1346

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DIVISION DE NUEVAS CREACIONES

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Apoderado: Ernesto Cavelier Franco

ASUNTO	Radicación	07-33374
	Trámite	002
	Evento	001
	Actuación	430
	Oficio	
	Folios	12082

Patente de Invención ⊗

Vía PCT (fase nacional) ⊗ Cap.I ⊗ Cap. II ☐

No. Sol. Internacional PCT/US2005/031146
Fecha de Presentación Internal. 31/03/2006

Como resultado del examen de fondo, realizado con fundamento en el artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le comunica:

1. Documentos estudiados

1.1. Descripción: Folios: 563 a 1263 Como se radicó inicialmente

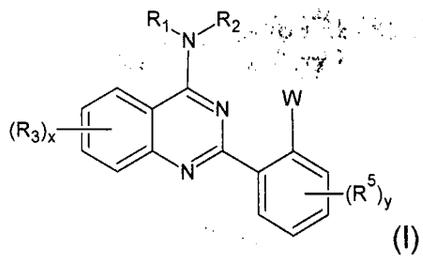
1.2. Reivindicaciones: Folios 1264 a 1292 como se radicó inicialmente

1.3. Prioridad: Folio 1: 60/607.150; 02/09/2004
60/607.037; 02/09/2004
60/607.033; 02/09/2004
60/607.245; 02/09/2004
60/607.036; 02/09/2004

2. Objeto de la invención

Título de la solicitud: QUINAZOLINAS ÚTILES COMO MODULADOR DE CANALES IÓNICOS.

El objeto de la invención se refiere a derivados de 2-fenilquinazolin-4-amina, que caen bajo el alcance de la fórmula Markush (I):



(I)

-Reivindicaciones 1–62: Un compuesto de la fórmula (I):
-Reivindicación 63: Composiciones que los contienen
-Reivindicación 64-69: Procedimiento de tratamiento que consiste en administrar un compuesto a un paciente

Se catalogó la invención, según la Clasificación Internacional de Patentes (IPC.): C07D239/94, C07D 401/04, C07D401/12, C07D403/04, C07D403/12, C07D403/14, C07D405/12, C07D405/14, A61K31/498, A61P9/06, A61P25/00

3. De la solicitud de Patente

4.2Reivindicaciones *(artículo 30 de la Decisión 486 de la CA.N.y/o art.22 Tratado PCT.*

-La reivindicación 1 no es clara, reclama compuestos bajo la denominación de "*derivados farmacéuticamente aceptables*". Es un intento por definir la materia en términos del resultado a conseguir. Por lo tanto, no es permisible una expresión de este tipo en las reivindicaciones. Son compuestos referenciados por una propiedad deseada sin tener un límite definido. Tampoco se encuentra definido el sustituyente secundario W que esta sobre el fenilo de la posición 2 del núcleo fenilquinazolina.

-La reivindicación 62, se refiere a la descripción, ya que la descripción no limita la invención, por lo cual no se acepta en las reivindicaciones. Entonces debe quedar explícitamente establecido los compuestos a que hace referencia.

No cumplen con el requisito de claridad, concisión o sustento por la descripción de acuerdo al art. 30 de la Decisión 486.

4. Excepción a la patentabilidad *(artículo 20 D486 literal d) de la C.A.N.)*

-Las reivindicaciones 64 a 69 reclaman un método terapéutico por lo tanto están incluidas en el alcance del artículo 20 D486 literal d) de la C.A.N.

5. Determinación del Estado de la Técnica

La fecha que se ha tenido en cuenta para determinar el estado de la técnica fecha de presentación de la solicitud de la cual se reclama prioridad, 02/sep/2004.
Teniendo en cuenta la fecha indicada se realizó la búsqueda del estado de la técnica, en bases de datos donde esta oficina tiene acceso libre, para búsqueda de documentos relacionados con la materia que se reclama como nueva e inventiva en presente solicitud, encontrándose los siguientes documentos más relevantes:

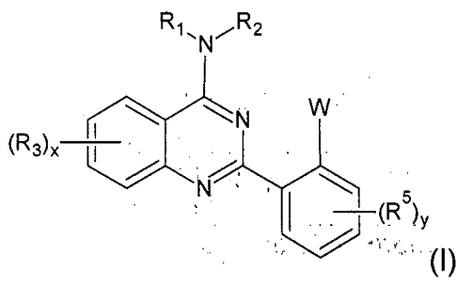
N°	Documento	Título	Fecha de Publicación*
D1	US3517005	Certain 2-and 4-quinazolines	23/jun/1970

D2	US3637963	Hydroxyarylquinazolines and their use as UV-absorbers	25/ene/1972
D3	JP2000229950	Production of quinazoline derivative or salt thereof	13/mar/2000
D4	WO2004	Quinazolines useful as modulators of ion chanels	16/sep/2004

6. Análisis de patentabilidad (artículo 14 D486)

6.1. Novedad (artículo 16 D486 de la C.A.N.)

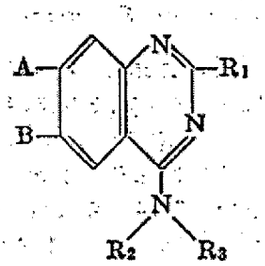
La solicitud en estudio reclama derivados de 2-fenilquinazolin-4-amina, que caen bajo el alcance de la fórmula Markush (I):



(I)

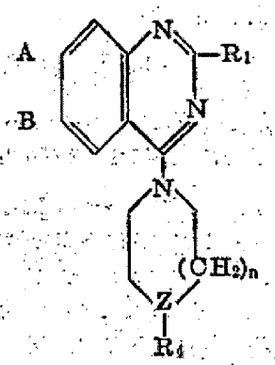
D1 enseña describe compuestos derivados de 2-fenilquinazolin-4-amina, de la fórmula:

The compounds of this invention are those of the following formulae:



I

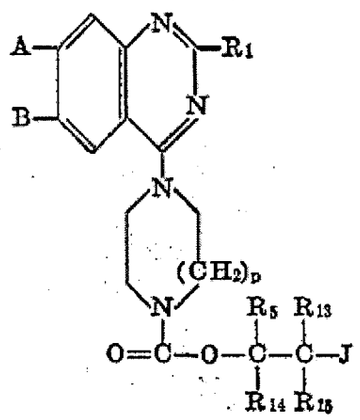
and



II

and

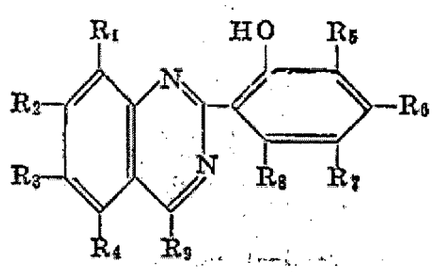
and



Pero R_1 no toma el significado de fenilo, por lo tanto la solicitud en estudio cumple con el requisito exigido en artículo 16 D486 de la C.A.N.

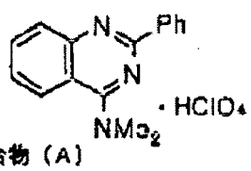
-D2 decribe derivados de 2-hidrofenil-quinazolina de fórmula:

These and other objectives are accomplished according to the present invention by novel 2-(o-hydroxyaryl) quinazolines of the formula

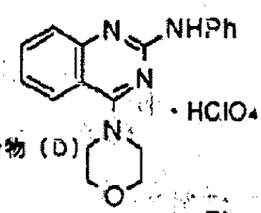


Pero R_9 no toma los significados de los sustituyentes (A), (B), (C), (D) ó (E) como la solicitud en estudio, por lo tanto la presente solicitud cumple con el requisito exigido en artículo 16 D486 de la C.A.N.

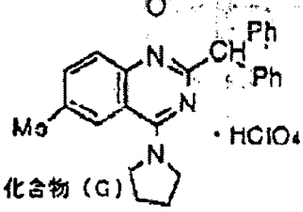
-D2 enseña compuestos 2-fenil-quinazolina-4-sustituida con heterociclo que comprende nitrógeno:



化合物 (A)



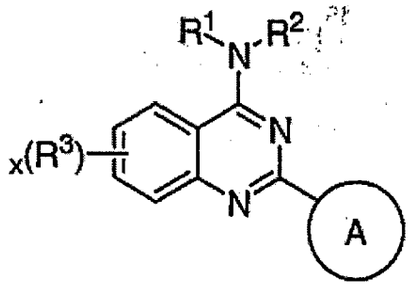
化合物 (D)

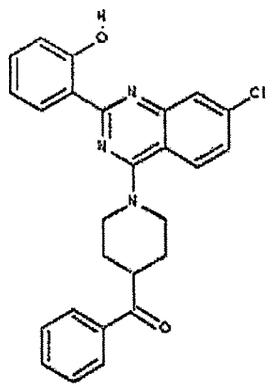
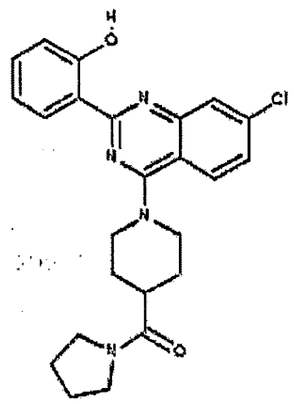


化合物 (G)

Pero sustituyente heterociclo con nitrógeno, unido a la posición 4 del núcleo quinazolina no contiene los sustituyentes secundarios, como la solicitud en estudio por lo tanto esta solicitud cumple con el requisito exigido en artículo 16 D486 de la C.A.N.

-D4 describe compuestos 2-fenil-quinazolina-4-sustituida con heterociclo sustituido con grupo carbinil y carboxiderivados:



	1016
	536

También véase ejemplos 633-635, 886, 916, 917, 942, 943, 964, 965, 1016 las **reivindicaciones 1-249**, donde está comprendida la materia que en la presente, ya que el núcleo quinazolina esta sustituido en la posición 2 por fenilo sustituido y en la posición 4 por un heterociclo con nitrógeno el cual está unido directamente a la quinazolina y además el heterociclo esta igualmente sustituido, que son la características esenciales de la invención, por lo tanto la solicitud en estudio no cumple cumple con el requisito exigido en artículo 16 D486 de la C.A.N.

7. Conclusión:

Los requisitos de patentabilidad de la presente solicitud se encuentran afectados así:

N°	Documento N°	Reivindicaciones Afectadas	Requisito que Afecta
D4	WO2004078733	1-69	novedad

En cumplimiento del artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le indica que debe dar respuesta dentro del término de sesenta días contados a partir de la fecha de notificación de la presente comunicación. En caso

de no dar respuesta al presente requerimiento, o si a pesar de la respuesta subsistieran los impedimentos para la concesión, se denegará la patente.

Notifíquese el presente oficio conforme a lo dispuesto en el artículo 8 de la resolución reglamentaria No. 00210 del 15 de enero de 2001, advirtiendo que contra él no procede recurso alguno en la vía gubernativa.

ALIX CARMENZA CESPEDES DE VERGEL
Directora de Nuevas Creaciones (c)

El anterior requerimiento fue notificado por fijación en lista, de fecha 17 SET. 2010

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

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Published:
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— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: QUINAZOLINES USEFUL AS MODULATORS OF ION CHANNELS

(57) Abstract: The present invention relates to quinazoline compounds of formula (I) useful as inhibitors of voltage-gated sodium channels and calcium channels. The invention also provides pharmaceutically acceptable compositions comprising the compounds of the invention and methods of using the compositions in the treatment of various disorders. or a pharmaceutically acceptable derivative thereof, wherein R^1, X, R^3, x, and ring A are as defined in the present application.

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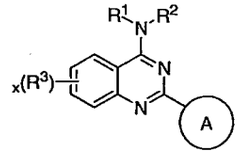
CLAIMS

1. A compound of formula **IA**:



IA

or a pharmaceutically acceptable salt thereof, wherein:

R^1 and R^2, taken together with the nitrogen atom to which they are bound, form an optionally substituted 3-12-membered monocyclic or bicyclic saturated, partially unsaturated, or fully unsaturated ring having 0-3 additional heteroatoms independently selected from nitrogen, sulfur, or oxygen; wherein the ring formed by R^1 and R^2 taken together, is optionally substituted at one or more substitutable carbon, nitrogen, or sulfur atoms with z independent occurrences of $-R^4$, wherein z is 0-5;

Ring A is a 5-7-membered monocyclic aryl ring or an 8-10-membered bicyclic aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or is a 3-12-membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein ring A is optionally substituted with y independent occurrences of $-R^5$, wherein y is 0-5, and is additionally optionally substituted with q independent occurrences of R^{5a}, wherein q is 0-2;

x is 0-4;

each occurrence of R^3, R^4, and R^5 is independently $Q\text{-}R^X$; wherein Q is a bond or is a C_1-C_6 alkylidene chain wherein up to two non-adjacent methylene units of Q are optionally and independently replaced by –NR-, -S-, -O-, -CS-, $-CO_2-$, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, $-NRCO_2-$, $-SO_2NR-$, $-NRSO_2-$, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, $-NRSO_2NR-$, -SO-, $-SO_2-$, -PO-, $-PO_2-$, -OP(O)(OR)-, or -POR-; and each occurrence of R^X is independently selected from -R', halogen, =O, =NR', $-NO_2$, -CN, -OR', -SR', $-N(R')_2$, $-NR'COR'$, $-NR'CON(R')_2$, $-NR'CO_2R'$, -COR', $-CO_2R'$, -OCOR', $-CON(R')_2$, $-OCON(R')_2$, -SOR', $-SO_2R'$, $-SO_2N(R')_2$, $-NR'SO_2R'$, $-NR'SO_2N(R')_2$, -COCOR', $-COCH_2COR'$, $-OP(O)(OR')_2$, $-P(O)(OR')_2$, $-OP(O)_2OR'$, $-P(O)_2OR'$, $-PO(R')_2$, or $-OPO(R')_2$;

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each occurrence of R^{5a} is independently an optionally substituted C_1-C_6aliphatic group, halogen, -OR', -SR', -N(R')$_2$, -NR'COR', -NR'CON(R')$_2$, -NR'CO_2R', -COR', -CO_2R', -OCOR', -CON(R')$_2$, -OCON(R')$_2$, -SOR', -SO_2R', -SO_2N(R')$_2$, -NR'SO_2R', -NR'SO_2N(R')$_2$, -COCOR', -$COCH_2$COR', -OP(O)(OR')$_2$, -P(O)(OR')$_2$, -$OP(O)_2$OR', -$P(O)_2$OR', -PO(R')$_2$, or -OPO(R')$_2$; and

each occurrence of R is independently hydrogen or an optionally substituted C_{1-6} aliphatic group; and each occurrence of R' is independently hydrogen or an optionally substituted C_{1-6} aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R', two occurrences of R, or two occurrences of R', are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

provided that:

a. when R^1 and R^2, taken together with the nitrogen atom to which they are bound, form an optionally substituted 4-membered monocyclic saturated or partially unsaturated ring having 0-3 additional heteroatoms independently selected from nitrogen, sulfur, or oxygen; then 2-Oxazolidinone, 3-[(3R,4R)-2-oxo-1-(2-phenyl-4-quinazolinyl)-4-[2-(3-pyridinyl)ethenyl]-3-azetidinyl]-4-phenyl-, (4S)- is excluded;

b. when R^1 and R^2, taken together with the nitrogen atom to which they are bound, form an optionally substituted 5-membered monocyclic saturated or partially unsaturated ring having 0-3 additional heteroatoms independently selected from nitrogen, sulfur, or oxygen; then:

i. ring A is not optionally substituted hexahydro-1H-1,4-diazepin-1-yl; and

ii. Benzenesulfonamide, 2-methoxy-5-[2-[[1-(2-phenyl-4-quinazolinyl)-3-pyrrolidinyl]amino]ethyl]-, (R)-, bis(trifluoroacetate), and Benzenesulfonamide, 2-methoxy-5-[2-[[1-(2-phenyl-4-quinazolinyl)-3-pyrrolidinyl]amino]ethyl]-, (S)-, bis(trifluoroacetate) are excluded;

iii. 3-Pyrrolidinamine, 1-(2-phenyl-4-quinazolinyl)-, and (R)- 3-Pyrrolidinamine, 1-(2-phenyl-4-quinazolinyl)-, (S)- are excluded;

iv. when R^1 and R^2, taken together are unsubstituted pyrrolidin-1-yl, ring A is unsubstituted phenyl, and x is 1, then R^3 is not 6-OMe or 6-OH;

v. when R^1 and R^2, taken together are unsubstituted pyrrolidin-1-yl, ring A is unsubstituted phenyl, and x is 2, then the two R^3 groups are not 6-OMe and 7-OMe;

vi. when R^1 and R^2, taken together are unsubstituted pyrrolidin-1-yl, then ring A is not unsubstituted pyrrolidin-1-yl, optionally substituted piperazin-1-yl, unsubstituted morpholin-1-yl; or unsubstituted piperidin-1-yl;

vii. when R^1 and R^2, taken together are pyrrolidin-1-yl, x is 0 and ring A is unsubstituted phenyl, then the pyrrolidin-1-yl group is not substituted at the 3-position with –OH or 2-methoxy-phenoxy;

viii. when R^1 and R^2, taken together are unsubstituted pyrrolidin-1-yl, and x is 0, then ring A is not 2,3-xylyl, 3-methylphenyl, unsubstituted phenyl, 4-bromo-phenyl, 4-chloro-phenyl, 3-nitro-phenyl, unsubstituted pyrid-3-yl, 2,4-dichlorophenyl, 3,4-dichlorophenyl, 4-propoxyphenyl, 3-methylphenyl, 3,4,5-trimethoxyphenyl, 2-chlorophenyl, unsubstituted pyrid-4-yl, 2-hydroxyphenyl, or 4-(1,1-dimethylethyl)phenyl;

c. when R^1 and R^2, taken together with the nitrogen atom to which they are bound, form an optionally substituted 6-membered monocyclic or bicyclic saturated or partially unsaturated ring having 0-3 additional heteroatoms independently selected from nitrogen, sulfur, or oxygen; then:

i. when R^1 and R^2, taken together form an unsubstituted morpholino ring, and ring A is unsubstituted phenyl, then x is not 0, or if x is 1 or 2, then R^3 is not: 6-fluoro, 6,7-dimethoxy, 6-nitro, 6-AcHN-, 6-methox, 6-NH2, 6-OCHN-, 6-OH, 6-AcMeN-, 6-TsHN-, 6-Me2N-, 7-OH, 6-amino-thiazol-2-yl, 6-NHCOCOOEt, or 6-(4-phenyl-amino-thiazol-2-yl);

ii. when R^1 and R^2, taken together form an unsubstituted morpholino ring, and ring A is unsubstituted cyclohexyl, unsubstituted pyrid-3-yl, unsubstituted 2-furyl, 2-fluorophenyl, 3-thienyl, benzofuran, pyridazine, phenyl substituted in one or more of the 3, 4, or 5-position of the phenyl ring, and x is 1 or 2, then R^3 is not 6-NH_2, 6-OHCHN-, 6-OH, 7-OH, 6-MsHN-, 6-AcHN-, 6-fluoro, or 6-OMe;

iii. when R^1 and R^2, taken together, form a piperid-4-one, piperid-4-ol, or thiomorpholino, or a dimethyl substituted morpholino ring, ring A is unsubstituted phenyl, and x is 1, then R^3 is not 6-OH;

iv. when x is 0 and A is unsubstituted phenyl, 3,4,5-trimethoxyphenyl, or 3,4-dimethoxyphenyl, then R^1 and R^2, taken together is not optionally substituted piperidinyl or optionally substituted piperazinyl;

v. when x is 2 or 3, and R^3 is 6,7-diOMe, or 6,7,8-triOMe, then R^1 and R^2, taken together is not optionally substituted piperidin-1-yl, piperazin-1-yl, or morpholin-1-yl;

vi. when x is 0 and ring A is unsubstituted phenyl, then R^1 and R_2, taken together is not optionally substituted or fused piperazinyl;

vii. when x is 0 and ring A is phenyl optionally substituted in one or more of the 3-,4-,or 5-positions of the phenyl ring, then R^1 and R^2, taken together is not optionally substituted piperazin-1-yl, or morpholin-1-yl;

viii. when x is 0 and ring A is 2-F-phenyl, then R^1 and R^2, taken together is not 4-(2-Cl-phenyl)-piperazin-1-yl, 4-(3-Cl-phenyl)-piperazin-1-yl, or unsubstituted morpholin-1-yl;

ix. when x is 0 and ring A is 2-Cl-phenyl, then R^1 and R^2, taken together is not unsubstituted morpholin-1-yl, 4-Me-piperazin-1-yl, 4-Et-piperazin-1-yl, 4-phenyl-piperazin-1-yl, or 4-CH_2Ph_2-piperazin-1-yl;

x. when x is 0 and ring A is 2-OH-phenyl, then R1 and R2, taken together is not unsubstituted morpholin-1-yl, 4-(2-OMe-phenyl)-piperazin-1-yl, 4-CH2Ph-piperazin-1-yl, 4-Et-piperazin-1-yl, or 4-Me-piperazin-1-yl;

xi. when x is 0, x is 1 and R^3 is 6-Br, or x is 2 and R^3 is 6-7-diOMe, and ring A is optionally substituted 2- or 3-thienyl, then R^1 and R^2, taken together is not 4-Ph-piperazin-1-yl, 4-(3-CF_3-phenyl)-piperazin-1-yl, 4-(2-OEt-phenyl)-piperazin-1-yl, 4-Me-piperazinyl, or unsubstituted morpholin-1-yl;

xii when x is 0, and ring A is unsubstituted pyrid-3-yl or pyrid-4-yl, then R^1 and R^2, taken together is not optionally substituted morpholin-1-yl, or optionally substituted piperazin-1-yl;

xiii. when x is 0, and ring A is optionally substituted 1H-imidazol-2-yl or 1H-imidazol-1-yl, then R^1 and R^2 taken together is not unsubstituted morpholin-1-yl, 4-Me-piperazin-1-yl, or 4-CH_2CH_2OH-piperazin-1-yl;

xiv. when x is 0 and ring A is 5-NO_2-thiazol-2-yl, then R^1 and R^2, taken together is not 4-Me-piperazin-1-yl;

xv. when x is 0 and ring A is 5-NO_2-2-furanyl, then R^1 and R^2, taken together is not 4-

CH_2CH_2OH-piperazin-1-yl, 4-Me-piperazin-1-yl, or unsubstituted morpholin-1-yl;

xvi. when x is 1, R^3 is 6-OH and ring A is unsubstituted phenyl, then R^1 and R^2, taken together is not unsubstituted morpholin-1-yl, or 4-Me-piperazin-1-yl;

xvii. when x is 0 and R^1 and R^2, taken together is unsubstituted piperidinyl, then ring A is not 2-OH-phenyl, 4-OMe-phenyl, 4-F-phenyl, 4-NO_2-phenyl, pyrid-3-yl, pyrid-4-yl, 2-Cl-phenyl, 4-O_nPr-phenyl, 3,4-dichlorophenyl, 2-F-phenyl, 4-Br-phenyl, 4-Cl-phenyl, 3-NO_2-phenyl, or 2,4-dichlorophenyl;

xviii. when x is 0, ring A is 4-Br-phenyl, 2-F-phenyl, 2-Cl-phenyl, 4-Cl-phenyl, 4-OnPr-phenyl, 2,4-dichlorophenyl, 3,4-dichlorophenyl, 4-Me-phenyl, 3-Me-phenyl, pyrid-3-yl, pyrid-4-yl, 2-OH-phenyl, 4-NO2-phenyl, 4-tBu-phenyl, then R^1 and R^2, taken together is not 2-Me-piperidin-1-yl, 4-CH2-Ph-piperidin-1-yl, 4-Me-piperidin-1-yl, 3-COOEt-piperidin-1-yl, 4-COOEt-piperidin-1-yl, 2-Et-piperidin-1-yl, 3-Me-piperidin-1-yl, 3,5-diMe-piperidin-1-yl, 4-$CONH_2$-piperidin-1-yl, (4-piperidinyl, 4-carboxamide)-piperidin-1-yl, 1,4-dioxa-8-azaspiro[4.5]decane, 3,4-dihydro-2(1H)-isoquinolinyl,or piperidin-4-one;

xix. when x is 1, R^3 is 6-Br, 6-Cl, 6-OH, 6-OMe, or 6-Me and ring A is 4-bromophenyl, 4-$CH_2P(O)(OH)(OEt)$phenyl, or unsubstituted phenyl, then R^1 and R^2, taken together, is not optionally substituted piperidinyl;

xx.when x is 2, and R^3 is 6,7-dimethoxy, and A is unsubstituted phenyl, then R^1 and R^2, taken together is not 1,4-dioxa-8-azaspiro[4.5]decane or 3,4-dihydro-2(1H)-isoquinolinyl;

xxi. when x is 3, and the three occurrences of R^3 are 5-OAc, 6-OAc, and 8-piperidinyl , and ring A is unsubstituted phenyl, then R^1 and R^2, taken together is not an unsubstituted piperidinyl ring;

xxii. when x is 3 and the three occurrences of R^3 are 6-Me, 7-COOEt, and 8-Me, and ring A is 2-Cl-phenyl, then R^1 and R^2, taken together, is not 4-phenyl-piperidin-1-yl, 4-(4-Cl-phenyl)-piperazin-1-yl, unsubstituted piperazin-1-yl, 4-CH_2Ph-piperazin-1-yl, 4(2-Cl-phenyl)piperazin-1-yl, or 4-COOEt-piperazin-1-yl;

c. when R^1 and R^2, taken together with the nitrogen atom to which they are bound, form an optionally substituted 7-membered monocyclic or bicyclic saturated or partially unsaturated ring having 0-3 additional heteroatoms independently selected from nitrogen, sulfur, or oxygen; then:

i. Benzenesulfonamide, 2-methoxy-5-[2-[5-(2-phenyl-4-quinazolinyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]ethyl]-, and bis(trifluoroacetate) 2,5-Diazabicyclo[2.2.1]heptane, 2-

(2-phenyl-4-quinazolinyl)- are excluded;

ii. when x is 2 and both occurrences of R^3 are OMe, and ring A is 4-Cl-phenyl, then R^1 and R^2, taken together is not unsubstituted hexahydro-1H-azepin-1-yl;

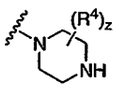
iii. when x is 0 and R^1 and R^2, taken together is unsubstituted hexahydro-1H-azepin-1-yl, then ring A is not unsubstituted phenyl, 4-F-phenyl, 4-NO_2-phenyl, pyrid-4-yl, 3,4-diCl-phenyl, 2-Cl-phenyl, 2,4-diCl-phenyl, 2,4-diCl-phenyl, 3-NO_2-phenyl, 4-Cl-phenyl, 4-O_nPr-phenyl, 3-Me-phenyl, 3,4-OMe-phenyl, 3,4,5-OMe-phenyl, pyrid-3-yl, or 2-OH-phenyl;

d. when R^1 and R^2, taken together with the nitrogen atom to which they are bound, form an optionally substituted 8-membered monocyclic or bicyclic saturated or partially unsaturated ring having 0-3 additional heteroatoms independently selected from nitrogen, sulfur, or oxygen; then:

i. Benzenesulfonamide, 2-methoxy-5-[2-[8-(2-phenyl-4-quinazolinyl)-3,8-diazabicyclo[3.2.1]oct-3-yl]ethyl]-, bis(trifluoroacetate) 3,8-Diazabicyclo[3.2.1]octane, 3-(phenylmethyl)-8-(2-phenyl-4-quinazolinyl)- 3,8-Diazabicyclo[3.2.1]octane, 8-(2-phenyl-4-quinazolinyl)-; Quinazoline, 2-(3-methylphenyl)-4-(1,3,3-trimethyl-6-azabicyclo[3.2.1]oct-6-yl)-, monohydrochloride; Quinazoline, 2-(4-nitrophenyl)-4-(1,3,3-trimethyl-6-azabicyclo[3.2.1]oct-6-yl)-, monohydrochloride; Quinazoline, 2-(3-methylphenyl)-4-(1,3,3-trimethyl-6-azabicyclo[3.2.1]oct-6-yl)-; Quinazoline, 2-(4-methylphenyl)-4-(1,3,3-trimethyl-6-azabicyclo[3.2.1]oct-6-yl)-; and Quinazoline, 2-(4-nitrophenyl)-4-(1,3,3-trimethyl-6-azabicyclo[3.2.1]oct-6-yl)-are excluded; and

e. when R^1 and R^2, taken together with the nitrogen atom to which they are bound, form an optionally substituted 9-membered monocyclic or bicyclic saturated or partially unsaturated ring having 0-3 additional heteroatoms independently selected from nitrogen, sulfur, or oxygen; then: Piperazine, 1-[4-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-6,7-dimethoxy-2-quinazolinyl]-4-(2-furanylcarbonyl)- is excluded.

2. The compound of claim 1, wherein the ring formed by R^1 and R^2 taken together is selected from:



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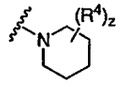

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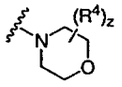

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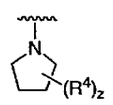

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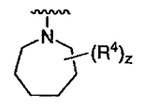

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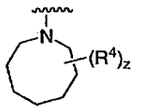

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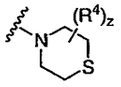

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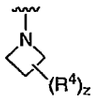

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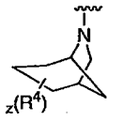

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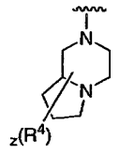

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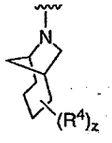

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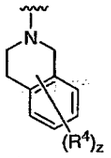

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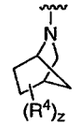


oo

wherein the ring formed by R^1 and R^2 taken together, is optionally substituted at one or more substitutable carbon, nitrogen, or sulfur atoms with z independent occurrences of $-R^4$, and z is 0-5.

3. The compound of claim 2, wherein R^1 and R^2 taken together is an optionally substituted ring selected from azetidin-1-yl (**jj**), pyrrolidin-1-yl (**ff**), piperidin1-yl (**dd**), piperazin-1-yl (**cc**), or morpholin-4-yl (**ee**).

4. The compound of claim 2, wherein R^1 and R^2 taken together is an optionally substituted ring selected from azetidin-1-yl (**jj**), pyrrolidin-1-yl (**ff**), piperidin1-yl (**dd**), or piperazin-1-yl (**cc**).

5. The compound of claim 2, wherein R^1 and R^2, taken together is selected from:

a. optionally substituted azetidin-1-yl (**jj**), wherein z is 1 or 2 and at least one occurrence of R^4 is $-NRSO_2R'$, -NRCOOR', or -NRCOR';

b. optionally substituted azetidin-1-yl (**jj**), wherein z is 1 and R^4 is $-NRSO_2R'$;

c. optionally substituted azetidin-1-yl **(jj)**, wherein z is 1 and R^4 is -NRCOOR';

d. optionally substituted azetidin-1-yl **(jj)**, wherein z is 1 and R^4 is –NRCOR';

e. optionally substituted pyrrolidin-1-yl **(ff)**, wherein z is 1 or 2 and R^4 is Cl, Br, F, CF_3, CH_3, $-CH_2CH_3$, -OR', or $-CH_2OR'$;

f. optionally substituted piperidin-1-yl **(dd)**, wherein z is 1 or 2 and at least one occurrence of R^4 is Cl, Br, F, CF_3, CH_3, $-CH_2CH_3$, -OR', or $-CH_2OR'$, $–NRSO_2R'$, -NRCOOR', or $–OCON(R')_2$;

g. optionally substituted piperidin-1-yl **(dd)**, wherein z is 1 and R^4 is F, CF_3, CH_3, $-CH_2CH_3$, -OR', or $-CH_2OR'$;

h. optionally substituted piperidin-1-yl **(dd)**, wherein z is 1 and R^4 is $–NRSO_2R'$;

i. optionally substituted piperidin-1-yl **(dd)**, wherein z is 1 and R^4 is -NRCOOR';

j. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 or 2 and at least one occurrence of R^4 is –SOR', $-CON(R')_2$, $-SO_2N(R')_2$, -COR', or –COOR';

k. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is –SOR'

l. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is –COOR';

m. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is $-CON(R')_2$;

n. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is $-SO_2N(R')_2$; or

o. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is -COR'.

6. The compound of claim 1, wherein z is 0-5, and R^4 groups, when present, are each independently halogen, CN, NO_2, $-N(R')_2$, $-CH_2N(R')_2$, -OR', $-CH_2OR'$, -SR', $-CH_2SR'$, -COOR', -NRCOR', $-CON(R')_2$, $-OCON(R')_2$, COR', -NHCOOR', $-SO_2R'$, $-SO_2N(R')_2$, or an optionally substituted group selected from C_1.C_6aliphatic, aryl, heteroaryl, cycloaliphatic, heterocycloaliphatic, arylC_1-C_6alkyl, heteroarylC_1-C_6alkyl, cycloaliphaticC_1-C_6alkyl, or heterocycloaliphaticC_1-C_6alkyl.

7. The compound of claim 1, wherein z is 0-5 and R^4 groups are each independently Cl, Br, F, CF_3, CH_3, $-CH_2CH_3$, CN, -COOH, $–N(CH_3)_2$, $-N(Et)_2$, $-N(iPr)_2$, $-O(CH_2)_2OCH_3$, $-CONH_2$, $-COOCH_3$, -OH, $-CH_2OH$, $-NHCOCH_3$, $-SO_2NH_2$, $-SO_2(CH_2)_3CH_3$, $-SO_2CH(CH_3)_2$, $-SO_2N(CH_3)_2$, $-SO_2CH_2CH_3$, $-C(O)OCH_2CH(CH_3)_2$, $-C(O)NHCH_2CH(CH_3)_2$, $-NHCOOCH_3$, $-C(O)C(CH_3)_3$, $-COO(CH_2)_2CH_3$, $-C(O)NHCH(CH_3)_2$, $-C(O)CH_2CH_3$, or an optionally substituted group selected from -piperidinyl, piperizinyl, morpholino, C_{1-4}alkoxy, phenyl, phenyloxy, benzyl, benzyloxy, $-CH_2$cyclohexyl, pyridyl, $-CH_2$pyridyl, or $-CH_2$thiazolyl.

8. The compound of claim 1, wherein x is 0-4, and R^3 groups, when present, are each independently halogen, CN, NO_2, $-N(R')_2$, $-CH_2N(R')_2$, -OR', $-CH_2OR'$, -SR', $-CH_2SR'$, -COOR', -NRCOR', $-CON(R')_2$, $-OCON(R')_2$, COR', -NHCOOR', $-SO_2R'$, $-SO_2N(R')_2$, or an optionally substituted group selected from C_1-C_6aliphatic, aryl, heteroaryl, cycloaliphatic, heterocycloaliphatic, arylC_1-C_6alkyl, heteroarylC_1-C_6alkyl, cycloaliphaticC_1-C_6alkyl, or heterocycloaliphaticC_1-C_6alkyl.

9. The compound of claim 1, wherein x is 1 or 2, and each occurrence of R^3 is independently Cl, Br, F, CF_3, $-OCF_3$, Me, Et, CN, -COOH, $-NH_2$, $–N(CH_3)_2$, $-N(Et)_2$, $-N(iPr)_2$, $-O(CH_2)_2OCH_3$, $-CONH_2$, $-COOCH_3$, -OH, $-OCH_3$, $-OCH_2CH_3$, $-CH_2OH$, $-NHCOCH_3$, $-NHCOCH(CH_3)_2$, $-SO_2NH_2$, -CONH(cyclopropyl), $-CONHCH_3$, $-CONHCH_2CH_3$, or an optionally substituted group selected from -piperidinyl, piperizinyl, morpholino, phenyl, phenyloxy, benzyl, or benzyloxy.

10. The compound of claim 1, wherein x is 1 or 2 and each R^3 group is independently halogen, CN, optionally substituted C_1-C_6alkyl, OR', $N(R')_2$, $CON(R')_2$, or NRCOR'.

11. The compound of claim 1, wherein x is 1 or 2, and each R^3 group is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-CONHCH_3$, $-CONHCH_2CH_3$, -CONH(cyclopropyl), $-OCH_3$, $-NH_2$, $-OCH_2CH_3$, or -CN.

12. The compound of claim 1, wherein x is 1 and R^3 is at the 6-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-CONHCH_3$, $-CONHCH_2CH_3$, -CONH(cyclopropyl), $-OCH_3$, $-NH_2$, $-OCH_2CH_3$, or -CN.

13. The compound of claim 1, wherein x is 1 and R^3 is at the 7-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-CONHCH_3$, $-CONHCH_2CH_3$, -CONH(cyclopropyl), $-OCH_3$, $-NH_2$, $-OCH_2CH_3$, or -CN.

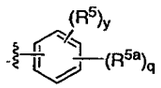
15. The compound of claim 1, wherein x is 1 and R^3 is at the 6-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-OCH_3$, or $-OCH_2CH_3$.

15. The compound of claim 1, wherein x is 1 and R^3 is at the 7-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-OCH_3$, or $-OCH_2CH_3$.

16. The compound of claim 1, wherein x is 1 and R^3 is at the 6-position of the quinazoline ring and is $-CON(R')_2$, or NRCOR'.

17. The compound of claim 1, wherein x is 1 and R^3 is at the 7-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-OCH_3$, or $-OCH_2CH_3$.

18. The compound of claim 1, wherein ring A is a group selected from:



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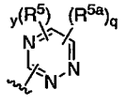

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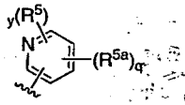

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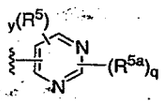

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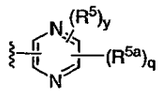

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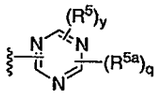

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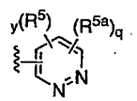

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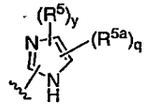

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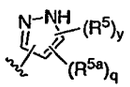

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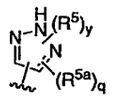

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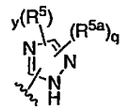

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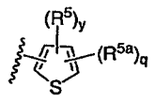

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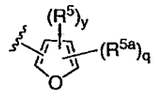

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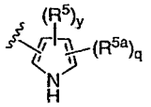

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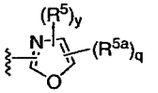

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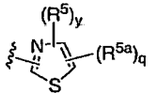

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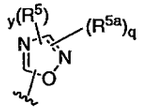

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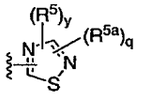

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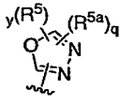

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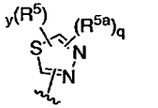

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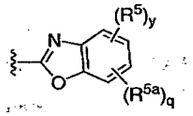

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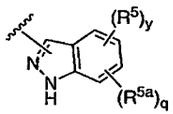

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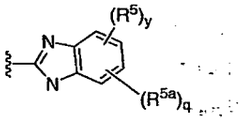

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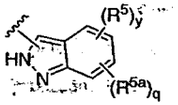

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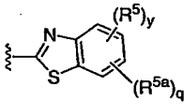

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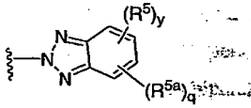

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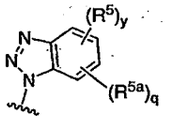

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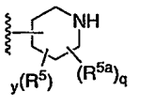

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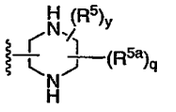

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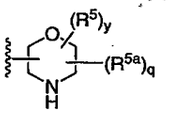

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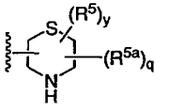

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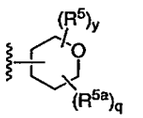

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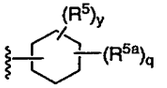

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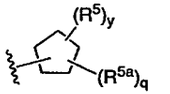

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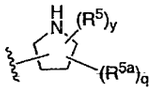
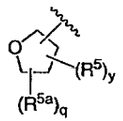


xxxv



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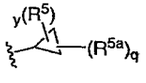


xxxvii

19. The compound of claim 17, wherein ring A is optionally substituted phenyl, 2-pyridyl, 3-pyridyl, or 4-pyridyl, or pyrrol-1-yl.

20. The compound of claim 1, wherein y is 0-5, q is 0-2, and R^5 and R^{5a} groups, when present, are each independently halogen, CN, NO_2, $-N(R')_2$, $-CH_2N(R')_2$, -OR', $-CH_2OR'$, -SR', $-CH_2SR'$, - -NRCOR', $-CON(R')_2$, $-S(O)_2N(R')_2$, -OCOR', -COR', $-CO_2R'$, $-OCON(R')_2$, $-NR'SO_2R'$, $-OP(O)(OR')_2$, $-P(O)(OR')_2$, $-OP(O)_2OR'$, $-P(O)_2OR'$, $-PO(R')_2$, $-OPO(R')_2$, or an optionally substituted group selected from C_1-C_6aliphatic, aryl, heteroaryl, cycloaliphatic, heterocycloaliphatic, arylC_1-C_6alkyl, heteroarylC_1-C_6alkyl, cycloaliphaticC_1-C_6alkyl, or heterocycloaliphaticC_1-C_6alkyl.

21. The compound of claim 1, wherein y is 0-5, and q is 1 or 2, and each occurrence of R^{5a} is independently Cl, Br, F, CF_3, Me, Et, CN, -COOH, $-NH_2$, $-N(CH_3)_2$, $-N(Et)_2$, $-N(iPr)_2$, $-O(CH_2)_2OCH_3$, $-CONH_2$, $-COOCH_3$, -OH, $-OCH_3$, $-OCH_2CH_3$, $-CH_2OH$, $-NHCOCH_3$, $-SO_2NH_2$, $-SO_2NHC(CH_3)_2$, $-OCOC(CH_3)_3$, $-OCOCH_2C(CH_3)_3$, $-O(CH_2)_2N(CH_3)_2$, 4-CH_3-piperazin-1-yl, $OCOCH(CH_3)_2$, OCO(cyclopentyl), $-COCH_3$, optionally substituted phenoxy, or optionally substituted benzyloxy.

22. The compound of claim 1, wherein:

a. y is 0, and q is 1 and R^{5a} is F;

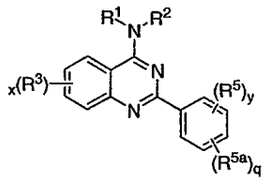
b. y is 0, q is 1, and R^{5a} is OR';

c. y is 0, q is 1 and R^{5a} is OH;

d. y is 0, q is 2 and one occurrence of R^{5a} is OR' and the other occurrence of R^{5a} is F;or

e. y is 0, q is 2 and one occurrence of R^{5a} is OH and the other occurrence of R^{5a} is F.

23. The compound of claim 1, wherein ring A is optionally substituted phenyl and compounds have the structure **IA-i**:



IA-i

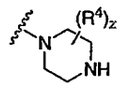
wherein:

y is 0-5;

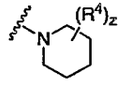
q is 0-2; and

each occurrence of R^{5a} is independently an optionally substituted C_1-C_6aliphatic group, halogen, -OR', -SR', -N(R')$_2$, -NR'COR', -NR'CON(R')$_2$, -NR'CO_2R', -COR', -CO_2R', -OCOR', -CON(R')$_2$, -OCON(R')$_2$, -SOR', -SO_2R', -SO_2N(R')$_2$, -NR'SO_2R', -NR'SO_2N(R')$_2$, -COCOR', -$COCH_2COR'$, -OP(O)(OR')$_2$, -P(O)(OR')$_2$, -OP(O)$_2$OR', -P(O)$_2$OR', -PO(R')$_2$, or -OPO(R')$_2$.

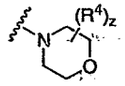
24. The compound of claim 23, wherein the ring formed by R^1 and R^2 taken together is selected from:



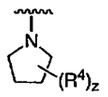
cc



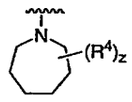
dd



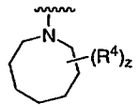
ee



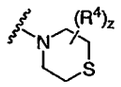
ff

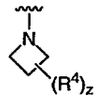


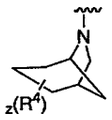
gg



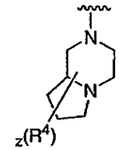
hh

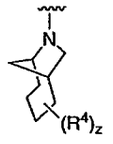


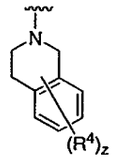


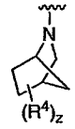


ii **jj** **kk**









ll **mm** **nn** **oo**

wherein the ring formed by R^1 and R^2 taken together, is optionally substituted at one or more substitutable carbon, nitrogen, or sulfur atoms with z independent occurrences of $-R^4$, and z is 0-5.

25. The compound of claim 24, wherein R^1 and R^2 taken together is an optionally substituted ring selected from azetidin-1-yl (**jj**), pyrrolidin-1-yl (**ff**), piperidin1-yl (**dd**), piperazin-1-yl (**cc**), or morpholin-4-yl (**ee**).

26. The compound of claim 24, wherein R^1 and R^2 taken together is an optionally substituted ring selected from azetidin-1-yl (**jj**), pyrrolidin-1-yl (**ff**), piperidin1-yl (**dd**), or piperazin-1-yl (**cc**).

27. The compound of claim 23, wherein z is 0-5, and R^4 groups, when present, are each independently halogen, CN, NO_2, -N(R')$_2$, -CH_2N(R')$_2$, -OR', -CH_2OR', -SR', -CH_2SR', -COOR', -NRCOR', -CON(R')$_2$, -OCON(R')$_2$, COR', -NHCOOR', -SO_2R', -SO_2N(R')$_2$, or an optionally substituted group selected from C_1-C_6aliphatic, aryl, heteroaryl, cycloaliphatic, heterocycloaliphatic, arylC_1-C_6alkyl, heteroarylC_1-C_6alkyl, cycloaliphaticC_1-C_6alkyl, or heterocycloaliphaticC_1-C_6alkyl.

28. The compound of claim 23, wherein z is 0-5 and R^4 groups are each independently Cl, Br, F, CF_3, CH_3, -CH_2CH_3, CN, -COOH, -N(CH_3)$_2$, -N(Et)$_2$, -N(iPr)$_2$, -O(CH_2)$_2$OCH_3, -$CONH_2$, -$COOCH_3$, -OH, -CH_2OH, -NHCOCH_3, -SO_2NH_2, -SO_2(CH_2)$_3CH_3$, -SO_2CH(CH_3)$_2$, -SO_2N(CH_3)$_2$, -$SO_2CH_2CH_3$, -C(O)OCH_2CH(CH_3)$_2$, -C(O)NHCH_2CH(CH_3)$_2$, -NHCOOCH_3, -C(O)C(CH_3)$_3$, -COO(CH_2)$_2CH_3$, -C(O)NHCH(CH_3)$_2$, -C(O)CH_2CH_3, or an optionally

substituted group selected from -piperidinyl, piperizinyl, morpholino, C_{1-4}alkoxy, phenyl, phenyloxy, benzyl, benzyloxy, -CH_2cyclohexyl, pyridyl, -CH_2pyridyl, or -CH_2thiazolyl.

29. The compound of claim 23, wherein R^1 and R^2, taken together is selected from:

a. optionally substituted azetidin-1-yl **(jj)**, wherein z is 1 or 2 and at least one occurrence of R^4 is –$NRSO_2R'$, -NRCOOR', or -NRCOR';

b. optionally substituted azetidin-1-yl **(jj)**, wherein z is 1 and R^4 is –$NRSO_2R'$;

c. optionally substituted azetidin-1-yl **(jj)**, wherein z is 1 and R^4 is -NRCOOR';

d. optionally substituted azetidin-1-yl **(jj)**, wherein z is 1 and R^4 is –NRCOR';

e. optionally substituted pyrrolidin-1-yl **(ff)**, wherein z is 1 or 2 and R^4 is Cl, Br, F, CF_3, CH_3, -CH_2CH_3, -OR', or -CH_2OR';

f. optionally substituted piperidin-1-yl **(dd)**, wherein z is 1 or 2 and at least one occurrence of R^4 is Cl, Br, F, CF_3, CH_3, -CH_2CH_3, -OR', or -CH_2OR', –$NRSO_2R'$, -NRCOOR', or –$OCON(R')_2$;

g. optionally substituted piperidin-1-yl **(dd)**, wherein z is 1 and R^4 is F, CF_3, CH_3, -CH_2CH_3, -OR', or -CH_2OR';

h. optionally substituted piperidin-1-yl **(dd)**, wherein z is 1 and R^4 is —$NRSO_2R'$;

i. optionally substituted piperidin-1-yl **(dd)**, wherein z is 1 and R^4 is -NRCOOR';

j. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 or 2 and at least one occurrence of R^4 is –SOR', -$CON(R')_2$, -$SO_2N(R')_2$, -COR', or –COOR';

k. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is –SOR'

l. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is –COOR';

m. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is -$CON(R')_2$;

n. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is -$SO_2N(R')_2$; or

o. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is -COR'.

30. The compound of claim 23, wherein x is 0-4, and R^3 groups, when present, are each independently halogen, CN, NO_2, -$N(R')_2$, -$CH_2N(R')_2$, -OR', -CH_2OR', -SR', -CH_2SR', -COOR', -NRCOR', -$CON(R')_2$, -$OCON(R')_2$, COR', -NHCOOR', -SO_2R', -$SO_2N(R')_2$, or an optionally substituted group selected from C_1-C_6aliphatic, aryl, heteroaryl, cycloaliphatic, heterocycloaliphatic, arylC_1-C_6alkyl, heteroarylC_1-C_6alkyl, cycloaliphaticC_1-C_6alkyl, or heterocycloaliphaticC_1-C_6alkyl.

31. The compound of claim 23, wherein x is 1 or 2, and each occurrence of R^3 is independently Cl, Br, F, CF_3, -OCF_3, Me, Et, CN, -COOH, -NH_2, –$N(CH_3)_2$, -$N(Et)_2$, -$N(iPr)_2$, -$O(CH_2)_2OCH_3$, -$CONH_2$, -$COOCH_3$, -OH, -OCH_3, -OCH_2CH_3, -CH_2OH, -$NHCOCH_3$, -$NHCOCH(CH_3)_2$, -SO_2NH_2, -CONH(cyclopropyl), -$CONHCH_3$, -$CONHCH_2CH_3$, or an optionally substituted group selected from -piperidinyl, piperizinyl, morpholino, phenyl, phenyloxy, benzyl, or benzyloxy.

32. The compound of claim 23 wherein x is 1 or 2 and each R^3 group is independently halogen, CN, optionally substituted C_1-C_6alkyl, OR', $N(R')_2$, $CON(R')_2$, or NRCOR'.

33. The compound of claim 23, wherein x is 1 or 2, and each R^3 group is -Cl, -CH_3, -CH_2CH_3, -F, -CF_3, -OCF_3, -$CONHCH_3$, -$CONHCH_2CH_3$, -CONH(cyclopropyl), -OCH_3, -NH_2, -OCH_2CH_3, or -CN.

34. The compound of claim 23, wherein x is 1 and R^3 is at the 6-position of the quinazoline ring and is -Cl, -CH_3, -CH_2CH_3, -F, -CF_3, -OCF_3, -$CONHCH_3$, -$CONHCH_2CH_3$, -CONH(cyclopropyl), -OCH_3, -NH_2, -OCH_2CH_3, or -CN.

35. The compound of claim 23, wherein x is 1 and R^3 is at the 7-position of the quinazoline ring and is -Cl, -CH_3, -CH_2CH_3, -F, -CF_3, -OCF_3, -$CONHCH_3$, -$CONHCH_2CH_3$, -CONH(cyclopropyl), -OCH_3, -NH_2, -OCH_2CH_3, or -CN.

36. The compound of claim 23, wherein x is 1 and R^3 is at the 6-position of the quinazoline ring and is -Cl, -CH_3, -CH_2CH_3, -F, -CF_3, -OCF_3, -OCH_3, or -OCH_2CH_3.

37. The compound of claim 23, wherein x is 1 and R^3 is at the 7-position of the quinazoline ring and is -Cl, -CH_3, -CH_2CH_3, -F, -CF_3, -OCF_3, -OCH_3, or -OCH_2CH_3.

38. The compound of claim 23, wherein x is 1 and R^3 is at the 6-position of the quinazoline ring and is –CON(R')$_2$, or NRCOR'.

39. The compound of claim 23, wherein x is 1 and R^3 is at the 7-position of the quinazoline ring and is –CON(R')$_2$, or NRCOR'.

40. The compound of claim 23, wherein y is 0-5, q is 0-2, and R^5 and R^{5a} groups, when present, are each independently halogen, CN, NO_2, -N(R')$_2$, -CH_2N(R')$_2$, -OR', -CH_2OR', -SR', -CH_2SR', - -NRCOR', -CON(R')$_2$, -S(O)$_2$N(R')$_2$, -OCOR', -COR', -CO_2R', -OCON(R')$_2$, -NR'SO_2R', -OP(O)(OR')$_2$, -P(O)(OR')$_2$, -OP(O)$_2$OR', -P(O)$_2$OR', -PO(R')$_2$, -OPO(R')$_2$, or an optionally substituted group selected from C_1-C_6aliphatic, aryl, heteroaryl, cycloaliphatic, heterocycloaliphatic, arylC_1-C_6alkyl, heteroarylC_1-C_6alkyl, cycloaliphaticC_1-C_6alkyl, or heterocycloaliphaticC_1-C_6alkyl.

41. The compound of claim 23, wherein y is 0-5, and q is 1 or 2, and each occurrence of R^{5a} is independently Cl, Br, F, CF_3, Me, Et, CN, -COOH, -NH_2, –N(CH_3)$_2$, -N(Et)$_2$, -N(iPr)$_2$, -O(CH_2)$_2$$OCH_3$, -$CONH_2$, -$COOCH_3$, -OH, -$OCH_3$, -$OCH_2CH_3$, -$CH_2$OH, -NHCO$CH_3$, -$SO_2NH_2$, -$SO_2$NHC($CH_3$)$_2$, -OCOC($CH_3$)$_3$, -OCO$CH_2$C($CH_3$)$_3$, -O($CH_2$)$_2$N($CH_3$)$_2$, 4-$CH_3$-piperazin-1-yl, OCOCH($CH_3$)$_2$, OCO(cyclopentyl), -$COCH_3$, optionally substituted phenoxy, or optionally substituted benzyloxy.

42. The compound of claim 23, wherein:

f. y is 0, and q is 1 and R^{5a} is F substituted at the 2-position of the phenyl ring;

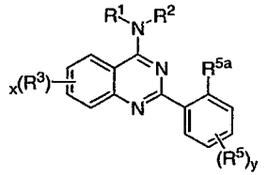
g. y is 0, q is 1, and R^{5a} is OR' substituted at the 2-position of the phenyl ring;

h. y is 0, q is 1 and R^{5a} is OH substituted at the 2-position of the phenyl ring;

i. y is 0, q is 2 and one occurrence of R^{5a} is OR' substituted at the 2-position of the phenyl ring and the other occurrence of R^{5a} is F substituted at the 6-position of the phenyl ring;or

j. y is 0, q is 2 and one occurrence of R^{5a} is OH substituted at the 2-position of the phenyl ring, and the other occurrence of R^{5a} is F substituted at the 6-position of the phenyl ring.

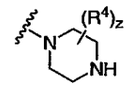
43. The compound of claim 23, wherein q is 1 and R^{5a} is at the 2-position of the phenyl ring, and compounds have the structure **IA-ii**:



IA-ii

wherein:

a) the ring formed by R^1 and R^2 taken together is selected from:



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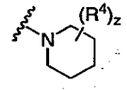
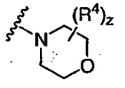


dd



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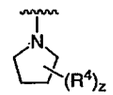

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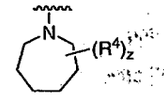

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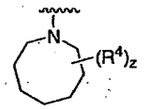

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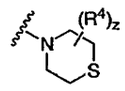
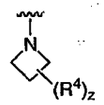
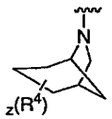


ii



jj



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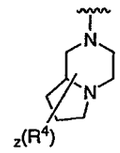
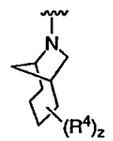
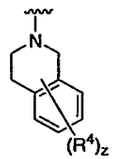


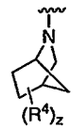
ll



mm



nn



oo

and the ring formed by R^1 and R^2 taken together, is optionally substituted at one or more substitutable carbon, nitrogen, or sulfur atoms with z independent occurrences of $-R^4$, and z is 0-5;

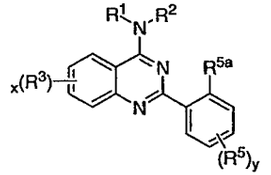
b) wherein z is 0-5, and R^4 groups, when present, are each independently halogen, CN, NO_2, $-N(R')_2$, $-CH_2N(R')_2$, -OR', $-CH_2OR'$, -SR', $-CH_2SR'$, -COOR', -NRCOR', $-CON(R')_2$, $-OCON(R')_2$, COR', -NHCOOR', $-SO_2R'$, $-SO_2N(R')_2$, or an optionally substituted group selected from C_1-C_6aliphatic, aryl, heteroaryl, cycloaliphatic, heterocycloaliphatic, arylC_1-C_6alkyl, heteroarylC_1-C_6alkyl, cycloaliphaticC_1-C_6alkyl, or heterocycloaliphaticC_1-C_6alkyl.

c) wherein x is 0-4, and R^3 groups, when present, are each independently halogen, CN, NO_2, $-N(R')_2$, $-CH_2N(R')_2$, -OR', $-CH_2OR'$, -SR', $-CH_2SR'$, -COOR', -NRCOR', $-CON(R')_2$, $-OCON(R')_2$, COR', -NHCOOR', $-SO_2R'$, $-SO_2N(R')_2$, or an optionally substituted group selected from C_1-C_6aliphatic, aryl, heteroaryl, cycloaliphatic, heterocycloaliphatic, arylC_1-C_6alkyl, heteroarylC_1-C_6alkyl, cycloaliphaticC_1-C_6alkyl, or heterocycloaliphaticC_1-C_6alkyl.

d) wherein y is 0-5, and R^5 groups, when present, are each independently halogen, CN, NO_2, $-N(R')_2$, $-CH_2N(R')_2$, -OR', $-CH_2OR'$, -SR', $-CH_2SR'$, -NRCOR', $-CON(R')_2$, $-S(O)_2N(R')_2$, -OCOR', -COR', $-CO_2R'$, $-OCON(R')_2$, $-NR'SO_2R'$, $-OP(O)(OR')_2$, $-P(O)(OR')_2$, $-OP(O)_2OR'$, $-P(O)_2OR'$, $-PO(R')_2$, $-OPO(R')_2$, or an optionally substituted group selected from C_1-C_6aliphatic, aryl, heteroaryl, cycloaliphatic, heterocycloaliphatic, arylC_1-C_6alkyl, heteroarylC_1-C_6alkyl, cycloaliphaticC_1-C_6alkyl, or heterocycloaliphaticC_1-C_6alkyl; and

e) R^{5a} is Cl, Br, F, CF_3, Me, Et, CN, -COOH, $-NH_2$, $-N(CH_3)_2$, $-N(Et)_2$, $-N(iPr)_2$, $-O(CH_2)_2OCH_3$, $-CONH_2$, $-COOCH_3$, -OH, $-OCH_3$, $-OCH_2CH_3$, $-CH_2OH$, $-NHCOCH_3$, $-SO_2NH_2$, $-SO_2NHC(CH_3)_2$, $-OCOC(CH_3)_3$, $-OCOCH_2C(CH_3)_3$, $-O(CH_2)_2N(CH_3)_2$, 4-CH_3-piperazin-1-yl, $OCOCH(CH_3)_2$, OCO(cyclopentyl), $-COCH_3$, optionally substituted phenoxy, or optionally substituted benzyloxy.

44. The compound of claim 23, wherein q is 1 and R^{5a} is at the 2-position of the phenyl ring, and compounds have the structure **IA-ii**:



IA-ii

wherein:

a) R^1 and R^2 taken together is an optionally substituted ring selected from azetidin-1-yl (**jj**), pyrrolidin-1-yl (**ff**), piperidin1-yl (**dd**), or piperazin-1-yl (**cc**);

b) z is 0-5 and R^4 groups are each independently Cl, Br, F, CF_3, CH_3, $-CH_2CH_3$, CN, -COOH, $-N(CH_3)_2$, $-N(Et)_2$, $-N(iPr)_2$, $-O(CH_2)_2OCH_3$, $-CONH_2$, $-COOCH_3$, -OH, $-CH_2OH$, $-NHCOCH_3$, $-SO_2NH_2$, $-SO_2(CH_2)_3CH_3$, $-SO_2CH(CH_3)_2$, $-SO_2N(CH_3)_2$, $-SO_2CH_2CH_3$, $-C(O)OCH_2CH(CH_3)_2$, $-C(O)NHCH_2CH(CH_3)_2$, $-NHCOOCH_3$, $-C(O)C(CH_3)_3$, $-COO(CH_2)_2CH_3$, $-C(O)NHCH(CH_3)_2$, $-C(O)CH_2CH_3$, or an optionally substituted group selected from -piperidinyl, piperizinyl, morpholino, C_{1-4}alkoxy, phenyl, phenyloxy, benzyl, benzyloxy, $-CH_2$cyclohexyl, pyridyl, $-CH_2$pyridyl, or $-CH_2$thiazolyl;

c) x is 1 or 2, and each occurrence of R^3 is independently Cl, Br, F, CF_3, $-OCF_3$, Me, Et, CN, -COOH, $-NH_2$, $-N(CH_3)_2$, $-N(Et)_2$, $-N(iPr)_2$, $-O(CH_2)_2OCH_3$, $-CONH_2$, $-COOCH_3$, -OH, $-OCH_3$, $-OCH_2CH_3$, $-CH_2OH$, $-NHCOCH_3$, $-NHCOCH(CH_3)_2$, $-SO_2NH_2$, -CONH(cyclopropyl), $-CONHCH_3$, $-CONHCH_2CH_3$, or an optionally substituted group selected from -piperidinyl, piperizinyl, morpholino, phenyl, phenyloxy, benzyl, or benzyloxy;

d) wherein y is 0-4, and R^5 groups, when present, are each independently Cl, Br, F, CF_3, Me, Et, CN, -COOH, $-NH_2$, $-N(CH_3)_2$, $-N(Et)_2$, $-N(iPr)_2$, $-O(CH_2)_2OCH_3$, $-CONH_2$, $-COOCH_3$, -OH, $-OCH_3$, $-OCH_2CH_3$, $-CH_2OH$, $-NHCOCH_3$, $-SO_2NH_2$, $-SO_2NHC(CH_3)_2$, $-OCOC(CH_3)_3$, $-OCOCH_2C(CH_3)_3$, $-O(CH_2)_2N(CH_3)_2$, 4-CH_3-piperazin-1-yl, $OCOCH(CH_3)_2$, OCO(cyclopentyl), $-COCH_3$, optionally substituted phenoxy, or optionally substituted benzyloxy; and

e) R^{5a} is Cl, F, CF_3, Me, Et, -OH, $-OCH_3$, $-OCH_2CH_3$, $-CH_2OH$, $-SO_2NH_2$, $-SO_2NHC(CH_3)_2$, $-OCOC(CH_3)_3$, $-OCOCH_2C(CH_3)_3$, $-O(CH_2)_2N(CH_3)_2$, 4-CH_3-piperazin-1-yl, $OCOCH(CH_3)_2$, OCO(cyclopentyl), or $-COCH_3$.

45. The compound of claim 44, wherein x is 1 and R^3 is at the 6-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-CONHCH_3$, $-CONHCH_2CH_3$, -CONH(cyclopropyl), $-OCH_3$, $-NH_2$, $-OCH_2CH_3$, or -CN.

46. The compound of claim 44, wherein x is 1 and R^3 is at the 7-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-CONHCH_3$, $-CONHCH_2CH_3$, -CONH(cyclopropyl), $-OCH_3$, $-NH_2$, $-OCH_2CH_3$, or -CN.

47. The compound of claim 44, wherein x is 1 and R^3 is at the 6-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-OCH_3$, or $-OCH_2CH_3$.

48. The compound of claim 44 wherein x is 1 and R^3 is at the 7-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-OCH_3$, or $-OCH_2CH_3$.

49. The compound of claim 44, wherein x is 1 and R^3 is at the 6-position of the quinazoline ring and is –CON(R')$_2$, or NRCOR'.

50. The compound of claim 44, wherein x is 1 and R^3 is at the 7-position of the quinazoline ring and is –CON(R')$_2$, or NRCOR'.

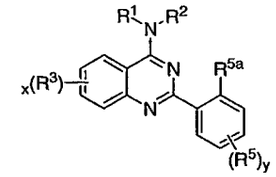
51. The compound of claim 44, wherein R^{5a} is Cl, F, CF_3, Me, Et, -OH, OR', $-OCH_3$, $-OCH_2CH_3$.

52. The compound of claim 44, wherein R^{5a} is OR'.

53. The compound of claim 44, wherein R^{5a} is OH.

54. The compound of claim 44, wherein R^{5a} is F.

55. The compound of claim 23, wherein q is 1 and R^{5a} is at the 2-position of the phenyl ring, and compounds have the structure **IA-ii**:



IA-ii

wherein:

a) R^1 and R^2 taken together is an optionally substituted ring selected from azetidin-1-yl (**jj**), pyrrolidin-1-yl (**ff**), piperidin1-yl (**dd**), or piperazin-1-yl (**cc**);

b) z is 0-5 and R^4 groups are each independently Cl, Br, F, CF_3, CH_3, $-CH_2CH_3$, CN, -COOH, $-N(CH_3)_2$, $-N(Et)_2$, $-N(iPr)_2$, $-O(CH_2)_2OCH_3$, $-CONH_2$, $-COOCH_3$, -OH, $-CH_2OH$, $-NHCOCH_3$, $-SO_2NH_2$, $-SO_2(CH_2)_3CH_3$, $-SO_2CH(CH_3)_2$, $-SO_2N(CH_3)_2$, $-SO_2CH_2CH_3$, $-C(O)OCH_2CH(CH_3)_2$, $-C(O)NHCH_2CH(CH_3)_2$, $-NHCOOCH_3$, $-C(O)C(CH_3)_3$, $-COO(CH_2)_2CH_3$, $-C(O)NHCH(CH_3)_2$, $-C(O)CH_2CH_3$, or an optionally substituted group selected from piperidinyl, piperizinyl, morpholino, C_{1-4}alkoxy, phenyl, phenyloxy, benzyl, benzyloxy, $-CH_2$cyclohexyl, pyridyl, $-CH_2$pyridyl, or $-CH_2$thiazolyl;

c) x is 1, and each occurrence of R^3 is independently Cl, Br, F, CF_3, $-OCF_3$, Me, Et, CN, -COOH, -OH, or $-OCH_3$;

d) y is 0 or 1, and R^5 groups, when present, are each independently Cl, Br, F, CF_3, Me, -OH, $-OCH_3$, $-OCH_2CH_3$, $-CH_2OH$, $-NHCOCH_3$, $-SO_2NH_2$, $-SO_2NHC(CH_3)_2$; and

e) R^{5a} is F, -OR', or $NHSO_2R'$.

56. The compound of claim 55, wherein x is 1 and R^3 is at the 6-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-CONHCH_3$, $-CONHCH_2CH_3$, -CONH(cyclopropyl), $-OCH_3$, $-NH_2$, $-OCH_2CH_3$, or -CN.

57. The compound of claim 55, wherein x is 1 and R^3 is at the 7-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-CONHCH_3$, $-CONHCH_2CH_3$, -CONH(cyclopropyl), $-OCH_3$, $-NH_2$, $-OCH_2CH_3$, or -CN.

58. The compound of claim 55, wherein x is 1 and R^3 is at the 6-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-OCH_3$, or $-OCH_2CH_3$.

59. The compound of claim 55, wherein x is 1 and R^3 is at the 7-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-OCH_3$, or $-OCH_2CH_3$.

60. The compound of claim 55, wherein x is 1 and R^3 is at the 6-position of the quinazoline ring and is $-CON(R')_2$, or NRCOR'.

61. The compound of claim 55, wherein x is 1 and R^3 is at the 7-position of the quinazoline ring and is $-CON(R')_2$, or NRCOR'.

62. The compound of claim 55, wherein R^{5a} is OR' and x is 1 and R^3 is at the 6-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-OCH_3$, or $-OCH_2CH_3$.

63. The compound of claim 55, wherein R^{5a} is OR' and x is 1 and R^3 is at the 7-position of the quinazoline ring and is -Cl, $-CH_3$, $-CH_2CH_3$, -F, $-CF_3$, $-OCF_3$, $-OCH_3$, or $-OCH_2CH_3$

64. The compound of claim 55, wherein R^1 and R^2, taken together is selected from:

a. optionally substituted azetidin-1-yl **(jj)**, wherein z is 1 or 2 and at least one occurrence of R^4 is $-NRSO_2R'$, -NRCOOR', or -NRCOR';

b. optionally substituted azetidin-1-yl **(jj)**, wherein z is 1 and R^4 is $-NRSO_2R'$;

c. optionally substituted azetidin-1-yl **(jj)**, wherein z is 1 and R^4 is -NRCOOR';

d. optionally substituted azetidin-1-yl **(jj)**, wherein z is 1 and R^4 is –NRCOR';

e. optionally substituted pyrrolidin-1-yl **(ff)**, wherein z is 1 or 2 and R^4 is Cl, Br, F, CF_3, CH_3, $-CH_2CH_3$, -OR', or $-CH_2OR'$;

f. optionally substituted piperidin-1-yl **(dd)**, wherein z is 1 or 2 and at least one occurrence of R^4 is Cl, Br, F, CF_3, CH_3, $-CH_2CH_3$, -OR', or $-CH_2OR'$, $-NRSO_2R'$, -NRCOOR', or $-OCON(R')_2$;

g. optionally substituted piperidin-1-yl **(dd)**, wherein z is 1 and R^4 is F, CF_3, CH_3, $-CH_2CH_3$, -OR', or $-CH_2OR'$;

h. optionally substituted piperidin-1-yl **(dd)**, wherein z is 1 and R^4 is $-NRSO_2R'$;

i. optionally substituted piperidin-1-yl **(dd)**, wherein z is 1 and R^4 is -NRCOOR';

j. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 or 2 and at least one occurrence of R^4 is –SOR', $-CON(R')_2$, $-SO_2N(R')_2$, -COR', or –COOR';

k. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is –SOR'

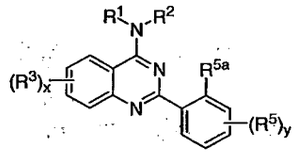
l. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is –COOR';

m. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is $-CON(R')_2$;

n. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is $-SO_2N(R')_2$; or

o. optionally substituted piperazin-1-yl **(cc)**, wherein z is 1 and R^4 is -COR'.

65. A compound of formula **IA-ii**:



IA-ii

wherein R^1 and R^2 are each independently an optionally substituted group selected from C_{1-6}aliphatic, Cy^1, wherein Cy^1 is a 5-7-membered monocyclic aryl ring or an 8-10-membered bicyclic aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or is a 3-12-membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein Cy^1 is bonded directly to the nitrogen atom or is bonded through an optionally substituted C_{1-4}aliphatic group, wherein one or more methylene units in the C_{1-4}aliphatic group are optionally replaced with -NR-, -O-, -COO, -OCO-, -NRCO-, -CONR-, $-SO_2NR$-, or $-NRSO_2$-; wherein R^1 and R^2, are each optionally and independently substituted at one or more substitutable carbon, nitrogen, or sulfur atoms with z independent occurrences of $-R^4$, wherein z is 0-5;

x is 0-4;

y is 0-4;

each occurrence of R^3, R^4, and R^5 is independently $Q\text{-}R^X$; wherein Q is a bond or is a C_1-C_6 alkylidene chain wherein up to two non-adjacent methylene units of Q are optionally and

independently replaced by –NR-, -S-, -O-, -CS-, -CO_2-, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, -$NRCO_2$-, -SO_2NR-, -$NRSO_2$-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -$NRSO_2NR$-, -SO-, -SO_2-, -PO-, -PO_2-, -OP(O)(OR)-, or -POR-; and each occurrence of R^X is independently selected from -R', =O, =NR', halogen, -NO_2, -CN, -OR', -SR', -$N(R')_2$, -NR'COR', -NR'CON$(R')_2$, -NR'CO_2R', -COR', -CO_2R', -OCOR', -CON$(R')_2$, -OCON$(R')_2$, -SOR', -SO_2R', -$SO_2N(R')_2$, -NR'SO_2R', -NR'$SO_2N(R')_2$, -COCOR', -$COCH_2$COR', -OP(O)$(OR')_2$, -P(O)$(OR')_2$, -OP$(O)_2$OR', -P$(O)_2$OR', -P$O(R')_2$, or -OP$O(R')_2$;

R^{5a} is an optionally substituted C_1-C_6aliphatic group, halogen, -OR', -SR', -$N(R')_2$, -NR'COR', -NR'CON$(R')_2$, -NR'CO_2R', -COR', -CO_2R', -OCOR', -CON$(R')_2$, -OCON$(R')_2$, -SOR', -SO_2R', -$SO_2N(R')_2$, -NR'SO_2R', -NR'$SO_2N(R')_2$, -COCOR', -$COCH_2$COR', -OP(O)$(OR')_2$, -P(O)$(OR')_2$, -OP$(O)_2$OR', -P$(O)_2$OR', -P$O(R')_2$, or -OP$O(R')_2$; and

each occurrence of R is independently hydrogen or an optionally substituted C_{1-6} aliphatic group; and each occurrence of R' is independently hydrogen or an optionally substituted C_{1-6} aliphatic group, a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R', two occurrences of R, or two occurrences of R', are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; provided that:

a. when x is 0, R^1 is hydrogen, and R^{5a} is Cl, Me, CF_3, Br, or F, then R^2 is not –$(CH_2)_2$-4-Cy^1, -$SO_2CH_2Cy^1$, or –$CH_2SO_2Cy^1$, wherein Cy^1 is a 5-7-membered monocyclic aryl ring or an 8-10-membered bicyclic aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or is a 3-8-membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

b. when x is 0, and R^{5a} is Cl, Me, NO_2, or OH, then:

i. when R^1 is hydrogen, R^2 is not Me, iBu, nBu, -$COCH_3$, -CH_2COOEt, -CH_2COOMe, -CH_2CH_2OH, iPr, -CH_2-pyridyl, -CH_2Ph, -$(CH_2)_3NH_2$, -$(CH_2)_2$-moropholinyl, or –CH_2CH_2Ph;