase orgánica se lavó con solución de  $\text{NaHCO}_3$ , salmuera, se secó sobre  $\text{MgSO}_4$ , y se concentró para dar el producto en bruto que



se purificó por cromatografía en columna eluyendo con EtOAc/hexanos para producir el compuesto **D5** ((S),  $R^6 = H$ ,  $R^7 = Ph$ ; 0,1 g, 0,457 mmol, 0,14 g).

**Método D, PASO 4,**

Se agregó  $NH_2NH_2 \cdot xH_2O$  (54,4 ul, 1,12 mmol) a una solución de compuesto **D5** ((S),  $R^6 = H$ ,  $R^7 = Ph$ ; 0,14 g, 0,373 mmol) en MeOH (2,0 ml) y  $CH_2Cl_2$  (2,0 ml) a temperatura ambiente. La mezcla resultante se agitó durante 2 horas antes de diluirse con EtOAc (50 ml) y solución de  $NaHCO_3$  (10 ml). La fase orgánica se lavó con agua, salmuera, se secó sobre  $MgSO_4$ , y se concentró para dar el producto en bruto que se disolvió en EtOH (3,0 ml) y se trató con  $P_2O_5$  (0,53 g, 3,72 mmol). La mezcla resultante se calentó a  $80^\circ C$  hasta la mañana siguiente. La mezcla se enfrió y se diluyó con EtOAc (50 ml) y solución de  $NaHCO_3$  (20 ml). La fase orgánica se lavó con solución de  $NaHCO_3$ , salmuera, se secó sobre  $MgSO_4$ , y se concentró para dar el producto en bruto que se purificó por cromatografía en columna eluyendo con EtOAc/hexanos para producir el compuesto **D6** ((S),  $R^6 = H$ ,  $R^7 = Ph$ ; 46 mg).

$^1H$  RMN ( $CDCl_3$ )  $\delta$ : 7,43-7,32 (m, 5 H); 4,30 (dd,  $J = 5,0, 4,0$  Hz, 1 H); 4,16 (AB cuart,  $J = 11,5, 4,0$  Hz, 1 H); 3,96 (AB cuart,  $J = 11,5, 5,0$  Hz, 1 H); 3,07 (m, 1 H); 2,89 (m, 1 H); 2,50 (m, 2 H); 1,84 (m, 2 H); 1,76 (m, 2 H). CLEM por Electroaspiración: Masa observada: 217,2.

**Método D, PASO 5,**

Se agregó t-BuLi (0,188 ml, 0,32 mmol, 1,7 M) gota a gota a una solución de compuesto **D6** ((S),  $R^6 = H$ ,  $R^7 = Ph$ ; 46 mg, 0,21 mmol) en THF (1,5 ml) a  $-78^\circ C$ . La mezcla se agitó durante 45 minutos antes de agregar el compuesto **D7** ( $R^{10} = 3-MeO-Fenilo$ ,  $R^9 = 4-(4-metilimidazol-1-il)$ ) en THF (1,0 ml) en goteo rápido. La mezcla resultante se agitó durante 2 horas antes de diluirse con EtOAc (50 ml) y solución de  $NH_4Cl$  (10 ml). La fase orgánica se lavó con salmuera, se secó sobre  $MgSO_4$ , y se concentró para dar el producto en bruto que se purificó

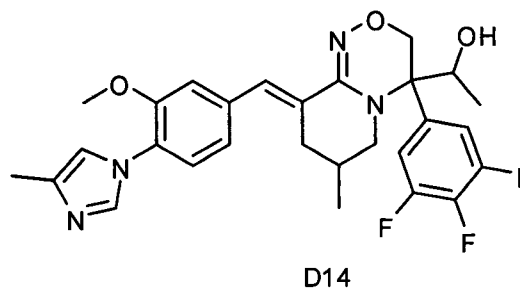
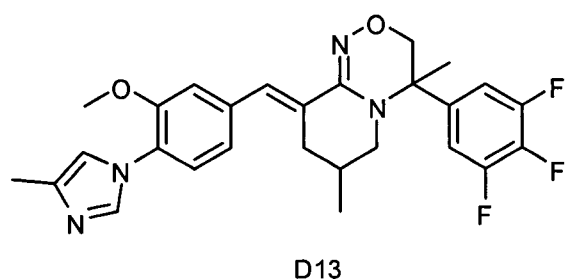
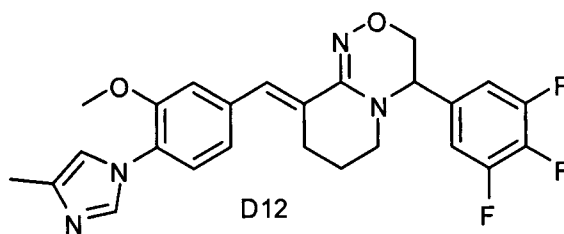
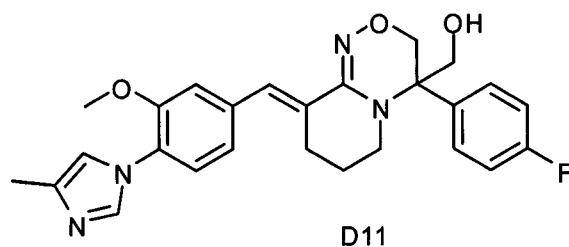
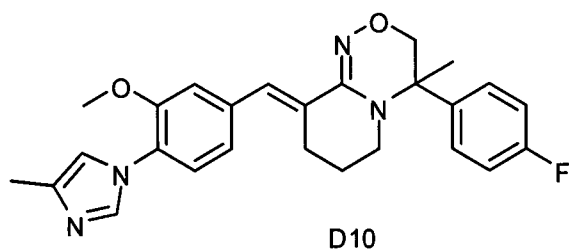
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por cromatografía en columna eluyendo con EtOAc/hexanos para producir el compuesto **D8** ((S),  $R^6 = H$ ,  $R^7 = Ph$ ;  $R^{10} = 3\text{-MeO-Fenilo}$ ,  $R^9 = 4\text{-(4-metilimidazol-1-il)}$ )).

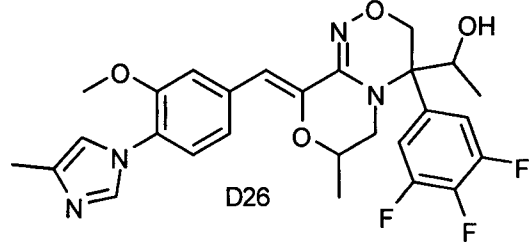
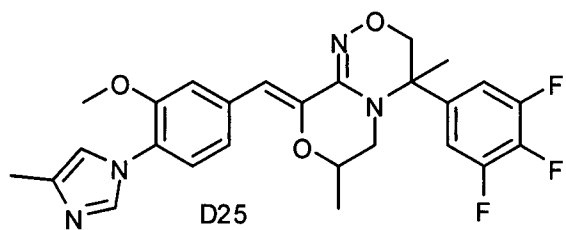
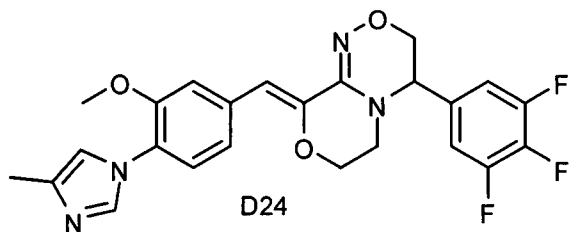
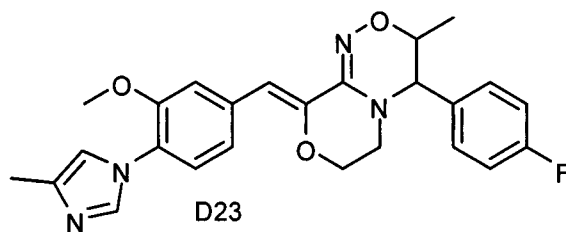
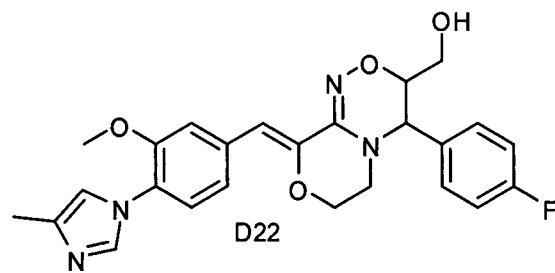
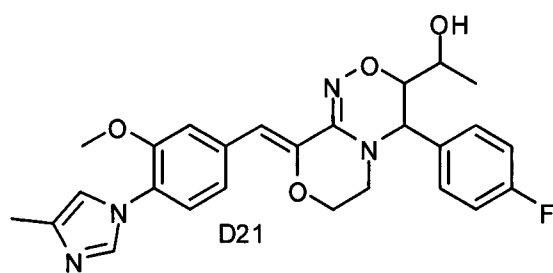
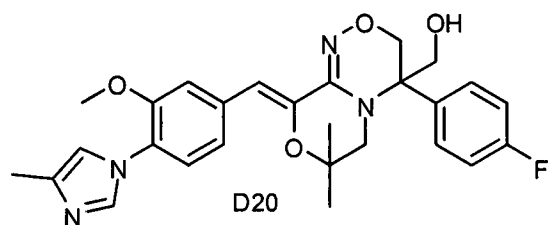
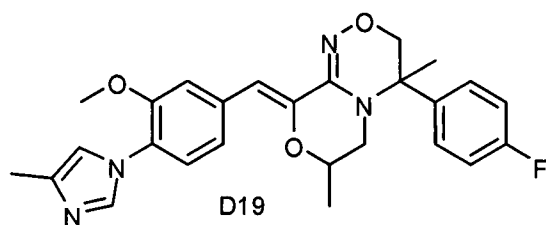
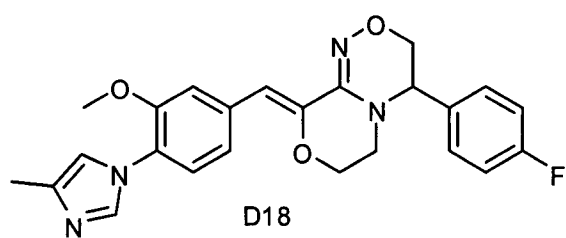
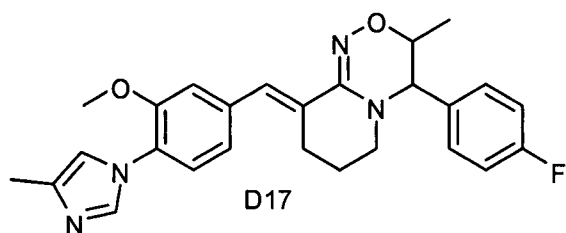
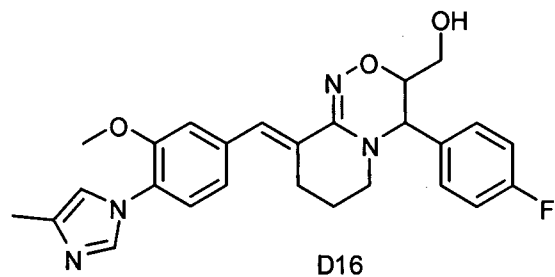
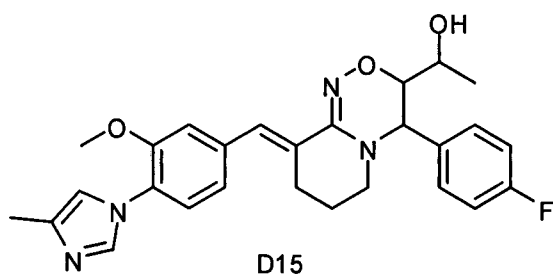
#### Método D, PASO 7,

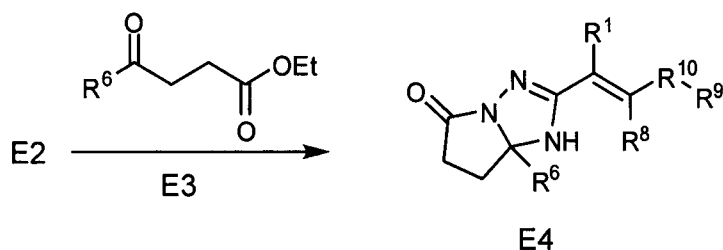
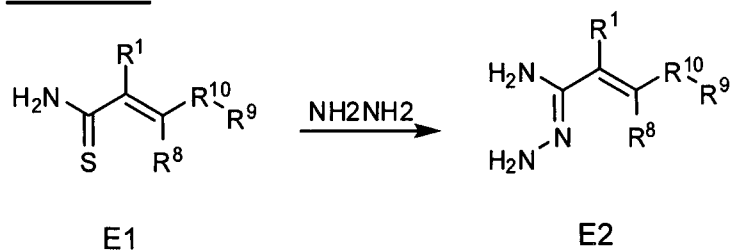
El Compuesto **D8** ((S),  $R^6 = H$ ,  $R^7 = Ph$ ;  $R^{10} = 3\text{-MeO-Fenilo}$ ,  $R^9 = 4\text{-(4-metilimidazol-1-il)}$ )) se disolverá en tolueno y se trató con p-TSA (10% en moles). La mezcla se calentará a reflujo con un aparato de Dean-Stark hasta la mañana siguiente. El solvente se eliminará y el residuo en bruto se purificará con cromatografía en columna para dar el compuesto **D9** ((S),  $R^6 = H$ ,  $R^7 = Ph$ ;  $R^{10} = 3\text{-MeO-Fenilo}$ ,  $R^9 = 4\text{-(4-metilimidazol-1-il)}$ )).

Los siguientes compuestos se sintetizan usando métodos similares al Método D:



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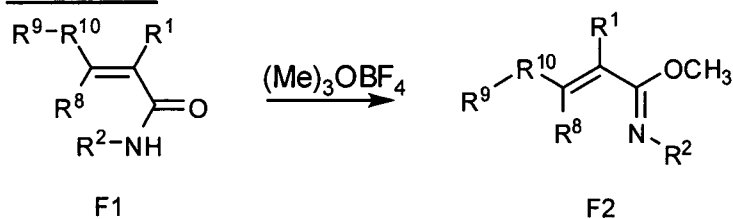


**Método E****Método E, Paso 1.**

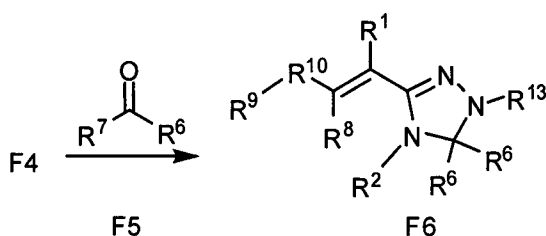
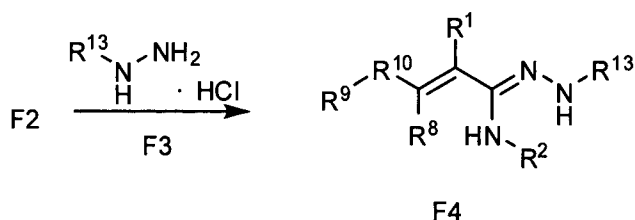
Los Compuestos de **E1** ( $\text{R}^1 = \text{R}^8 = \text{H}$ ,  $\text{R}^{10} = 3\text{-MeOFenilo}$ ,  $\text{R}^9 = 4\text{-(4-Me-imidazol-1-il)}$ ) se preparan a partir de las correspondientes tioamidas o nitrilos por tratamiento con hidrazina con una cantidad catalítica de ácido en un solvente tal como etanol con aplicación de calor.

**Método E, Paso 2.**

Se hace reaccionar **E1** ( $\text{R}^1 = \text{R}^8 = \text{H}$ ,  $\text{R}^{10} = 3\text{-MeOFenilo}$ ,  $\text{R}^9 = 4\text{-(4-Me-imidazol-1-il)}$ ) con los ceto ésteres de **E3** ( $\text{R}^6 = \text{p-F-fenilo}$ ) en condiciones de deshidratación tales como tratamiento con una cantidad catalítica de (por ej.  $\text{TsOH}$ , o  $\text{AcOH}$ ) en solventes tales como Tolueno o DCM. En algunos casos el calentamiento en tolueno para eliminar el agua a través de destilación azeotrópica facilitará la reacción para producir los compuestos **E4** ( $\text{R}^1 = \text{R}^8 = \text{H}$ ,  $\text{R}^{10} = 3\text{-MeOFenilo}$ ,  $\text{R}^9 = 4\text{-(4-Me-imidazol-1-il)}$ ,  $\text{R}^6 = \text{p-F-fenilo}$ ).

**Método F.**

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### Método F, Paso1,

A una solución en diclorometano de **F1** ( $\text{R}^1 = \text{H}$ ,  $\text{R}^2 = \text{H}$ ,  $\text{R}^8 = \text{H}$ ,  $\text{R}^{10} = 3$ -(metoxi)fenilo,  $\text{R}^9 = 4$ -(4-Me-imidazol-1-ilo) se agrega tetrafluoroborato de trimetiloxonio, y la mezcla de reacción se agita a temperatura ambiente hasta la mañana siguiente. El solvente se evapora para producir el iminoéter en bruto **B2** como la sal de tetrafluoroborato. Opcionalmente, la sal de tetrafluoroborato en bruto se tritura con éter y la sal de tetrafluoroborato precipitada resultante de **F2** ( $\text{R}^1 = \text{H}$ ,  $\text{R}^2 = \text{H}$ ,  $\text{R}^8 = \text{H}$ ,  $\text{R}^{10} = 3$ -(metoxi)fenilo,  $\text{R}^9 = 4$ -(4-Me-imidazol-1-ilo) se filtra y se seca. Esta se convierte en la base libre repartiendo entre diclorometano y exceso de NaOH 1M. La fase de cloruro de metileno se seca sobre  $\text{K}_2\text{CO}_3$  y se evapora para dar la base libre de **F2** ( $\text{R}^1 = \text{H}$ ,  $\text{R}^2 = \text{H}$ ,  $\text{R}^8 = \text{H}$ ,  $\text{R}^{10} = 3$ -(metoxi)fenilo,  $\text{R}^9 = 4$ -(4-Me-imidazol-1-ilo)), la cual se usa inmediatamente.

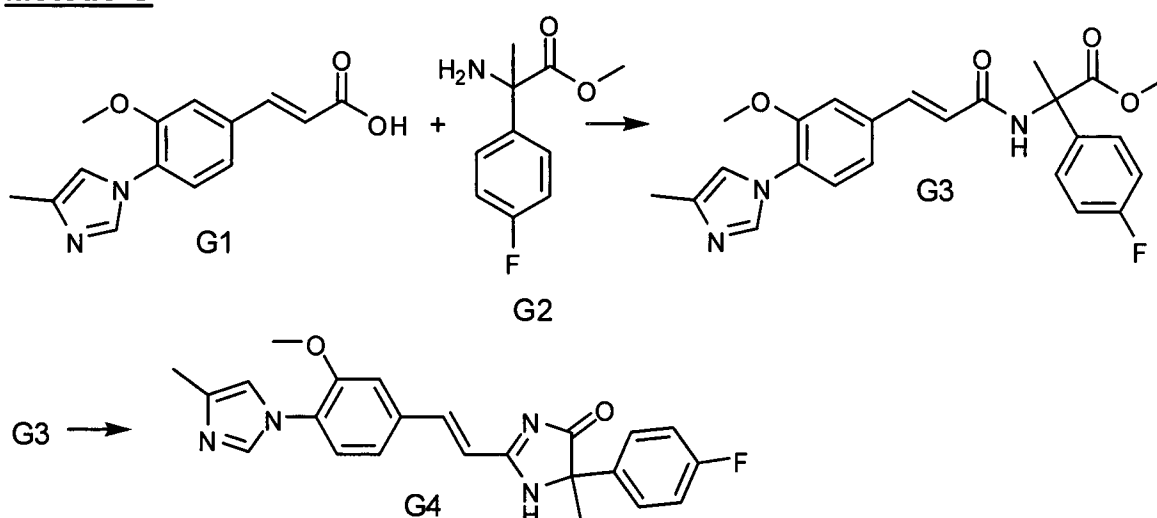
### Método F, Paso 2:

Se trata **F2** ( $\text{R}^1 = \text{H}$ ,  $\text{R}^2 = \text{H}$ ,  $\text{R}^8 = \text{H}$ ,  $\text{R}^{10} = 3$ -(metoxi)fenilo,  $\text{R}^9 = 4$ -(4-Me-imidazol-1-il)) con hidrazina **F3** ( $\text{R}^{13} = \text{H}$ ) opcionalmente como el clorhidrato o el hidrato en metanol a reflujo hasta la mañana siguiente. La mezcla de reacción se neutraliza con bicarbonato de sodio, se filtra y se evapora para dar la amidohidrazida **F4** en bruto ( $\text{R}^1 = \text{H}$ ,  $\text{R}^2 = \text{H}$ ,  $\text{R}^{13} = \text{H}$ ,  $\text{R}^8 = \text{H}$ ,  $\text{R}^{10} = 3$ -(metoxi)fenilo,  $\text{R}^9 = 4$ -(4-Me-imidazol-1-ilo)).

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**Método F, Paso 3:**

Se trata **F4** ( $R^1 = H$ ,  $R^2=H$ ,  $R^{13}=H$ ,  $R^8 = H$ ,  $R^{10} = 3\text{-(metoxi)fenilo}$ ,  $R^9 = 4\text{-(4-Me-imidazol-1-il)}$ ) con la cetona **F5** ( $R^6 = Me$ ,  $R^7 = 4\text{-fluorofenilo}$ ) y ácido p-toluensulfónico en etanol a reflujo hasta la mañana siguiente para dar, luego de la neutralización y evaporación, el compuesto **F6** ( $R^1 = H$ ,  $R^2=H$ ,  $R^{13}=H$ ,  $R^8 = H$ ,  $R^{10} = 3\text{-(metoxi)fenilo}$ ,  $R^9 = 4\text{-(4-Me-imidazol-1-ilo)}$ ,  $R^6 = Me$ ,  $R^7 = 4\text{-fluorofenilo}$ ).

**Método G****Método G, Paso 1**

El Compuesto **G1** (200 mg), generado a partir del correspondiente aldehído y dietil fosfonato de carbometoximetilo, seguido de hidrólisis con LiOH, se hizo reaccionar con compuesto **G2** (230 mg) con HOBT (135 mg) y EDCI (197 mg) en 10 ml DMF para dar el compuesto **G3** luego del procesamiento de rutina y purificación en un 66% de rendimiento.

$^1\text{H}$  RMN de G3 ( $\text{CDCl}_3$ , ppm);  $\delta$  7,35 s, 1H; 7,55 d, 1H; 7,45 m, 2H; 7,25, d, 1H; 7,15, m, 3H; 7,10, m, 1H; 6,95, s, 1H; 6,5, s, 1H; 3,9 s, 3H; 3,75 s, 3H; 2,3 s, 3H; 2,15 s, 3H.

**Método G, Paso 2**

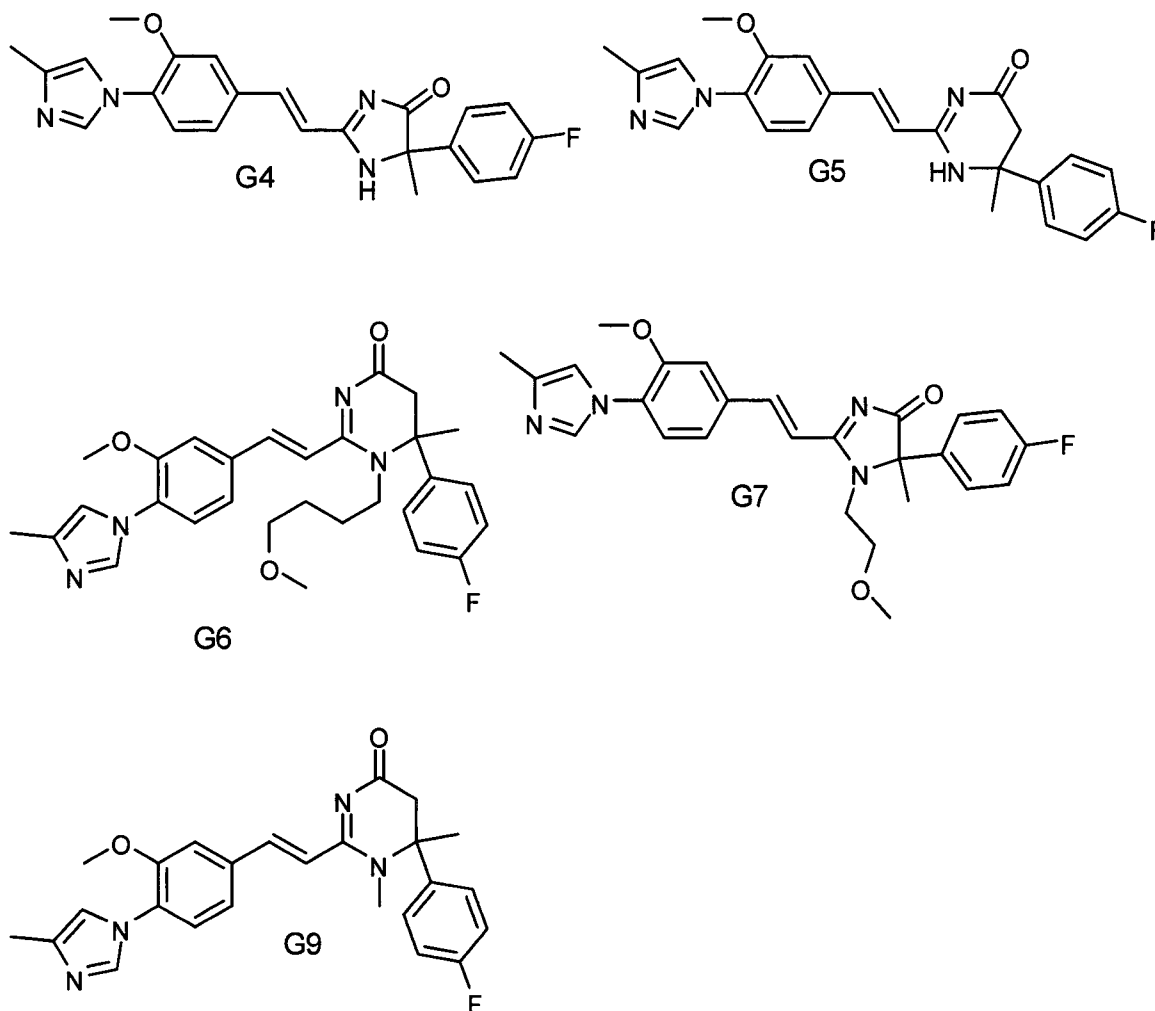
Una solución de amoníaco en THF se trató con  $\text{Me}_3\text{Al}$  en hexano antes de agregar lentamente el compuesto **G3**. La mezcla final se reflujo hasta la mañana

siguiente antes de desactivar con cloruro de amonio acuoso sat. y se extrajo con EtOAc. La fase orgánica se lavó con salmuera, se secó sobre solvente y el solvente se evaporó. El residuo se cromatografió para dar la correspondiente amida. El producto amida se disolvió en 1 ml de EtOH y 2 ml de NaOH 1N. Luego de que el material de partida desapareció, la mezcla de reacción se repartió en DCM/cloruro de amonio ac. sat. La fase orgánica se secó y el solvente se evaporó. El residuo se cromatografió para dar el compuesto **G4**.

$^1\text{H}$  RMN de G4 ( $\text{CDCl}_3$ , ppm);  $\delta$  10,5 br. 1H; 7,9, s, 1H; 7,6 m, 2H; 7,4, m, 1H; 7,3, m 2H; 7,2, m, 1H; 7,05, m, 2H; 7,0 s, 1H; 6,9 m 1H; 3,9 s, 3H; 2,3 s, 3H.

Los siguientes compuestos se obtienen usando métodos similares al

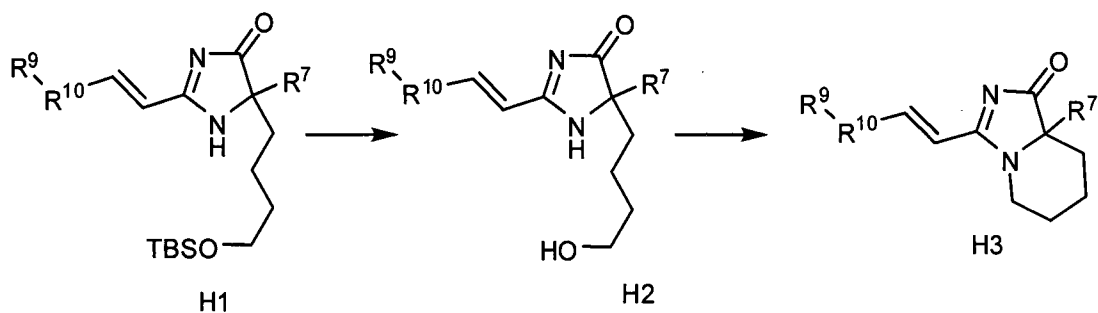
Método G:



**Método H**



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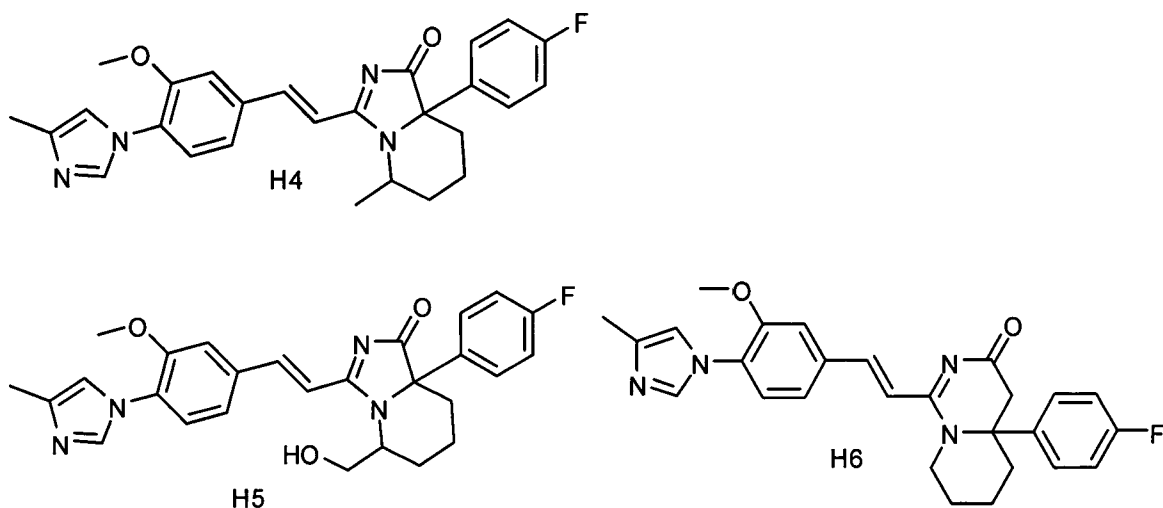
### Método H, Paso 1

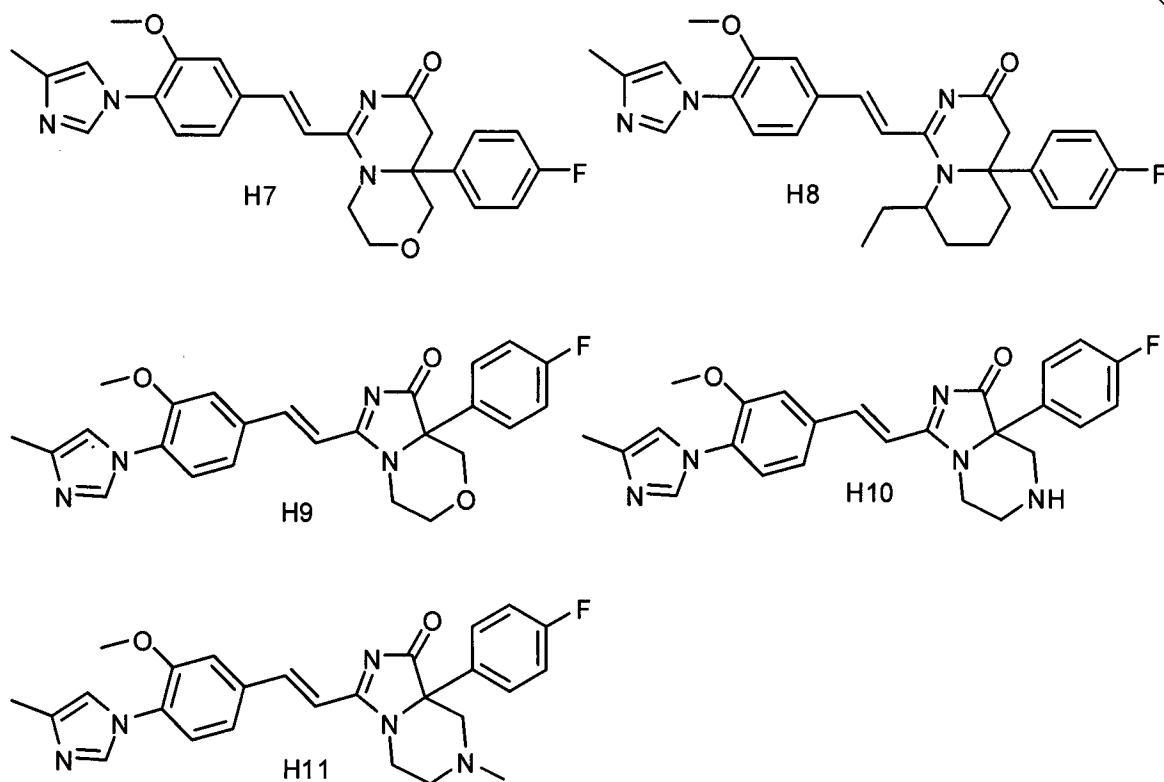
El Compuesto **H1** ( $R^7$  = p-F-fenilo,  $R^{10}$  = 3-MeO-Fenilo,  $R^9$  = 4-(4-metilo-imidazol-1-ilo), se prepara usando métodos similares al Método G, se trata con TBAF para dar el compuesto **H2** ( $R^7$  = p-F-fenilo,  $R^{10}$  = 3-MeO-Fenilo,  $R^9$  = 4-(4-metilo-imidazol-1-ilo) luego de la purificación.

### Método H, Paso 2

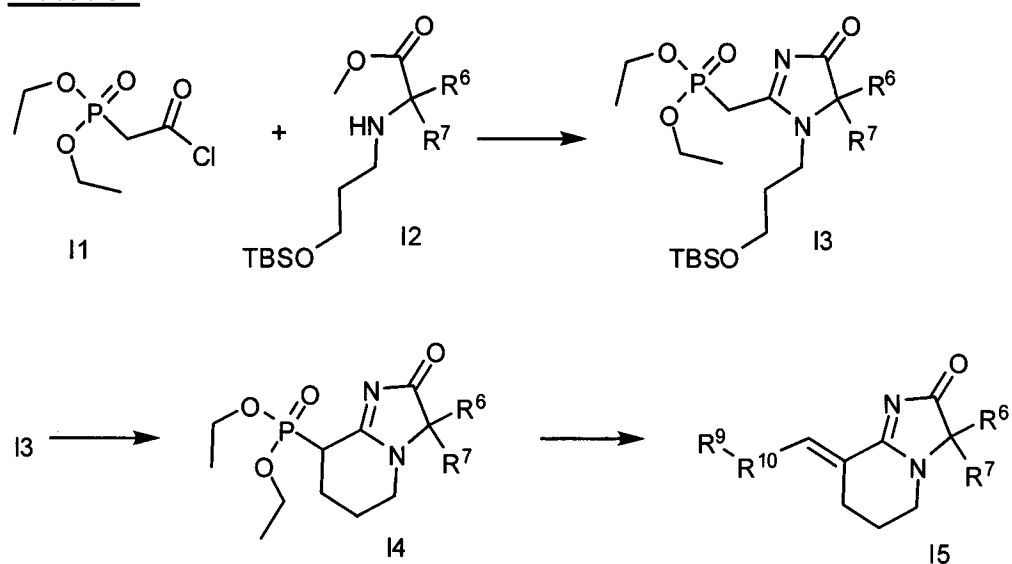
El Compuesto **H2** ( $R^7$  = p-F-fenilo,  $R^{10}$  = 3-MeO-Fenilo,  $R^9$  = 4-(4-metilo-imidazol-1-ilo) se convierte en el filtrado. El filtrado del producto se trata con NaH en DMF para dar el compuesto **H3** ( $R^7$  = p-F-fenilo,  $R^{10}$  = 3-MeO-Fenilo,  $R^9$  = 4-(4-metilo-imidazol-1-ilo) luego del procesamiento de rutina y purificación.

Los siguientes compuestos se obtienen usando métodos similares al Método H:





### Método I



### Método I, Paso 1

El Compuesto I3 ( $R^6$  = p-F-Fenilo,  $R^7$  = Me) se obtiene usando métodos similares al Método G usando material de partida I1 y I2 ( $R^6$  = p-F-Fenilo,  $R^7$  = Me).

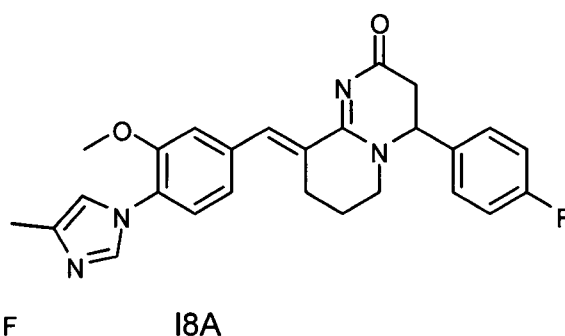
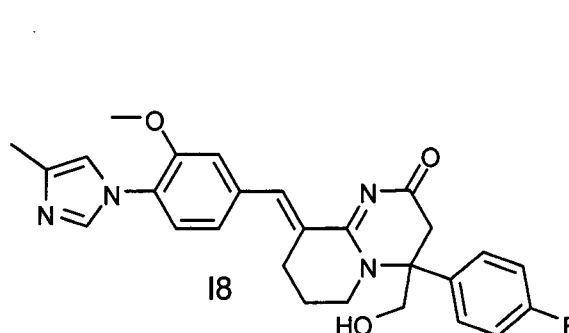
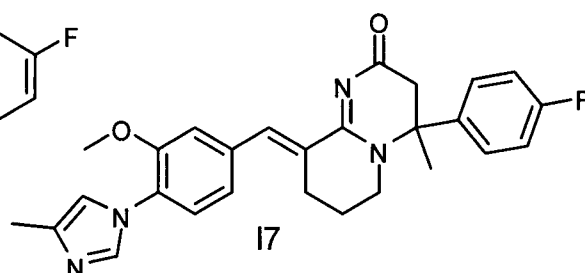
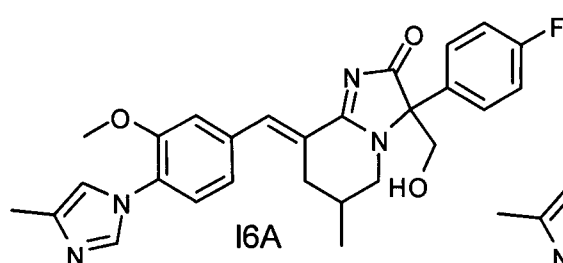
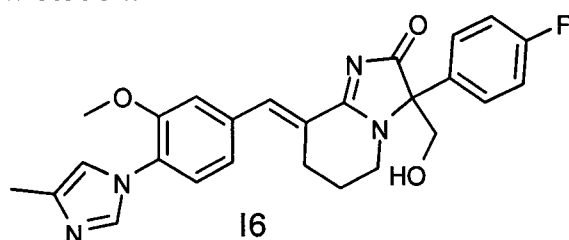
### Método I, Paso 2

El Compuesto **I3** ( $R^6 = p\text{-F-Fenilo}$ ,  $R^7 = \text{Me}$ ) se trata con TBAF a lo que le sigue purificación para dar el correspondiente alcohol que se transforma en el triflato. El triflato se trata con NaH en DMF para dar el compuesto **I4** ( $R^6 = p\text{-F-Fenilo}$ ,  $R^7 = \text{Me}$ ).

### Método I, Paso 3

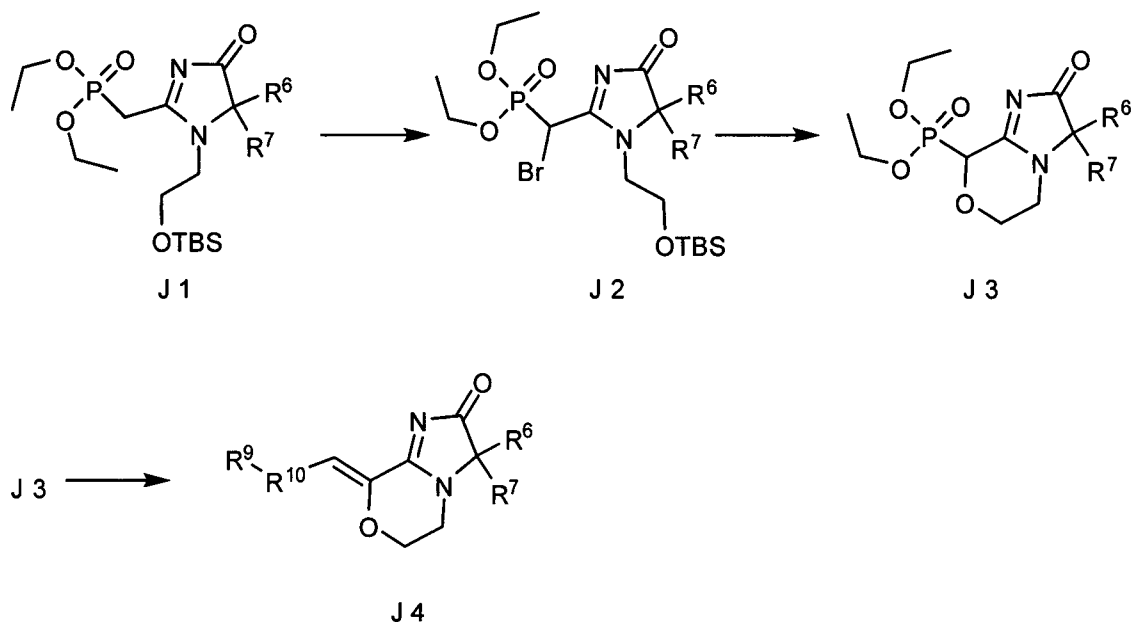
El Compuesto **I5** ( $R^6 = p\text{-F-Fenilo}$ ,  $R^7 = \text{Me}$ ,  $R^{10} = 3\text{-MeOfenilo}$ ,  $R^9 = 4\text{-(4-metilimidazol-1-il)}$ ) se obtiene usando compuesto **I4** ( $R^6 = p\text{-F-Fenilo}$ ,  $R^7 = \text{Me}$ ) haciendo reaccionar con **D7** ( $R^{10} = 3\text{-MeOfenilo}$ ,  $R^9 = 4\text{-(4-metilimidazol-1-il)}$ ) y una base luego de la purificación.

Los siguientes compuestos se obtienen usando un método similar al método I.



### Método J

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### Método J, Paso 1

El Compuesto **J1** (R<sup>6</sup> = p- F-Ph y R<sup>7</sup> = metilo), que se obtiene usando un método similar al Método I, Paso 1, se trata con NBS en Benceno con un iniciador radical (tal como AIBN) a reflujo para dar el compuesto **J2** (R<sup>6</sup> = p- F-Ph y R<sup>7</sup> = metilo).

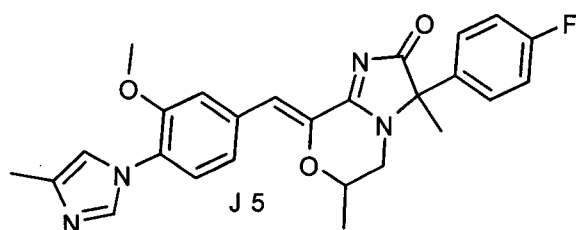
### Método J, paso 2

El Compuesto **J2** (R<sup>6</sup> = p- F-Ph y R<sup>7</sup> = metilo) se trata con TBAF en DMF para dar el compuesto **J3** (R<sup>6</sup> = p- F-Ph y R<sup>7</sup> = metilo) luego de la purificación.

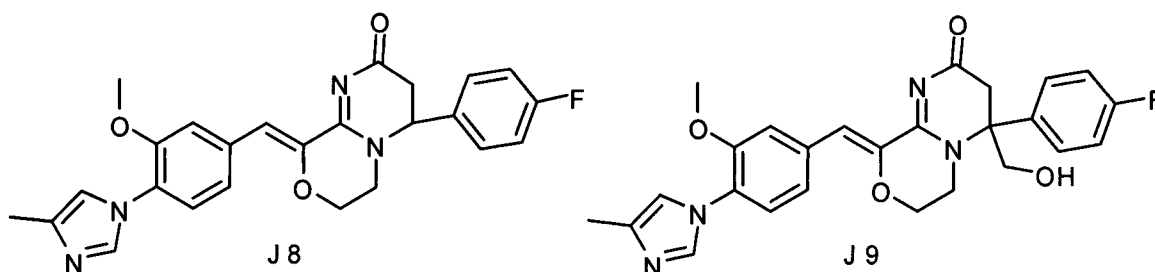
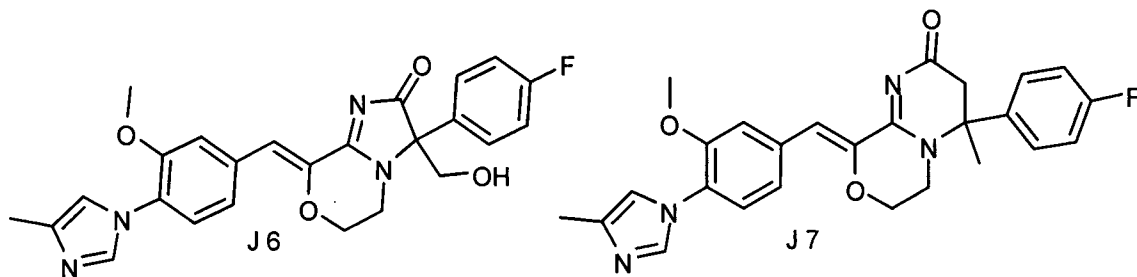
### Método J Paso3

El Compuesto **J4** (R<sup>6</sup> = p- F-Ph y R<sup>7</sup> = metilo, R<sup>10</sup> = 3-MeOfenilo, R<sup>9</sup> = 4-(4-metilimidazol-1-il)) se obtiene usando un método similar al Método I paso 3.

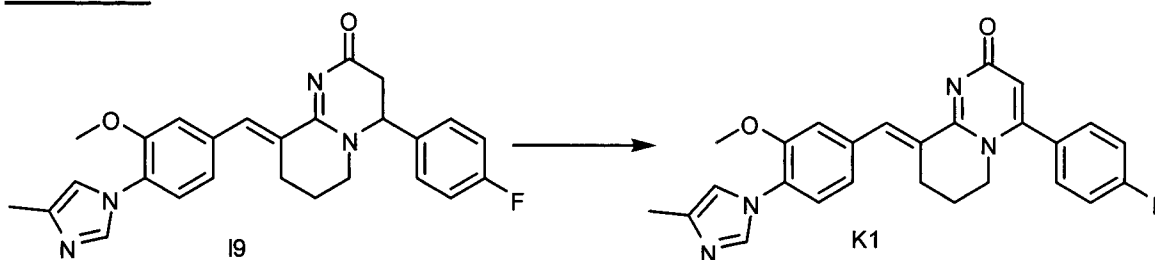
Los siguientes compuestos se obtienen usando métodos similares al Método J:



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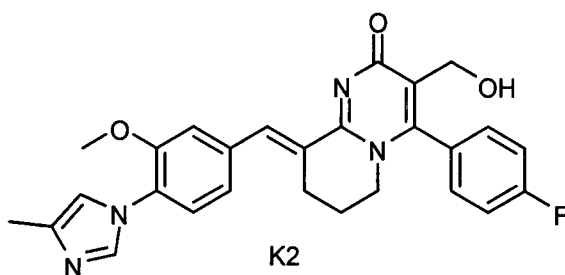


### Método K

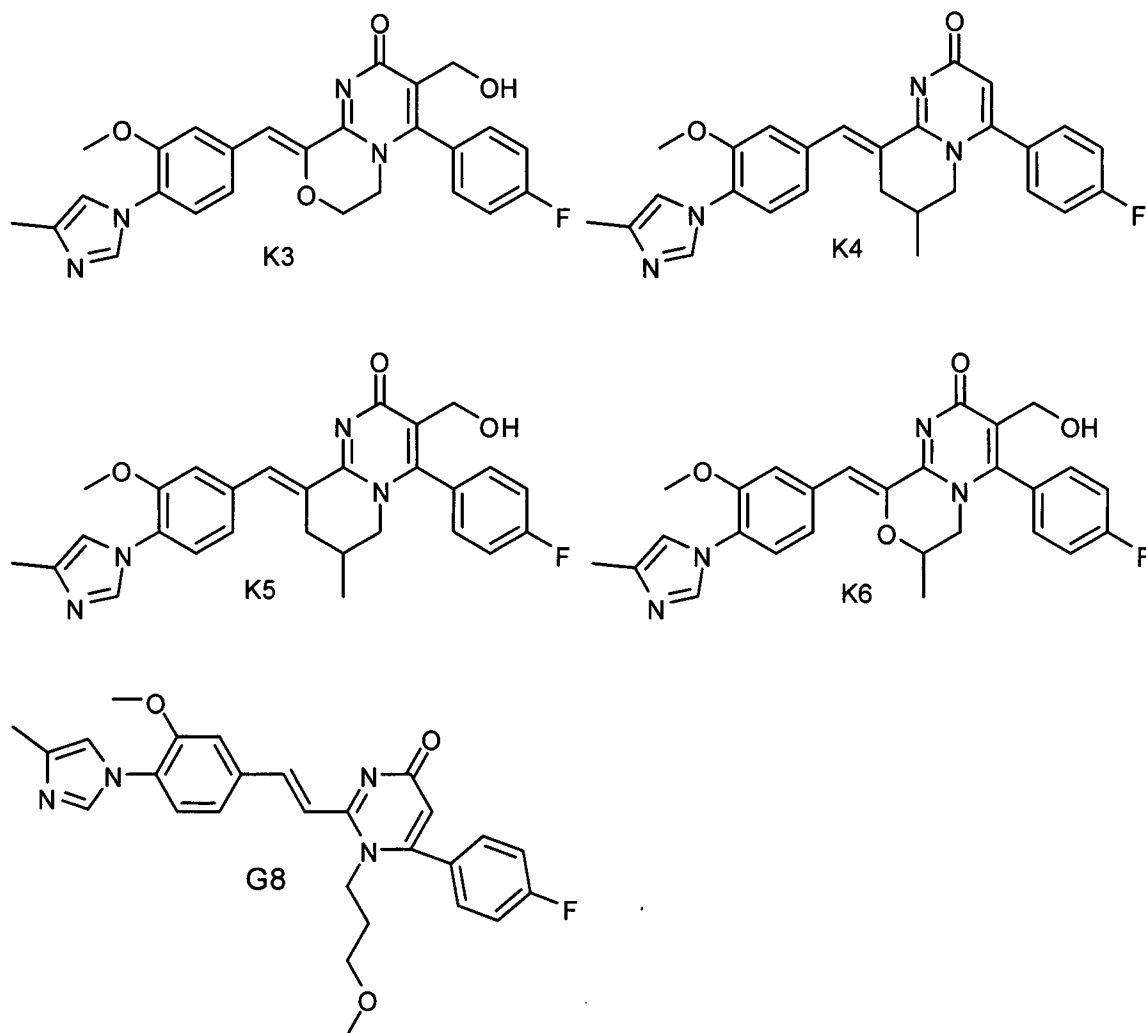
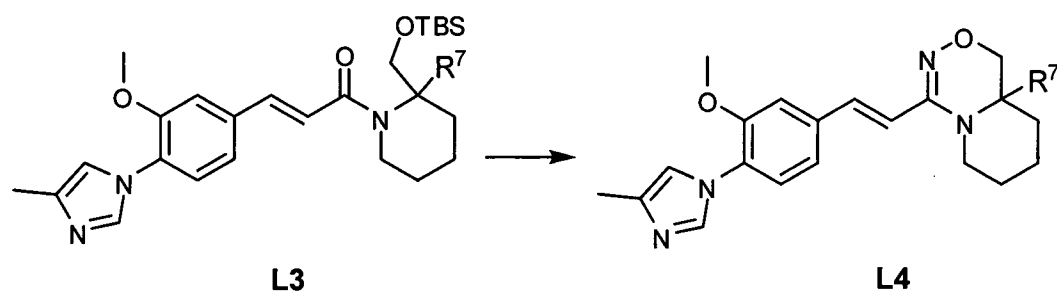
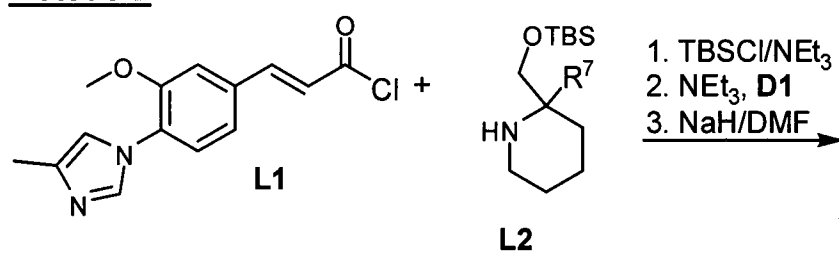


El Compuesto **I9** se trata con 1,2 eq. de LDA a  $-78^{\circ}\text{C}$  antes de hacerse reaccionar con bromuro de fenilselenio. Luego de entibiar la reacción hasta la temperatura ambiente, se trata con  $\text{H}_2\text{O}_2$  y se procesa, y se purifica para dar el compuesto **K1**.

Los siguientes compuestos se obtienen usando métodos similares al Método K:



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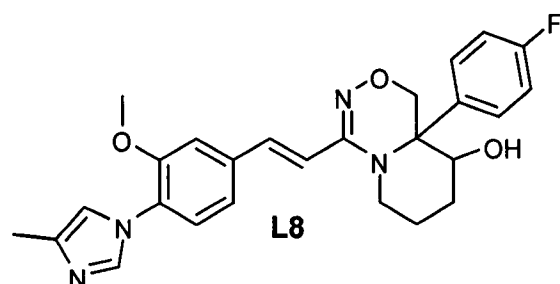
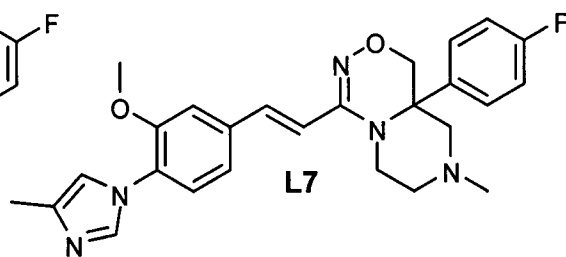
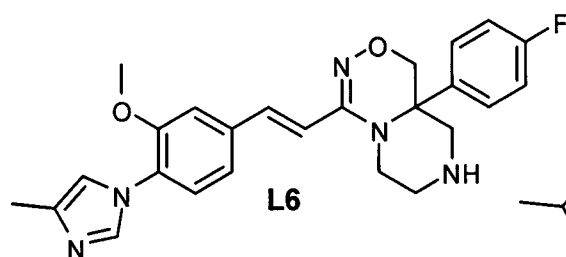
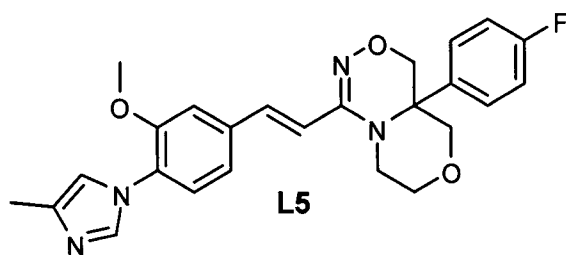
**Método L****Método L, Paso 1**

El Compuesto **L3** ( $R^7$  = p-F-Fenilo) se obtiene usando química de acoplamiento de amida de **L1** y **L2**

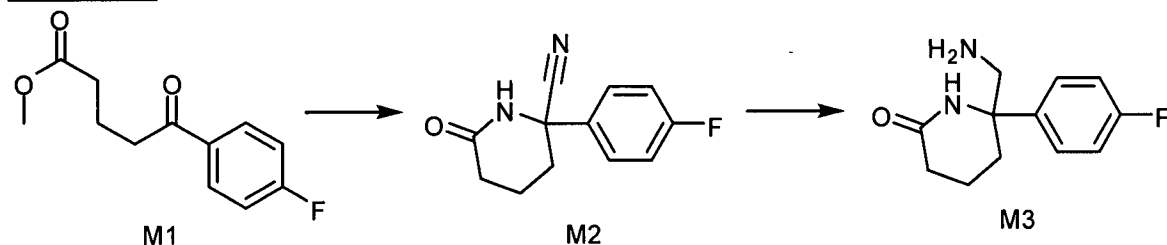
### Método L, Paso 2

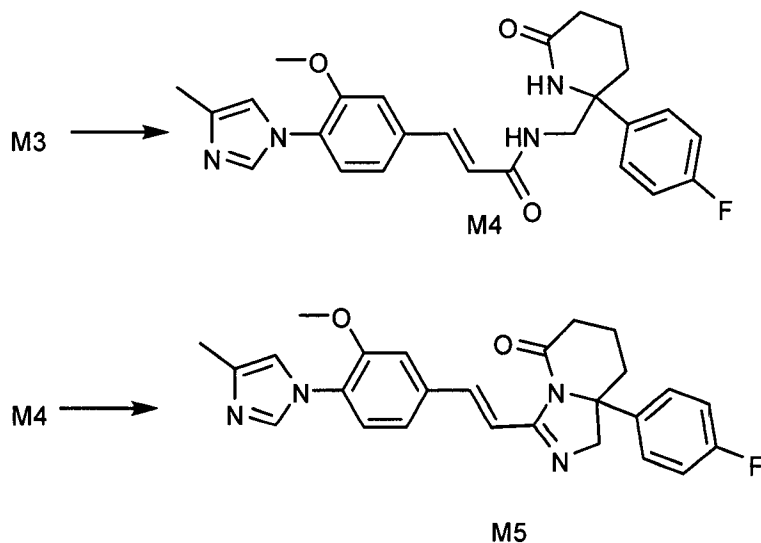
El Compuesto **L4** ( $R^7$  = p-F-Fenilo) se obtiene usando métodos similares al Método D, Pasos 2 a 5.

Los siguientes compuestos se obtienen usando métodos similares al Método L:



### Método M





### Método M, paso 1

El Compuesto **M1** se convierte en **M2** a través de síntesis de amina de Strecker haciendo reaccionar **M1** con Cianuro de Amonio en alcohol.

### Método M, Paso 2

El Compuesto **M3** se obtiene usando una hidrogenación mediada por Ni de **M2**.

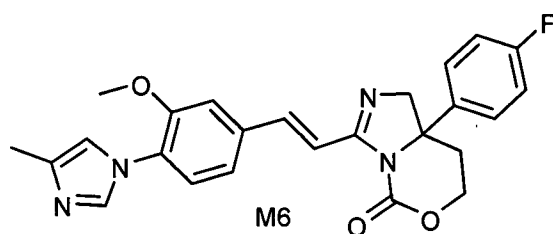
### Método M, Paso 3

El Compuesto **M4** se obtiene usando condiciones de acoplamiento de amida normales.

### Método M, Paso 4

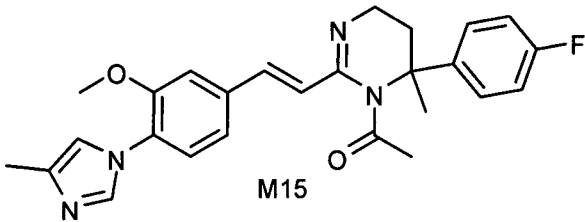
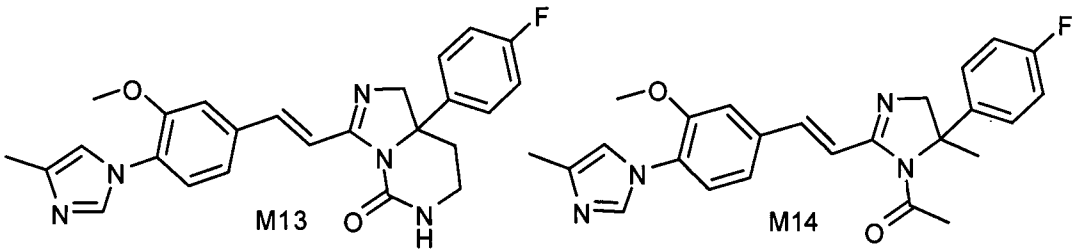
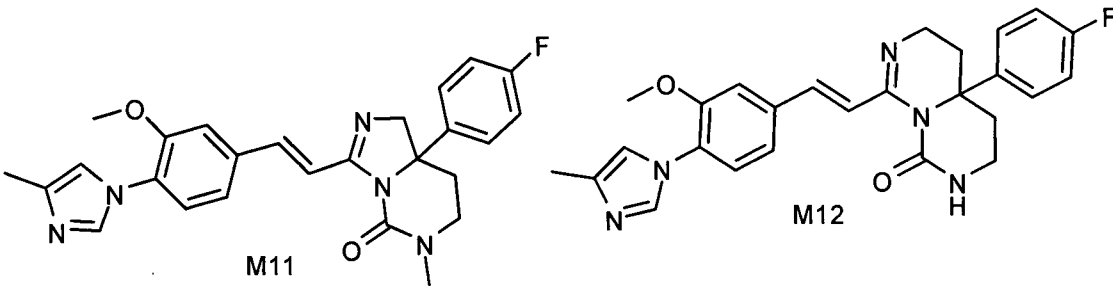
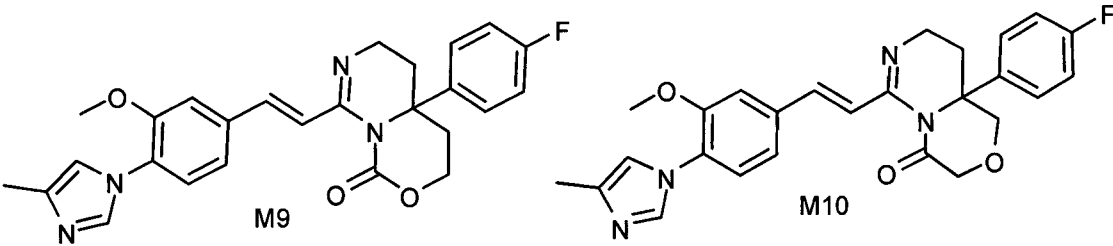
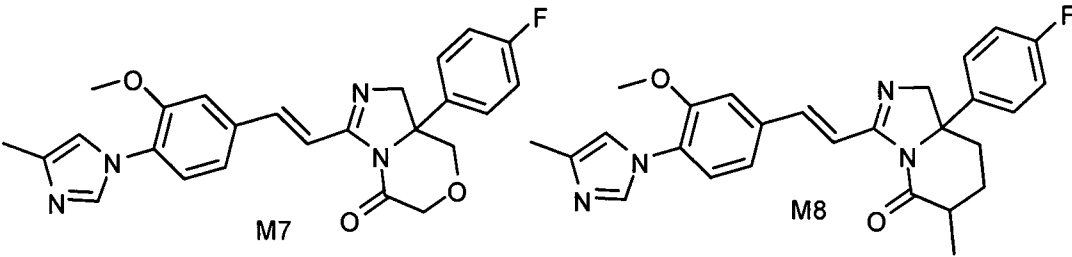
El Compuesto **M5** se obtiene a través del tratamiento de **M4** con  $\text{POCl}_3$  en tolueno a reflujo.

Los siguientes compuestos se obtendrán usando un método similar al método M.

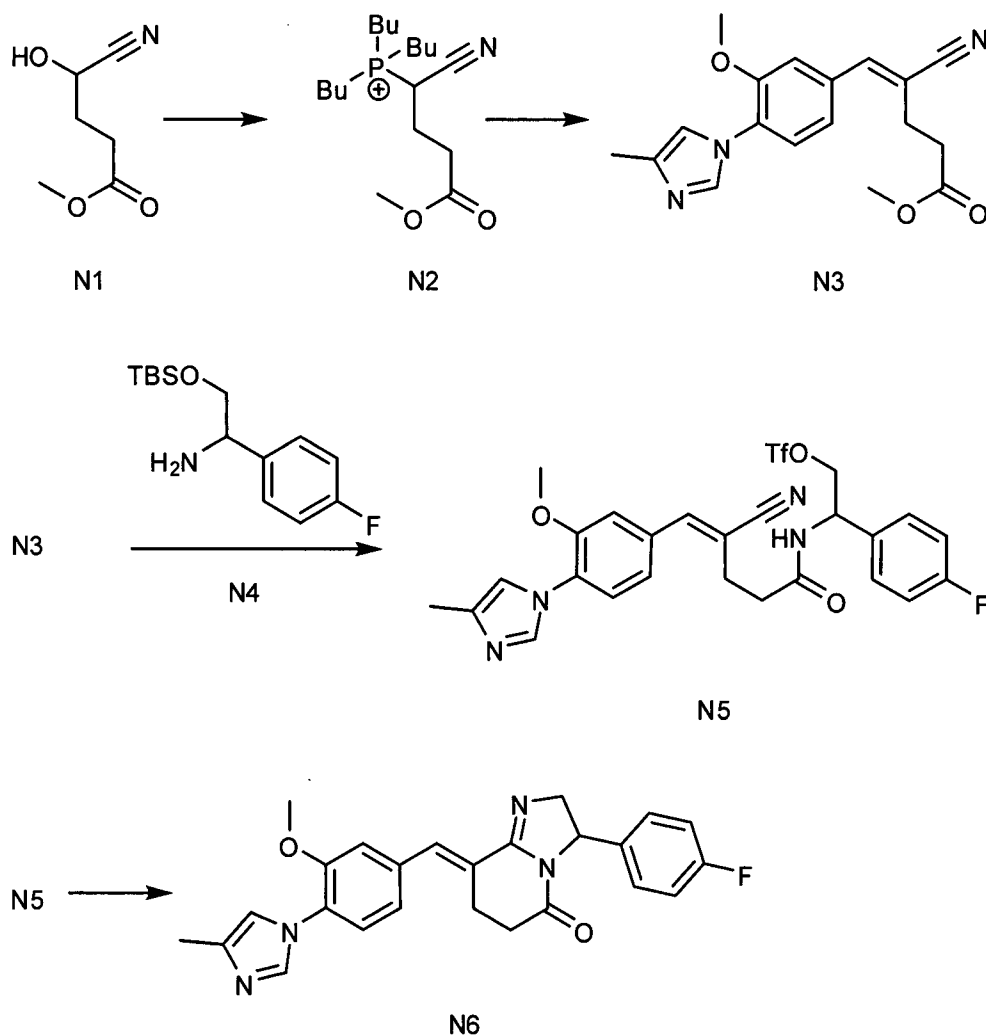




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**Método N**



### Método N, Paso 1

**N2** se obtiene a partir de **N1** luego de la generación del éster de triflato a lo que le sigue tratamiento de tributilfosfina.

### Método N, Paso 2

El Compuesto **N3** se obtiene a través de reacción de Wittig con el aldehído apropiado con **N2**

### Método N, Paso 3

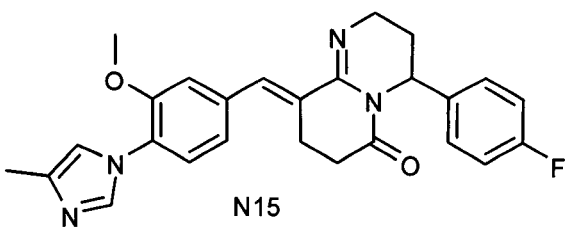
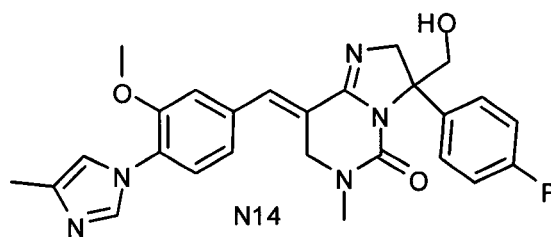
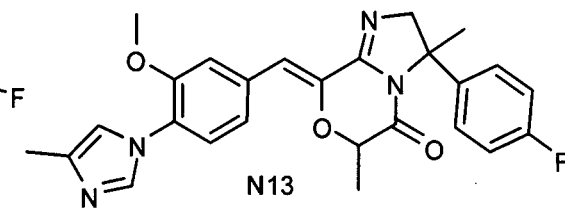
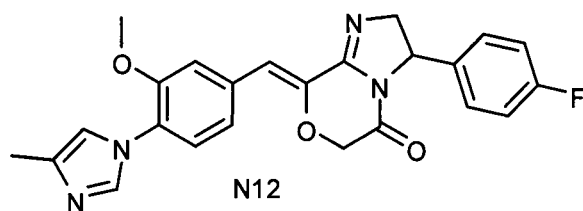
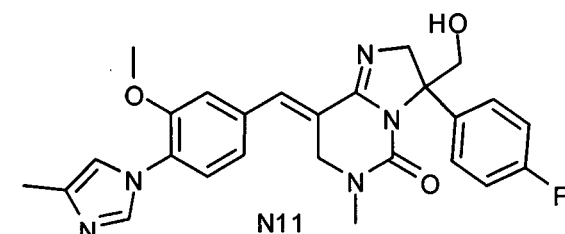
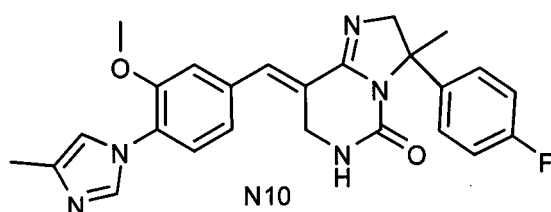
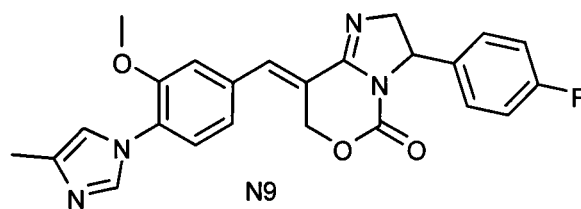
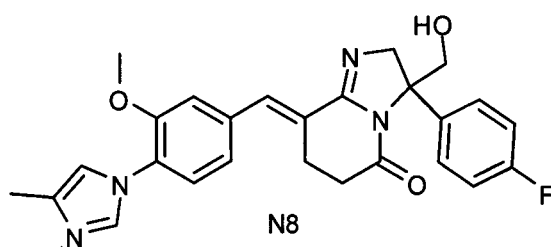
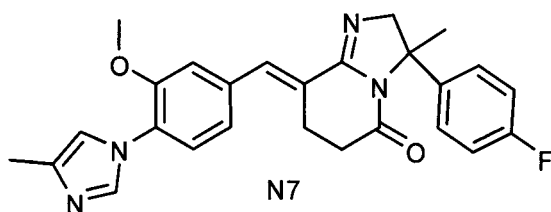
El Compuesto **N5** se obtiene a través de la hidrólisis de **N3** a su correspondiente ácido a lo que le sigue acoplamiento de amida estándar con compuesto **N4** a lo que le sigue desprotección de TBS y generación de triflato.

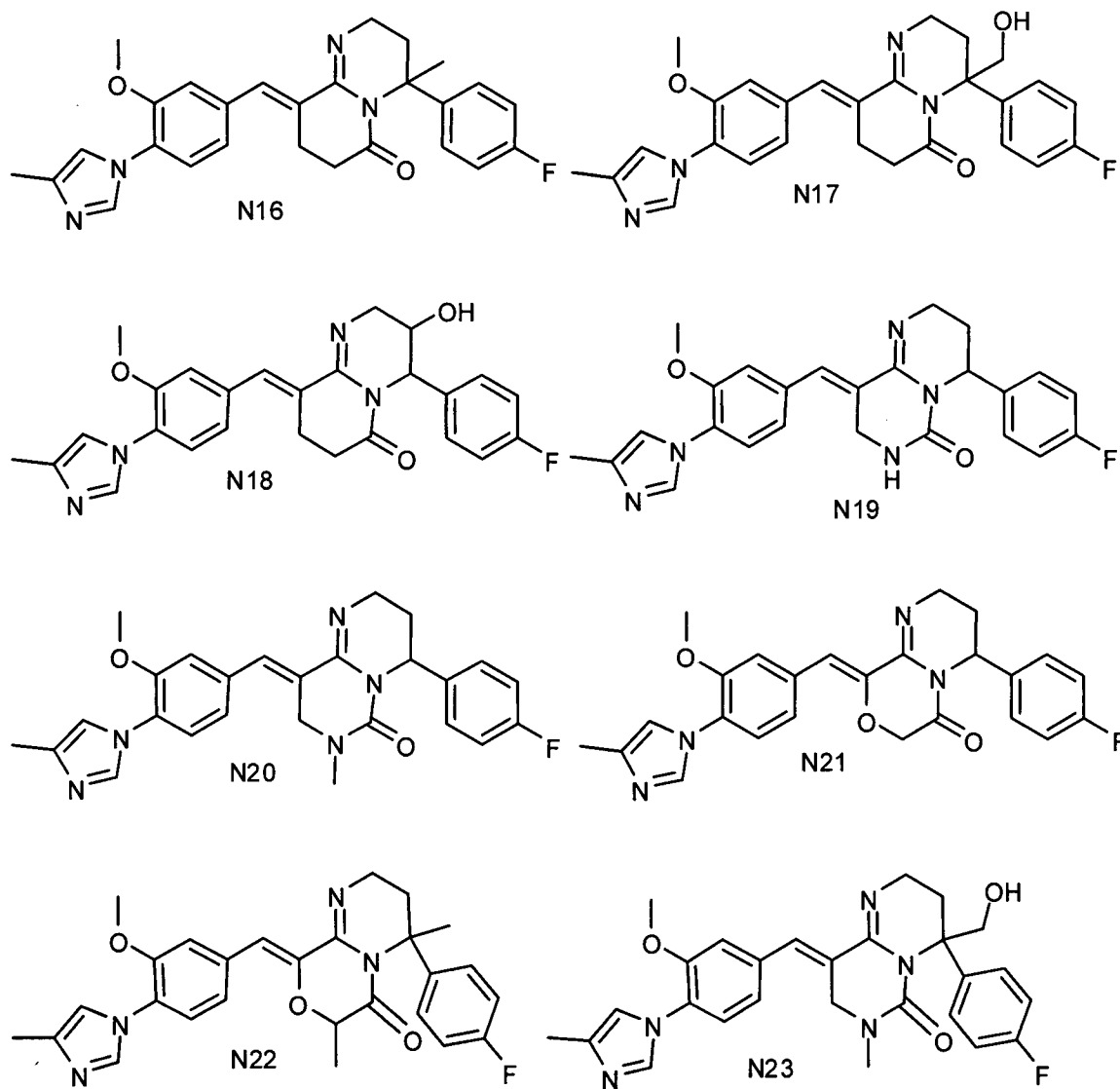
### Método N, Paso 4

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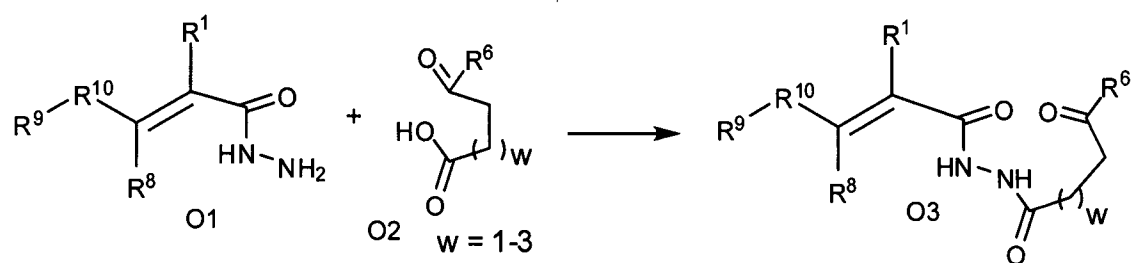
El Compuesto **N6** se obtiene usando compuesto **N5** siguiendo el tratamiento de NaH en DMF.

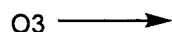
Los siguientes compuestos se obtienen usando métodos similares al Método N:





### Método O

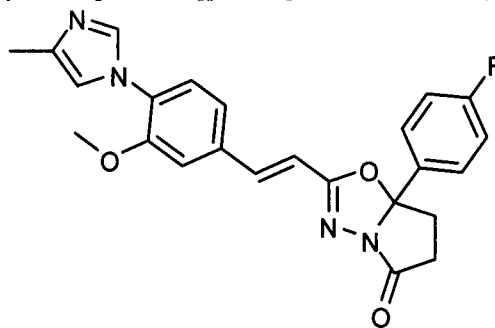
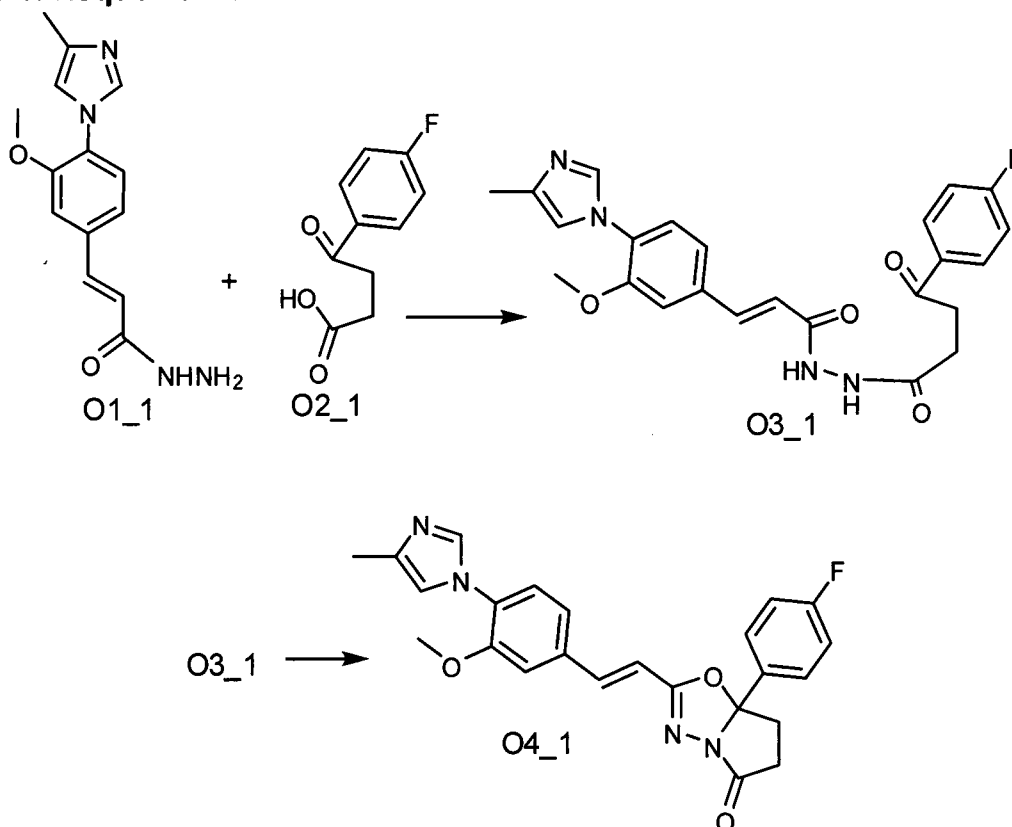




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**Ejemplo Método O**

(E)—7a—(4—fluorofenil)—2—(3—metoxi—4—(4—metil—1H—imidazol—1—il)estiril)—7,7a—dihidropirrolo[2,1—b][1,3,4]oxadiazol—5(6H)—ona

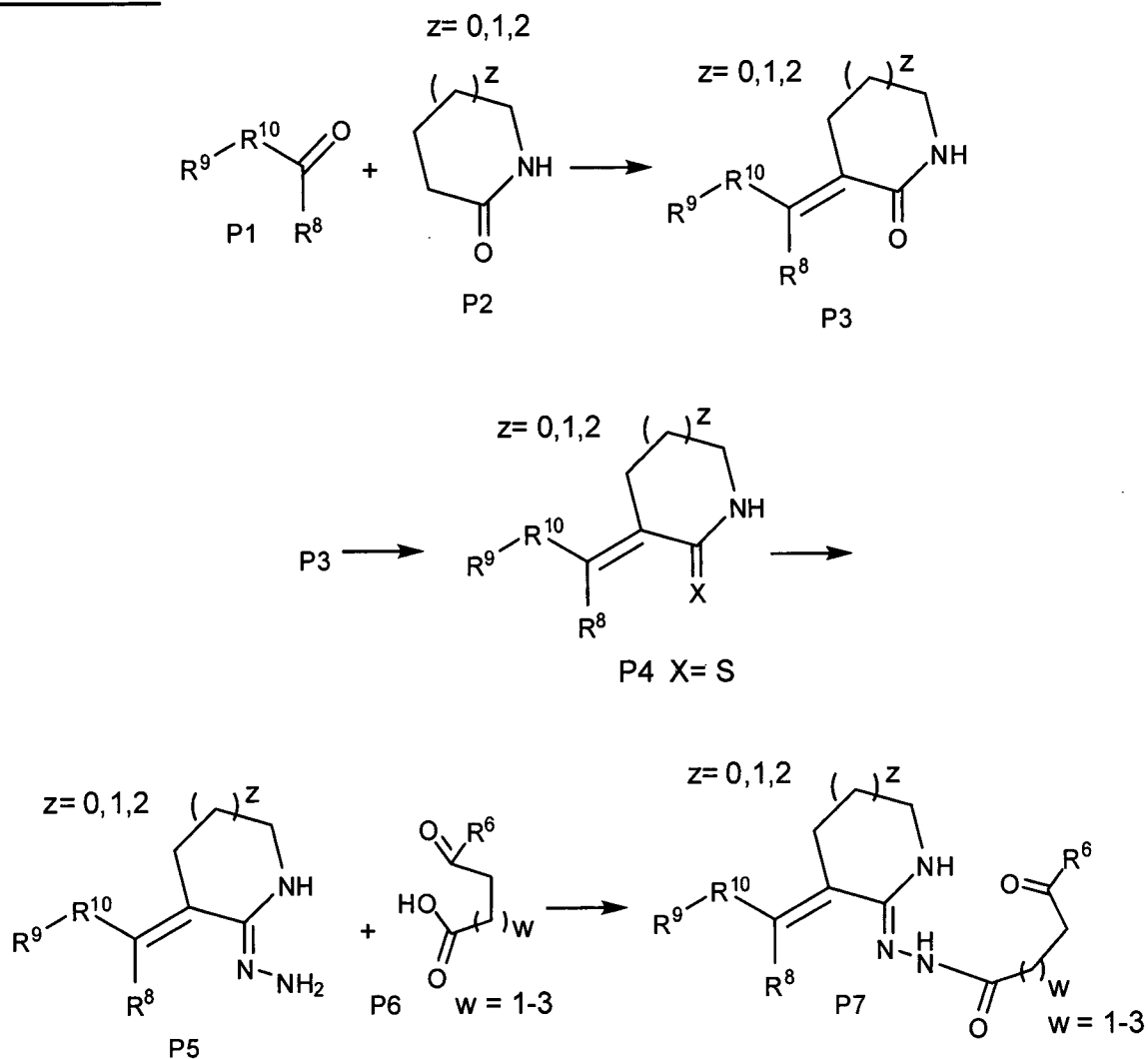
**O4\_1****Paso 1: Esquema de Reacción****Paso 1**

El Compuesto **O3\_1** se prepara por tratamiento de una solución de 1 gramo de compuesto **O1\_1** en DCM (100 ml), y 1 equivalente de DCC con 1 equivalente de compuesto conocido **O2\_1**. Luego de agitar durante 12 hrs, agregar salmuera (100 ml) y separar la fase orgánica. Evaporar esto hasta la

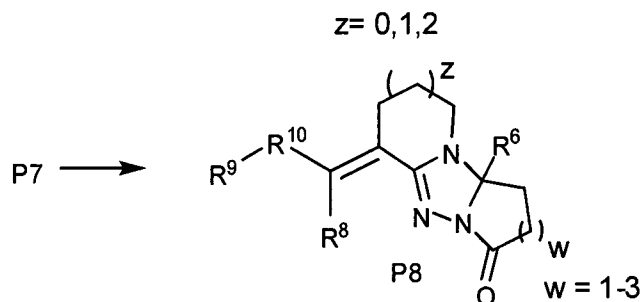
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sequedad y purificar el residuo por cromatografía flash para obtener **O3\_1**. Tratar el compuesto **O3\_1** en tolueno con TsOH (0,1 equivalentes) y calentar hasta el reflujo bajo una trampa de Dean Stark hasta la mañana siguiente. Luego de enfriar hasta la temperatura ambiente agregar solución diluida de  $\text{NaHCO}_3$  y salmuera y separar la fase orgánica. Evaporar esto hasta la sequedad y purificar el residuo por cromatografía flash para obtener el compuesto **O4\_1**.

### MÉTODO P



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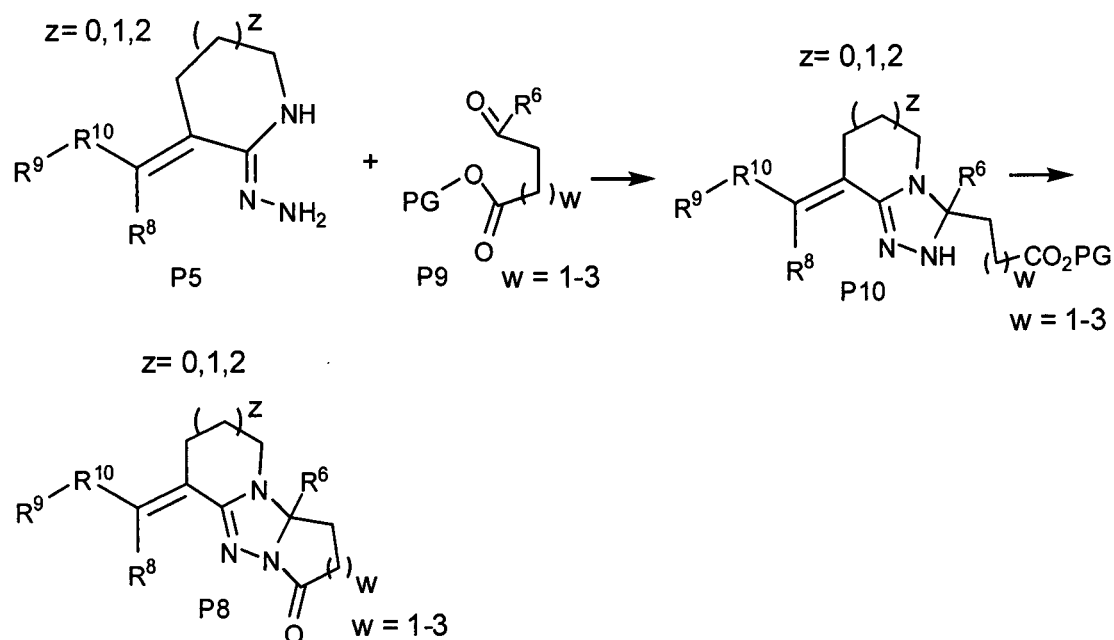


La condensación de un compuesto que contiene carbonilo tales como **P1** con las lactamas **P2** en condiciones ácidas (usando por ejemplo NaH y LDA para formar el dianión de **P2**, y luego el tratamiento con **P1**) proveerá los compuestos **P3**. La reacción de **P3** con reactivo de Lawesson proporciona las tioamidas **P4**. Estas pueden convertirse en los compuestos del tipo **P5**, por tratamiento directo con hidrazina en un solvente tal como isopropanol o tolueno. En forma alternativa, en algunos casos la reacción puede facilitarse haciendo reaccionar primero **P4** con MeI para preparar el tiometil éter como intermediario que luego se trata con hidrazina para proporcionar los compuestos del tipo **P5**. La reacción de **P5** con un ceto ácido **P6** y un agente deshidratante tal como DCC en DCM proveerá un intermediario **P7** que puede convertirse en los compuestos de fórmula **P8** luego del calentamiento adicional o el uso de un catalizador ácido tal como TsOH en tolueno a reflujo.

En forma alternativa, un Esquema de Reacción modificado brindará los compuestos de fórmula **P8**. Por ejemplo, la amina **P5** puede hacerse reaccionar con la cetona **P9** (donde PG es un grupo protector tal como un tBu, Et, TMSCH<sub>2</sub>CH<sub>2</sub>) en condiciones de deshidratación para proveer la triazina **P10**. Luego de eliminar el PG, el ácido se convierte en los compuestos de fórmula **P8** por tratamiento con DCC en DCM u otras condiciones de deshidratación.

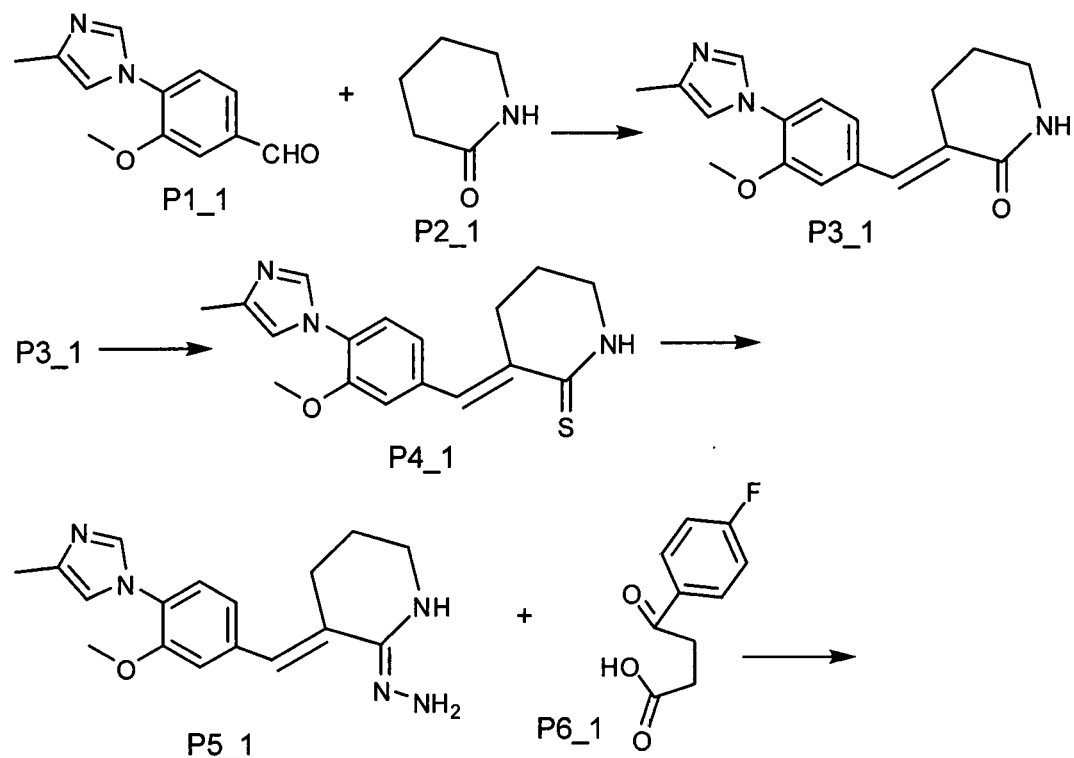


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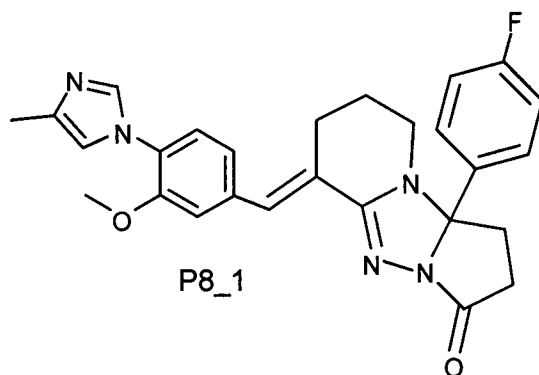


En algunos casos será beneficioso proteger el NH de las lactamas iniciales **P2** con un grupo protector tales como a p-metoxi fenilo, o tritilo. En estos casos el p-metoxi fenilo, o grupo protector tritilo puede eliminarse (por tratamiento con CAN o ácido respectivamente) de los intermediarios **P5**, **P3** o **P4** y completarse la secuencia como se indicó con anterioridad.

#### MÉTODO P EJEMPLOS



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### Paso 1

Agregar una solución de la lactama **P2\_1** (1 gramo) en THF (100 ml) a una suspensión de NaH (1,5 equivalentes) en THF a temperatura ambiente en una atmósfera inerte. Luego de agitar durante 15 minutos, enfriar la mezcla de reacción hasta  $-78^{\circ}\text{C}$  y luego agregar a esto 1 equivalente de LDA en THF con el uso de una jeringa. Dejar entibiar hasta  $0^{\circ}\text{C}$  durante 1 hr luego enfriar nuevamente esto hasta  $-78^{\circ}\text{C}$  y agregar una solución en THF del aldehído **P1\_1** con el uso de una jeringa. Dejar que la mezcla de reacción se entibie hasta la temperatura ambiente seguido de la incorporación de solución saturada de  $\text{NH}_4\text{Cl}$ . Repartir la mezcla con EtOAc, separar la fase orgánica, evaporar hasta la sequedad y purificar por cromatografía flash para proveer el compuesto **P3\_1**.

### Paso 2

Tratar 1 gramo de compuesto **P3\_1** con 1 equivalente de reactivo de Lawesson en tolueno (100 ml) a entre  $50$  y  $100^{\circ}\text{C}$  hasta la mañana siguiente. Luego de enfriar hasta la temperatura ambiente repartir con salmuera y separar la fase orgánica. Evaporar esto hasta la sequedad y purificar el residuo por cromatografía flash para obtener el intermediario **P4\_1**.

### Paso 3:

Tratar 1 gramo de compuesto **P4\_1** en DCM (100 ml) con 1 equivalente de MeI y 1 equivalente de trietilamina. Luego de 3 hrs a temperatura ambiente, concentrar hasta la sequedad y disolver nuevamente el residuo en dioxano y agregar un exceso de hidrazina. Luego de calentar durante 6 hrs a  $50^{\circ}\text{C}$  enfriar

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hasta la temperatura ambiente, evaporar hasta la sequedad y repartir el residuo entre DCM y salmuera. Separar la fase orgánica, evaporar esto hasta la sequedad y purificar el residuo por cromatografía flash para obtener el intermediario **P5\_1**.

#### **Paso 4**

El Compuesto **P8\_1** puede prepararse tratando una solución de 1 gramo de compuesto **P5\_1** en DCM (100 ml), y 1 equivalente de DCC con 1 equivalente de ácido conocido **P6\_1**. Luego de agitar durante 12 hrs, agregar salmuera (100 ml) y separar la fase orgánica. Evaporar esto hasta la sequedad y purificar el residuo por cromatografía flash para obtener el intermediario **P7\_1**. Tratar el compuesto **P7\_1** en tolueno (100 ml) con TsOH (0,1 equivalentes) y calentar hasta el reflujo bajo una trampa de Dean Stark hasta la mañana siguiente. Luego de enfriar hasta la temperatura ambiente, agregar solución diluida de  $\text{NaHCO}_3$  y salmuera y separar la fase orgánica. Evaporar esto hasta la sequedad y purificar el residuo por cromatografía flash para obtener el compuesto deseado **P8\_1**.

#### **Ensayo:**

Reacción de Secretasa y Análisis de  $\text{A}\beta$  en Células Totales: Se trataron células HEK293 que sobre-expresan APP con mutaciones Suecas y de Londres con los compuestos especificados durante 5 horas a  $37^\circ\text{C}$  en 100 ml de medio de DMEM que contiene 10% de suero fetal de bovino. Al final de la incubación, se midió el total de  $\text{A}\beta$ ,  $\text{A}\beta_{40}$  y  $\text{A}\beta_{42}$  usando inmunoensayos tipo sándwich basados en electroquimioluminiscencia (ECL). Se determinó el total de  $\text{A}\beta$  usando un par de anticuerpos TAG-W02 y biotin-4G8,  $\text{A}\beta_{40}$  se identificó con pares de anticuerpo TAG-G2-10 y biotin-4G8, mientras que  $\text{A}\beta_{42}$  se identificó con TAG-G2-11 y biotin-4G8. La señal de ECL se midió usando Sector Imager 2400 (Meso Scale Discovery).

Análisis de EM del Perfil de A $\beta$ : El perfil de A $\beta$  en medio acondicionado se determinó usando espectrometría de masa con desorción/ionización con láser potenciado en la superficie (SELDI). Se incubó el medio acondicionado con disposición PS20 ProteinChip recubierto con anticuerpo W02. Los espectros de masa de A $\beta$  capturado en la disposición se leyeron en un SELDI ProteinChip Reader (Bio-Rad) de acuerdo con las instrucciones del fabricante.

Análisis de CSF A $\beta$ : A $\beta$  en CSF de rata se determinó usando tecnología de MSD como se describió con anterioridad. Se midió A $\beta$ 40 usando el par de anticuerpos Tag-G2-10 y biotin-4G8, mientras que A $\beta$ 42 se midió usando Tag-anti A $\beta$ 42 (Meso Scale Discovery) y biotin-4G8. La señal de ECL se midió usando Sector Imager 2400 (Meso Scale Discovery).

El análisis espectrométrico de masa con desorción/ionización asistida con matriz (MALDI MS) de A $\beta$  se realiza en un espectrómetro de masa Voyager-DE STR (ABI, Framingham, MA). El instrumento se equipa con un láser de nitrógeno pulsado (337 nm). Los espectros de masa se adquieren en un modo lineal con un acelerador de voltaje de 20 kV. El espectro presentado en este trabajo representa un promedio de 256 disparos de láser. Para preparar la solución de matriz de muestra, 1  $\mu$ l de muestra de A $\beta$  inmunoprecipitada se mezcla con 3  $\mu$ l de solución saturada de ácido  $\alpha$ -ciano-4-hidroxicinámico en 0,1% de TFA/acetonitrilo. La solución muestra-matriz luego se aplica a la placa de muestra y se seca a temperatura ambiente antes del análisis de espectrometría de masa. Todos los espectros se calibran externamente con una mezcla de insulina de bovino y ACTH (18-39 clip).

El Compuesto G4 presentó un IC<sub>50</sub> de Ab42 de 1114 nM con una selectividad Abtotal/Ab42 de 11 veces.

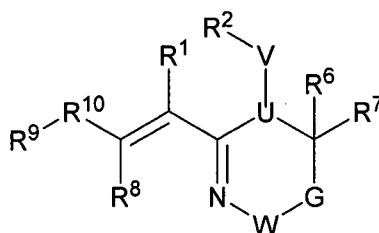
Mientras que la presente invención se ha descrito en conjunción con las realizaciones específicas que se describieron con anterioridad, muchas

alternativas, modificaciones y otras variaciones de la misma resultarán obvias para aquellas personas con experiencia en el arte. Todas dichas alternativas, modificaciones y variaciones se encuentran comprendidas dentro del espíritu y el alcance de la presente invención.

### REIVINDICACIONES

Habiendo así especialmente descrito y determinado la naturaleza de la presente invención y la forma como la misma ha de ser llevada a la práctica, se declara reivindicar como de propiedad y derecho exclusivo.

1. Un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula:



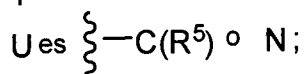
Fórmula I

en la cual:

cualquiera de (i)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (ii)  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (iii)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8

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miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (iv)  $R^6$  y cualquiera de  $R^3$  o  $R^4$  del resto  $-C(R^3)(R^4)-G$ , están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o (v)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con dicho resto heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y



W se selecciona del grupo que consiste en un enlace,  $-O-$ ,  $-C(O)-$ ,  $-S-$ ,  $-S(O)-$ ,

$-S(O_2)-$ , y  $-C(R^{11})(R^{12})-$ ;

G se selecciona del grupo que consiste en  $-C(R^3)(R^4)-$ ,  $-C(O)-$  y  $-N(R^{13})-$ , con la salvedad de que cuando W es  $-O-$  o  $-S-$ , G no es  $-N(R^{13})-$  o  $-C(O)-$ ;

V se selecciona del grupo que consiste en un enlace,  $-O-$ ,  $-C(O)-$  y  $-N(R^{14})-$ ;

$R^1$  (cuando  $R^1$  no está unido a  $R^2$ ),  $R^2$  (cuando  $R^2$  no está unido a  $R^1$  o  $R^6$ ),  $R^5$ ,  $R^6$  (cuando  $R^6$  no está unido a  $R^2$ ), y  $R^7$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

o, de manera alternativa,  $R^1$  (cuando  $R^1$  no está unido a  $R^2$ ) y  $R^8$  se toman juntos para formar un enlace;

$R^3$  se selecciona del grupo que consiste en H, halo,  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o



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estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; o

$R^3$  y  $R^6$  tomados juntos forman un enlace, siempre que cuando  $R^3$  y  $R^6$  forman un enlace: (1) W no es un enlace, (2)  $R^2$  y  $R^6$  no se unen para formar un resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo (como se describió en los puntos (ii) y (iii) anteriores) (3)  $R^6$  y cualquiera de  $R^3$  o  $R^4$  del resto  $-C(R^3)(R^4)-G$  no se unen para formar un resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo (como se describió en el punto (iv) más arriba), y (4)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$  no se unen para formar un resto heterociclilo o heterociclenilo (como se describió en el punto (v) más arriba);

$R^4$ ,  $R^{11}$  y  $R^{12}$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, halo,  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

siempre que cuando uno de  $R^3$  o  $R^4$  se selecciona del grupo que consiste en:

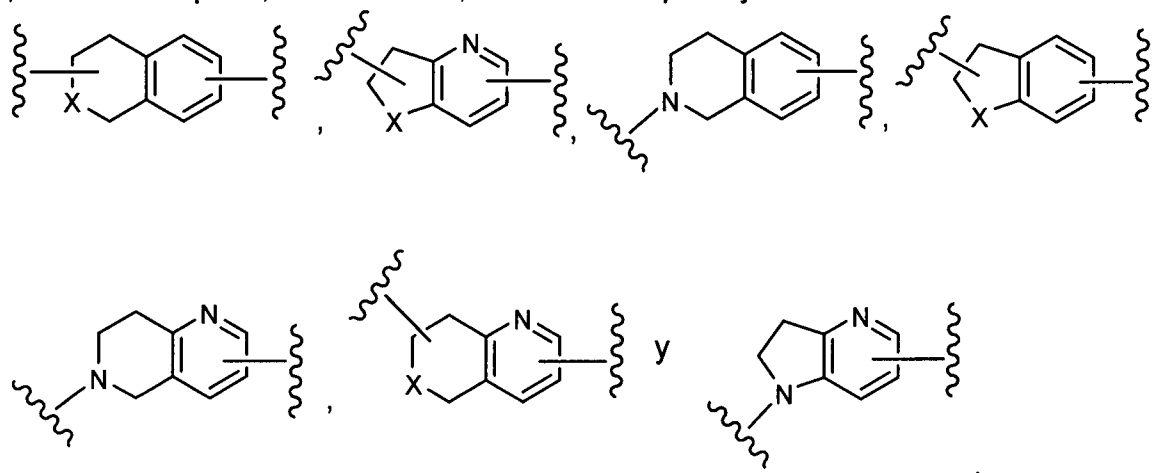
$-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ ;

siempre que cuando uno de  $R^{11}$  o  $R^{12}$  se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ ;

$R^{13}$  se selecciona en forma independiente del grupo que consiste en H, alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo-, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo,

arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-,  
 arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-,  
 arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo,  
 cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-,  
 heterocicloalquenilarilo-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  
 $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  y  $-N(R^8)_2$ ;  
 y donde dichos grupos  $R^{13}$  alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-,  
 heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-,  
 arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo,  
 arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo, arilheterocicloalquilo-,  
 heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo,  
 arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-,  
 arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-,  
 arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo,  
 cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, y  
 heterocicloalquenilarilo- están sustituidos en forma opcional con 1 a 5 grupos  
 seleccionados en forma independiente del grupo que consiste en: alquilo,  
 alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterocicilo,  
 heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo,  $-CN$ ,  
 $-OR^{15}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-SR^{15}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  
 $-CH(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ ,  
 $-P(O)(OR^{15})(OR^{16})$ ,  $-N(R^{15})(R^{16})$ ,  $-alquil-N(R^{15})(R^{16})$ ,  $-N(R^{15})C(O)R^{16}$ ,  
 $-CH_2-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-R^{15}$ ,  $-CH_2N(R^{15})(R^{16})$ ,  
 $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-CH_2-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)OR^{16}$ ,  $-CH_2-N(R^{15})C(O)OR^{16}$ ,  $-S(O)R^{15}$ ,  $=NOR^{15}$ ,  $-N_3$ ,  $-NO_2$  y  
 $-S(O)_2R^{15}$ ;

R<sup>10</sup> se selecciona del grupo que consiste en un enlace, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo-, heterociclilalquilo- y los restos:



en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-,



heterociclilo- heterocicilalquilo- para  $R^{10}$  como también los restos mencionados anteriormente para  $R^{10}$  puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y

$R^9$  se selecciona del grupo que consiste en alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

$R^{15}$ ,  $R^{16}$  y  $R^{17}$  se seleccionan de manera independiente del grupo que consiste en H, alquilo, alqueno, alquino, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, arilcicloalquilo-, arilheterociclilo-,  $R^{18}$ -alquilo,  $R^{18}$ -cicloalquilo,  $R^{18}$ -cicloalquilalquilo-,  $R^{18}$ -heterociclilo,  $R^{18}$ -heterocicilalquilo-,  $R^{18}$ -arilo,  $R^{18}$ -arilalquilo-,  $R^{18}$ -heteroarilo y  $R^{18}$ -heteroarilalquilo-;

$R^{18}$  es de 1-5 sustituyentes seleccionados en forma independiente del grupo que consiste en alquilo, alqueno, alquino, arilo, arilalquilo-, arilalqueno-, arilalquino-,  $-\text{NO}_2$ , halo, heteroarilo, HO-alquioxialquilo-,  $-\text{CF}_3$ ,  $-\text{CN}$ , alquil-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alquil})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{heteroarilo})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{NH}(\text{arilo})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterociclilo})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,

-O-heterociclilo, -O-cicloalquilalquilo, -O-heterociclilalquilo,  $\text{-NH}_2$ ,  $\text{-NHR}^{20}$ ,  
 $\text{-N(alquil)}_2$ ,  $\text{-N(arilalquil)}_2$ ,  $\text{-N(arilalquil)-(heteroarilalquilo)}$ ,  $\text{-NHC(O)R}^{20}$ ,  
 $\text{-NHC(O)NH}_2$ ,  $\text{-NHC(O)NH(alquilo)}$ ,  $\text{-NHC(O)N(alquil)(alquilo)}$ ,  
 $\text{-N(alquil)C(O)NH(alquilo)}$ ,  $\text{-N(alquil)C(O)N(alquil)(alquilo)}$ ,  $\text{-NHS(O)}_2\text{R}^{20}$ ,  
 $\text{-NHS(O)}_2\text{NH(alquilo)}$ ,  $\text{-NHS(O)}_2\text{N(alquil)(alquilo)}$ ,  $\text{-N(alquil)S(O)}_2\text{NH(alquilo)}$  y  
 $\text{-N(alquil)S(O)}_2\text{N(alquil)(alquilo)}$ ;

o, en forma alternativa, dos restos  $\text{R}^{18}$  en los carbonos adyacentes pueden

ligarse para formar:

$\text{R}^{19}$  es alquilo, cicloalquilo, arilo, arilalquilo- o heteroarilalquilo-;

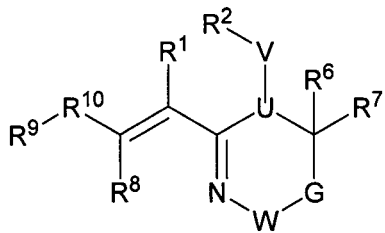
$\text{R}^{20}$  es alquilo, cicloalquilo, arilo, arilo sustituido por halo, arilalquilo-, heteroarilo o heteroarilalquilo-;

donde cada uno de los grupos alquilo, cicloalquilo, cicloalquenilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, alquilarilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^1\text{-R}^2$ ,  $\text{R}^2\text{-R}^6$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ ,  $\text{R}^8$ ,  $\text{R}^9$ ,  $\text{R}^{10}$ ,  $\text{R}^{11}$ ,  $\text{R}^{12}$  y  $\text{R}^{14}$  está no sustituido o sustituido en forma opcional e independiente por 1 a 5 grupos  $\text{R}^{21}$  seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo,  $\text{-CN}$ ,  $\text{-OR}^{15}$ ,  $\text{-C(O)R}^{15}$ ,  $\text{-C(O)OR}^{15}$ ,  $\text{-C(O)N(R}^{15})(\text{R}^{16})$ ,  $\text{-SR}^{15}$ ,  $\text{-S(O)N(R}^{15})(\text{R}^{16})$ ,  $\text{-CH(R}^{15})(\text{R}^{16})$ ,  $\text{-S(O)}_2\text{N(R}^{15})(\text{R}^{16})$ ,  $\text{-C(=NOR}^{15})\text{R}^{16}$ ,  $\text{-P(O)(OR}^{15})(\text{OR}^{16})$ ,  $\text{-N(R}^{15})(\text{R}^{16})$ ,  $\text{-alquil-N(R}^{15})(\text{R}^{16})$ ,  $\text{-N(R}^{15})\text{C(O)R}^{16}$ ,  $\text{-CH}_2\text{-N(R}^{15})\text{C(O)R}^{16}$ ,  $\text{-CH}_2\text{-N(R}^{15})\text{C(O)N(R}^{16})(\text{R}^{17})$ ,  $\text{-CH}_2\text{-R}^{15}$ ,  $\text{-CH}_2\text{N(R}^{15})(\text{R}^{16})$ ,  $\text{-N(R}^{15})\text{S(O)R}^{16}$ ,  $\text{-N(R}^{15})\text{S(O)}_2\text{R}^{16}$ ,  $\text{-CH}_2\text{-N(R}^{15})\text{S(O)}_2\text{R}^{16}$ ,  $\text{-N(R}^{15})\text{S(O)}_2\text{N(R}^{16})(\text{R}^{17})$ ,  $\text{-N(R}^{15})\text{S(O)N(R}^{16})(\text{R}^{17})$ ,  $\text{-N(R}^{15})\text{C(O)N(R}^{16})(\text{R}^{17})$ ,  $\text{-CH}_2\text{-N(R}^{15})\text{C(O)N(R}^{16})(\text{R}^{17})$ ,  $\text{-N(R}^{15})\text{C(O)OR}^{16}$ ,  $\text{-CH}_2\text{-N(R}^{15})\text{C(O)OR}^{16}$ ,  $\text{-S(O)R}^{15}$ ,  $\text{=NOR}^{15}$ ,  $\text{-N}_3$ ,  $\text{-NO}_2$  y  $\text{-S(O)}_2\text{R}^{15}$ ;

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donde cada uno de los grupos alquilo, cicloalquenilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en  $R^{21}$  está en forma independiente no sustituido o sustituido por 1 a 5 grupos  $R^{22}$  seleccionados en forma independiente del grupo que consiste en alquilo, cicloalquilo, cicloalquenilo, heterociclilo, arilo, heteroarilo, halo,  $-CF_3$ ,  $-CN$ ,  $-OR^{15}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-alquil-C(O)OR^{15}$ ,  $C(O)N(R^{15})(R^{16})$ ,  $-SR^{15}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-C(=NOR^{15})R^{16}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $-N(R^{15})(R^{16})$ ,  $-alquil-N(R^{15})(R^{16})$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-CH_2-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-CH_2-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-CH_2-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-CH_2-N(R^{15})C(O)OR^{16}$ ,  $-N_3$ ,  $=NOR^{15}$ ,  $-NO_2$ ,  $-S(O)R^{15}$  y  $-S(O)_2R^{15}$ .

2. Un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula:



en la cual:

$R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

U es  $\begin{matrix} \diagup \\ \diagdown \end{matrix} -C(R^5) \circ N$ ;

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W se selecciona del grupo que consiste en un enlace, -O-, -C(O)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, y -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G es -C(R<sup>3</sup>)(R<sup>4</sup>)-; -C(O)- y -N(R<sup>13</sup>)-; con la salvedad de que cuando W es -O- o -S-, G no es -N(R<sup>13</sup>)- o -C(O)- ;

V se selecciona del grupo que consiste en un enlace, -O-, -C(O)- y -N(R<sup>14</sup>)-;

R<sup>5</sup>, R<sup>6</sup>, y R<sup>7</sup> pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alqueno-, alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

R<sup>3</sup> se selecciona del grupo que consiste en H, halo, -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alquilo-, alqueno-, alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma



independiente del grupo que consiste en los restos que se muestran más adelante; o

$R^3$  y  $R^6$  tomados juntos forman un enlace, siempre que cuando  $R^3$  y  $R^6$  forman un enlace W no es un enlace;

$R^4$ ,  $R^{11}$  y  $R^{12}$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, halo,  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

siempre que cuando uno de  $R^3$  o  $R^4$  se selecciona del grupo que consiste en:

$-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,

$-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , y  $-N_3$ ;

siempre que cuando uno de  $R^{11}$  o  $R^{12}$  se selecciona del grupo que consiste  
 en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  
 $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  
 $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se  
 selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , y  $-N_3$ ;

$R^{13}$  se selecciona en forma independiente del grupo que consiste en H,  
 alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-,  
 arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-,  
 heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-,  
 heteroarilcicloalquilo-, heterocicloalquilo, arilheterocicloalquilo-,  
 heteroarilheterocicloalquilo-, alquenilo, arilalquenilo, cicloalquenilo,  
 arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-,  
 arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-,  
 arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo,  
 cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-,  
 heterocicloalquenilarilo-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  
 $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  y  
 $-N(R^8)_2$ ; y donde dichos grupos  $R^{13}$  alquilo, arilalquilo-, heteroarilalquilo-,  
 cicloalquilalquilo-, heterocicloalquilalquilo-, arilcicloalquilalquilo-,

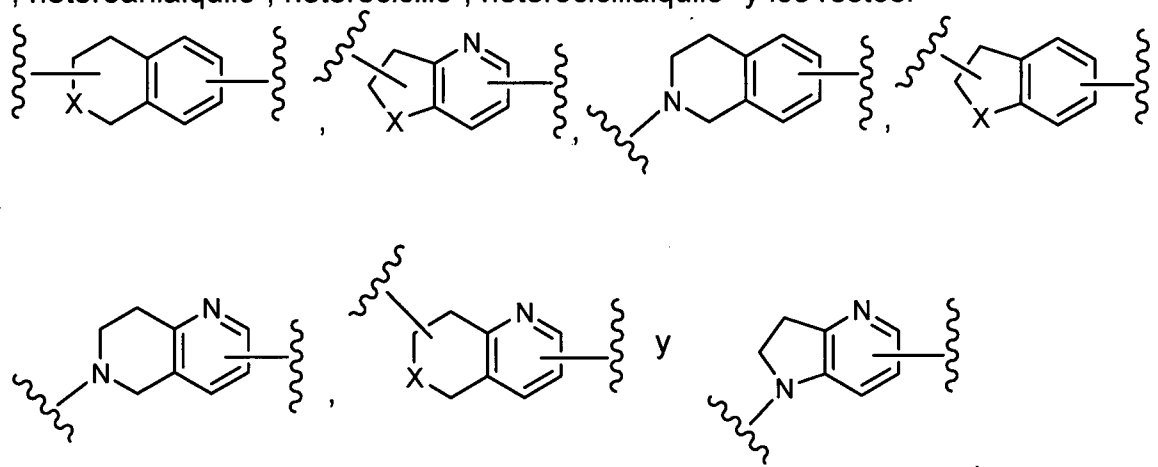
heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-,  
heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-,  
heteroarilcicloalquilo-, heterocicloalquilo, arilheterocicloalquilo-,  
heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo,  
arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo,  
arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-,  
arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo,  
cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, y  
heterocicloalquenilarilo- están sustituidos en forma opcional con 1 a 5 grupos  
seleccionados en forma independiente del grupo que consiste en: alquilo,  
alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo,  
heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo, -CN,  
-OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>),  
-CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>),  
-N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>,  
-CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>; -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>),  
-N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y  
-S(O)<sub>2</sub>R<sup>15</sup>;

R<sup>14</sup> se selecciona del grupo que consiste en H, alquilo, alquenilo, alquinilo,  
cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-,  
arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>,  
-C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, y  
-P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);

R<sup>8</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-,  
arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-,

heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, con cada uno de dicho alquilo-, alquenoilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- que no está sustituido o está sustituido en forma independiente y opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

$R^{10}$  se selecciona del grupo que consiste en un enlace, alquilo-, alquenoilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo-, heterociclilalquilo- y los restos:



donde X es O,  $N(R^{14})$  o S;

en los cuales cada uno de dicho alquilo-, alquenoilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- heterociclilalquilo- para  $R^{10}$  como también los restos mencionados anteriormente para  $R^{10}$  puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y

$R^9$  se selecciona del grupo que consiste en alquilo-, alquenoilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-,

heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

$R^{15}$ ,  $R^{16}$  y  $R^{17}$  se seleccionan de manera independiente del grupo que consiste en H, alquilo, alqueno, alquino, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, arilcicloalquilo-, arilheterociclilo-,  $R^{18}$ -alquilo,  $R^{18}$ -cicloalquilo,  $R^{18}$ -cicloalquilalquilo-,  $R^{18}$ -heterociclilo,  $R^{18}$ -heterociclilalquilo-,  $R^{18}$ -arilo,  $R^{18}$ -arilalquilo,  $R^{18}$ -heteroarilo y  $R^{18}$ -heteroarilalquilo-;

$R^{18}$  es de 1-5 sustituyentes seleccionados en forma independiente del grupo que consiste en alquilo, alqueno, alquino, arilo, arilalquilo-, arilalqueno-, arilalquino-,  $-\text{NO}_2$ , halo, heteroarilo, HO-alquioxialquilo-,  $-\text{CF}_3$ ,  $-\text{CN}$ , alquil-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alquil})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{heteroarilo})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{NH}(\text{arilo})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterociclilo})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  $-\text{O-heterociclilo}$ ,  $-\text{O-cicloalquilalquilo}$ ,  $-\text{O-heterociclilalquilo}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alquil})_2$ ,  $-\text{N}(\text{arilalquil})_2$ ,  $-\text{N}(\text{arilalquil})-(\text{heteroarilalquilo})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alquilo})$ ,

-NHS(O)<sub>2</sub>N(alquil)(alquilo), -N(alquil)S(O)<sub>2</sub>NH(alquilo) y  
-N(alquil)S(O)<sub>2</sub>N(alquil)(alquilo);

o, en forma alternativa, dos restos R<sup>18</sup> en los carbonos adyacentes pueden

ligarse para formar:

R<sup>19</sup> es alquilo, cicloalquilo, arilo, arilalquilo o heteroarilalquilo;

R<sup>20</sup> es alquilo, cicloalquilo, arilo, arilo sustituido por halo, arilalquilo, heteroarilo o heteroarilalquilo;

donde cada uno de los grupos alquilo, cicloalquilo, cicloalquenilo, cicloalquilalquilo-, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, alquilarilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en R<sup>1</sup>-R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> y R<sup>14</sup> está no sustituido o sustituido en forma opcional e independiente por 1 a 5 grupos R<sup>21</sup> seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>;

donde cada uno de los grupos alquilo, cicloalquenilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en R<sup>21</sup> está en forma independiente no sustituido o sustituido por 1 a 5 grupos R<sup>22</sup> seleccionados en forma independiente


$$Ues \begin{Bmatrix} \\ \\ \end{Bmatrix} -C(R^5) \circ N;$$

G es  $-C(R^3)(R^4)-$ ;  $-C(O)-$  y  $-N(R^{13})-$ ; con la salvedad de que cuando W es  $-S-$ , G no es  $-N(R^{13})-$  o  $-C(O)-$ ;

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V se selecciona del grupo que consiste en un enlace, -O-, -C(O)- y -N(R<sup>14</sup>)-;

R<sup>1</sup> (cuando R<sup>1</sup> no está unido a R<sup>2</sup>), R<sup>5</sup>, R<sup>6</sup> (cuando R<sup>6</sup> no está unido a R<sup>2</sup>), y R<sup>7</sup> pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

o, de manera alternativa, R<sup>1</sup> (cuando R<sup>1</sup> no está unido a R<sup>2</sup>) y R<sup>8</sup> se toman juntos para formar un enlace;

R<sup>3</sup> se selecciona del grupo que consiste en H, halo, -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma



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independiente del grupo que consiste en los restos que se muestran más adelante;

$R^4$ ,  $R^{11}$  y  $R^{12}$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, halo,  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

siempre que cuando uno de  $R^3$  o  $R^4$  se selecciona del grupo que consiste en:

$-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,

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$-\text{S}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})\text{R}^{15}$ ,  $-\text{S}(\text{O})_2\text{R}^{15}$ ,  $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ,  $=\text{NOR}^{15}$ , y  $-\text{N}_3$ ;

siempre que cuando uno de  $\text{R}^{11}$  o  $\text{R}^{12}$  se selecciona del grupo que consiste en:  $-\text{OR}^{15}$ ,  $-\text{CN}$ ,  $-\text{SR}^{15}$ ,  $-\text{NR}^{15}\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{OR}^{16}$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})\text{R}^{15}$ ,  $-\text{S}(\text{O})_2\text{R}^{15}$ ,  $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ,  $=\text{NOR}^{15}$ , y  $-\text{N}_3$ , entonces el otro no se selecciona del grupo que consiste en:  $-\text{OR}^{15}$ ,  $-\text{CN}$ ,  $-\text{SR}^{15}$ ,  $-\text{NR}^{15}\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{R}^{16}$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})_2\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{N}(\text{R}^{15})\text{S}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{N}(\text{R}^{16})(\text{R}^{17})$ ,  $-\text{N}(\text{R}^{15})\text{C}(\text{O})\text{OR}^{16}$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{15})(\text{R}^{16})$ ,  $-\text{S}(\text{O})\text{R}^{15}$ ,  $-\text{S}(\text{O})_2\text{R}^{15}$ ,  $-\text{P}(\text{O})(\text{OR}^{15})(\text{OR}^{16})$ ,  $=\text{NOR}^{15}$ , y  $-\text{N}_3$ ;

$\text{R}^{13}$  se selecciona en forma independiente del grupo que consiste en H, alquilo, arilalquilo, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo, arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo, arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-, arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo, heterocicloalquenilarilo-,  $-\text{OR}^{15}$ ,  $-\text{CN}$ ,  $-\text{C}(\text{O})\text{R}^8$ ,  $-\text{C}(\text{O})\text{OR}^9$ ,  $-\text{S}(\text{O})\text{R}^{10}$ ,  $-\text{S}(\text{O})_2\text{R}^{10}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{11})(\text{R}^{12})$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{11})(\text{R}^{12})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{11})(\text{R}^{12})$ ,  $-\text{NO}_2$ ,  $-\text{N}=\text{C}(\text{R}^8)_2$  y  $-\text{N}(\text{R}^8)_2$ ; y donde dichos grupos  $\text{R}^{13}$  alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo, arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo, arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-, arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo, heterocicloalquenilarilo-,  $-\text{OR}^{15}$ ,  $-\text{CN}$ ,  $-\text{C}(\text{O})\text{R}^8$ ,  $-\text{C}(\text{O})\text{OR}^9$ ,  $-\text{S}(\text{O})\text{R}^{10}$ ,  $-\text{S}(\text{O})_2\text{R}^{10}$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{11})(\text{R}^{12})$ ,  $-\text{S}(\text{O})\text{N}(\text{R}^{11})(\text{R}^{12})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{R}^{11})(\text{R}^{12})$ ,  $-\text{NO}_2$ ,  $-\text{N}=\text{C}(\text{R}^8)_2$  y  $-\text{N}(\text{R}^8)_2$ ;

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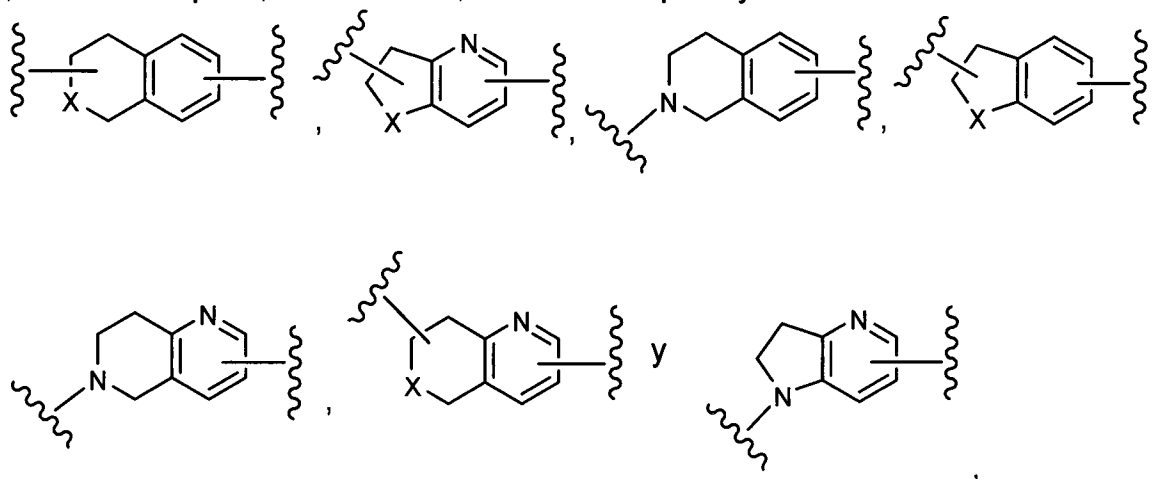
heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo, arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo, arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo, arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, y heterocicloalquenilarilo- están sustituidos en forma opcional con 1 a 5 grupos seleccionados en forma independiente del grupo que consiste en: alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>; -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>;

R<sup>14</sup> se selecciona del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, y -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);

R<sup>8</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-,

heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, con cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- que no está sustituido o está sustituido en forma independiente y opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

$R^{10}$  se selecciona del grupo que consiste en un enlace, alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo-, heterociclilalquilo- y los restos:



donde X es O,  $N(R^{14})$  o S;

en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- heterociclilalquilo- para  $R^{10}$  como también los restos mencionados anteriormente para  $R^{10}$  puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y

$R^9$  se selecciona del grupo que consiste en alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-,

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heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

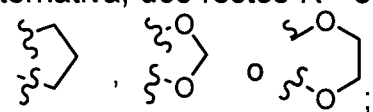
$R^{15}$ ,  $R^{16}$  y  $R^{17}$  se seleccionan de manera independiente del grupo que consiste en H, alquilo, alqueno, alquinilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, arilcicloalquilo, arilheterociclilo-,  $R^{18}$ -alquilo-,  $R^{18}$ -cicloalquilo-,  $R^{18}$ -cicloalquilalquilo-,  $R^{18}$ -heterociclilo-,  $R^{18}$ -heterociclilalquilo-,  $R^{18}$ -arilo-,  $R^{18}$ -arilalquilo-,  $R^{18}$ -heteroarilo- y  $R^{18}$ -heteroarilalquilo-;

$R^{18}$  es de 1-5 sustituyentes seleccionados en forma independiente del grupo que consiste en alquilo, alqueno, alquinilo, arilo, arilalquilo, arilalqueno, arilalquino,  $-\text{NO}_2$ , halo, heteroarilo, HO-alquioxialquilo,  $-\text{CF}_3$ ,  $-\text{CN}$ , alquil-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alquil})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{heteroarilo})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{NH}(\text{arilo})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterociclilo})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  $-\text{O-heterociclilo}$ ,  $-\text{O-cicloalquilalquilo}$ ,  $-\text{O-heterociclilalquilo}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alquil})_2$ ,  $-\text{N}(\text{arilalquil})_2$ ,  $-\text{N}(\text{arilalquil})-(\text{heteroarilalquilo})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{NH}(\text{alquilo})$  y  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ;

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o, en forma alternativa, dos restos  $R^{18}$  en los carbonos adyacentes pueden

ligarse para formar:



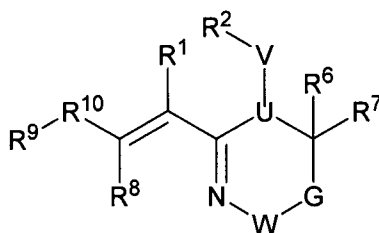
$R^{19}$  es alquilo, cicloalquilo, arilo, arilalquilo o heteroarilalquilo;

$R^{20}$  es alquilo, cicloalquilo, arilo, arilo sustituido por halo, arilalquilo, heteroarilo o heteroarilalquilo;

donde cada uno de los grupos alquilo, cicloalquilo, cicloalquenilo, cicloalquilalquilo-, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, alquilarilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en  $R^1$ ,  $R^2$ - $R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  y  $R^{14}$  está no sustituido o sustituido en forma opcional e independiente por 1 a 5 grupos  $R^{21}$  seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>;

donde cada uno de los grupos alquilo, cicloalquenilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, alquenilo y alquinilo en  $R^{21}$  está en forma independiente no sustituido o sustituido por 1 a 5 grupos  $R^{22}$  seleccionados en forma independiente del grupo que consiste en alquilo, cicloalquilo, cicloalquenilo, heterociclilo, arilo, heteroarilo, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>,

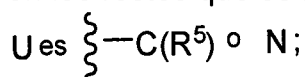
4. Un compuesto, o las sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico de dicho compuesto, donde dicho compuesto tiene la estructura general que se muestra en la fórmula:



R<sup>1</sup> y R<sup>2</sup> están unidos para formar un cicloalquilo C<sub>4</sub>-C<sub>8</sub>, cicloalqueno C<sub>4</sub>-C<sub>8</sub>, resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y R<sup>2</sup> y R<sup>6</sup> están unidos para formar un cicloalquilo C<sub>4</sub>-C<sub>8</sub>, cicloalqueno C<sub>4</sub>-C<sub>8</sub>, resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, con cada uno de dichos restos cicloalquilo o heterociclilo no sustituido o sustituido en forma independiente y opcional con 1-5 sustituyentes que pueden ser iguales o diferentes, cada

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sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;



W se selecciona del grupo que consiste en un enlace, -O-, -C(O)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, y -C(R<sup>11</sup>)(R<sup>12</sup>)-;

G es -C(R<sup>3</sup>)(R<sup>4</sup>)-, -C(O)- y -N(R<sup>13</sup>)-; con la salvedad de que cuando W es -O- o -S-, G no es -N(R<sup>13</sup>)- o -C(O)-;

V se selecciona del grupo que consiste en un enlace, -O-, -C(O)- y -N(R<sup>14</sup>)-;

R<sup>5</sup>, R<sup>6</sup>, y R<sup>7</sup> pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, alquilo-, alqueno-, alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

R<sup>3</sup> se selecciona del grupo que consiste en H, halo, -OR<sup>15</sup>, -CN, -SR<sup>15</sup>, -NR<sup>15</sup>R<sup>16</sup>, -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(=NOR<sup>15</sup>)R<sup>16</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)R<sup>15</sup>, -S(O)<sub>2</sub>R<sup>15</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), =NOR<sup>15</sup>, -N<sub>3</sub>, alquilo-, alqueno-, alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterocicilalquilo-, en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-,



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heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

$R^4$ ,  $R^{11}$  y  $R^{12}$  pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en H, halo,  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,

$-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-C(O)R^{15}$ ,  $-C(O)OR^{15}$ ,  $-C(=NOR^{15})R^{16}$ ,  $-C(O)N(R^{15})(R^{16})$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ ,  $-N_3$ , alquilo-, alquenilo-, alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-5 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

siempre que cuando uno de  $R^3$  o  $R^4$  se selecciona del grupo que consiste en:

$-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ , y  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,

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$-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , y  $-N_3$ ;

siempre que cuando uno de  $R^{11}$  o  $R^{12}$  se selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  
 $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  
 $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  
 $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  $=NOR^{15}$ , y  $-N_3$ , entonces el otro no se  
 selecciona del grupo que consiste en:  $-OR^{15}$ ,  $-CN$ ,  $-SR^{15}$ ,  $-NR^{15}R^{16}$ ,  
 $-N(R^{15})C(O)R^{16}$ ,  $-N(R^{15})S(O)R^{16}$ ,  $-N(R^{15})S(O)_2R^{16}$ ,  $-N(R^{15})S(O)_2N(R^{16})(R^{17})$ ,  
 $-N(R^{15})S(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)N(R^{16})(R^{17})$ ,  $-N(R^{15})C(O)OR^{16}$ ,  
 $-S(O)N(R^{15})(R^{16})$ ,  $-S(O)_2N(R^{15})(R^{16})$ ,  $-S(O)R^{15}$ ,  $-S(O)_2R^{15}$ ,  $-P(O)(OR^{15})(OR^{16})$ ,  
 $=NOR^{15}$ , y  $-N_3$ ;

$R^{13}$  se selecciona en forma independiente del grupo que consiste en H,  
 alquilo, arilalquilo, heteroarilalquilo-, cicloalquilalquilo-, heterocicloalquilalquilo-,  
 arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-,  
 heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-,  
 heteroarilcicloalquilo-, heterocicloalquilo, arilheterocicloalquilo-,  
 heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo,  
 arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo,  
 arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-,  
 arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo,  
 cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-,  
 heterocicloalquenilarilo-,  $-OR^{15}$ ,  $-CN$ ,  $-C(O)R^8$ ,  $-C(O)OR^9$ ,  $-S(O)R^{10}$ ,  $-S(O)_2R^{10}$ ,  
 $-C(O)N(R^{11})(R^{12})$ ,  $-S(O)N(R^{11})(R^{12})$ ,  $-S(O)_2N(R^{11})(R^{12})$ ,  $-NO_2$ ,  $-N=C(R^8)_2$  y  
 $-N(R^8)_2$ ; y donde dicho  $R^{13}$  alquilo, arilalquilo-, heteroarilalquilo-, cicloalquilalquilo-,

heterocicloalquilalquilo-, arilcicloalquilalquilo-, heteroarilcicloalquilalquilo-, arilheterocicloalquilalquilo-, heteroarilheterocicloalquilalquilo-, cicloalquilo, arilcicloalquilo-, heteroarilcicloalquilo-, heterocicloalquilo, arilheterocicloalquilo-, heteroarilheterocicloalquilo-, alquenilo, arilalquenilo-, cicloalquenilo, arilcicloalquenilo-, heteroarilcicloalquenilo-, heterocicloalquenilo-, arilheterocicloalquenilo-, heteroarilheterocicloalquenilo-, alquinilo, arilalquinilo-, arilo, cicloalquilarilo-, heterocicloalquilarilo-, heterocicloalquenilarilo-, heteroarilo, cicloalquilheteroarilo-, heterocicloalquilheteroarilo-, cicloalquenilarilo-, y heterocicloalquenilarilo- grupos están sustituidos en forma opcional con 1 a 5 grupos seleccionados en forma independiente del grupo que consiste en: alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterocicilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>; -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>;

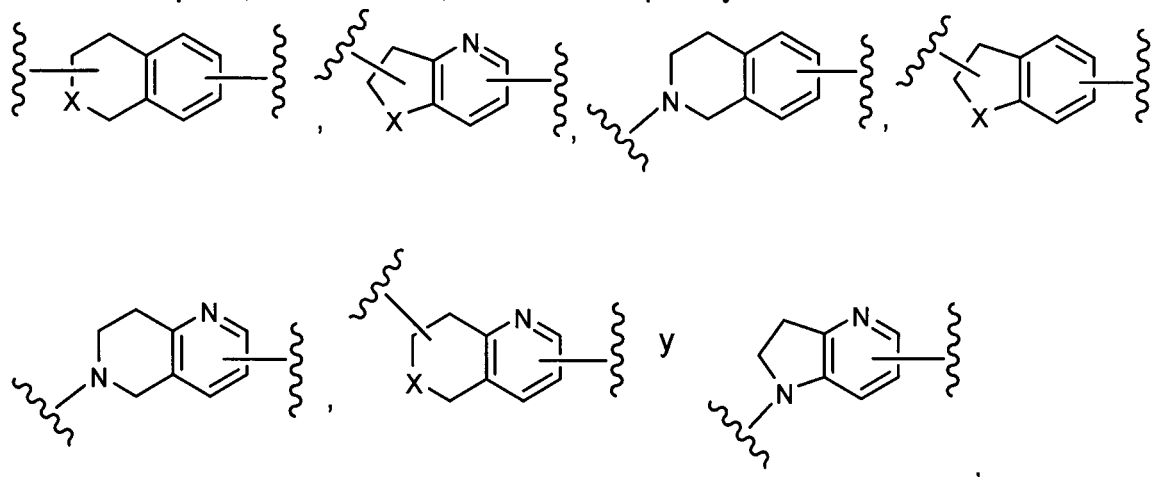
R<sup>14</sup> se selecciona del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, cicloalquenilo, heterocicilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, -CN, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, y -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>);

R<sup>8</sup> se selecciona del grupo que consiste en H, alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-,

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heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, con cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- que no está sustituido o está sustituido en forma independiente y opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante;

$R^{10}$  se selecciona del grupo que consiste en un enlace, alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo-, heterociclilalquilo- y los restos:



donde X es O,  $N(R^{14})$  o S;

en los cuales cada uno de dicho alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- heterociclilalquilo- para  $R^{10}$  como también los restos mencionados anteriormente para  $R^{10}$  puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante; y

$R^9$  se selecciona del grupo que consiste en alquilo-, alqueno- y alquino-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-,

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heteroarilalquilo-, heterociclilo- y heterociclilalquilo-, en los cuales cada uno de dicho alquilo-, alquenilo- y alquinilo-, arilo-, arilalquilo-, alquilarilo-, cicloalquilo-, cicloalquilalquilo-, heteroarilo-, heteroarilalquilo-, heterociclilo- y heterociclilalquilo- puede no estar sustituido o estar sustituido en forma opcional e independiente con 1-3 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en los restos que se muestran más adelante,

$R^{15}$ ,  $R^{16}$  y  $R^{17}$  se seleccionan de manera independiente del grupo que consiste en H, alquilo, alquenilo, alquinilo, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterociclilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, arilcicloalquilo-, arilheterociclilo-,  $R^{18}$ -alquilo-,  $R^{18}$ -cicloalquilo-,  $R^{18}$ -cicloalquilalquilo-,  $R^{18}$ -heterociclilo-,  $R^{18}$ -heterociclilalquilo-,  $R^{18}$ -arilo-,  $R^{18}$ -arilalquilo-,  $R^{18}$ -heteroarilo- y  $R^{18}$ -heteroarilalquilo

$R^{18}$  es de 1-5 sustituyentes seleccionados en forma independiente del grupo que consiste en alquilo, alquenilo, alquinilo, arilo, arilalquilo-, arilalquenilo-, arilalquinilo-,  $-\text{NO}_2$ , halo, heteroarilo, HO-alquioxialquilo-,  $-\text{CF}_3$ ,  $-\text{CN}$ , alquil-CN,  $-\text{C}(\text{O})\text{R}^{19}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^{19}$ ,  $-\text{C}(\text{O})\text{NHR}^{20}$ ,  $-\text{C}(\text{O})\text{NH}_2$ ,  $-\text{C}(\text{O})\text{NH}_2-\text{C}(\text{O})\text{N}(\text{alquil})_2$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{C}(\text{O})\text{N}(\text{alquil})(\text{heteroarilo})$ ,  $-\text{SR}^{19}$ ,  $-\text{S}(\text{O})_2\text{R}^{20}$ ,  $-\text{S}(\text{O})\text{NH}_2$ ,  $-\text{S}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{S}(\text{O})\text{NH}(\text{arilo})$ ,  $-\text{S}(\text{O})_2\text{NH}_2$ ,  $-\text{S}(\text{O})_2\text{NHR}^{19}$ ,  $-\text{S}(\text{O})_2\text{NH}(\text{heterociclilo})$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})_2$ ,  $-\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{arilo})$ ,  $-\text{OCF}_3$ ,  $-\text{OH}$ ,  $-\text{OR}^{20}$ ,  $-\text{O-heterociclilo}$ ,  $-\text{O-cicloalquilalquilo}$ ,  $-\text{O-heterociclilalquilo}$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^{20}$ ,  $-\text{N}(\text{alquil})_2$ ,  $-\text{N}(\text{arilalquil})_2$ ,  $-\text{N}(\text{arilalquil})-(\text{heteroarilalquilo})$ ,  $-\text{NHC}(\text{O})\text{R}^{20}$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{NHC}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{NH}(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{C}(\text{O})\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{R}^{20}$ ,  $-\text{NHS}(\text{O})_2\text{NH}(\text{alquilo})$ ,  $-\text{NHS}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ,  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{NH}(\text{alquilo})$  y  $-\text{N}(\text{alquil})\text{S}(\text{O})_2\text{N}(\text{alquil})(\text{alquilo})$ ;

o, en forma alternativa, dos restos  $R^{18}$  en los carbonos adyacentes pueden

ligarse para formar:

$R^{19}$  es alquilo, cicloalquilo, arilo, arilalquilo- o heteroarilalquilo-;

$R^{20}$  es alquilo, cicloalquilo, arilo, arilo sustituido por halo, arilalquilo-, heteroarilo o heteroarilalquilo-;

donde cada uno de los alquilo, cicloalquilo, cicloalqueno, cicloalquilalquilo, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, alquilarilo-, heteroarilo, heteroarilalquilo-, alqueno y alquino grupos in  $R^1$ - $R^2$ ,  $R^2$ - $R^6$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  y  $R^{14}$  está no sustituido o sustituido en forma opcional e independiente por 1 a 5 grupos  $R^{21}$  seleccionados en forma independiente del grupo que consiste en alquilo, alqueno, alquino, cicloalquilo, cicloalquilalquilo-, cicloalqueno, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, halo, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>, -C(O)OR<sup>15</sup>, -C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>), -CH(R<sup>15</sup>)(R<sup>16</sup>), -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>), -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-R<sup>15</sup>, -CH<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)S(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -S(O)R<sup>15</sup>, =NOR<sup>15</sup>, -N<sub>3</sub>, -NO<sub>2</sub> y -S(O)<sub>2</sub>R<sup>15</sup>;

donde cada uno de los grupos alquilo, cicloalqueno, cicloalquilo, cicloalquilalquilo-, heterociclilo, heterocicilalquilo-, arilo, arilalquilo-, heteroarilo, heteroarilalquilo-, alqueno y alquino en  $R^{21}$  está en forma independiente no sustituido o sustituido por 1 a 5 grupos  $R^{22}$  seleccionados en forma independiente del grupo que consiste en alquilo, cicloalquilo, cicloalqueno, heterociclilo, arilo, heteroarilo, halo, -CF<sub>3</sub>, -CN, -OR<sup>15</sup>, -C(O)R<sup>15</sup>,

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-C(O)OR<sup>15</sup>, -alquil-C(O)OR<sup>15</sup>, C(O)N(R<sup>15</sup>)(R<sup>16</sup>), -SR<sup>15</sup>, -S(O)N(R<sup>15</sup>)(R<sup>16</sup>),  
 -S(O)<sub>2</sub>N(R<sup>15</sup>)(R<sup>16</sup>), -C(=NOR<sup>15</sup>)R<sup>16</sup>, -P(O)(OR<sup>15</sup>)(OR<sup>16</sup>), -N(R<sup>15</sup>)(R<sup>16</sup>),  
 -alquil-N(R<sup>15</sup>)(R<sup>16</sup>), -N(R<sup>15</sup>)C(O)R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)R<sup>16</sup>, -N(R<sup>15</sup>)S(O)R<sup>16</sup>,  
 -N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)S(O)<sub>2</sub>R<sup>16</sup>, -N(R<sup>15</sup>)S(O)<sub>2</sub>N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)S(O)N(R<sup>16</sup>)(R<sup>17</sup>), -N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>), -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)N(R<sup>16</sup>)(R<sup>17</sup>),  
 -N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -CH<sub>2</sub>-N(R<sup>15</sup>)C(O)OR<sup>16</sup>, -N<sub>3</sub>, =NOR<sup>15</sup>, -NO<sub>2</sub>, -S(O)R<sup>15</sup> y  
 -S(O)<sub>2</sub>R<sup>15</sup>.

5. El compuesto de la reivindicación 1, en el cual R<sup>1</sup> es H.
6. El compuesto de la reivindicación 1, en el cual R<sup>1</sup> es alquilo.
7. El compuesto de la reivindicación 1, en el cual R<sup>1</sup> es metilo.
8. El compuesto de la reivindicación 1, en el cual U es C(R<sup>5</sup>).
9. El compuesto de la reivindicación 1, en el cual U es N.
10. El compuesto de la reivindicación 1, en el cual W es un enlace.
11. El compuesto de la reivindicación 1, en el cual W es -O-.
12. El compuesto de la reivindicación 1, en el cual R<sup>2</sup> y R<sup>6</sup> están unidos para formar un anillo ciclohexilo.
13. El compuesto de la reivindicación 1, en el cual W es -C(O)-.
14. El compuesto de la reivindicación 1, en el cual =N-W-G- es =N-C(R<sup>11</sup>R<sup>12</sup>)-C(O)-.
15. El compuesto de la reivindicación 1, en el cual W es -C(R<sup>11</sup>)(R<sup>12</sup>)-.
16. El compuesto de la reivindicación 1, en el cual:

(a) U es N, y R<sup>2</sup> y R<sup>6</sup> están unidos para formar un anillo pirrolidinilo incluyendo el N de U como el nitrógeno de dicho anillo pirrolidinilo, que no está sustituido; o

(b) U es N, y R<sup>2</sup> y R<sup>6</sup> están unidos para formar un anillo pirrolidinilo incluyendo el N de U como el nitrógeno de dicho anillo pirrolidinilo, donde dicho anillo pirrolidinilo está sustituido con 1-3 sustituyentes que pueden ser iguales o

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diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi; o

(c) U es N, y R<sup>2</sup> y R<sup>6</sup> están unidos para formar un anillo piperazinilo incluyendo el N de U como el nitrógeno de dicho anillo piperazinilo, que no está sustituido; o

(d) U es N, y R<sup>2</sup> y R<sup>6</sup> están unidos para formar un anillo piperazinilo incluyendo el N de U como el nitrógeno de dicho anillo piperazinilo, donde dicho anillo piperazinilo está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi; o

(e) R<sup>2</sup> y R<sup>6</sup> están unidos para formar un anillo morfolinilo que no está sustituido; o

(f) R<sup>2</sup> y R<sup>6</sup> están unidos para formar un anillo morfolinilo, que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi; o

(g) R<sup>2</sup> y R<sup>6</sup> están unidos para formar un anillo piranilo que no está sustituido; o

(h) R<sup>2</sup> y R<sup>6</sup> están unidos para formar un anillo piranilo, que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi; o

(i) R<sup>2</sup> y R<sup>6</sup> están unidos para formar un anillo pirrolidinilo que no está sustituido; o

(j) R<sup>2</sup> y R<sup>6</sup> están unidos para formar un anillo pirrolidinilo, que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se



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selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

17. El compuesto de la reivindicación 1, en el cual:

(a) U es N y R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo pirrolidinilo, que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi; o

(b) U es N y R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo piperidinilo, que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi; o

(c) U es N y R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo piperazinilo, que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi.

18. El compuesto de la reivindicación 1, en el cual R<sup>7</sup> es 4-fluorofenilo.

19. El compuesto de la reivindicación 1, en el cual:

(a) U es N, R<sup>1</sup> y R<sup>2</sup> están unidos para formar un anillo pirrolidinilo, cuyo anillo no está sustituido o está sustituido en forma opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi, y R<sup>2</sup> y R<sup>6</sup> están unidos para formar un anillo pirrolidinilo, cuyo anillo no está sustituido o está sustituido en forma opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxí y alcoxi; o

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(b) U es N,  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo, cuyo anillo no está sustituido o está sustituido en forma opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxilo y alcoxi, y  $R^2$  y  $R^6$  están unidos para formar un anillo piperidinilo, cuyo anillo no está sustituido o está sustituido en forma opcional con 1-3 sustituyentes que pueden ser iguales o diferentes, cada uno se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxilo y alcoxi.

20. El compuesto de la reivindicación 1, en el cual:

(a)  $R^7$  es bifenilo no sustituido; o

(b)  $R^7$  es bifenilo que está sustituido con 1-4 sustituyentes que pueden ser iguales o diferentes, cada sustituyente se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, -CN, -NH<sub>2</sub>, -NH(alquilo), -N(alquil)<sub>2</sub>, hidroxilo y alcoxi;

(c)  $R^7$  es 3-(1,1'-bifenil)-ilo; o

(d)  $R^7$  es 4-(1,1'-bifenil)-ilo.

21. El compuesto de la reivindicación 1, en el cual  $R^8$  es H.

22. El compuesto de la reivindicación 1, en el cual  $R^8$  es alquilo.

23. El compuesto de la reivindicación 1, en el cual  $R^8$  es metilo.

24. El compuesto de la reivindicación 1, en el cual  $R^{10}$  es arilo.

25. El compuesto de la reivindicación 1, en el cual  $R^{10}$  es fenilo.

26. El compuesto de la reivindicación 1, en el cual  $R^{10}$  es heteroarilo.

27. El compuesto de la reivindicación 1, en el cual  $R^9$  es heteroarilo no sustituido.

28. El compuesto de la reivindicación 1, en el cual  $R^9$  es heteroarilo que está sustituido con 1-3 sustituyentes que pueden ser iguales o diferentes, cada

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sustituyente se selecciona en forma independiente del grupo que consiste en grupos halo, alquilo, CN, NH<sub>2</sub>, NH(alquilo), N(alquil)<sub>2</sub>, hidroxilo y alcoxi.

29. El compuesto de la reivindicación 1, en el cual R<sup>9</sup> es imidazol-1-ilo.
30. El compuesto de la reivindicación 1, en el cual R<sup>9</sup> es 4-metil-imidazol-1-ilo.
31. El compuesto de la reivindicación 1, en el cual R<sup>9</sup> es 5-cloro-4-metilo-imidazol-1-ilo.
32. El compuesto de la reivindicación 1 en el cual:

(a)

U es C(R<sup>5</sup>);

R<sup>1</sup> es H;

R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo cicloalquilo de 4-7 miembros;

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

R<sup>8</sup> es H;

R<sup>10</sup> se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo; y

R<sup>9</sup> es 4-metil-imidazolilo-1-ilo; o

(b)

U es C(R<sup>5</sup>) o N;

R<sup>1</sup> es H;

R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo heterociclilo de 5-8 miembros;

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;

R<sup>8</sup> es H;

R<sup>10</sup> se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo; y

R<sup>9</sup> es 4-metil-imidazolilo-1-ilo; o

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(c)

U es C(R<sup>5</sup>) o N;

R<sup>1</sup> y R<sup>2</sup> están conectados para formar un anillo heterociclilo de 5-8 miembros;

R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo heterociclilo de 5-8 miembros;

R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;R<sup>8</sup> es H;

R<sup>10</sup> se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo; y

R<sup>9</sup> es 4-metil-imidazolilo-1-ilo; o

(d)

U es C(R<sup>5</sup>);

R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo cicloalquilo de 4-7 miembros;

R<sup>1</sup> y R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;R<sup>8</sup> es H;

R<sup>10</sup> se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo; y

R<sup>9</sup> es 4-metil-imidazolilo-1-ilo; o

(e)

U es C(R<sup>5</sup>) o N;R<sup>1</sup> y R<sup>2</sup> están conectados para formar un anillo piperidinilo;R<sup>2</sup> y R<sup>6</sup> están conectados para formar un anillo piperidinilo;R<sup>7</sup> es 3-(1,1'-bifenil)-ilo;R<sup>8</sup> es H;

$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo; y

$R^9$  es 4-metil-imidazolilo-1-ilo; o

(f)

U es C( $R^5$ ) o N;

$R^1$  y  $R^2$  están conectados para formar un anillo piperazinilo;

$R^2$  y  $R^6$  están conectados para formar un anillo piperazinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo; y

$R^9$  es 4-metil-imidazolilo-1-ilo; o

(g)

U es C( $R^5$ ) o N;

$R^1$  y  $R^2$  están conectados para formar un anillo piperidinilo;

$R^2$  y  $R^6$  están conectados para formar un anillo piperazinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo; y

$R^9$  es 4-metil-imidazolilo-1-ilo; o

(h)

U es N;

$R^1$  y  $R^2$  están conectados para formar un anillo piperazinilo;

$R^2$  y  $R^6$  están conectados para formar un anillo piperidinilo;

$R^7$  es 3-(1,1'-bifenil)-ilo;

$R^8$  es H;

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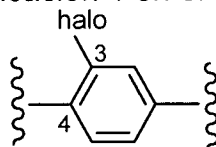
$R^{10}$  se selecciona del grupo que consiste en: 3-metoxi-fenilo y 3-F-fenilo; y

$R^9$  es 4-metil-imidazolilo-1-ilo.

33. El compuesto de la reivindicación 1 en el cual  $R^{10}$  es fenilo sustituido con 1 halo.

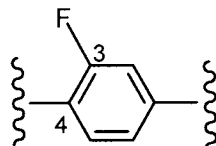
34. El compuesto de la reivindicación 1 en el cual  $R^{10}$  es fenilo sustituido con 1 halo, y dicho halo es F.

35. El compuesto de la reivindicación 1 en el cual  $R^{10}$  es:



(donde el enlace del carbono marcado como 4 es para el resto  $R^9$ ).

36. El compuesto de la reivindicación 1 en el cual  $R^{10}$  es:

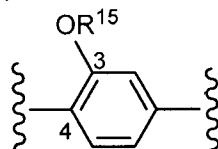


(donde el enlace del carbono marcado como 4 es para el resto  $R^9$ ).

37. El compuesto de la reivindicación 1 en el cual  $R^{10}$  es fenilo sustituido con un grupo  $-OR^{15}$ .

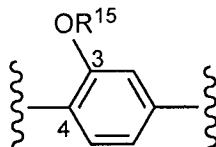
38. El compuesto de la reivindicación 1 en el cual  $R^{10}$  es fenilo sustituido con un grupo  $-OR^{15}$ , y dicho  $R^{15}$  es alquilo.

39. En otra realización  $R^{10}$  es:



(donde el enlace del carbono marcado como 4 es para el resto  $R^9$ ).

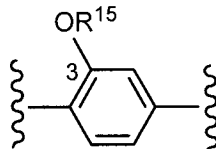
40. El compuesto de la reivindicación 1 en el cual  $R^{10}$  es:



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en la cual  $R^{15}$  es alquilo (donde el enlace del carbono marcado como 4 es para el resto  $R^9$ ).

41. El compuesto de la reivindicación 1 en el cual  $R^{10}$  es:



en la cual  $R^{15}$  es metilo (es decir,  $R^{10}$  es 3-metoxi-fenilo).

42. El compuesto de la reivindicación 1 en el cual  $R^9$  es heteroarilo sustituido con 1 a 3 grupos alquilo seleccionados en forma independiente.

43. El compuesto de la reivindicación 1 en el cual  $R^9$  es heteroarilo sustituido con uno es un grupo alquilo.

44. El compuesto de la reivindicación 1 en el cual:

(a)  $R^1$  y  $R^2$  están unidos para formar un anillo sustituido en forma opcional con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y dicho anillo está fusionado con un anillo arilo o heteroarilo, y dicho anillo fusionado resultante está sustituido en forma opcional con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(b)  $R^1$  y  $R^2$  están unidos para formar un anillo sustituido con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y dicho anillo está fusionado con un anillo arilo o heteroarilo, y dicho anillo fusionado resultante está sustituido en forma opcional con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(c)  $R^1$  y  $R^2$  están unidos para formar un anillo sustituido en forma opcional con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(d)  $R^1$  y  $R^2$  están unidos para formar un anillo; o

(e)  $R^1$  y  $R^2$  están unidos para formar un anillo, y dicho anillo está fusionado con un anillo arilo o heteroarilo, y dicho anillo fusionado resultante está sustituido

en forma opcional con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

45. El compuesto de la reivindicación 1 en el cual:

(a)  $R^1$  y  $R^2$  están unidos para formar un anillo heterociclilo sustituido en forma opcional con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente;

o

(b)  $R^1$  y  $R^2$  están unidos para formar un anillo heterociclilo sustituido con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(c) U es N, y  $R^1$  y  $R^2$  están unidos para formar un anillo heterociclilo sustituido en forma opcional con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(d) U es N, y  $R^1$  y  $R^2$  están unidos para formar un anillo heterociclilo sustituido con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(e)  $R^1$  y  $R^2$  están unidos para formar un anillo heterociclilo; o

(f) U es N, y  $R^1$  y  $R^2$  están unidos para formar un anillo heterociclilo.

46. El compuesto de la reivindicación 1 en el cual:

(a)  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido en forma opcional con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente;

o

(b)  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(c)  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido en forma opcional con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente;

o

(d) U es N, y  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido con 1 a 5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o



(e)  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido en forma opcional con un resto =O; o

(f) U es N, y  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido en forma opcional con un resto =O; o

(g)  $R^1$  y  $R^2$  están unidos para formar un piperidinilo; o

(h) U es N, y  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo; o

(i)  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido con un resto =O; o

(j) U es N, y  $R^1$  y  $R^2$  están unidos para formar un anillo piperidinilo sustituido con un resto =O.

47. El compuesto de la reivindicación 1 en el cual  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

48. El compuesto de la reivindicación 1 en el cual:

(a)  $R^1$  y  $R^2$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (1) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y

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(b)  $R^2$  y  $R^6$  están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (1) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; y

(c) dicho resto  $R^2$  y  $R^6$  cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

49. El compuesto de la reivindicación 1 en el cual  $R^6$  y cualquiera de  $R^3$  o  $R^4$  del resto  $-C(R^3)(R^4)-G$ , están unidos para formar un cicloalquilo  $C_4-C_8$ , cicloalquenilo  $C_4-C_8$ , resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (a) dicho resto cicloalquilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, (b) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (c) dicho resto cicloalquilo, cicloalquenilo, heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

50. El compuesto de la reivindicación 1 en el cual:

(a)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-G$ , están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (1) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho resto heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y

el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(b)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, donde dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(c)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, donde dicho resto heterociclilo está sustituido con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(d)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros; o

(e)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (1) dicho resto heterociclilo está sustituido en forma opcional con un  $=O$ , y (2) dicho resto heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(f)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, donde dicho resto heterociclilo está sustituido en forma opcional con a  $=O$ ; o

(g)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, donde dicho resto heterociclilo heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

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(h)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros;

(i)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, en la cual: (1) dicho resto heterociclilo está sustituido con un  $=O$ , y (2) dicho resto heterociclilo o heterociclenilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente;

(j)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5-8 miembros o resto heterociclenilo de 5-8 miembros, donde dicho resto heterociclilo está sustituido con a  $=O$ .

51. El compuesto de la reivindicación 1 en el cual:

(a)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5 miembros, en la cual: (1) dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho resto heterociclilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(b)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5 miembros, donde dicho resto heterociclilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(c)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5 miembros, en la cual: (1) dicho resto heterociclilo está sustituido en forma opcional con un  $=O$ , y (2) dicho resto heterociclilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la

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fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(d)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5 miembros, donde dicho resto heterociclilo está sustituido en forma opcional con  $a=O$ ; o

(e)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5 miembros, donde dicho resto heterociclilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(f)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5 miembros; o

(g)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5 miembros, en la cual: (1) dicho resto heterociclilo está sustituido con un  $=O$ , y (2) dicho resto heterociclilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(h)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5 miembros, donde dicho resto heterociclilo está sustituido con  $a=O$ ; o

(i)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5 miembros, en la cual: (1) dicho resto heterociclilo está sustituido con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho resto heterociclilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

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(j)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un resto heterociclilo de 5 miembros, donde dicho resto heterociclilo está sustituido con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

52. El compuesto de la reivindicación 1 en el cual:

(a)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un anillo pirrolidinilo, en la cual: (1) dicho anillo pirrolidinilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho anillo pirrolidinilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(b)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un 5 anillo pirrolidinilo, donde dicho anillo pirrolidinilo está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(c)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un anillo pirrolidinilo, en la cual: (1) dicho anillo pirrolidinilo está sustituido en forma opcional con un  $=O$ , y (2) dicho anillo pirrolidinilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(d)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un anillo pirrolidinilo, donde dicho anillo pirrolidinilo está sustituido en forma opcional con a  $=O$ ; o

(e)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un anillo pirrolidinilo, donde dicho anillo pirrolidinilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

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(f)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un anillo pirrolidinilo; o

(g)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un anillo pirrolidinilo, en la cual: (1) dicho anillo pirrolidinilo está sustituido con un  $=O$ , y (2) dicho anillo pirrolidinilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(h)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un anillo pirrolidinilo, donde dicho anillo pirrolidinilo está sustituido con a  $=O$ ; o

(i)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un anillo pirrolidinilo, en la cual: (1) dicho anillo pirrolidinilo está sustituido con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente, y (2) dicho anillo pirrolidinilo está fusionado en forma opcional con un anillo arilo o heteroarilo, y el resto arilo que resulta de la fusión está sustituido en forma opcional con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente; o

(j)  $R^6$  y  $R^{13}$  del resto  $-N(R^{13})-$  G, están unidos para formar un 5 anillo pirrolidinilo, donde dicho anillo pirrolidinilo está sustituido con 1-5 sustituyentes  $R^{21}$  seleccionados en forma independiente.

53. El compuesto de la reivindicación 1 en el cual:

(a)  $R^{10}$  se selecciona del grupo que consiste en arilo y arilo sustituido con uno o más grupos  $R^{21}$ , y  $R^9$  se selecciona del grupo que consiste en heteroarilo y heteroarilo sustituido con uno o más grupos  $R^{21}$ , y donde cada  $R^{21}$  se selecciona en forma independiente; o

(b)  $R^{10}$  se selecciona del grupo que consiste en fenilo y fenilo sustituido con 1-3 grupos  $R^{21}$  sustituidos en forma independiente, y  $R^9$  se selecciona del grupo que consiste en imidazolilo y imidazolilo sustituido con 1-3 grupos  $R^{21}$  sustituidos en forma independiente; o

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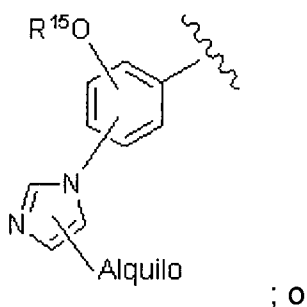
(c)  $R^{10}$  es fenilo sustituido con 1-3 grupos  $R^{21}$  sustituidos en forma independiente, y  $R^9$  se selecciona del grupo que consiste en imidazolilo y imidazolilo sustituido con 1-3 grupos  $R^{21}$  sustituidos en forma independiente; o

(d)  $R^{10}$  se selecciona del grupo que consiste en heteroarilo y heteroarilo sustituido con 1-3 grupos  $R^{21}$ , y el grupo  $R^9$  se selecciona del grupo que consiste en heteroarilo y heteroarilo sustituido con 1-3 grupos  $R^{21}$ , y donde cada  $R^{21}$  se selecciona en forma independiente; o

(e)  $R^{10}$  se selecciona del grupo que consiste en piridilo y piridilo sustituido con 1-3 grupos  $R^{21}$ , y el grupo  $R^9$  se selecciona del grupo que consiste en imidazolilo y imidazolilo sustituido con 1-3 grupos  $R^{21}$ , y donde cada  $R^{21}$  se selecciona en forma independiente; o

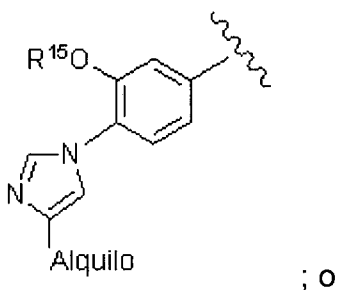
(f)  $R^{10}$  es piridilo, y el grupo  $R^9$  es imidazolilo sustituido con 1-3 grupos  $R^{21}$ , y donde cada  $R^{21}$  se selecciona en forma independiente; o

(g) el resto  $R^9$ - $R^{10}$  es:



; o

(h) el resto  $R^9$ - $R^{10}$  es:

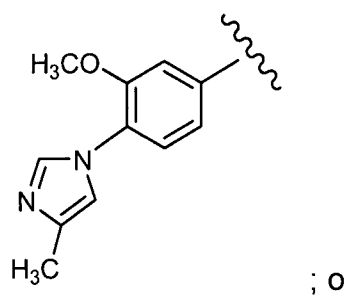


; o

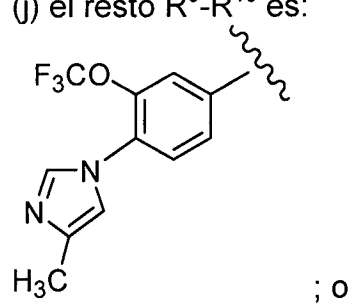
(i) el resto  $R^9$ - $R^{10}$  es:



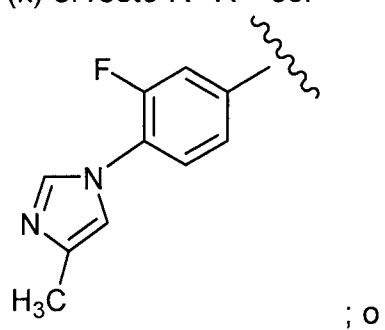
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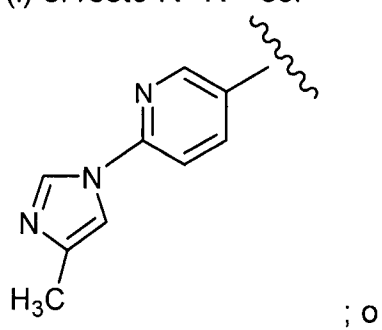
(j) el resto  $R^9$ - $R^{10}$  es:



(k) el resto  $R^9$ - $R^{10}$  es:

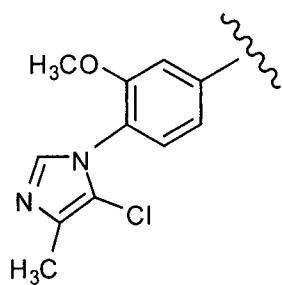


(l) el resto  $R^9$ - $R^{10}$  es:

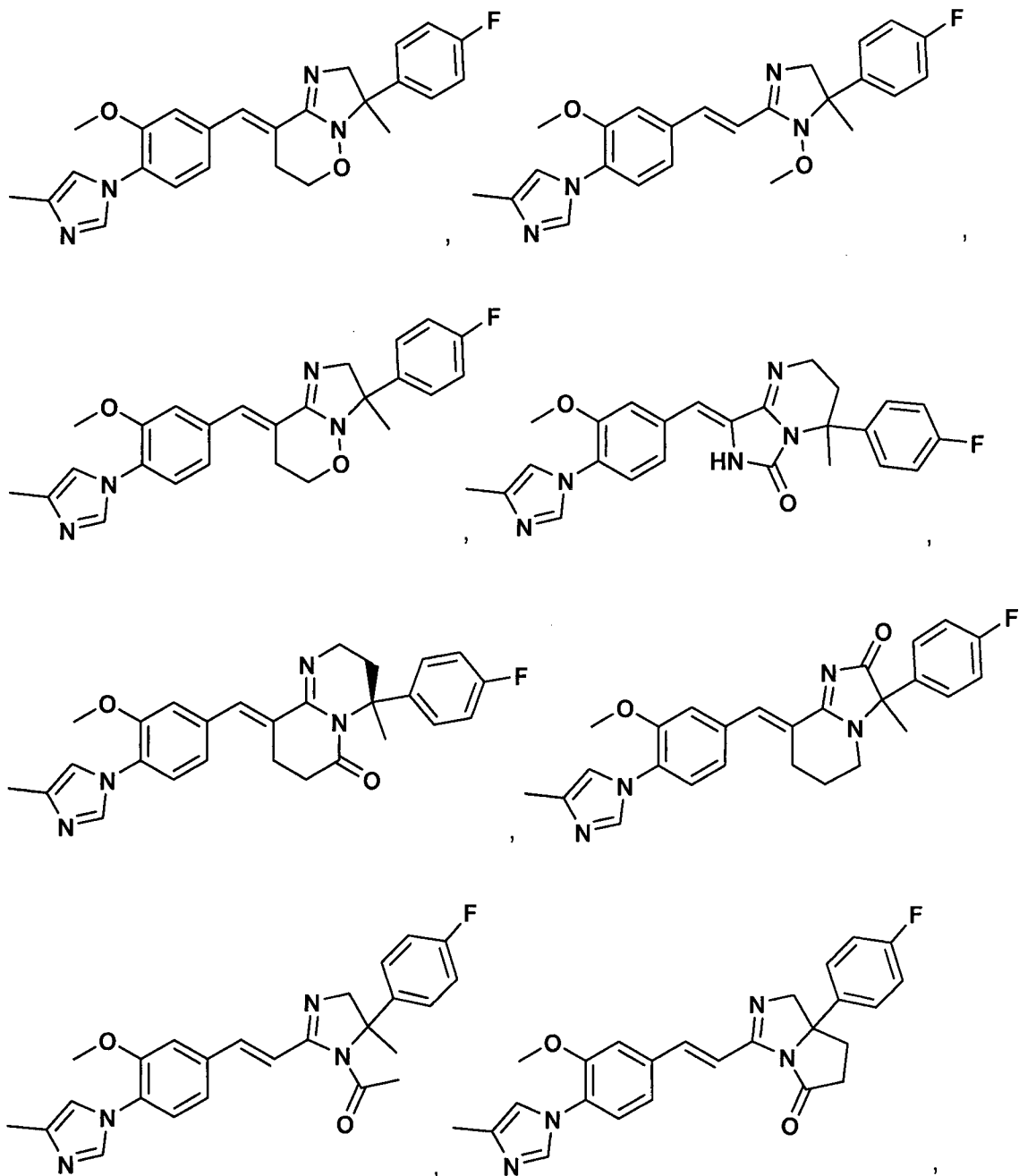


(m) el resto  $R^9$ - $R^{10}$  es:

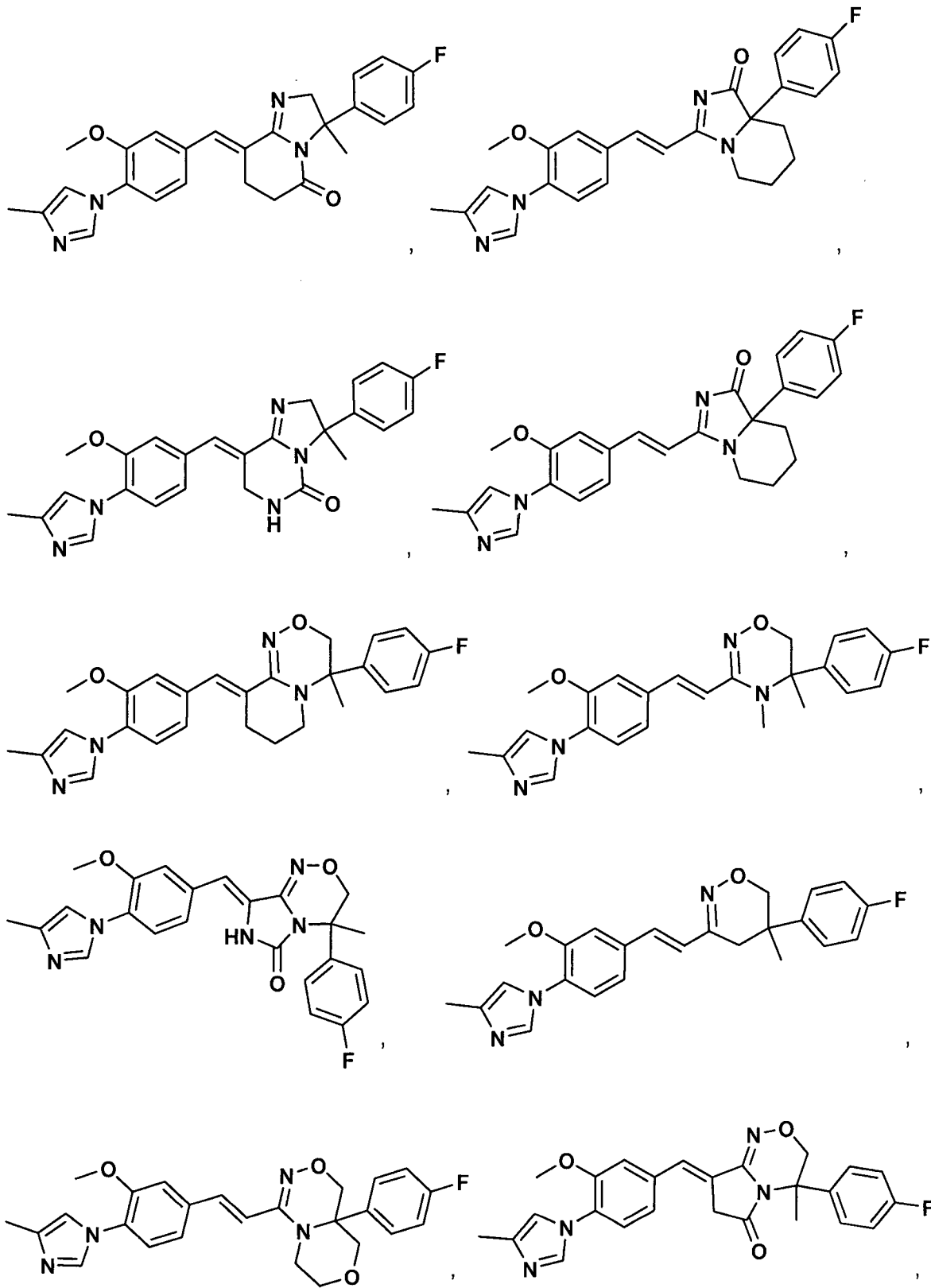
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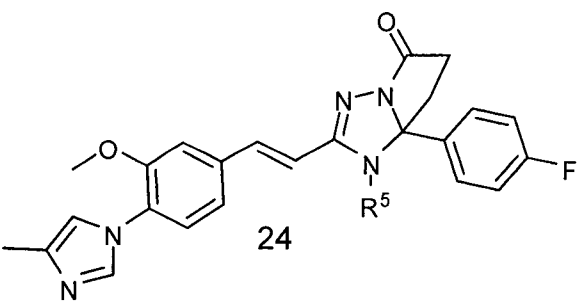
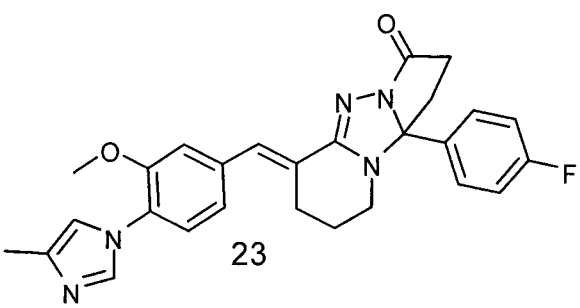
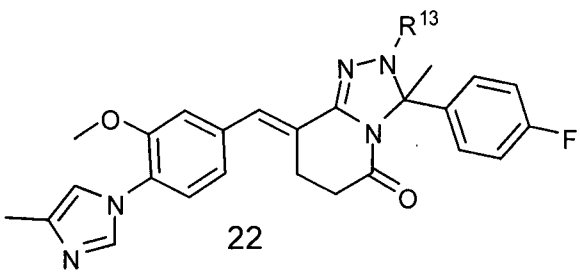
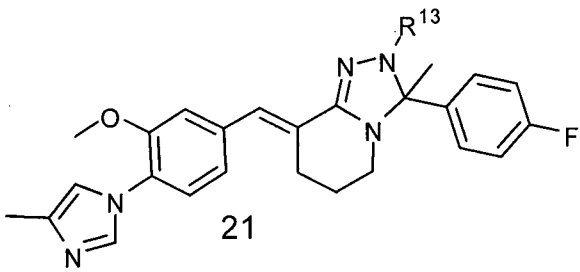
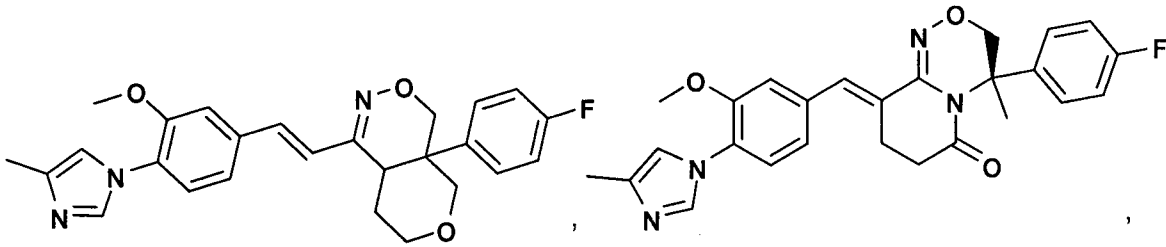
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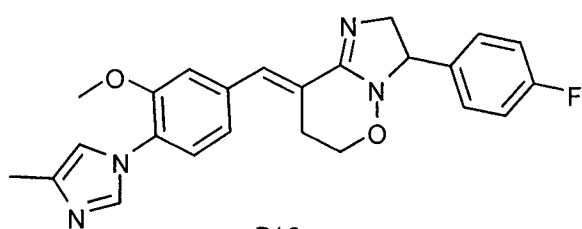


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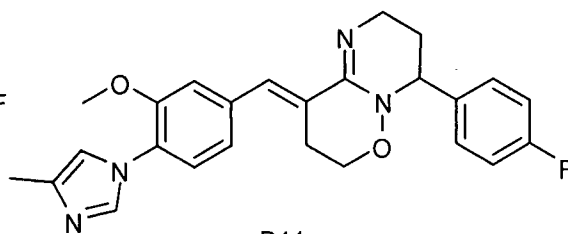


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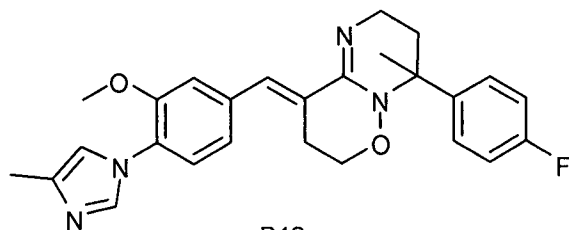




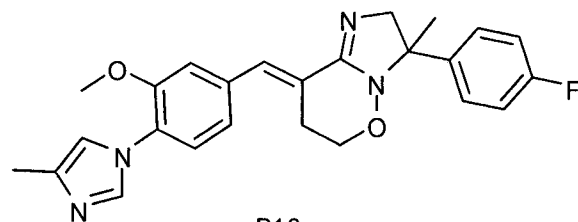
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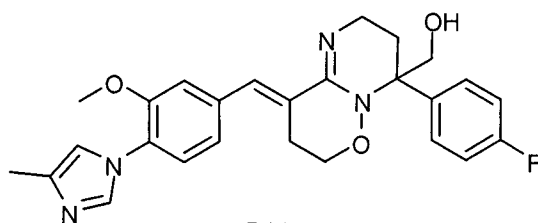
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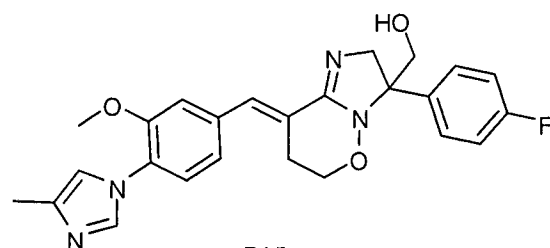
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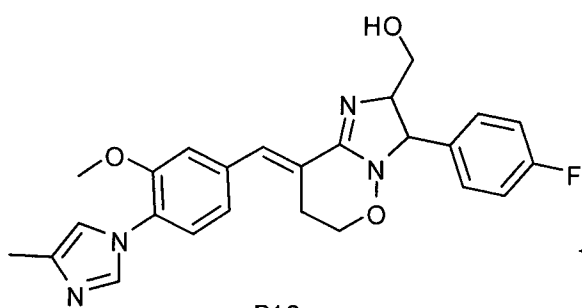
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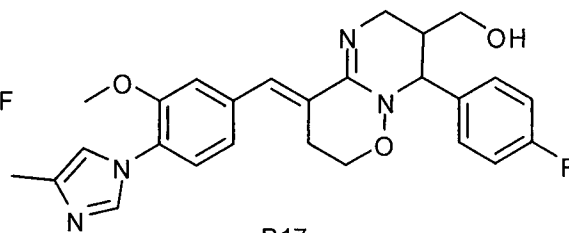
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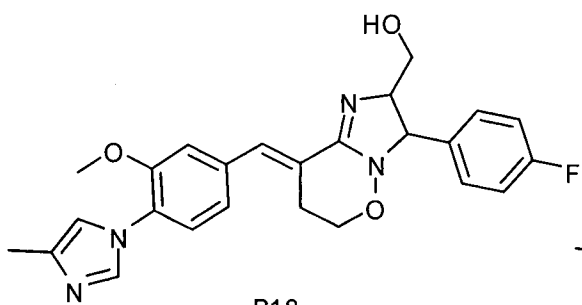
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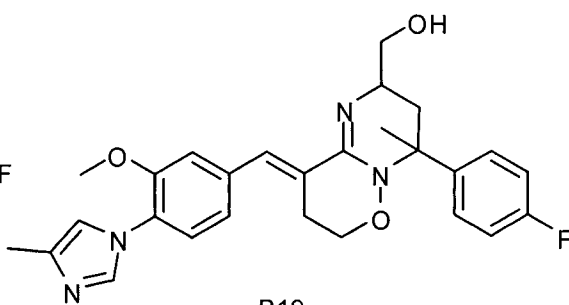
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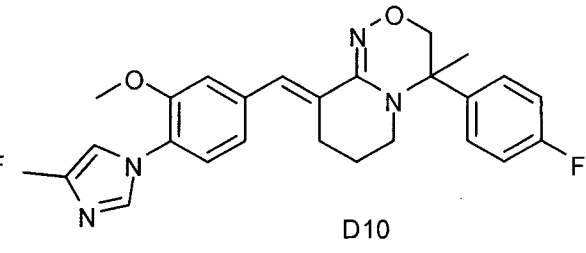
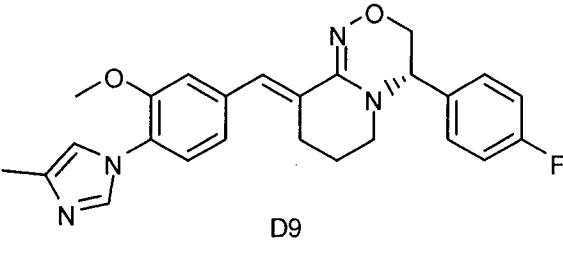
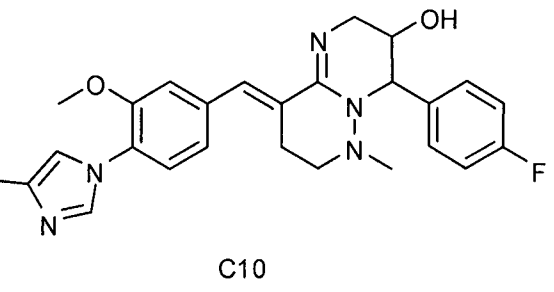
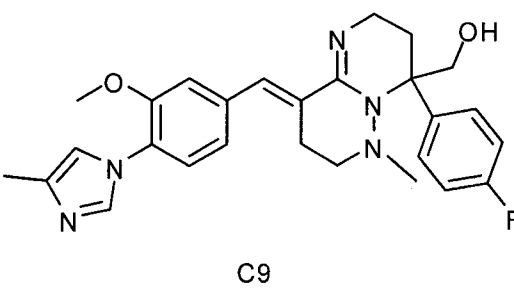
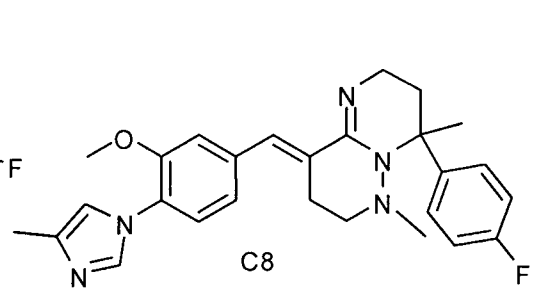
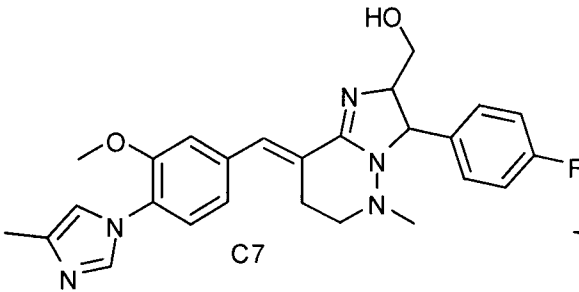
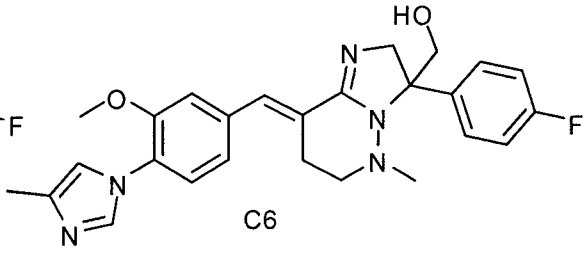
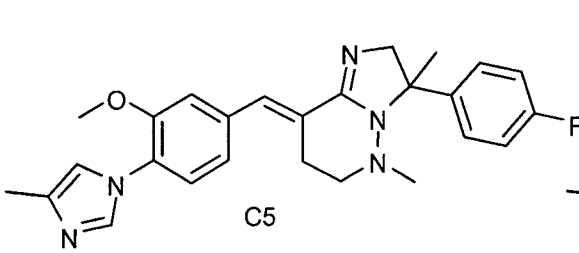
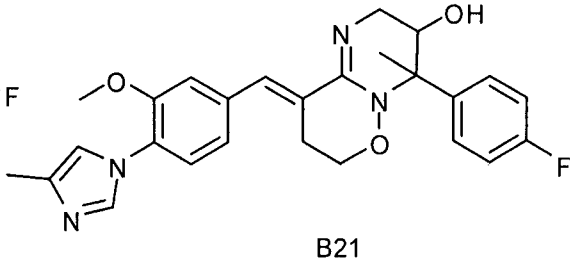
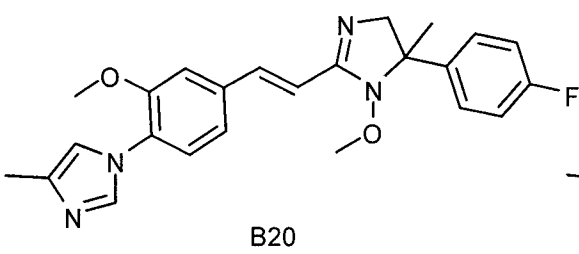


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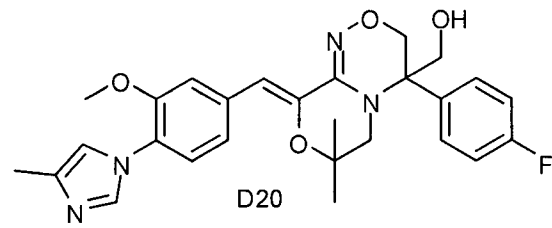
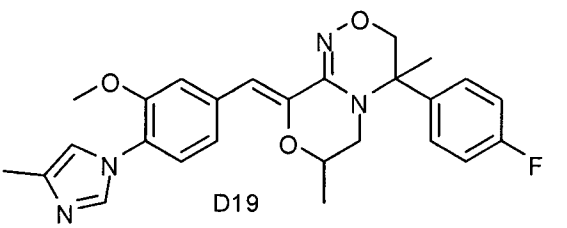
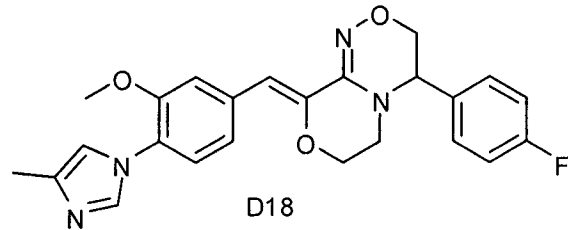
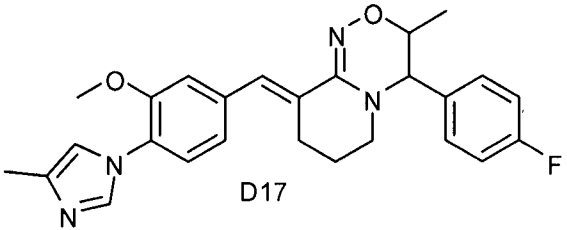
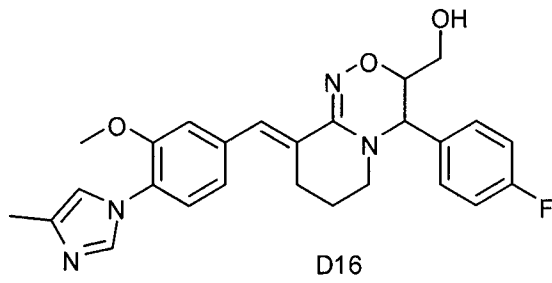
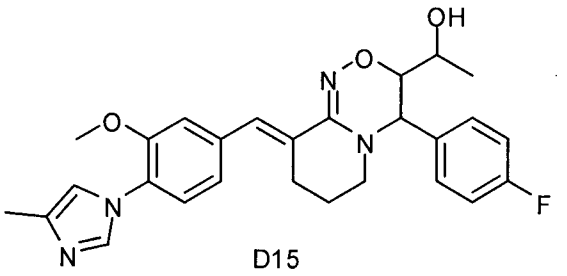
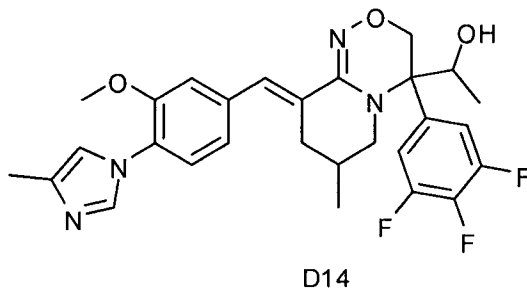
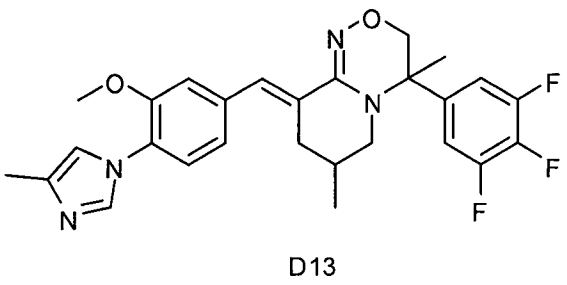
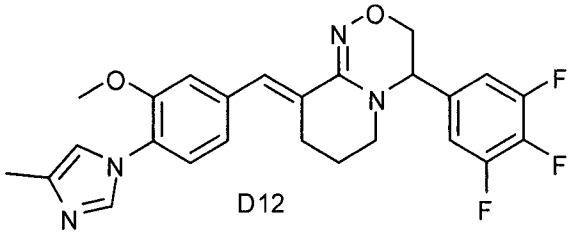
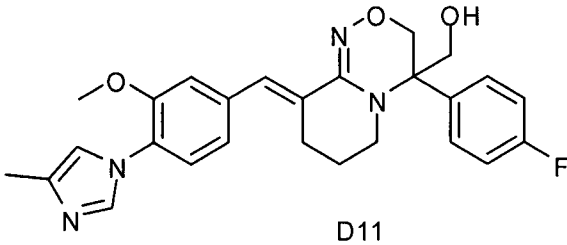


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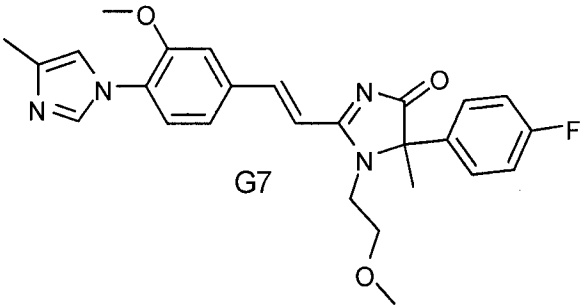
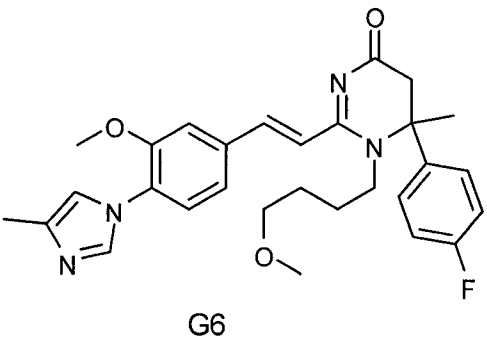
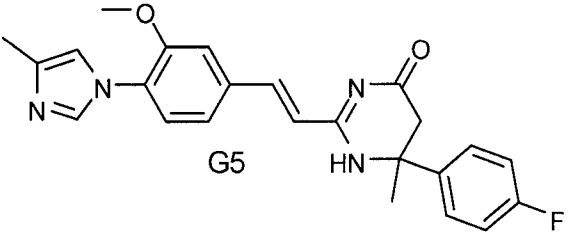
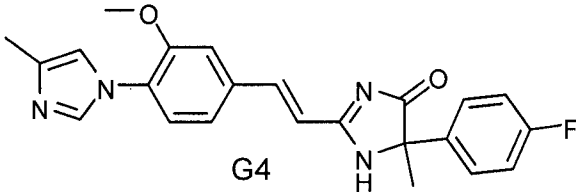
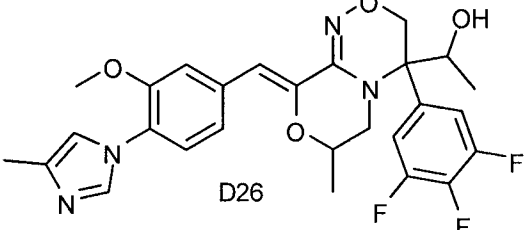
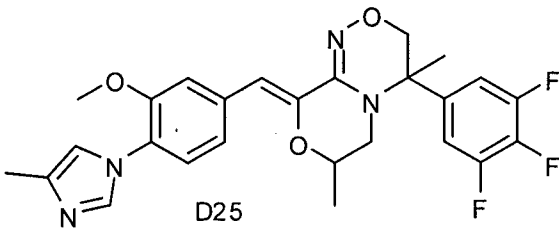
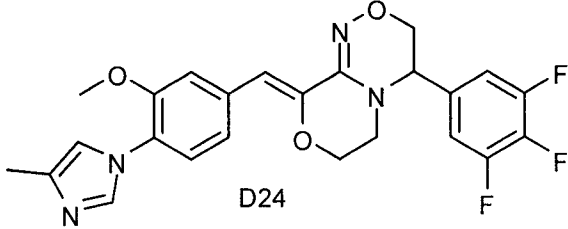
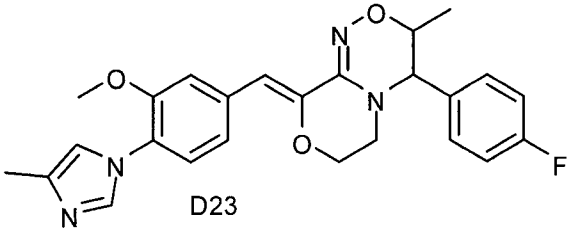
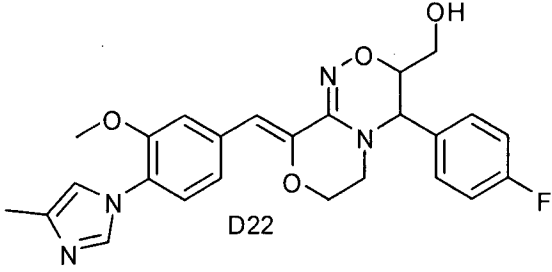
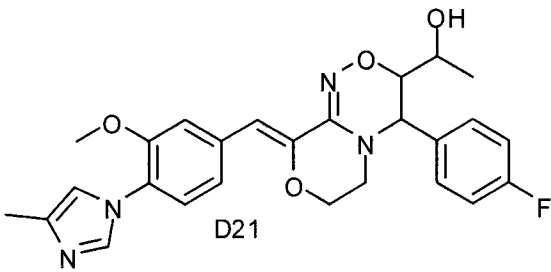
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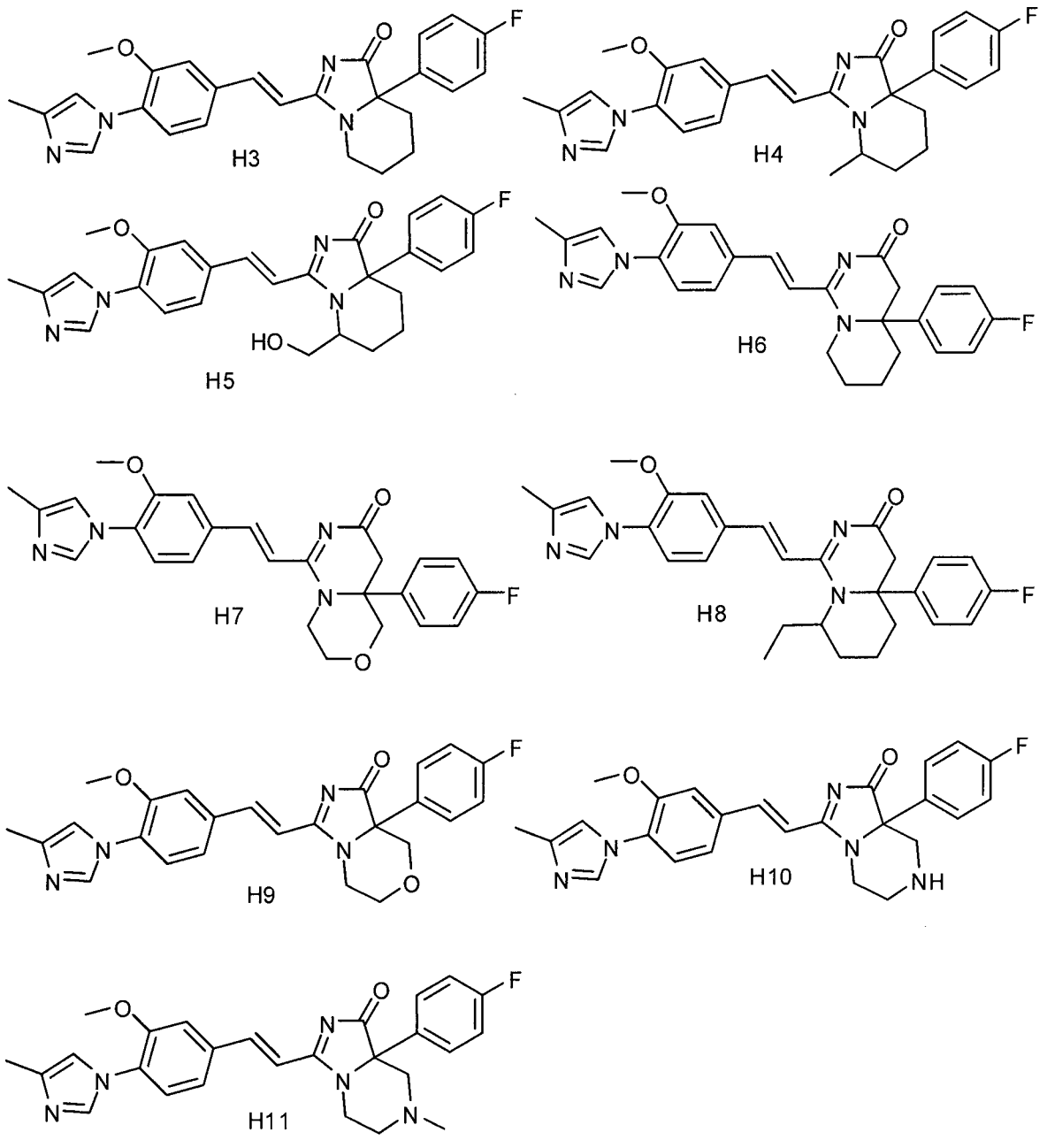
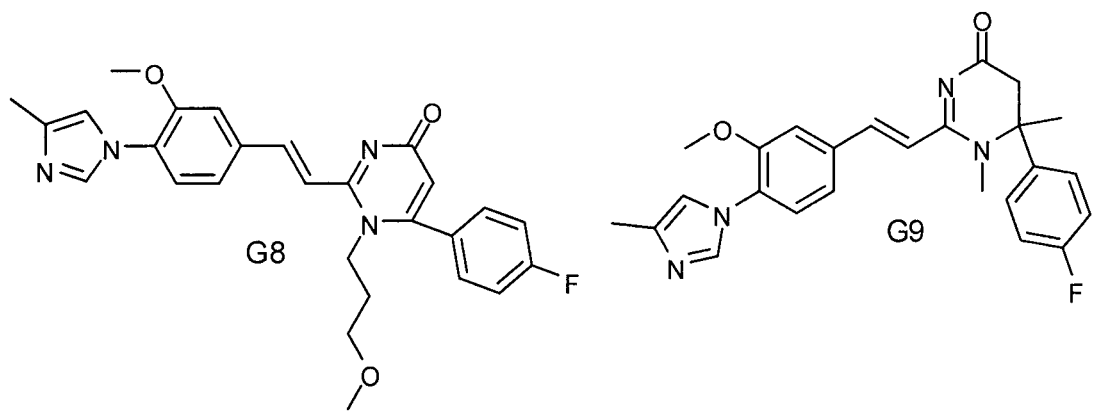


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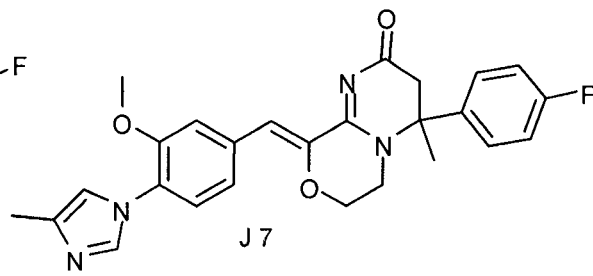
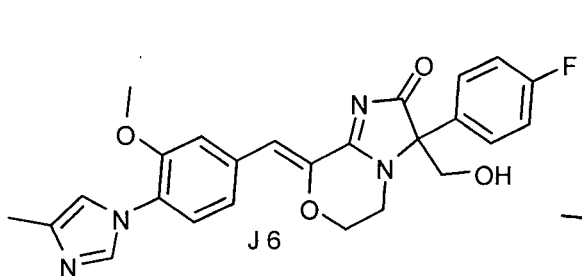
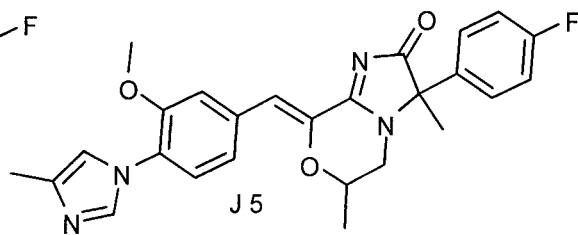
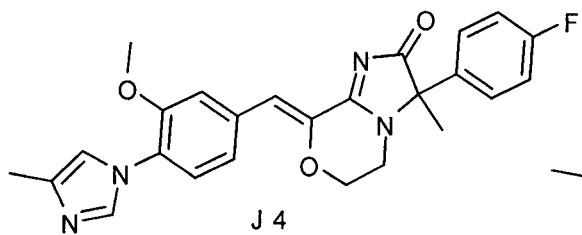
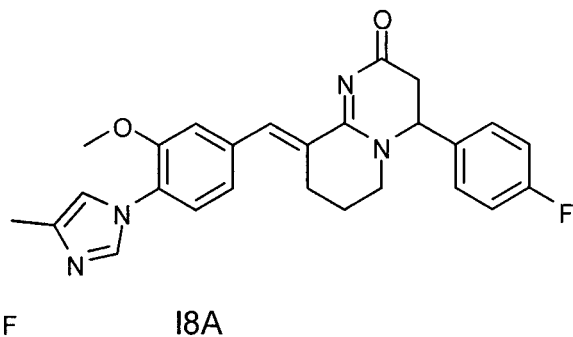
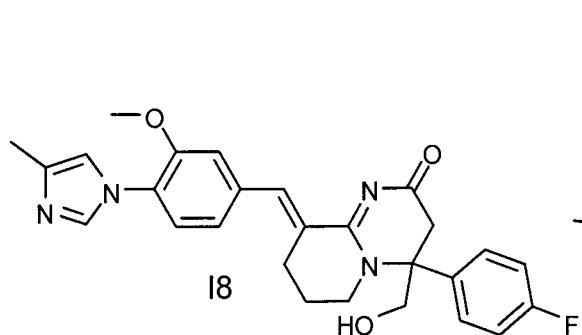
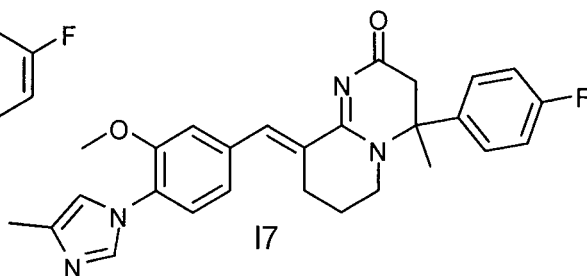
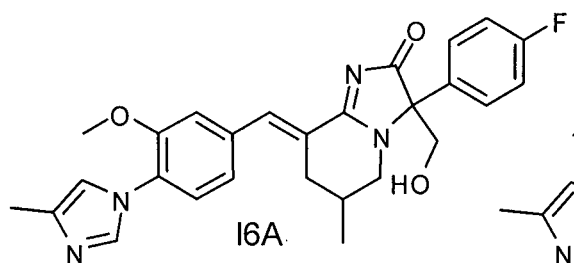
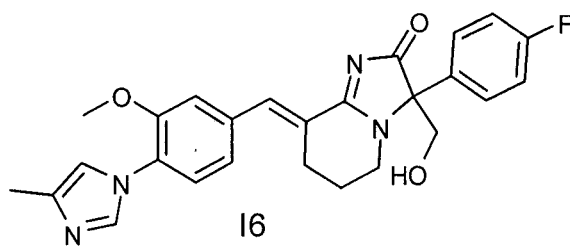
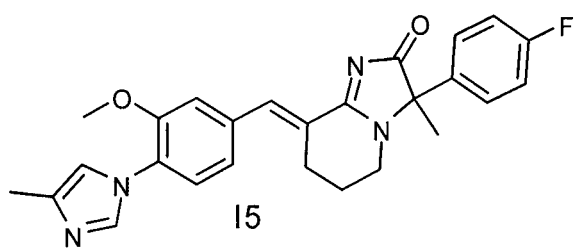




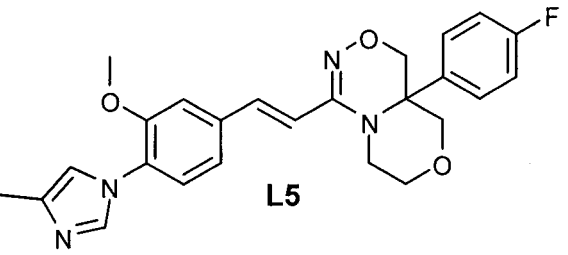
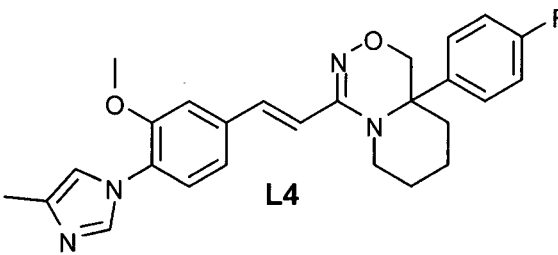
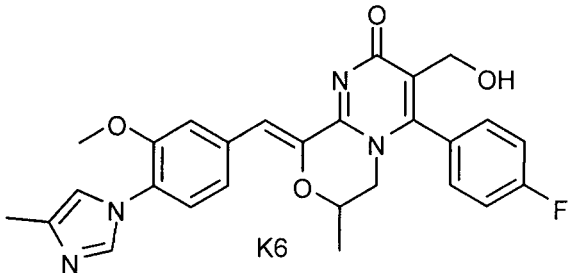
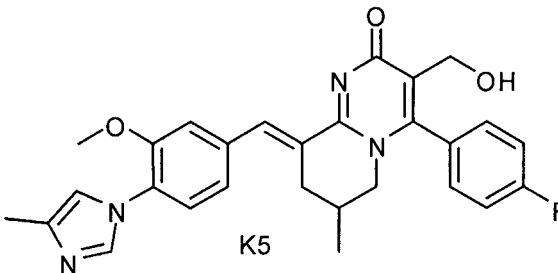
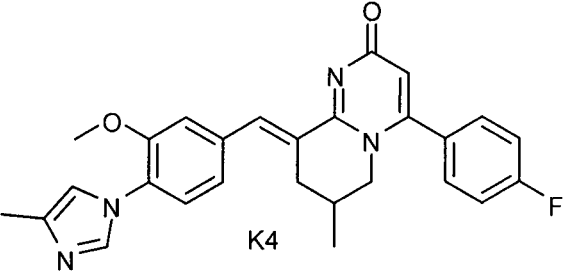
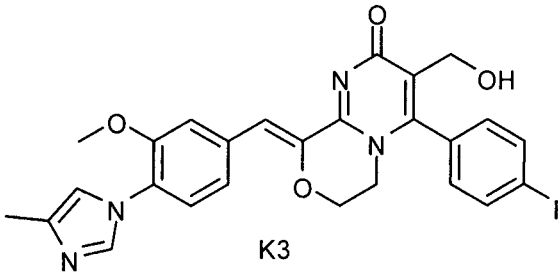
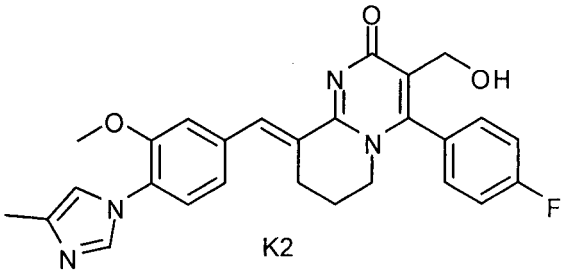
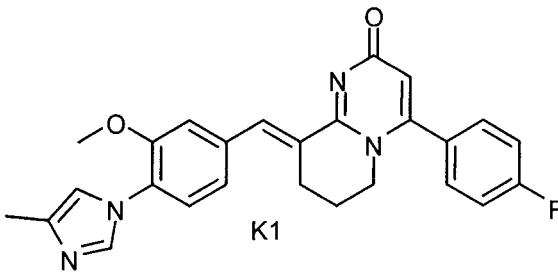
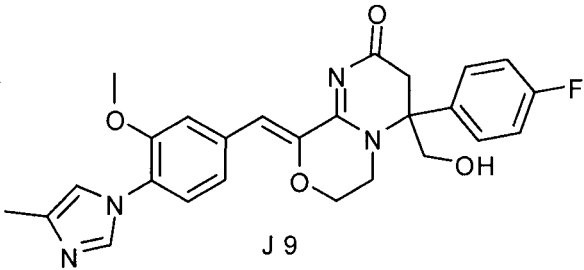
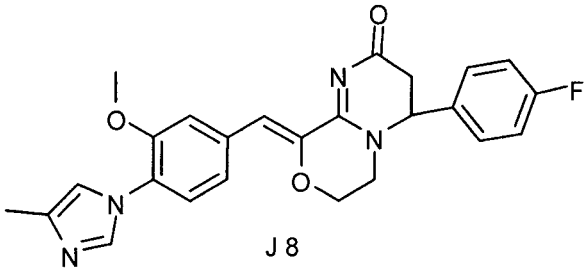
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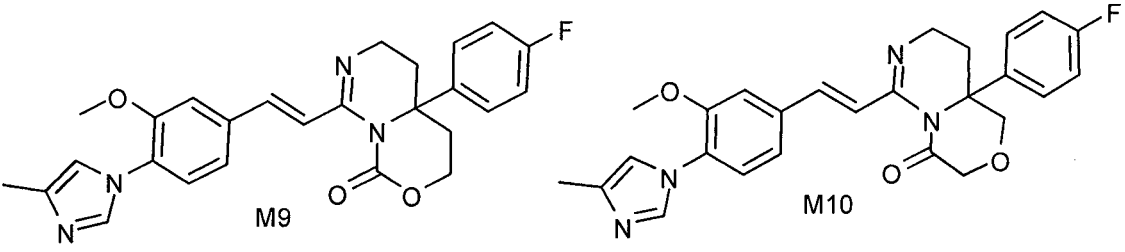
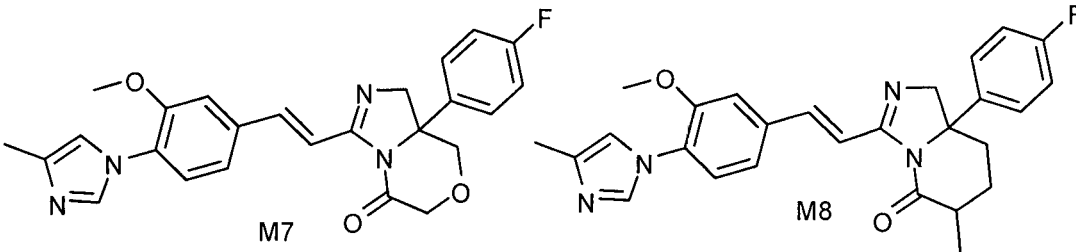
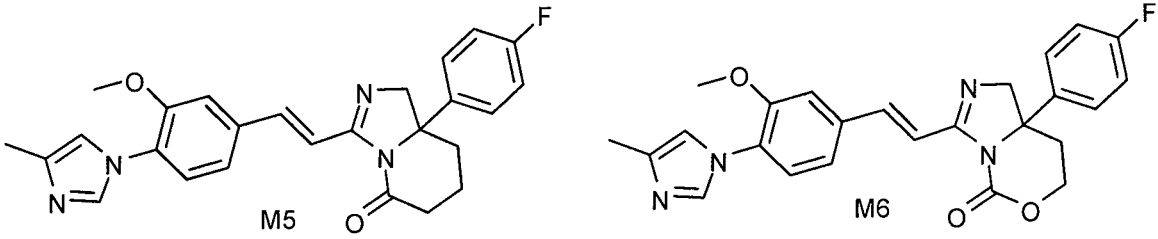
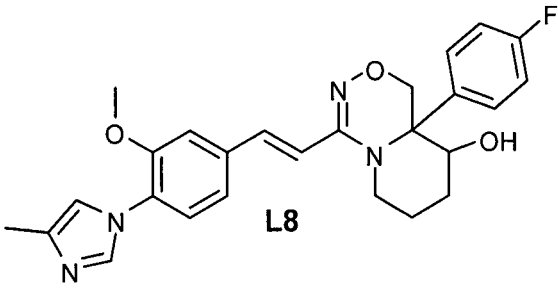
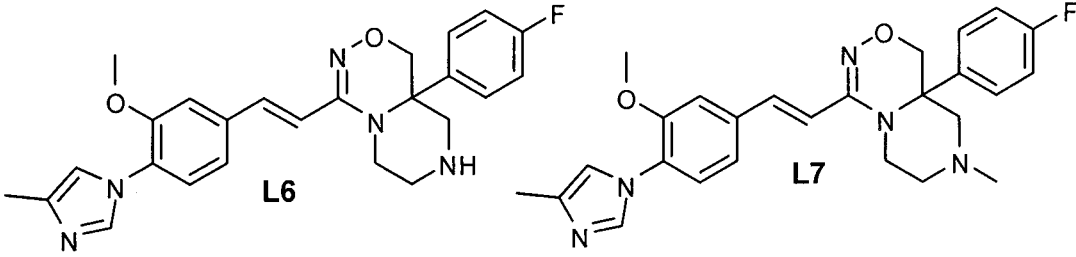
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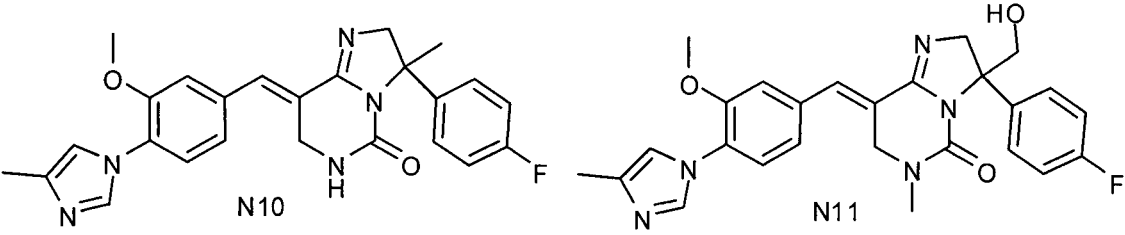
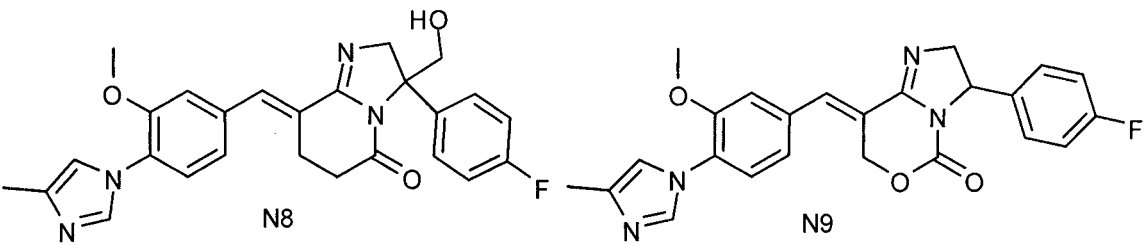
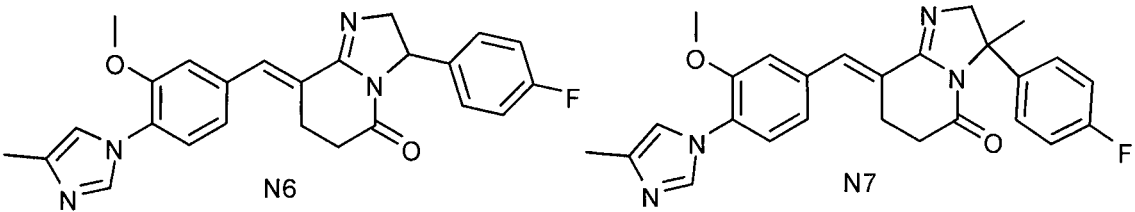
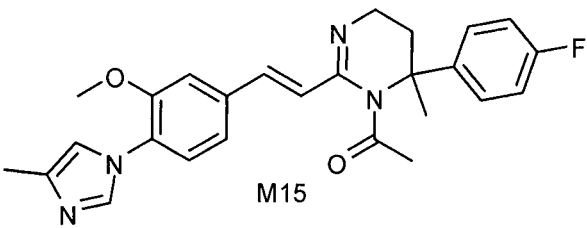
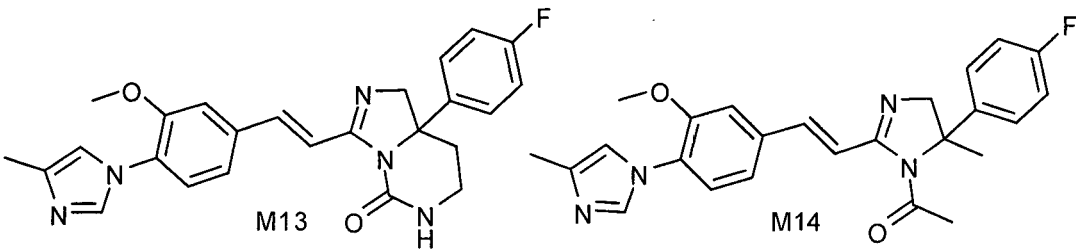
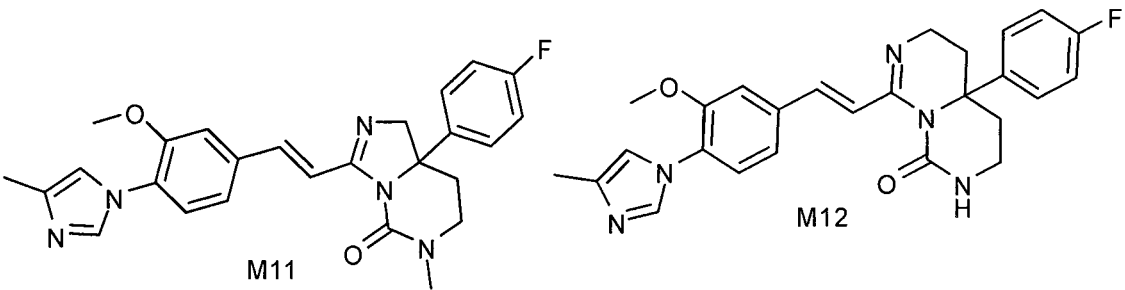
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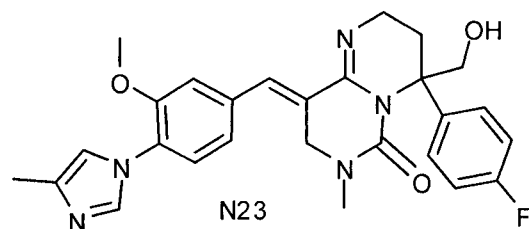
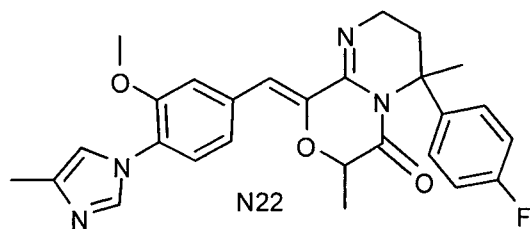
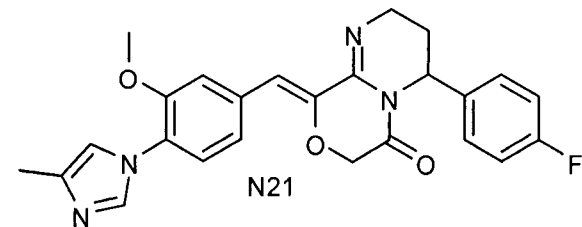
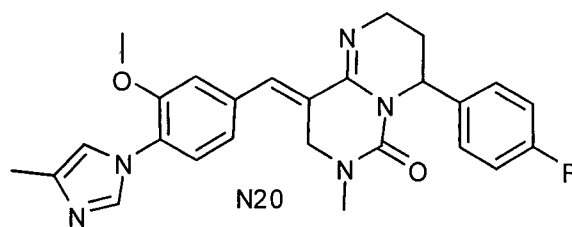
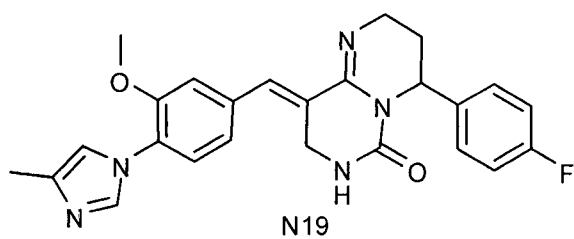
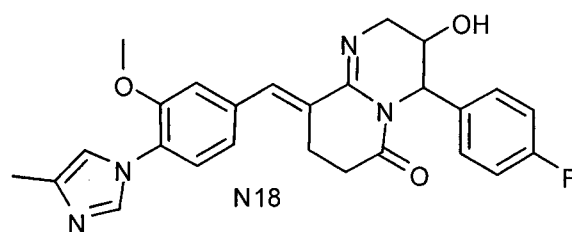
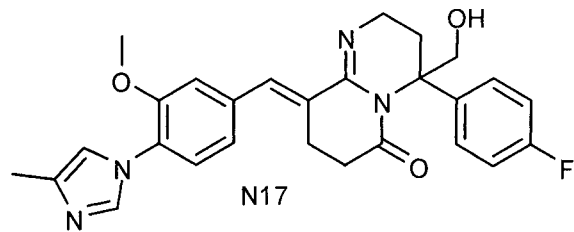
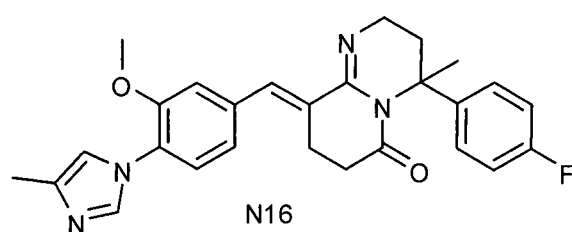
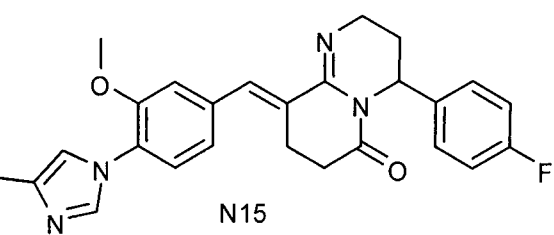
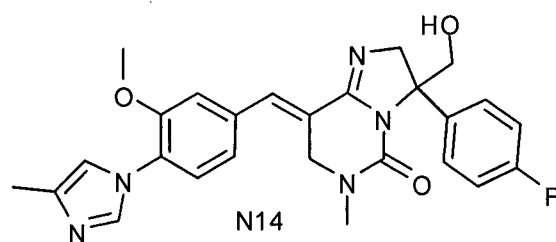
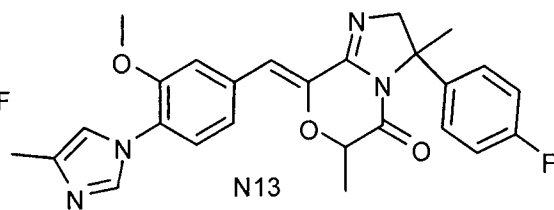
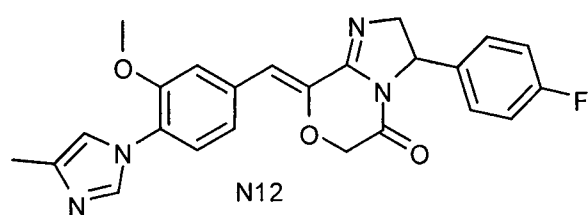
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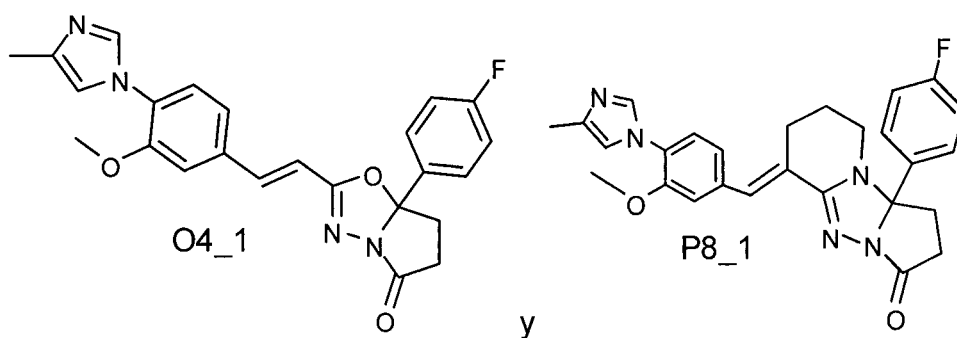
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o una de sus sales, solvatos, ésteres o prodrogas aceptables desde el punto de vista farmacéutico.

55. El compuesto de la reivindicación 56 en el cual dicho compuesto es una sal aceptable desde el punto de vista farmacéutico de un compuesto de la reivindicación 56.

56. El compuesto de la reivindicación 56 en el cual dicho compuesto es un solvato de un compuesto de la reivindicación 56.

57. El compuesto de la reivindicación 56 en el cual dicho compuesto es un éster de un compuesto de la reivindicación 56.

58. Una composición farmacéutica que comprende una cantidad efectiva para uso terapéutico de un compuesto de la reivindicación 1, y un vehículo aceptable desde el punto de vista farmacéutico.

59. Una composición farmacéutica que comprende una cantidad efectiva para uso terapéutico de un compuesto de la reivindicación 56, y un vehículo aceptable desde el punto de vista farmacéutico.

60. Una composición farmacéutica que comprende una cantidad efectiva para uso terapéutico de un compuesto de la reivindicación 1, y un vehículo aceptable desde el punto de vista farmacéutico, y una cantidad efectiva de uno o más fármacos farmacéuticamente activos distintos seleccionados del grupo que consiste en: (a) drogas útiles para el tratamiento de la enfermedad de Alzheimer,

(b) drogas útiles para inhibir la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico, (c) drogas útiles para tratar varias enfermedades neurodegenerativas, y (d) drogas útiles para inhibir la gamma-secretasa.

61. Una composición farmacéutica que comprende una cantidad efectiva para uso terapéutico de un compuesto de la reivindicación 56, y un vehículo aceptable desde el punto de vista farmacéutico, y una cantidad efectiva de uno o más fármacos farmacéuticamente activos distintos seleccionados del grupo que consiste en: (a) drogas útiles para el tratamiento de la enfermedad de Alzheimer, (b) drogas útiles para inhibir la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico, (c) drogas útiles para tratar varias enfermedades neurodegenerativas, y (d) drogas útiles para inhibir la gamma-secretasa.

62. Una composición farmacéutica que comprende una cantidad efectiva para uso terapéutico de un compuesto de la reivindicación 1, y un vehículo aceptable desde el punto de vista farmacéutico, y una cantidad efectiva de uno o más inhibidores de BACE.

63. Una composición farmacéutica que comprende una cantidad efectiva para uso terapéutico de un compuesto de la reivindicación 56, y un vehículo aceptable desde el punto de vista farmacéutico, y una cantidad efectiva de uno o más inhibidores de BACE.

64. Una composición farmacéutica:

(1) que comprende una cantidad efectiva para uso terapéutico de por lo menos un compuesto de la reivindicación 1, o una de sus sales, solvatos, o ésteres aceptables desde el punto de vista farmacéutico, y por lo menos un vehículo aceptable desde el punto de vista farmacéutico, o



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(2) que comprende una cantidad efectiva para uso terapéutico de por lo menos un compuesto de la reivindicación 1, o una de sus sales, solvatos, o ésteres aceptables desde el punto de vista farmacéutico, y por lo menos un vehículo aceptable desde el punto de vista farmacéutico, y una cantidad efectiva de uno o más fármacos farmacéuticamente activos distintos seleccionados del grupo que consiste en: (a) drogas útiles para el tratamiento de la enfermedad de Alzheimer, (b) drogas útiles para inhibir la deposición de la proteína amiloide (por ej., proteína beta amiloide) en, o alrededor de un tejido neurológico, (c) drogas útiles para tratar varias enfermedades neurodegenerativas, y (d) drogas útiles para inhibir la gamma-secretasa, o

(3) que comprende una cantidad efectiva para uso terapéutico de por lo menos un compuesto de la reivindicación 1, o una de sus sales, solvatos, o ésteres aceptables desde el punto de vista farmacéutico, y por lo menos un vehículo aceptable desde el punto de vista farmacéutico, y una cantidad efectiva de uno o más inhibidores de BACE,

(4) que comprende una cantidad efectiva para uso terapéutico de por lo menos un compuesto de la reivindicación 1, o una de sus sales, solvatos, o ésteres aceptables desde el punto de vista farmacéutico, y por lo menos un vehículo aceptable desde el punto de vista farmacéutico, y cantidad efectiva de uno o más inhibidores de colinesterasa, o

(5) que comprende una cantidad efectiva para uso terapéutico de por lo menos un compuesto de la reivindicación 1, y por lo menos un vehículo aceptable desde el punto de vista farmacéutico, y cantidad efectiva de uno o más inhibidores de colinesterasa, o

(6) que comprende una cantidad efectiva para uso terapéutico de por lo menos un compuesto de la reivindicación 1, o una de sus sales, solvatos, o ésteres aceptables desde el punto de vista farmacéutico, y por lo menos un

vehículo aceptable desde el punto de vista farmacéutico, y cantidad efectiva de uno o más inhibidores de BACE, antagonistas muscarínicos, inhibidores de colinesterasa; inhibidores de la gamma secretasa; moduladores de la gamma secretasa; inhibidores de la HMG-CoA reductasa; agentes anti-inflamatorios no esteroides; antagonistas del receptor de N-metil-D-aspartato; anticuerpos anti-amiloides; vitamina E; agonistas del receptor nicotínico de acetilcolina; agonistas inversos del receptor de CB1 o antagonistas del receptor de CB1; un antibiótico, secretagogos de la hormona del crecimiento; antagonistas de histamina H3; agonistas de AMPA; inhibidores de PDE4; agonistas inversos de GABA<sub>A</sub>; inhibidores de agregación amiloide; inhibidores de glucógeno sintasa quinasa beta; promotores de la actividad de alfa secretasa; inhibidores de PDE-10 e inhibidores de la absorción del colesterol, o

(7) que comprende una cantidad efectiva para uso terapéutico de por lo menos un compuesto de la reivindicación 1, y por lo menos un vehículo aceptable desde el punto de vista farmacéutico, y cantidad efectiva de uno o más inhibidores de BACE, antagonistas muscarínicos, inhibidores de colinesterasa; inhibidores de la gamma secretasa; moduladores de la gamma secretasa; inhibidores de la HMG-CoA reductasa; agentes anti-inflamatorios no esteroides; antagonistas del receptor de N-metil-D-aspartato; anticuerpos anti-amiloides; vitamina E; agonistas del receptor nicotínico de acetilcolina; agonistas inversos del receptor de CB1 o antagonistas del receptor de CB1; un antibiótico, secretagogos de la hormona del crecimiento; antagonistas de histamina H3; agonistas de AMPA; inhibidores de PDE4; agonistas inversos de GABA<sub>A</sub>; inhibidores de agregación amiloide; inhibidores de glucógeno sintasa quinasa beta; promotores de la actividad de alfa secretasa; inhibidores de PDE-10 e inhibidores de la absorción del colesterol, o

(8) que comprende una cantidad efectiva para uso terapéutico de por lo menos un compuesto de la reivindicación 1, o una de sus sales, solvatos, o



ésteres aceptables desde el punto de vista farmacéutico, y por lo menos un vehículo aceptable desde el punto de vista farmacéutico, y una cantidad efectiva de clorhidrato de donepezilo, o

(9) que comprende una cantidad efectiva para uso terapéutico de por lo menos un compuesto de la reivindicación 1, y por lo menos un vehículo aceptable desde el punto de vista farmacéutico, y una cantidad efectiva de clorhidrato de donepezilo.

65. Un método para modular la gamma-secretasa que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1 a un paciente que necesita de dicho tratamiento.

66. Un método de tratamiento de una o más de varias enfermedades neurodegenerativas, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1 a un paciente que necesita de tratamiento.

67. Un método de inhibición de la deposición de la proteína amiloide en, o alrededor de un tejido neurológico, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1 a un paciente que necesita de tratamiento.

68. Un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1 a un paciente que necesita de tratamiento.

69. Un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 56 a un paciente que necesita de tratamiento.

70. Un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de un compuesto de la reivindicación 1 a un paciente que necesita de tratamiento.

71. Un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de un compuesto de la reivindicación 56 a un paciente que necesita de tratamiento.

72. Un método para (a) modular la gamma-secretasa, (b) tratar una o más de varias enfermedades neurodegenerativas, (c) inhibir la deposición de la proteína amiloide en, o alrededor de un tejido neurológico, o (d) tratar la enfermedad de Alzheimer, que comprende administrar:

(1) una cantidad efectiva de un compuesto de la reivindicación 1, y

(2) una cantidad efectiva de uno o más principios farmacéuticamente activos distintos seleccionados del grupo que consiste en: inhibidores de BACE, antagonistas muscarínicos, inhibidores de colinesterasa; inhibidores de la gamma secretasa; moduladores de la gamma secretasa; inhibidores de la HMG-CoA reductasa; agentes anti-inflamatorios no esteroides; antagonistas del receptor de N-metil-D-aspartato; anticuerpos anti-amiloides; vitamina E; agonistas del receptor nicotínico de acetilcolina; agonistas inversos del receptor de CB1 o antagonistas del receptor de CB1; un antibiótico, secretagogos de la hormona del crecimiento; antagonistas de histamina H3; agonistas de AMPA; inhibidores de PDE4; agonistas inversos de GABA<sub>A</sub>; inhibidores de agregación amiloide; inhibidores de glucógeno sintasa quinasa beta; promotores de la actividad de alfa secretasa; inhibidores de PDE-10 e inhibidores de la absorción del colesterol,

a un paciente que necesita de dicho tratamiento.

73. Un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de un compuesto de la reivindicación 1, y una cantidad efectiva de uno o más compuestos seleccionados del grupo que consiste en inhibidores del anticuerpo A $\beta$ , inhibidores de la gamma secretasa e inhibidores de la beta secretasa, a un paciente que necesita de dicho tratamiento.

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74. Un método de tratamiento de la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de un compuesto de la reivindicación 1, y una cantidad efectiva de uno o más inhibidores de BACE, a un paciente que necesita de dicho tratamiento.

75. Un método para:

(1) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de una o más colinesterasa, a un paciente que necesita de tratamiento, o

(2) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de clorhidrato de donepezilo, a un paciente que necesita de tratamiento, o

(3) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de un compuesto de la reivindicación 1, en combinación con una cantidad efectiva de una o más colinesterasa, a un paciente que necesita de tratamiento, o

(4) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de un compuesto de la reivindicación 1, en combinación con una cantidad efectiva de clorhidrato de donepezilo, a un paciente que necesita de tratamiento, o

(5) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de (rivastigmina, a un paciente que necesita de dicho tratamiento, o

(6) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en

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combinación con una cantidad efectiva de tacrina, a un paciente que necesita de dicho tratamiento, o

(7) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de un inhibidor de quinasa Tau, a un paciente que necesita de dicho tratamiento, o

(8) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más inhibidores de quinasa Tau seleccionados del grupo que consiste en: inhibidores de GSK3beta, inhibidores de cdk5, inhibidores de ERK, a un paciente que necesita de dicho tratamiento, o

(9) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de una vacunación anti-Abeta, a un paciente que necesita de dicho tratamiento, o

(10) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más ligandos de APP, a un paciente que necesita de dicho tratamiento, o

(11) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más agentes que regulan en sentido ascendente la enzima degradante de insulina y/o neprilisina, a un paciente que necesita de dicho tratamiento, o

(12) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en

combinación con una cantidad efectiva de uno o más agentes reductores del colesterol, a un paciente que necesita de dicho tratamiento, o

(13) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más agentes reductores del colesterol seleccionados del grupo que consiste en: Atorvastatina, Fluvastatina, Lovastatina, Mevastatina, Pitavastatina, Pravastatina, Rosuvastatina, Simvastatina, y Ezetimibe, a un paciente que necesita de dicho tratamiento, o

(14) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más fibratos, a un paciente que necesita de dicho tratamiento, o

(15) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más fibratos seleccionados del grupo que consiste en, clofibrato, Clofibrade, Etofibrate, Clofibrato de aluminio, a un paciente que necesita de dicho tratamiento, o

(16) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más agonistas de LXR, a un paciente que necesita de dicho tratamiento, o

(17) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más imitadores de LRP, a un paciente que necesita de dicho tratamiento, o

(18) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en

combinación con una cantidad efectiva de uno o más antagonistas del receptor 5-HT6, a un paciente que necesita de dicho tratamiento, o

(19) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más agonistas del receptor nicotínico, a un paciente que necesita de dicho tratamiento, o

(20) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más antagonistas del receptor H3, a un paciente que necesita de dicho tratamiento, o

(21) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más inhibidores de histona desacetilasa, a un paciente que necesita de dicho tratamiento, o

(22) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más inhibidores de hsp90, a un paciente que necesita de dicho tratamiento, o

(23) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más agonistas del receptor muscarínico m1, a un paciente que necesita de dicho tratamiento, o

(24) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más moduladores o agonistas alostéricos positivos de antagonistas del receptor 5-HT6 mGluR1 o mGluR5, a un paciente que necesita de dicho tratamiento, o



(25) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más antagonistas de mGluR2/3, a un paciente que necesita de dicho tratamiento, o

(26) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de fórmula I, en combinación con una cantidad efectiva de uno o más agentes anti-inflamatorios que pueden reducir la neuroinflamación, a un paciente que necesita de dicho tratamiento, o

(27) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más antagonistas del receptor de Prostaglandina EP2, a un paciente que necesita de dicho tratamiento, o

(28) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más inhibidores de PAI-1, a un paciente que necesita de dicho tratamiento, o

(29) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más agentes que pueden inducir el eflujo Abeta, a un paciente que necesita de dicho tratamiento, o

(30) tratar la enfermedad de Alzheimer, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de gelsolin, a un paciente que necesita de dicho tratamiento, o

(31) tratar el Síndrome de Down, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1 a un paciente que necesita de tratamiento, o

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(32) tratar el Síndrome de Down, que comprende administrar una cantidad efectiva de un compuesto de la reivindicación 1 a un paciente que necesita de tratamiento, o

(33) tratar el Síndrome de Down, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de uno o más inhibidores de colinesterasa, a un paciente que necesita de tratamiento.

(34) tratar el Síndrome de Down, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1, en combinación con una cantidad efectiva de clorhidrato de donepezilo, a un paciente que necesita de tratamiento, o

(35) tratar el Síndrome de Down, que comprende administrar una cantidad efectiva de un compuesto de la reivindicación 1, en combinación con una cantidad efectiva de uno o más inhibidores de colinesterasa, a un paciente que necesita de tratamiento.

(37) tratar el Síndrome de Down, que comprende administrar una cantidad efectiva de un compuesto de la reivindicación 1, en combinación con una cantidad efectiva de clorhidrato de donepezilo, a un paciente que necesita de tratamiento, o

(38) tratar la insuficiencia cognitiva leve, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1 a un paciente que necesita de tratamiento, o

(39) tratar el glaucoma, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1 a un paciente que necesita de tratamiento, o

(40) tratar la angiopatía amiloide cerebral, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1 a un paciente que necesita de tratamiento, o

(41) tratar el infarto, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1 a un paciente que necesita de tratamiento, o

(42) Esta invención provee, además, un método de tratamiento de demencia, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1 a un paciente que necesita de tratamiento, o

(43) tratar la microgliosis, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1 a un paciente que necesita de tratamiento, o

(44) tratar la inflamación cerebral, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1 a un paciente que necesita de tratamiento, o

(45) tratar la pérdida de la función olfativa, que comprende administrar una cantidad efectiva de uno o más compuestos de la reivindicación 1 a un paciente que necesita de tratamiento.

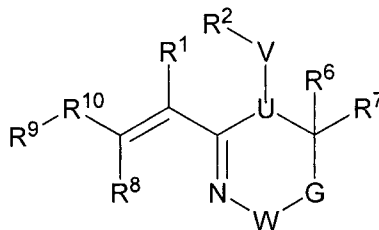
76. Un kit que comprende, en envases separados, en un envase individual, composiciones farmacéuticas para usar en forma combinada, en el cual un envase comprende una cantidad efectiva de un compuesto de la reivindicación 1 en un vehículo aceptable desde el punto de vista farmacéutico, y otro envase comprende una cantidad efectiva de otro principio farmacéuticamente activo, las cantidades combinadas del compuesto de la reivindicación 1 y otro principio farmacéuticamente activo efectivo para: (a) tratar la enfermedad de Alzheimer, o (b) inhibir la deposición de la proteína amiloide en, o alrededor de un tejido neurológico, o (c) tratar varias enfermedades neurodegenerativas, o (d) modular la actividad de gamma-secretasa.

p. de: SCHERING CORPORATION

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### RESUMEN DE LA INVENCIÓN

En sus muchas realizaciones, la presente invención proporciona una novedosa clase de compuestos heterocíclicos de la fórmula:



Fórmula I

como moduladores de la gamma secretasa, métodos para la preparación de dichos compuestos, composiciones farmacéuticas que contienen uno o más de dichos compuestos, métodos para la preparación de formulaciones farmacéuticas que comprenden uno o más de dichos compuestos, y métodos de tratamiento, prevención, inhibición, o alivio de una o más de varias enfermedades asociadas con la sistema nervioso central usando dichos compuestos o composiciones farmacéuticas.

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C07D 487/04 (2006.01) A61K 31/5365 (2006.01)  
C07D 498/04 (2006.01) A61P 25/28 (2006.01)  
A61K 31/4166 (2006.01)

(US). PALANI, Anandan [US/US]; 25 Reinhart Way,  
Bridgewater, New Jersey 08807 (US).

(74) Agent: JEANETTE, Henry, C.; Schering Corporation,  
2000 Galloping Hill Road, Patent Dept. K-6-1 1990, Ke-  
nilworth, New Jersey 07033 (US).

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(71) Applicant (for all designated States except US): SCHER-  
ING CORPORATION [US/US]; 2000 Galloping Hill  
Road, Kenilworth, New Jersey 07033 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): ZHU, Zhaoning  
[US/US]; 6 Cypress Court, Plainsboro, New Jersey 08536  
(US). GREENLEE, William, J. [US/US]; 115 Herrick  
Avenue, Teaneck, New Jersey 07666 (US). HUANG,  
Xianhai [CN/US]; 16 Hemlock Circle, Warren, New  
Jersey 07059 (US). MCKITTRICK, Brian, A. [US/US];  
14 Millbrook Road, New Vernon, New Jersey 07976 (US).  
CLADER, John, W. [US/US]; 428 North Union Avenue,  
Cranford, New Jersey 07016 (US). MCBRIAR, Mark, D.  
[US/US]; 14 Crestview Drive, Clinton, New Jersey 08809

(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,  
CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE,  
EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID,  
IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC,  
LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN,  
MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,  
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ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL,  
NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG,  
CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report  
— before the expiration of the time limit for amending the  
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(88) Date of publication of the international search report:  
19 March 2009

(54) Title: GAMMA SECRETASE MODULATORS

(57) Abstract: In its many embodiments, the present invention provides a novel class of heterocyclic compounds of the formula: as modulators of gamma secretase, methods of preparing such compounds, pharmaceutical compositions containing one or more such compounds, methods of preparing pharmaceutical formulations comprising one or more such compounds, and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the central nervous system using such compounds or pharmaceutical compositions.

WO 2008/153793 A3

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2008/006734

673

## A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D403/10 C07D471/04 C07D487/04 C07D498/04 A61K31/4166  
A61K31/517 A61K31/519 A61K31/5365 A61P25/28

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages              | Relevant to claim No. |
|-----------|-------------------------------------------------------------------------------------------------|-----------------------|
| A         | US 2007/117798 A1 (KIMURA TEIJI [JP] ET AL) 24 May 2007 (2007-05-24)<br>claims 1,17-20<br>----- | 1                     |

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the International filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \* & \* document member of the same patent family

Date of the actual completion of the international search

27 January 2009

Date of mailing of the international search report

03/02/2009

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040,  
Fax: (+31-70) 340-3016

Authorized officer

Beyss-Kahana, Ellen

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2008/006734

17H

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|-------------------------------------------|---------------------|----------------------------|---------------------|
| US 2007117798 A1                          | 24-05-2007          | AR 058198 A1               | 23-01-2008          |
|                                           |                     | AU 2006317457 A1           | 31-05-2007          |
|                                           |                     | CA 2629745 A1              | 31-05-2007          |
|                                           |                     | EP 1953154 A1              | 06-08-2008          |
|                                           |                     | WO 2007060810 A1           | 31-05-2007          |
|                                           |                     | KR 20080069221 A           | 25-07-2008          |



No. 09-137086- -00000-0000

Fecha: 2009-12-01 16:37:09 Dep. 2020 DIR.NUEVASCR  
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI  
Act. 411 PRESENTACION Folios: 674**REQUISITOS MÍNIMOS PARA ADMISIÓN A TRAMITE  
PCT**

PATENTE DE INVENCION

[ ]

MODELO DE UTILIDAD [ ]

- ◆ Indicación de que se solicita la concesión de una patente [ ]
- ◆ Datos de identificación del solicitante o de la persona que presenta la solicitud [ ]
- ◆ Descripción de la invención [ ]
- ◆ Dibujos de ser estos pertinentes [ ]
- ◆ Comprobante de pago de las tasas establecidas [ ]

COMPLETA [ ]

INCOMPLETA [ ]

DISEÑO INDUSTRIAL [ ]

- ◆ Indicación de que se solicita el registro de Diseño Industrial [ ]
- ◆ Datos de identificación del solicitante o de la persona que presenta la solicitud [ ]
- ◆ Representación gráfica y fotográfica del Diseño Industrial o muestra del material que incorpora el diseño [ ]
- ◆ Comprobante de pago de las tasas establecidas [ ]

COMPLETA [ ]

INCOMPLETA [ ]

ESQUEMA DE TRAZADO [ ]

- ◆ Indicación de que se solicita el registro de un Esquema de Trazado [ ]
- ◆ Datos de identificación del solicitante o de la persona que presenta la solicitud [ ]
- ◆ Representación gráfica del esquema trazado [ ]
- ◆ Comprobante de pago de las tasas establecidas [ ]

COMPLETA [ ]

INCOMPLETA [ ]

Edson Navarro

Firma Responsable

Fecha 01-12-2009

Carrera 13 No. 27-00 Piso 5,7y10  
Conmutador: 3 82 0840  
Fax: 3505220  
E-mail: [info@sic.gov.co](mailto:info@sic.gov.co)  
[www.sic.gov.co](http://www.sic.gov.co)  
Bogotá D.C. - Colombia





Bogotá,  
2020

Doctor(a)  
OLARTE GARCIA CARLOS REYNALDO  
Apoderado(a) y/o Representante de  
SCHERING CORPORATION

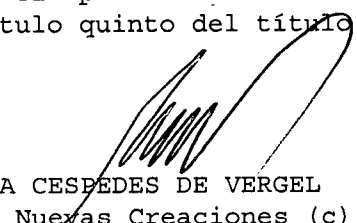
|            |                            |                   |
|------------|----------------------------|-------------------|
| REFERENCIA | Radicación No.             | 9 137086          |
|            | Solicitud internacional    | PCT/US2008/006734 |
|            | Fecha inicio fase nacional | 01/01/2010        |
|            | Trámite                    | 11                |
|            | Evento                     | 378               |
|            | Actuación                  | 430               |
|            | Oficio No.                 | 1295              |

Como resultado del examen de forma, realizado con fundamento en el artículo 38 de la Decisión 486 de la Comisión de la Comunidad Andina, artículo 27 del Tratado de Cooperación en Materia de Patentes (PCT), regla 51 bis del Reglamento y Circular Única de la Superintendencia de Industria y Comercio, se le comunica que:

1. La solicitud no contiene la copia del documento en que consta la cesión del derecho a la patente del inventor al solicitante o a su causante, conforme a lo establecido por el artículo 26 literal k) de la Decisión 486 de la Comisión de la Comunidad Andina. Cuando se trate de documentos otorgados en el extranjero, estos deberán legalizarse de conformidad con lo dispuesto por los artículos 259 y 260 del Código de Procedimiento Civil. Cuando se trate de las declaraciones a que hace referencia la Regla 4.17 ii) del Tratado de Cooperación en Materia de Patentes PCT., el alcance de las tales declaraciones se determinará según indiquen claramente una cesión de derechos del inventor al solicitante o su causante, de conformidad con lo dispuesto en el numeral 5.2.15 del Capítulo Quinto, Título X de la Circular Única de Superintendencia de Industria y Comercio.

En cumplimiento de lo dispuesto por el artículo 39 de la Decisión 486, se le requiere para que dentro del término de dos meses siguientes a la fecha de notificación del presente oficio, complete los requisitos anteriormente enunciados. En caso de no dar cumplimiento al presente requerimiento, la solicitud se considerará abandonada y perderá su prelación.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única No.10 de 2001.

  
ALIX CARMENZA CESPEDES DE VERGEL  
Directora de Nuevas Creaciones (c)

El anterior requerimiento fue notificado por fijación en lista de fecha 05 FEB. 2010  
adpall

Al contestar favor indique el número de radicación consignado en el rótulo

Sede Centro: Carrera 13 No. 27-00 pisos 2, 5, 7 y 10 PBX: 5870000  
Sede CAN: Av. Carrera 50 No. 26 - 55 int.2. Tel 5880070  
Call Center 6513240. Línea 01800-910165  
Web: www.sic.gov.co e-mail: info@sic.gov.co  
Bogotá D.C. Colombia



Bogotá,  
2020

Doctor(a)  
OLARTE GARCIA CARLOS REYNALDO  
Apoderado(a) y/o Representante de  
SCHERING CORPORATION

|            |                            |                   |
|------------|----------------------------|-------------------|
| REFERENCIA | Radicación No.             | 9 137086          |
|            | Solicitud internacional    | PCT/US2008/006734 |
|            | Fecha inicio fase nacional | 01/01/2010        |
|            | Trámite                    | 11                |
|            | Evento                     | 378               |
|            | Actuación                  | 430               |
|            | Oficio No.                 | 1236              |

Teniendo en cuenta que el capítulo reivindicatorio presentado excede de quince reivindicaciones, es necesario que cancele la tasa establecida por cada reivindicación adicional presentada, de conformidad con lo dispuesto en la resolución de tasas vigente para la fecha de presentación de la solicitud, so pena de que no sean tenidas en cuenta dentro del presente trámite administrativo.

En consecuencia, con fundamento en lo previsto por el artículo 12 del Código Contencioso Administrativo, se le requiere para que dentro del término de dos (2) meses siguientes a la fecha de notificación del presente oficio atienda el requerimiento aquí señalado. Lo anterior, con el alcance que para tal efecto establece el artículo 13 de la misma codificación, respecto de las reivindicaciones adicionales.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única N° 10 de 2001.

ALIX CARMENZA CESPEDES DE VERGEL  
Directora de Nuevas Creaciones (c)

El anterior requerimiento fue notificado por fijación en lista de  
fecha 05 FEB. 2010  
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