

Doctor

José Luis Salazar

Jefe de División de Nuevas Creaciones

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

E. _____ S. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

No. 06-007912-A-00002-0000

Fecha: 2012-02-13 16:37:10
Tra. 11 PATENTE/II
Act. 523 RESPUESTADep. 2020 DIR.NUEVASCR
Eve: 378 FASENACIONALI
Folios: 76

Referencia: Expediente No. 06.007.912A

Solicitud de Patente de Invención titulada: "Derivados de Piridazina y sus composiciones farmacéuticas".

Solicitante: Xenon Pharmaceuticals Inc.

RESPUESTA AL AUTO NOTIFICADO POR FIJACIÓN EN LISTA NO. 435**DEL 18 DE NOVIEMBRE DE 2011, OFICIO NO. 17921 (EXAMEN DE FONDO)**

ÁLVARO CORREA ORDÓÑEZ, mayor de edad y vecino de Bogotá D.C., identificado tal como aparece al pie de mi firma, en mi carácter de apoderado de la sociedad en referencia, doy respuesta al auto emanado por ese Despacho dentro del término legal:

1. Objeciones del Examinador**1.1 Título de la invención:**

Con el fin de atender la sugerencia del examinador, se presenta el siguiente título:

"Derivados de Piridazina y sus composiciones farmacéuticas"

El título ya no se refiere al uso y se dirige a la materia reclamada, por lo tanto se da por superada la anterior observación.

1.2 Excepciones a la patentabilidad:

Su Despacho menciona que el método de tratamiento de las reivindicaciones 1-9, 18, 43, 53, 58 y 61 no son patentables.

Con relación a esta observación, informamos a su Despacho que se cancelaron las reivindicaciones 1-9, 18, 43, 53, 58 y 61 del nuevo pliego reivindicatorio que se presenta.

Por lo tanto, se da por superada esta observación.

1.3 Claridad del capítulo reivindicatorio:

Su Despacho considera que las reivindicaciones 10-11, 17, 20-21, 23-30, 32, 34-36, 45-50, 55-57, 60 no son concisas, y menciona que con el fin de realizar una generalización razonable de los ejemplos se sugiere restringir la solicitud a los compuestos que corresponden a derivados de piridazin-diazepam (cuando se define x como 2, y como 1 ó x como 1, y como 2); además definir de manera apropiada los términos objetados estableciendo el número de átomos de carbono o de miembros que conforman los sistemas de anillos y de la parte alquelino y finalmente, en la definición de los radicales R2 y R3 eliminar la expresión “....algunos o todos los anillos pueden estar fusionados entre sí....”, con el fin de darle concisión al capítulo reivindicatorio.

1.3.1 Modificación a una solicitud en trámite

De conformidad con el artículo 34 de la Decisión 486 que permite al solicitante en cualquier momento del trámite presentar modificaciones o correcciones en su solicitud, siempre que no se amplíe la protección inicialmente presentada, me permito presentar un nuevo pliego reivindicatorio conformado por 48 reivindicaciones.

En particular se presentan las siguientes modificaciones:

Se colocó el número de carbonos apropiado para los términos “cicloalquilo”, “heterociclilo”, arilo, heteroarilo.

Por otro lado, la expresión “....*algunos o todos los anillos pueden estar fusionados entre sí....*”, opcional para los radicales R^2 y R^3 se ha eliminado.

Así mismo, se agregó C1-C2 para especificar la longitud del puente alquileo.

Por último, “x” e “y” se limitaron a “x es 2 e y es 1”. La expresión sugerida “x es 2, y es 1 o x es 1, y es 2” parece ser redundante dada la simetría de las estructuras reivindicadas.

2. Modificación a la solicitud de patente inicial ya otorgada que tiene número de solicitud No. 06.007.912.

Hacemos notar a su Despacho que por un error tipográfico la solicitud inicial se otorgó con el compuesto piridazin-diazepan cuando (x es 2 e y es 1). Por favor, ver la reivindicación 21 de la solicitud 06.007.912.

(2-ciclopropiletil)-amida del ácido 6-[4-(5-fluoro-2-trifluorometilbenzoil)-[1,4]diazepan-1-il]-piridazin-3-carboxílico;

Esto corresponde a un error tipográfico, ya que las reivindicaciones otorgadas en la solicitud 06.007.912 requieren que x e y sean ambos 1.

Así mismo, hacemos notar a su Despacho, que el anterior compuesto que se cancela de la solicitud inicial 06.007.912, se reivindica ahora en la solicitud divisional 06.007.912 A en la reivindicación 14.

3. Solicitudes concedidas en otros países para esta misma invención.

A manera informativa, pongo en conocimiento del Examinador que solicitudes de patentes equivalentes a la presente solicitud Colombiana han sido otorgadas o aceptadas en las respectivas jurisdicciones. Por favor nótese, que dichas patentes fueron otorgadas con reivindicaciones dirigidas a derivados de piridazina, en las cuales x e y pueden ser 1,2, o 3, las cuales son más amplias que la combinación x es 2 e y es 1 de la solicitud en estudio.

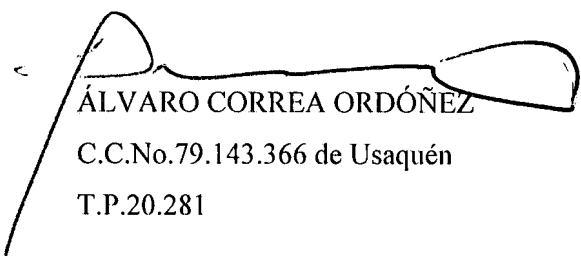
Estamos adjuntando la carátula de la patente Estadounidense No. US 7,754, 711 así como las reivindicaciones otorgadas. Por favor, ver reivindicación 2.

Se adjunta también las reivindicaciones aprobadas para la solicitud Europea No. 06748193.7. Por favor, ver también reivindicación 2.

De igual forma estamos adjuntando las reivindicaciones en inglés otorgadas en Japón con número de patente JP 4808616. Por favor, ver todas las reivindicaciones.

En virtud de lo anterior, solicito que se acepten las razones expuestas en el presente documento y en consecuencia, se otorgue el privilegio de patente de invención para el invento que se tramita en este expediente.

Atentamente,



ÁLVARO CORREA ORDÓÑEZ

C.C.No.79.143.366 de Usaquén

T.P.20.281

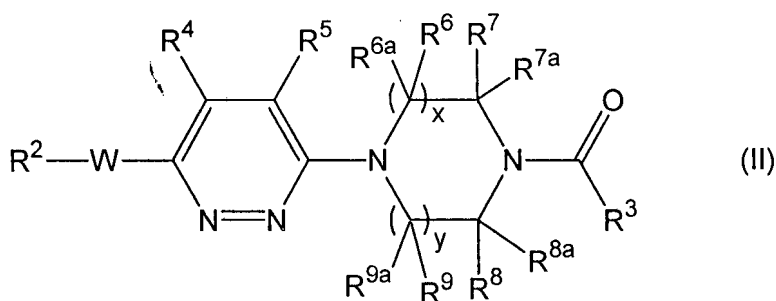
Anexos:

- Capítulo reivindicatorio modificado conformado por 48 reivindicaciones
- Copia de la carátula y reivindicaciones de la Patente US 7,754,711.
- Copia de las reivindicaciones admitidas y próximas a otorgar de la solicitud europea No. 06748193.7.
- Copia de las reivindicaciones en inglés de la patente japonesa No. 4808616.

BOGMGT/BOGDMS-966753-V1-P2006_000012A-0720.DOC

REIVINDICACIONES

1. Un compuesto de la fórmula (II):



que se caracteriza porque:

x es 2 e y es 1;

W se selecciona de $-C(O)N(R^1)-$ y $-N(R^1)C(O)-$;

cada R^1 se selecciona independientemente del grupo que consiste en hidrógeno; alquilo C_1-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, metilo o trifluorometilo; y alquilo C_2-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en metoxi e hidroxilo;

R^2 se selecciona del grupo que consiste en alquilo C_7-C_{12} , alquenilo C_3-C_{12} , hidroxialquilo C_7-C_{12} , alcoxialquilo C_2-C_{12} , hidroxialquenilo C_3-C_{12} , cicloalquilo C_3-C_{12} , cicloalquilalquilo C_4-C_{12} , aralquilo $C_{13}-C_{19}$, heterociclilalquilo C_3-C_{12} y heteroarilalquilo C_3-C_{12} ;

R^3 se selecciona del grupo que consiste en alquilo C_3-C_{12} , alquenilo C_3-C_{12} , hidroxialquilo C_3-C_{12} , hidroxialquenilo C_3-C_{12} , alcoxi C_3-C_{12} , alcoxialquilo C_3-C_{12} , cicloalquilo C_3-C_{12} , cicloalquilalquilo C_4-C_{12} , arilo C_6-C_{19} , aralquilo C_7-C_{12} , heterociclilo C_3-C_{12} , heterociclilalquilo C_3-C_{12} , heteroarilo C_5-C_{12} y heteroarilalquilo C_3-C_{12} ;

R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi y trifluorometilo; y

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

o R^6 y R^{6a} juntos, o R^9 y R^{9a} juntos son un grupo oxo, mientras que los restantes R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

o uno de los R^6 , R^{6a} , R^7 y R^{7a} junto con uno de los R^8 , R^{8a} , R^9 y R^{9a} forman un puente alquileo C_{1-2} , mientras que los restantes R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

incluidos un estereoisómero, enantiómero o tautómero del mismo, una sal farmacéuticamente aceptable del mismo o una composición farmacéutica del mismo.

2. El compuesto de la Reivindicación 1 que se caracteriza porque:

W se selecciona de $-C(O)N(R^1)-$ y $-N(R^1)C(O)-$;

cada R^1 se selecciona independientemente de hidrógeno o alquilo C_1-C_6 ;

R^2 se selecciona del grupo que consiste en alquilo C_7-C_{12} , alqueno C_3-C_{12} , hidroxialquilo C_7-C_{12} , alcóxialquilo C_2-C_{12} , hidroxialqueno C_3-C_{12} , cicloalquilo C_3-C_{12} , cicloalquilalquilo C_4-C_{12} , aralquilo $C_{13}-C_{19}$, heterociclilalquilo C_3-C_{12} , y heteroarilalquilo C_3-C_{12} ;

cada R^2 está opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, alquilo C_1-C_3 , $-OR^{11}$, $-C(O)OR^{11}$, trihaloalquilo C_1-C_6 , cicloalquilo C_3-C_{12} , heterociclilo C_3-C_{12} , arilo C_6-C_{19} , heteroarilo C_1-C_{12} y heteroarilo C_1-C_{12} cicloalquilo C_3-C_{12} ;

R^3 se selecciona del grupo que consiste en alquilo C_3-C_{12} , alqueno C_3-C_{12} , hidroxialquilo C_3-C_{12} , hidroxialqueno C_3-C_{12} , alcóxido C_3-C_{12} , alcóxialquilo C_3-C_{12} , cicloalquilo C_3-C_{12} , cicloalquilalquilo C_4-C_{12} , aralquilo C_7-C_{12} , heterociclilo C_3-C_{12} , heterociclilalquilo C_3-C_{12} , heteroarilo C_5-C_{12} y heteroarilalquilo C_3-C_{12} ;

cada R^3 está opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en alquilo C_1-C_6 , trihaloalquilo C_1-C_6 , trihaloalcóxido C_1-C_6 , alcóxido C_1-C_6 , alquilsulfonilo C_1-C_6 , halo, ciano, nitro, hidróxido, $-N(R^{12})_2$, $-C(O)OR^{11}$, $-S(O)_2N(R^{12})_2$, cicloalquilo C_3-C_{12} , heterociclilo C_3-C_{12} , arilo C_6-C_{19} , aralquilo C_7-C_{19} , heteroarilo C_1-C_{12} y heteroaril C_1-C_{12} cicloalquilo C_3-C_{12} ;

R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi y trifluorometilo; y

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

cada R^{11} se selecciona independientemente de hidrógeno, alquilo C_1-C_6 , arilo C_6-C_{19} o aralquilo C_7-C_{19} ; y

cada R^{12} se selecciona independientemente de hidrógeno o alquilo C_1-C_6 .

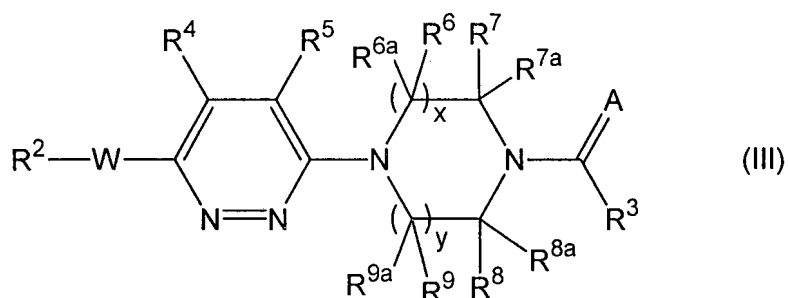
- 7
3. El compuesto de la Reivindicación 2 que se caracteriza porque:
W es $-N(R^1)C(O)-$;
 R^1 es hidrógeno;
 R^2 es cicloalquilalquilo C_4-C_{12} ;
 R^3 es alquilo C_3-C_{12} o alquenilo C_3-C_{12} , cada uno opcionalmente sustituido con uno o más grupos halo;
 R^4 y R^5 son cada uno hidrógeno; y
 R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} son cada uno hidrógeno.
4. El compuesto de la Reivindicación 2 que se caracteriza porque:
W es $-N(R^1)C(O)-$;
 R^1 es hidrógeno;
 R^2 es cicloalquilalquilo C_4-C_{12} ;
 R^3 es cicloalquilo C_3-C_{12} opcionalmente sustituido con uno o más sustituyentes seleccionados de hidroxilo, trihaloalquilo C_1-C_6 o alquilo C_1-C_6 ;
 R^4 y R^5 son cada uno hidrógeno; y
 R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} son cada uno hidrógeno.
5. El compuesto de la Reivindicación 2 que se caracteriza porque:
W es $-N(R^1)C(O)-$;
 R^2 es cicloalquilalquilo C_4-C_{12} y
 R^3 es hidroxialquilo C_3-C_{12} opcionalmente sustituido con uno o más grupos halo;
 R^4 y R^5 son cada uno hidrógeno; y
 R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} son cada uno hidrógeno.
6. El compuesto de la Reivindicación 2 que se caracteriza porque:
W es $-N(R^1)C(O)-$;
 R^1 es hidrógeno;
 R^2 es cicloalquilalquilo C_4-C_{12} ;
 R^3 es alcoxi C_3-C_{12} ;
 R^4 y R^5 son cada uno hidrógeno; y
 R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} son cada uno hidrógeno.

7. El compuesto de la Reivindicación 2 que se caracteriza porque:
W es -N(R¹)C(O)-;
R¹ es hidrógeno;
R² es cicloalquilalquilo C₄-C₁₂;
R³ es aralquilo C₇-C₁₂ opcionalmente sustituido con uno o más sustituyentes independientemente seleccionados de halo o trihaloalquilo C₁-C₆;
R⁴ y R⁵ son cada uno hidrógeno; y
R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹ y R^{9a} son cada uno hidrógeno.

8. El compuesto de la Reivindicación 2 que se caracteriza porque:
W es -N(R¹)C(O)-;
R¹ es hidrógeno;
R² es cicloalquilalquilo C₄-C₁₂;
R³ es heterociclilo C₃-C₁₂ o heteroarilo C₅-C₁₂, cada uno opcionalmente sustituido con uno o más sustituyentes independientemente seleccionado de halo, alquilo C₁-C₆, trihaloalquilo C₁-C₆ o aralquilo C₇-C₁₉;
R⁴ y R⁵ son cada uno hidrógeno; y
R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹ y R^{9a} son cada uno hidrógeno.

9. Una composición farmacéutica que comprende un excipiente farmacéuticamente aceptable y una cantidad terapéuticamente eficaz de un compuesto de la Reivindicación 1.

10. Un compuesto de la fórmula (III):



que se caracteriza porque:

x es 2 e y es 1;

A es oxígeno o azufre;

W se selecciona de -C(O)N(R¹)- y -N(R¹)C(O)-;

cada R^1 se selecciona independientemente del grupo que consiste en hidrógeno; alquilo C_1-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, metilo o trifluorometilo; y alquilo C_2-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en metoxi e hidroxi;

R^2 se selecciona del grupo que consiste en alquilo C_1-C_{12} , alquenilo C_2-C_{12} , hidroxialquilo C_2-C_{12} , hidroxialquenilo C_2-C_{12} , alcoxi C_1-C_6 , alcoxialquilo C_3-C_{12} , cicloalquilo C_3-C_{12} , cicloalquilalquilo C_4-C_{12} , arilo C_6-C_{19} , aralquilo C_7-C_{12} , heterociclilo C_3-C_{12} , heterocicilalquilo C_3-C_{12} , heteroarilo C_1-C_{12} y heteroarilalquilo C_3-C_{12} ;

R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, nitro, hidroxi, alquilo C_1-C_6 , trihaloalquilo C_1-C_6 , trihaloalcoxi C_1-C_6 , alquilsulfonilo C_1-C_6 , $-N(R^{11})_2$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-S(O)_2N(R^{11})_2$, cicloalquilo C_3-C_{12} , heterociclilo C_3-C_{12} , heteroarilo C_1-C_{12} y heteroaril C_1-C_{12} cicloalquilo C_3-C_{12} , siempre que R^3 no sea fenilo sustituido con tienilo opcionalmente sustituido;

R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi y trifluorometilo;

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

o R^6 y R^{6a} juntos, o R^7 y R^{7a} juntos, o R^8 y R^{8a} juntos o R^9 y R^{9a} juntos forman un grupo oxo, siempre que cuando A sea oxígeno, R^7 y R^{7a} juntos o R^8 y R^{8a} juntos no formen un grupo oxo, mientras que los restantes R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

o uno de los R^6 , R^{6a} , R^7 y R^{7a} junto con uno de los R^8 , R^{8a} , R^9 y R^{9a} forman un puente alquilenos C_{1-2} , mientras que los restantes R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ; y

cada R^{11} se selecciona independientemente de hidrógeno, alquilo C_1-C_6 , cicloalquilo C_3-C_6 , arilo C_6-C_{19} o aralquilo C_7-C_{19} ;

un estereoisómero, enantiómero o tautómero del mismo, una sal farmacéuticamente aceptable del mismo, o una composición farmacéutica del mismo.

11. El compuesto de la Reivindicación 10 que se caracteriza porque:

A es oxígeno o azufre;

W se selecciona de $-C(O)N(R^1)-$ y $-N(R^1)C(O)-$;

cada R^1 se selecciona independientemente de hidrógeno o alquilo C_1-C_6 ;

R^2 se selecciona del grupo que consiste de alquilo C_1-C_{12} , alquenilo C_2-C_{12} , hidroxialquilo C_2-C_{12} , hidroxialquenilo C_2-C_{12} , alcoxi C_1-C_6 , alcoxialquilo C_3-C_{12} , cicloalquilo C_3-C_{12} , cicloalquilalquilo C_4-C_{12} , arilo C_6-C_{19} , aralquilo C_7-C_{12} , heterociclilo C_3-C_{12} , heterocicilalquilo C_3-C_{12} , heteroarilo C_1-C_{12} y heteroarilalquilo C_3-C_{12} ;

cada R^2 está opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, oxo, tioxo, alquilo C_1-C_3 , $-OR^{11}$, $-C(O)R^{11}$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-C(O)N(R^{12})_2$, $-N(R^{12})_2$, trihaloalquilo C_1-C_6 , cicloalquilo C_3-C_{12} , heterociclilo C_3-C_{12} , arilo C_6-C_{19} , heteroarilo C_1-C_{12} y heteroaril C_1-C_{12} cicloalquilo C_3-C_{12} ;

R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, nitro, hidroxilo, alquilo C_1-C_6 , trihaloalquilo C_1-C_6 , trihaloalcoxi C_1-C_6 , alquilsulfonilo C_1-C_6 , $-N(R^{12})_2$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-S(O)_2N(R^{12})_2$, cicloalquilo C_3-C_{12} , heterociclilo C_3-C_{12} y heteroaril C_1-C_{12} cicloalquilo C_3-C_{12} ;

R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi y trifluorometilo;

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

o R^6 y R^{6a} juntos o R^9 y R^{9a} juntos forman un grupo oxo, mientras que los restantes R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

cada R^{11} se selecciona independientemente de hidrógeno, alquilo C_1-C_6 , cicloalquilo C_3-C_6 , arilo C_6-C_{19} o aralquilo C_7-C_{19} ; y

cada R^{12} se selecciona independientemente de hidrógeno o alquilo C_1-C_6 .

12. El compuesto de la Reivindicación 11 que se caracteriza porque:

A es oxígeno o azufre;

W es $-N(R^1)C(O)-$;

R^1 es hidrógeno, metilo o etilo;

R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi y trifluorometilo; y

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 .

13. El compuesto de la Reivindicación 12 que se caracteriza porque:

R^2 es cicloalquilalquilo C_4-C_{12} opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en $-OR^{11}$, alquilo C_1-C_3 o arilo C_6-C_{19} ;

R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, nitro, hidroxilo, alquilo C_1-C_6 , trihaloalquilo C_1-C_6 , trihaloalcoxi C_1-C_6 , alquilsulfonilo C_1-C_6 , $-N(R^{12})_2$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-S(O)_2N(R^{12})_2$ y cicloalquilo C_3-C_{12} ;

cada R^{11} se selecciona independientemente de hidrógeno, alquilo C_1-C_6 , cicloalquilo C_3-C_6 , arilo C_6-C_{19} o aralquilo C_7-C_{19} ; y

cada R^{12} se selecciona independientemente de hidrógeno o alquilo C_1-C_6 .

14. El compuesto de la Reivindicación 13, en donde el compuesto es:

(2-ciclopropiletil)-amida del ácido 6-[4-(5-fluoro-2-trifluorometilbenzoil)-[1,4]diazepan-1-il]-piridazin-3-carboxílico.

15. El compuesto de la Reivindicación 12 que se caracteriza porque:

A es oxígeno;

R^2 es alquilo C_1-C_{12} o alquenilo C_2-C_{12} , cada uno opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ariloxi, $-C(O)R^{11}$, $-OC(O)R^{11}$ o $-C(O)OR^{11}$;

R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, nitro, hidroxilo, alquilo C_1-C_6 , trihaloalquilo C_1-C_6 , trihaloalcoxi C_1-C_6 , alquilsulfonilo C_1-C_6 , $-N(R^{12})_2$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-S(O)_2N(R^{12})_2$ y cicloalquilo C_3-C_{12} ;

cada R^{11} se selecciona independientemente de hidrógeno, alquilo C_1-C_6 , cicloalquilo C_3-C_6 , aralquilo C_7-C_{19} o arilo C_6-C_{19} (opcionalmente sustituido con uno o más grupos halo); y

cada R^{12} se selecciona independientemente de hidrógeno o alquilo C_1-C_6 .

16. El compuesto de la Reivindicación 12 que se caracteriza porque:

A es oxígeno;

R^2 es hidroxialquilo C_2-C_{12} , hidroxialquenilo C_2-C_{12} , cada uno

opcionalmente sustituido con uno o más grupos halo;

R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, nitro, hidroxilo, alquilo C_1-C_6 , trihaloalquilo C_1-C_6 , trihaloalcoxi C_1-C_6 , alquilsulfonilo C_1-C_6 , $-N(R^{12})_2$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-S(O)_2N(R^{12})_2$ y cicloalquilo C_3-C_{12} ;

cada R^{11} se selecciona independientemente de hidrógeno, alquilo C_1-C_6 , cicloalquilo C_3-C_6 , aralquilo C_7-C_{19} o arilo C_6-C_{19} (opcionalmente sustituido con uno o más grupos halo); y

cada R^{12} se selecciona independientemente de hidrógeno o alquilo C_1-C_6 .

17. El compuesto de la Reivindicación 12 que se caracteriza porque:

A es oxígeno;

R^2 es aralquilo C_7-C_{12} , donde la parte arilo del grupo aralquilo C_7-C_{12} está opcionalmente sustituida por uno o más sustituyentes independientemente seleccionados de halo, alquilo C_1-C_3 , $-OR^{11}$, $-C(O)OR^{11}$, trihaloalquilo C_1-C_6 , cicloalquilo C_3-C_{12} y arilo C_6-C_{19} y la parte alquilo del grupo aralquilo C_7-C_{12} está opcionalmente sustituida por uno o más sustituyentes independientemente seleccionados de halo, $-OR^{11}$ y $-OC(O)R^{11}$;

R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, nitro, hidroxilo, alquilo C_1-C_6 , trihaloalquilo C_1-C_6 , trihaloalcoxi C_1-C_6 , alquilsulfonilo C_1-C_6 , $-N(R^{12})_2$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-S(O)_2N(R^{12})_2$ y cicloalquilo C_3-C_{12} ;

cada R^{11} se selecciona independientemente de hidrógeno, alquilo, C_1-C_6 , cicloalquilo C_3-C_6 , aralquilo C_7-C_{19} o arilo C_6-C_{19} (opcionalmente sustituido con uno o más grupos halo); y

cada R^{12} se selecciona independientemente de hidrógeno o alquilo C_1-C_6 .

18. El compuesto de la Reivindicación 12 que se caracteriza porque:

A es oxígeno;

R^2 es alcoxi C_1-C_6 o alcoxialquilo C_3-C_{12} , cada uno opcionalmente sustituido con uno o más sustituyentes independientemente seleccionados de halo o cicloalquilo C_3-C_6 ;

R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, nitro, hidroxilo, alquilo C_1-C_6 ,

trihaloalquilo C₁-C₆, trihaloalcoxi C₁-C₆, alquilsulfonilo C₁-C₆, -N(R¹²)₂, -OC(O)R¹¹, -C(O)OR¹¹, -S(O)₂N(R¹²)₂ y cicloalquilo C₃-C₁₂;

cada R¹¹ se selecciona independientemente de hidrógeno, alquilo C₁-C₆, cicloalquilo C₃-C₆, aralquilo C₇-C₁₉ o arilo C₆-C₁₉ (opcionalmente sustituido con uno o más grupos halo); y

cada R¹² se selecciona independientemente de hidrógeno o alquilo C₁-C₆.

19. El compuesto de la Reivindicación 12 que se caracteriza porque:

A es oxígeno;

R² es arilo opcionalmente sustituido con uno o más sustituyentes independientemente seleccionados de halo, ciano, alquilo C₁-C₃, -OR¹¹, -C(O)R¹¹, -OC(O)R¹¹, -C(O)OR¹¹, -C(O)N(R¹²)₂, trihaloalquilo C₁-C₆, cicloalquilo C₃-C₁₂, heterociclilo C₃-C₁₂, arilo C₆-C₁₉, heteroarilo C₁-C₁₂ y heteroaril C₁-C₁₂ cicloalquilo C₃-C₁₂;

R³ es fenilo opcionalmente sustituido con trihaloalquilo C₁-C₆ o trihaloalcoxi C₁-C₆;

cada R¹¹ se selecciona independientemente de hidrógeno, alquilo C₁-C₆, cicloalquilo C₃-C₆, aralquilo C₇-C₁₉ o arilo C₆-C₁₉ (opcionalmente sustituido con uno o más grupos halo); y

cada R¹² se selecciona independientemente de hidrógeno o alquilo C₁-C₆.

20. El compuesto de la Reivindicación 12 que se caracteriza porque:

A es oxígeno;

R² es heteroarilo C₁-C₁₂ opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, oxo, tioxo, alquilo C₁-C₃, -OR¹¹, -C(O)R¹¹, -OC(O)R¹¹, -C(O)OR¹¹, -C(O)N(R¹²)₂ y trihaloalquilo C₁-C₆;

R³ es fenilo opcionalmente sustituido por trihaloalquilo C₁-C₆ o trihaloalcoxi C₁-C₆;

cada R¹¹ se selecciona independientemente de hidrógeno, alquilo C₁-C₆, cicloalquilo C₃-C₆, aralquilo C₇-C₁₉ o arilo C₆-C₁₉ (opcionalmente sustituido con uno o más grupos halo); y

cada R¹² se selecciona independientemente de hidrógeno o alquilo C₁-C₆.

21. El compuesto de la Reivindicación 20 que se caracteriza porque el heteroarilo C₁-C₁₂ se selecciona del grupo que consiste en piridinilo, purinilo, pirazinilo,

indolilo, indazolilo, benzoimidazolilo, imidazolilo, tetrazolilo, triazolilo, isoxazolilo, pirazolilo, pirimidinilo, tiadiazolilo, tiazolilo y piridazinilo.

22. El compuesto de la Reivindicación 12 que se caracteriza porque:

A es oxígeno;

R^2 es heterociclilo C_3-C_{12} , heterociclilalquilo C_3-C_{12} o heteroarilalquilo C_3-C_{12} , cada uno opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, oxo, tioxo, alquilo C_1-C_3 , $-OR^{11}$, $-C(O)R^{11}$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-C(O)N(R^{12})_2$ y trihaloalquilo C_1-C_6 ;

R^3 es fenilo opcionalmente sustituido por halo, trihaloalquilo C_1-C_6 o trihaloalcoxi C_1-C_6 ;

cada R^{11} se selecciona independientemente de hidrógeno, alquilo C_1-C_6 , cicloalquilo C_3-C_6 , aralquilo C_7-C_{19} o arilo C_6-C_{19} (opcionalmente sustituido con uno o más grupos halo); y

cada R^{12} se selecciona independientemente de hidrógeno o alquilo C_1-C_6 .

23. El compuesto de la Reivindicación 11 que se caracteriza porque:

A es oxígeno;

W es $-C(O)N(R^1)-$;

R^1 es hidrógeno, metilo o etilo;

R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi y trifluorometilo; y

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 .

24. El compuesto de la Reivindicación 23 que se caracteriza porque:

R^2 es cicloalquilo C_3-C_{12} o cicloalquilalquilo C_4-C_{12} , cada uno opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en $-OR^{11}$, alquilo C_1-C_3 , trihaloalquilo C_1-C_6 o arilo C_6-C_{19} ;

R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, trihaloalquilo C_1-C_6 y trihaloalcoxi C_1-C_6 ; y

cada R^{11} se selecciona independientemente de hidrógeno, alquilo C_1-C_6 , cicloalquilo C_3-C_6 , arilo C_6-C_{19} o aralquilo C_7-C_{19} .

25. El compuesto de la Reivindicación 23 que se caracteriza porque:

R^2 es alquilo C_1-C_{12} , alquenilo C_2-C_{12} , alcoxi C_1-C_6 o alcoxialquilo C_3-C_{12} , cada de los cuales está opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, oxo, tioxo, alquilo C_1-C_3 , $-OR^{11}$, $-C(O)R^{11}$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-C(O)N(R^{12})_2$, $-N(R^{12})_2$, trihaloalquilo C_1-C_6 , cicloalquilo C_3-C_{12} y arilo C_6-C_{19} ;

R^3 es fenilo opcionalmente sustituido con halo, trihaloalquilo C_1-C_6 o trihaloalcoxi C_1-C_6 ;

cada R^{11} se selecciona independientemente de hidrógeno, alquilo C_1-C_6 , cicloalquilo C_3-C_6 , aralquilo C_7-C_{19} o arilo C_6-C_{19} (opcionalmente sustituido con uno o más grupos halo); y

cada R^{12} se selecciona independientemente de hidrógeno o alquilo C_1-C_6 .

26. El compuesto de la Reivindicación 23 que se caracteriza porque:

R^2 es aralquilo C_7-C_{12} opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, oxo, tioxo, alquilo C_1-C_3 , $-OR^{11}$, $-C(O)R^{11}$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-C(O)N(R^{12})_2$, $-N(R^{12})_2$, trihaloalquilo C_1-C_6 , cicloalquilo C_3-C_{12} y arilo C_6-C_{19} ;

R^3 es fenilo opcionalmente sustituido con halo, trihaloalquilo C_1-C_6 o trihaloalcoxi C_1-C_6 ;

cada R^{11} se selecciona independientemente de hidrógeno, alquilo C_1-C_6 , cicloalquilo C_3-C_6 , aralquilo C_7-C_{19} o arilo C_6-C_{19} (opcionalmente sustituido con uno o más grupos halo); y

cada R^{12} se selecciona independientemente de hidrógeno o alquilo C_1-C_6 .

27. El compuesto de la Reivindicación 13 que se caracteriza porque:

A es oxígeno;

W es $-N(R^1)C(O)-$;

R^1 es hidrógeno, metilo o etilo;

R^2 es ciclopropiletilo o ciclopropilmetilo;

R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en fluoro, cloro y trifluorometilo;

R^4 y R^5 son cada uno hidrógeno; y

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} son cada uno hidrógeno.

28. El compuesto de la Reivindicación 15 que se caracteriza porque:
A es oxígeno;
W es $-N(R^1)C(O)-$;
 R^1 es hidrógeno, metilo o etilo;
 R^2 es alquilo C_1-C_6 opcionalmente sustituido con $-C(O)OR^{11}$;
 R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en fluoro, cloro y trifluorometilo;
 R^4 y R^5 son cada uno hidrógeno;
 R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} son cada uno hidrógeno; y
 R^{11} es hidrógeno, metilo, etilo o 1,1-dimetiletilo.
29. El compuesto de la Reivindicación 17 que se caracteriza porque:
A es oxígeno;
W es $-N(R^1)C(O)-$;
 R^1 es hidrógeno, metilo o etilo;
 R^2 es 2-feniletilo o 3-fenilpropilo donde el grupo fenilo está opcionalmente sustituido con uno o más sustituyentes independientemente seleccionados de cloro, fluoro o $-OR^{11}$;
 R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en fluoro, cloro y trifluorometilo;
 R^4 y R^5 son cada uno hidrógeno;
 R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} son cada uno hidrógeno; y
 R^{11} es hidrógeno, metilo, etilo o 1,1-dimetiletilo.
30. El compuesto de la Reivindicación 24 que se caracteriza porque:
A es oxígeno;
W es $-C(O)N(R^1)-$;
 R^1 es hidrógeno, metilo o etilo;
 R^2 es ciclopropiletilo, ciclopropilmetilo o ciclopentiletilo;
 R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en fluoro, cloro y trifluorometilo;
 R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi y trifluorometilo; y

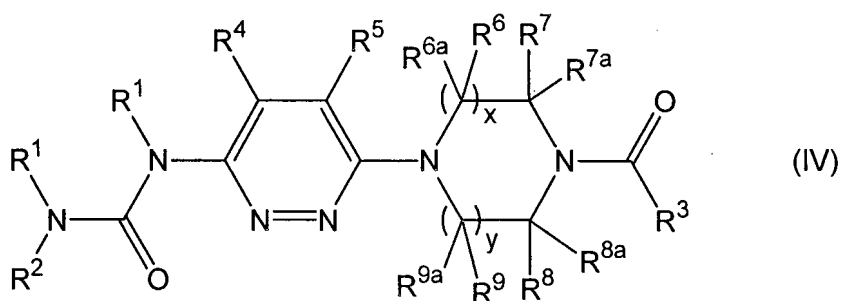
R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} son cada uno hidrógeno.

31. El compuesto de la Reivindicación 25 que se caracteriza porque:
- A es oxígeno;
 - W es $-C(O)N(R^1)-$;
 - R^1 es hidrógeno, metilo o etilo;
 - R^2 es alquilo C_1-C_6 ;
 - R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en fluoro, cloro y trifluorometilo;
 - R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi y trifluorometilo; y
 - R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} son cada uno hidrógeno.

32. El compuesto de la Reivindicación 26 que se caracteriza porque:
- A es oxígeno;
 - W es $-C(O)N(R^1)-$;
 - R^1 es hidrógeno, metilo o etilo;
 - R^2 es 3-fenilpropilo;
 - R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en fluoro, cloro y trifluorometilo;
 - R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi y trifluorometilo; y
 - R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} son cada uno hidrógeno.

33. Una composición farmacéutica que comprende un excipiente farmacéuticamente aceptable y una cantidad terapéuticamente eficaz de un compuesto de la Reivindicación 10.

34. Un compuesto de la fórmula (IV):



que se caracteriza porque:

x es 2 e y es 1;

cada R^1 se selecciona independientemente del grupo que consiste en hidrógeno; alquilo C_1-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, metilo o trifluorometilo; y alquilo C_2-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en metoxi e hidroxi;

R^2 se selecciona del grupo que consiste en alquilo C_1-C_{12} , alquenilo C_2-C_{12} , hidroxialquilo C_2-C_{12} , hidroxialquenilo C_2-C_{12} , alcoxialquilo C_2-C_{12} , cicloalquilo C_3-C_{12} , cicloalquilalquilo C_4-C_{12} , heterociclilo C_3-C_{12} , heterociclilalquilo C_3-C_{12} , arilo C_6-C_{19} , aralquilo C_7-C_{12} , heteroarilo C_1-C_{12} , y heteroarilalquilo C_3-C_{12} ;

R^3 se selecciona del grupo que consiste en alquilo C_1-C_{12} , alquenilo C_2-C_{12} , hidroxialquilo C_2-C_{12} , hidroxialquenilo C_2-C_{12} , alcoxi C_1-C_{12} , alcoxialquilo C_2-C_{12} , cicloalquilo C_3-C_{12} , cicloalquilalquilo C_4-C_{12} , arilo C_6-C_{19} , aralquilo C_7-C_{12} , heterociclilo C_3-C_{12} , heterociclilalquilo C_3-C_{12} , heteroarilo C_1-C_{12} y heteroarilalquilo C_3-C_{12} ;

R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi y trifluorometilo; y

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

o R^6 y R^{6a} juntos, o R^9 y R^{9a} juntos forman un grupo oxo, mientras que los restantes R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

o uno de los R^6 , R^{6a} , R^7 y R^{7a} junto con uno de los R^8 , R^{8a} , R^9 y R^{9a} forman un puente alquilenos C_{1-2} , mientras que los restantes R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

un estereoisómero, enantiómero o tautómero del mismo, una sal farmacéuticamente aceptable del mismo o una composición farmacéutica del mismo.

35. El compuesto de la Reivindicación 34 que se caracteriza porque:

cada R^1 es hidrógeno o alquilo C_1-C_6 ;

R^2 se selecciona del grupo que consiste en alquilo C_3-C_{12} , alquenilo C_3-C_{12} , hidroxialquilo C_3-C_{12} , hidroxialquenilo C_3-C_{12} , alcoxialquilo C_3-C_{12} , cicloalquilo C_3-C_{12} , cicloalquilalquilo C_4-C_{12} , heterociclilo C_3-C_{12} , heterociclilalquilo C_3-C_{12} , arilo C_6-C_{19} , aralquilo C_7-C_{12} , heteroarilo C_1-C_{12} y heteroarilalquilo C_3-C_{12} ;

cada R^2 está opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, oxo, tioxo, alquilo C_1-C_3 , $-OR^{11}$, $-C(O)OR^{11}$, trihaloalquilo C_1-C_6 , cicloalquilo C_3-C_{12} , heterociclilo C_3-C_{12} , arilo C_6-C_{19} , heteroarilo C_1-C_{12} y heteroaril C_1-C_{12} cicloalquilo C_3-C_{12} ;

R^3 se selecciona del grupo que consiste en alquilo C_3-C_{12} , alquenilo C_3-C_{12} , hidroxialquilo C_3-C_{12} , hidroxialquenilo C_3-C_{12} , alcoxi C_3-C_{12} , alcoxialquilo C_3-C_{12} , cicloalquilo C_3-C_{12} , cicloalquilalquilo C_4-C_{12} , arilo C_6-C_{19} , aralquilo C_7-C_{12} , heterociclilo C_3-C_{12} , heterociclilalquilo C_3-C_{12} , heteroarilo C_1-C_{12} y heteroarilalquilo C_3-C_{12} ;

donde cada uno de los anteriores grupos R^3 están opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en alquilo C_1-C_6 , trihaloalquilo C_1-C_6 , trihaloalcoxi C_1-C_6 , alcoxi C_1-C_6 , alquilsulfonilo C_1-C_6 , halo, ciano, nitro, hidroxilo, $-N(R^{12})_2$, $-C(O)OR^{11}$, $-S(O)_2N(R^{12})_2$, cicloalquilo C_3-C_{12} , heterociclilo C_3-C_{12} , arilo C_6-C_{19} , heteroarilo C_1-C_{12} y heteroaril C_1-C_{12} cicloalquilo C_3-C_{12} ;

R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi y trifluorometilo;

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

R^6 y R^{6a} juntos o R^7 y R^{7a} juntos forman un grupo oxo mientras que los restantes R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

o uno de los R^6 , R^{6a} , R^7 y R^{7a} junto con uno de los R^8 , R^{8a} , R^9 y R^{9a} forman un puente alquilenos C_{1-2} , mientras que los restantes R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

cada R^{11} se selecciona independientemente de hidrógeno, alquilo C_1-C_6 ,

cicloalquilo C₃-C₆, arilo C₆-C₁₉ o aralquilo C₇-C₁₉; y

cada R¹² se selecciona independientemente de hidrógeno o alquilo C₁-C₆.

36. El compuesto de la Reivindicación 35 que se caracteriza porque:

R² es cicloalquilo C₃-C₁₂ o cicloalquilalquilo C₄-C₁₂, cada uno opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en -OR¹¹, alquilo C₁-C₃ o arilo C₆-C₁₉;

R³ es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, trihaloalquilo C₁-C₆ y trihaloalcoxi C₁-C₆; y
cada R¹¹ se selecciona independientemente de hidrógeno, alquilo C₁-C₆,

cicloalquilo C₃-C₆, arilo C₆-C₁₉ o aralquilo C₇-C₁₉.

37. El compuesto de la Reivindicación 35 que se caracteriza porque:

R² es aralquilo C₇-C₁₂ opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, -OR¹¹ o alquilo C₁-C₃;

R³ es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, trihaloalquilo C₁-C₆ y trihaloalcoxi C₁-C₆; y
cada R¹¹ se selecciona independientemente de hidrógeno, alquilo C₁-C₆,

cicloalquilo C₃-C₆, arilo C₆-C₁₉ o aralquilo C₇-C₁₉.

38. El compuesto de la Reivindicación 35 que se caracteriza porque:

R² es arilo C₆-C₁₉ opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, -OR¹¹ o alquilo C₁-C₃;

R³ es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, trihaloalquilo C₁-C₆ y trihaloalcoxi C₁-C₆; y
cada R¹¹ se selecciona independientemente de hidrógeno, alquilo C₁-C₆,

cicloalquilo C₃-C₆, arilo C₆-C₁₉ o aralquilo C₇-C₁₉.

39. El compuesto de la Reivindicación 35 que se caracteriza porque:

R² es alquilo C₃-C₁₂, hidroxialquilo C₃-C₁₂ o alcoxialquilo C₃-C₁₂, cada uno opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, -OR¹¹ o -C(O)OR¹¹;

R³ es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, trihaloalquilo C₁-C₆ y trihaloalcoxi C₁-C₆; y

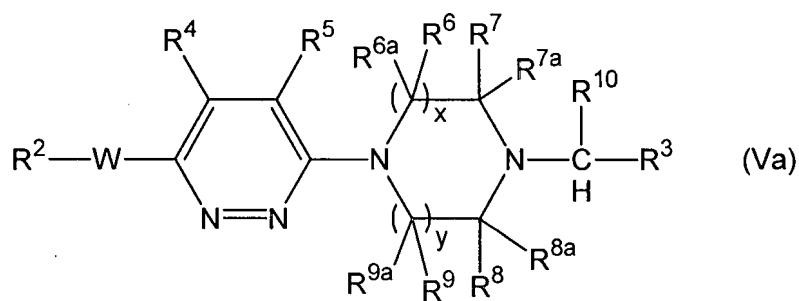
cada R^{11} se selecciona independientemente de hidrógeno, alquilo C_1-C_6 , cicloalquilo C_3-C_6 , arilo C_6-C_{19} o aralquilo C_7-C_{19} .

40. El compuesto de la Reivindicación 37 que se caracteriza porque:
 cada R^1 es hidrógeno, metilo o etilo;
 R^2 es bencilo;
 R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en fluoro, cloro y trifluorometilo;
 R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi y trifluorometilo; y
 $R^6, R^{6a}, R^7, R^{7a}, R^8, R^{8a}, R^9$ y R^{9a} son cada uno hidrógeno.

41. El compuesto de la Reivindicación 39 que se caracteriza porque:
 cada R^1 es hidrógeno, metilo o etilo;
 R^2 es pentilo;
 R^3 es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en fluoro, cloro y trifluorometilo;
 R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi y trifluorometilo; y
 $R^6, R^{6a}, R^7, R^{7a}, R^8, R^{8a}, R^9$ y R^{9a} son cada uno hidrógeno.

42. Una composición farmacéutica que comprende un excipiente farmacéuticamente aceptable y una cantidad terapéuticamente eficaz de un compuesto de la Reivindicación 34.

43. Un compuesto de la fórmula (Va):



que se caracteriza porque:

x es 2 e y es 1;

W es $-C(O)N(R^1)-$; $-N(R^1)C(O)N(R^1)-$ o $-N(R^1)C(O)-$;

cada R^1 se selecciona independientemente del grupo que consiste en hidrógeno; alquilo C_1-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, metilo o trifluorometilo; y alquilo C_2-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en metoxi e hidroxi;

R^2 se selecciona del grupo que consiste en alquilo C_7-C_{12} , alquenilo C_2-C_{12} , hidroxialquilo C_7-C_{12} , hidroxialquenilo C_2-C_{12} , alcoxi C_1-C_{12} , alcoxialquilo C_2-C_{12} , cicloalquilo C_3-C_{12} , cicloalquilalquilo C_4-C_{12} , aralquilo $C_{13}-C_{19}$, heterociclilo C_3-C_{12} , heterocicilalquilo C_3-C_{12} , heteroarilo C_1-C_{12} y heteroarilalquilo C_3-C_{12} ;

R^3 se selecciona del grupo que consiste en alquilo C_1-C_{12} , alquenilo C_2-C_{12} , hidroxialquilo C_2-C_{12} , hidroxialquenilo C_2-C_{12} , alcoxi C_1-C_{12} , alcoxialquilo C_2-C_{12} , cicloalquilo C_3-C_{12} , cicloalquilalquilo C_4-C_{12} , arilo C_6-C_{19} , aralquilo C_7-C_{12} , heterociclilo C_3-C_{12} , heterocicilalquilo C_3-C_{12} , heteroarilo C_1-C_{12} y heteroarilalquilo C_3-C_{12} ;

R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi, trifluorometilo, ciano, nitro o $-N(R^{12})_2$;

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

o R^6 y R^{6a} juntos o R^7 y R^{7a} juntos o R^8 y R^{8a} juntos o R^9 y R^{9a} juntos forman un grupo oxo, mientras que los restantes R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

o uno de los R^6 , R^{6a} , R^7 y R^{7a} junto con uno de los R^8 , R^{8a} , R^9 y R^{9a} forman un puente alquilenos C_{1-2} , mientras que los restantes R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

R^{10} es hidrógeno o alquilo C_1-C_3 ; y

cada R^{12} se selecciona independientemente de hidrógeno o alquilo C_1-C_6 ;

siempre que R^2 no sea pirazinilo, piridinonilo, pirrolidinonilo o imidazolilo;

un estereoisómero, enantiómero o tautómero del mismo, una sal farmacéuticamente aceptable del mismo o una composición farmacéutica del mismo.

44. El compuesto de la Reivindicación 43 que se caracteriza porque:

W es $-N(R^1)C(O)-$;

cada R^1 es hidrógeno o alquilo C_1-C_6 ;

R^2 se selecciona del grupo que consiste en alquilo C_7-C_{12} , alquenilo

C₂-C₁₂, hidroxialquilo C₇-C₁₂, hidroxialquenilo C₂-C₁₂, alcoxi C₁-C₁₂, alcoxialquilo C₂-C₁₂, cicloalquilo C₃-C₁₂, cicloalquilalquilo C₄-C₁₂, aralquilo C₁₃-C₁₉, heterociclilo C₃-C₁₂, heterocicilalquilo C₃-C₁₂, heteroarilo C₁-C₁₂ y heteroarilalquilo C₃-C₁₂;

cada R² está opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, oxo, tioxo, alquilo C₁-C₃, -OR¹¹, -C(O)R¹¹, -OC(O)R¹¹, -C(O)OR¹¹, -C(O)N(R¹²)₂, -N(R¹²)₂, trihaloalquilo C₁-C₆, cicloalquilo C₃-C₁₂, heterociclilo C₃-C₁₂, arilo C₆-C₁₉, heteroarilo C₁-C₁₂ y heteroaril C₁-C₁₂ cicloalquilo C₃-C₁₂;

R³ se selecciona del grupo que consiste en alquilo C₁-C₁₂, alquenilo C₂-C₁₂, hidroxialquilo C₂-C₁₂, hidroxialquenilo C₂-C₁₂, alcoxi C₁-C₁₂, alcoxialquilo C₂-C₁₂, cicloalquilo C₃-C₁₂, cicloalquilalquilo C₄-C₁₂, arilo C₆-C₁₉, aralquilo C₇-C₁₂, heterociclilo C₃-C₁₂, heterocicilalquilo C₃-C₁₂, heteroarilo C₁-C₁₂ y heteroarilalquilo C₃-C₁₂;

cada R³ está opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, nitro, hidroxilo, alquilo C₁-C₆, trihaloalquilo C₁-C₆, trihaloalcoxi C₁-C₆, alquilsulfonilo C₁-C₆, -N(R¹²)₂, -OC(O)R¹¹, -C(O)OR¹¹, -S(O)₂N(R¹²)₂, cicloalquilo C₃-C₁₂, heterociclilo C₃-C₁₂ y heteroaril C₁-C₁₂ cicloalquilo C₃-C₁₂;

R⁴ y R⁵ se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi, trifluorometilo, ciano, nitro o -N(R¹²)₂;

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹ y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C₁-C₃;

R¹⁰ es hidrógeno o alquilo C₁-C₃;

cada R¹¹ se selecciona independientemente de hidrógeno, alquilo C₁-C₆, cicloalquilo C₃-C₆, arilo C₆-C₁₉ o aralquilo C₇-C₁₉; y

cada R¹² se selecciona independientemente de hidrógeno o alquilo C₁-C₆.

45. El compuesto de la Reivindicación 44 que se caracteriza porque:

R² es cicloalquilo C₃-C₁₂ o cicloalquilalquilo C₄-C₁₂, cada uno opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, trihaloalquilo C₁-C₆, -OR¹¹, alquilo C₁-C₃ o arilo C₆-C₁₉;

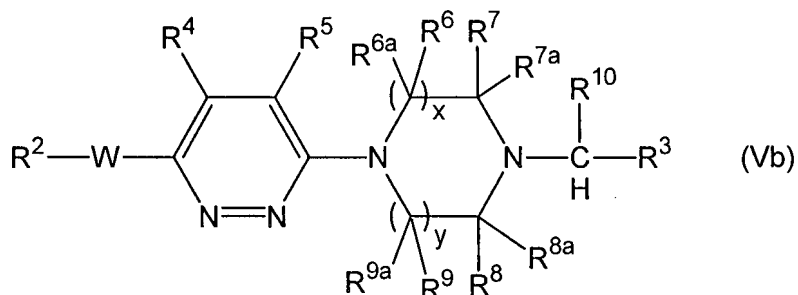
R³ es fenilo opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, ciano, nitro, hidroxilo, alquilo C₁-C₆, trihaloalquilo C₁-C₆, trihaloalcoxi C₁-C₆, alquilsulfonilo C₁-C₆, -N(R¹²)₂, -OC(O)R¹¹, -C(O)OR¹¹, -S(O)₂N(R¹²)₂ y cicloalquilo C₃-C₁₂;

cada R^{11} se selecciona independientemente de hidrógeno, alquilo C_1-C_6 , cicloalquilo C_3-C_6 , arilo C_6-C_{19} o aralquilo C_7-C_{19} ; y

cada R^{12} se selecciona independientemente de hidrógeno o alquilo C_1-C_6 .

46. Una composición farmacéutica que comprende un excipiente farmacéuticamente aceptable y una cantidad terapéuticamente eficaz de un compuesto de la Reivindicación 43.

47. Un compuesto de la fórmula (Vb):



que se caracteriza porque:

x es 2 e y es 1;

W es $-C(O)N(R^1)-$; $-N(R^1)C(O)N(R^1)-$ o $-N(R^1)C(O)-$;

cada R^1 se selecciona independientemente del grupo que consiste en hidrógeno; alquilo C_1-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en halo, metilo o trifluorometilo; y alquilo C_2-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados del grupo que consiste en metoxi y hidroxilo;

R^2 se selecciona del grupo que consiste en alquilo C_1-C_{12} , alquenilo C_2-C_{12} , hidroxialquilo C_2-C_{12} , hidroxialquenilo C_2-C_{12} , alcoxi C_1-C_{12} , alcoxialquilo C_2-C_{12} , cicloalquilo C_3-C_{12} , cicloalquilalquilo C_4-C_{12} , arilo C_6-C_{19} , aralquilo C_7-C_{12} , heterociclilo C_3-C_{12} , heterociclilalquilo C_3-C_{12} , heteroarilo C_1-C_{12} y heteroarilalquilo C_3-C_{12} ;

R^3 se selecciona del grupo que consiste en alquilo C_7-C_{12} , alquenilo C_2-C_{12} , hidroxialquilo C_2-C_{12} , hidroxialquenilo C_2-C_{12} , alcoxi C_1-C_{12} o alcoxialquilo C_2-C_{12}

R^4 y R^5 se seleccionan cada uno independientemente de hidrógeno, fluoro, cloro, metilo, metoxi, trifluorometilo, ciano, nitro o $-N(R^{12})_2$;

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

o R^6 y R^{6a} juntos o R^7 y R^{7a} juntos o R^8 y R^{8a} juntos o R^9 y R^{9a} juntos

forman un grupo oxo, mientras que los restantes R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

o uno de los R^6 , R^{6a} , R^7 y R^{7a} junto con uno de los R^8 , R^{8a} , R^9 y R^{9a} forman un puente alquileo C_{1-2} , mientras que los restantes R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 y R^{9a} se seleccionan cada uno independientemente de hidrógeno o alquilo C_1-C_3 ;

R^{10} es hidrógeno o alquilo C_1-C_3 ; y

cada R^{12} se selecciona independientemente de hidrógeno o alquilo C_1-C_6 ;

como un estereoisómero, enantiómero o tautómero del mismo, una sal farmacéuticamente aceptable del mismo o una composición farmacéutica del mismo.

48. Una composición farmacéutica que comprende un excipiente farmacéuticamente aceptable y una cantidad terapéuticamente eficaz de un compuesto de la Reivindicación 47.



US007754711B2

(12) **United States Patent**
Chakka et al.

(10) **Patent No.:** **US 7,754,711 B2**
(45) **Date of Patent:** ***Jul. 13, 2010**

(54) **PYRIDAZINE DERIVATIVES AND THEIR USE AS THERAPEUTIC AGENTS**

(75) **Inventors:** Nagasree Chakka, Burnaby (CA); Mikhail Chafeev, Vancouver (CA); Sultan Chowdhury, Scarborough (CA); Jian-Min Fu, Burnaby (CA); Duanjie Hou, Burnaby (CA); Rajender Kamboj, Burnaby (CA); Vishnumurthy Kodumuru, Burnaby (CA); Shifeng Liu, Port Coquitlam (CA); Vandna Raina, Vancouver (CA); Shaoyi Sun, Vancouver (CA); Serguei Sviridov, Burnaby (CA); Michael D. Winther, Vancouver (CA); Zailui Zhang, Vancouver (CA); Melwyn Abreo, Jamul (CA); Mark W. Holladay, San Diego, CA (US); Wenbao Li, San Diego, CA (US); Sengen Sun, San Diego, CA (US); Chi Tu, San Diego, CA (US); Heinz W. Gschwend, Santa Rosa, CA (US)

(73) **Assignee:** Xenon Pharmaceuticals Inc., Burnaby, British Columbia (CA)

(*) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 480 days.

This patent is subject to a terminal disclaimer.

(21) **Appl. No.:** 11/055,034

(22) **Filed:** Feb. 9, 2005

(65) **Prior Publication Data**
US 2006/0009459 A1 Jan. 12, 2006

Related U.S. Application Data

(63) Continuation-in-part of application No. 10/901,563, filed on Jul. 29, 2004, now Pat. No. 7,335,658.
(60) Provisional application No. 60/553,491, filed on Mar. 16, 2004, provisional application No. 60/553,404, filed on Mar. 16, 2004, provisional application No. 60/553,403, filed on Mar. 16, 2004, provisional application No. 60/553,446, filed on Mar. 16, 2004, provisional application No. 60/553,416, filed on Mar. 16, 2004, provisional application No. 60/546,815, filed on Feb. 23, 2004, provisional application No. 60/546,898, filed on Feb. 23, 2004, provisional application No. 60/546,786, filed on Feb. 23, 2004, provisional application No. 60/546,934, filed on Feb. 23, 2004, provisional application No. 60/491,095, filed on Jul. 30, 2003.

(51) **Int. Cl.**
A61K 31/551 (2006.01)
A61K 31/5513 (2006.01)
A61K 31/50 (2006.01)
A61K 31/502 (2006.01)
A61K 31/501 (2006.01)

C07D 245/02 (2006.01)
C07D 243/04 (2006.01)
C07D 243/08 (2006.01)
C07D 403/04 (2006.01)
C07D 401/14 (2006.01)
C07D 403/14 (2006.01)
A61P 7/12 (2006.01)

(52) **U.S. Cl.** 514/218; 540/470; 540/492; 540/575; 544/238; 514/252.01; 514/252.02

(58) **Field of Classification Search** 514/183, 514/218, 252.13, 252.01, 252.02; 540/470, 540/492, 575; 544/238

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,001,125 A * 3/1991 Stokbroekx et al. 514/252.02
5,883,094 A * 3/1999 Fliri et al. 514/242
5,985,878 A * 11/1999 Stokbroekx et al. 514/252.02
7,119,086 B2 * 10/2006 Di Malta et al. 514/218

FOREIGN PATENT DOCUMENTS

EP 0-156-433 10/1985
EP 0-211-457 2/1987
EP 0-320-032 6/1989
EP 1-396-487 3/2004
WO WO-97/37975 10/1997
WO WO-99/00386 1/1999
WO WO-01/62954 8/2001

(Continued)

OTHER PUBLICATIONS

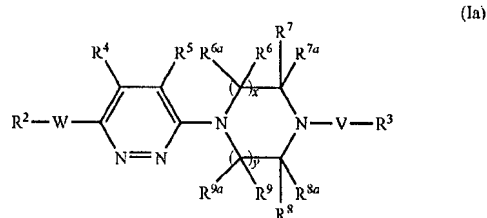
Dobrzyn, et al., Obesity Reviews 6, 169-174, 2005.*

(Continued)

Primary Examiner Mark L Berch
Assistant Examiner—Cecilia M Jaisle
(74) *Attorney, Agent, or Firm*—Osha • Liang LLP

(57) **ABSTRACT**

Methods of treating an SCD-mediated disease or condition in a mammal, preferably a human, are disclosed, wherein the methods comprise administering to a mammal in need thereof a compound of formula (Ia):



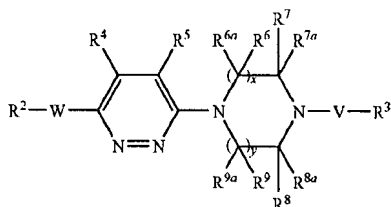
where x, y, W, V, R², R³, R⁴, R⁵, R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹ and R^{9a} are defined herein. Pharmaceutical compositions comprising the compounds of formula (I) are also disclosed.

6 Claims, No Drawings

be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

What is claimed is:

1. An in vivo method of inhibiting human stearyl-CoA desaturase (hSCD) activity comprising contacting a source of hSCD with a compound of formula (Ia)



wherein:

x and y are each independently 1, 2 or 3;

W is —C(O)N(R¹)—; —C(O)N[C(O)R^{1a}]—, —N(R¹)C(O)N(R¹)—, —N(R¹)C(O)—, —OC(O)N(R¹)—, —N(R¹)S(O)_p— (where p is 1 or 2), —S(O)_pN(R¹)— (where p is 1 or 2), —C(O)—, —OS(O)₂N(R¹)—, —OC(O)—, —C(O)O—, —N(R¹)C(O)O—, —N(R¹)C(=NR^{1a})N(R¹)—, —N(R¹)C(=S)N(R¹)—, —N(R¹)C(=NR^{1a})—, or —C(=NR^{1a})N(R¹)—;

V is —C(O)—, —C(O)O—, —C(S)—, —C(O)N(R¹)—, —S(O)_t— (where t is 0, 1 or 2), —S(O)_pN(R¹)— (where p is 1 or 2), —C(R¹⁰)H—, or —C(=NR^{1a})—;

each R¹ is independently selected from the group consisting of hydrogen; C₁-C₆alkyl optionally substituted with one or more substituents selected from the group consisting of halo, methyl or trifluoromethyl; and C₂-C₆alkyl optionally substituted with one or more substituents selected from the group consisting of methoxy and hydroxyl;

R^{1a} is selected from the group consisting of hydrogen, —OR¹, cyano, C₁-C₆alkyl and cycloalkylalkyl;

R² is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclalkyl, C₃-C₁₂heterocyclalkylalkyl, C₁-C₁₂heteroaryl, and C₃-C₁₂heteroarylalkyl;

or R² is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclalkyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

R³ is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclalkyl, C₃-C₁₂heterocyclalkylalkyl, C₁-C₁₂heteroaryl and C₃-C₁₂heteroarylalkyl;

or R³ is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclalkyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

R⁴ and R⁵ are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or —N(R¹²)₂;

or R⁶ and R^{6a} together, or R⁷ and R^{7a} together, or R⁸ and R^{8a} together, or R⁹ and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

or R⁶ and R^{6a} together, or R⁷ and R^{7a} together, or R⁸ and R^{8a} together, or R⁹ and R^{9a} together are an oxo group, provided that when V is —C(O)—, R⁷ and R^{7a} together or R⁸ and R^{8a} together do not form an oxo group, while the remaining R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

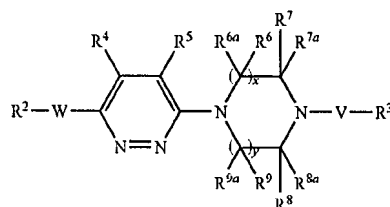
or one of R⁶, R^{6a}, R⁷, and R^{7a} together with one of R⁸, R^{8a}, R⁹ and R^{9a} form an alkylene bridge, while the remaining R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

R¹⁰ is hydrogen or C₁-C₃alkyl; and

each R¹² is independently selected from hydrogen or C₁-C₆alkyl;

a stereoisomer, enantiomer or tautomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutical composition thereof.

2. A compound of formula (Ia):



wherein:

x and y are each independently 1, 2 or 3;

W is —C(O)N(R¹)—; —C(O)N[C(O)R^{1a}]—, —N(R¹)C(O)N(R¹)—, —N(R¹)C(O)—, —OC(O)N(R¹)—, —N(R¹)S(O)_p— (where p is 1 or 2), —S(O)_pN(R¹)— (where p is 1 or 2), —C(O)—, —OS(O)₂N(R¹)—, —OC(O)—, —C(O)O—, —N(R¹)C(O)O—, —N(R¹)C(=NR^{1a})N(R¹)—, —N(R¹)C(=S)N(R¹)—, —N(R¹)C(=NR^{1a})—, or —C(=NR^{1a})N(R¹)—;

V is —C(O)—, —C(O)O—, —C(S)—, —C(O)N(R¹)—, —S(O)_t— (where t is 0, 1 or 2), —S(O)_pN(R¹)— (where p is 1 or 2), —C(R¹⁰)H—, or —C(=NR^{1a})—;

each R¹ is independently selected from the group consisting of hydrogen;

C₁-C₆alkyl optionally substituted with one or more substituents selected from the group consisting of halo, methyl or trifluoromethyl; and C₂-C₆alkyl optionally substituted with one or more substituents selected from the group consisting of methoxy and hydroxyl;

R^{1a} is selected from the group consisting of hydrogen, —OR¹, cyano, C₁-C₆alkyl and cycloalkylalkyl;

R² is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclalkyl, C₃-C₁₂heterocyclalkylalkyl, C₁-C₁₂heteroaryl, and C₃-C₁₂heteroarylalkyl;

or R² is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group con-

119

sisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

R³ is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkenyl, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl and C₃-C₁₂heteroarylalkyl;

or R³ is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of cycloalkyl, heterocyclyl, aryl and heteroaryl and where some or all of the rings may be fused to each other;

R⁴ and R⁵ are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or —N(R¹²)₂;

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

or R⁶ and R^{6a} together, or R⁷ and R^{7a} together, or R⁸ and R^{8a} together, or R⁹ and R^{9a} together are an oxo group, provided that when V is —C(O)—, R⁷ and R^{7a} together or R⁸ and R^{8a} together do not form an oxo group, while

120

the remaining R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

or one of R⁶, R^{6a}, R⁷, and R^{7a} together with one of R⁸, R^{8a}, R⁹ and R^{9a} form an alkylene bridge, while the remaining R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

R¹⁰ is hydrogen or C₁-C₃alkyl; and

each R¹² is independently selected from hydrogen or C₁-C₆alkyl;

a stereoisomer, enantiomer or tautomer thereof, a pharmaceutically acceptable salt thereof, a pharmaceutical composition thereof.

3. The compound of claim 2 wherein W is —N(R¹)C(O)— and V is —C(=NH)—.

4. The compound of claim 2 wherein W is —N(R¹)C(=NR^{1a})—.

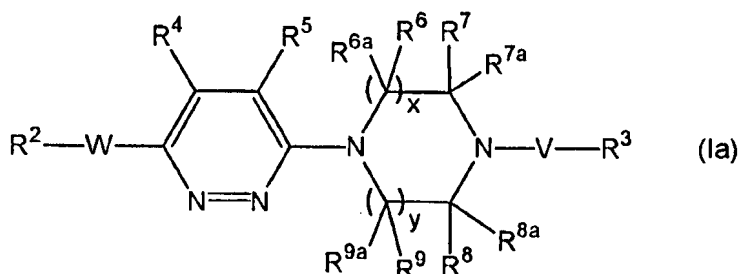
5. The compound of claim 2 wherein W is —N(R¹)C(=NR^{1a})N(R¹)— or —N(R¹)C(=S)N(R¹)—.

6. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of claim 2.

* * * * *

CLAIMS

1. An in-vitro method of inhibiting human stearyl-CoA desaturase (hSCD) activity comprising contacting a source of hSCD with a compound of formula (Ia)



wherein:

x and y are each independently 1, 2 or 3;

W is -OC(O)N(R¹)-, -N(R¹)S(O)_p- (where p is 1), -S(O)_pN(R¹)- (where p is 1 or 2), -OS(O)₂N(R¹)-, -N(R¹)C(O)O-, -N(R¹)C(=NR^{1a})N(R¹)-, -N(R¹)C(=S)N(R¹)-, -N(R¹)C(=NR^{1a})-, or -C(=NR^{1a})N(R¹)-;

V is -C(O)-, -C(O)O-, -C(S)-, -C(O)N(R¹)-, -S(O)- (where t is 0, 1 or 2), -S(O)_pN(R¹)- (where p is 1 or 2), -C(R¹⁰)H-, or -C(=NR^{1a})-;

each R¹ is independently selected from the group consisting of hydrogen; C₁-C₆alkyl optionally substituted with one or more substituents selected from the group consisting of halo, methyl or trifluoromethyl; and C₂-C₆alkyl optionally substituted with one or more substituents selected from the group consisting of methoxy and hydroxyl;

R^{1a} is selected from the group consisting of hydrogen, -OR¹, cyano, C₁-C₆alkyl and C₄-C₁₂cycloalkylalkyl;

R² is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl, and C₃-C₁₂heteroarylalkyl;

or R² is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl, C₆-C₁₉aryl and C₁-C₁₂heteroaryl and where some or all of the rings may be fused to each other;

R³ is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl and C₃-C₁₂heteroarylalkyl;

or R^3 is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of C_3 - C_{12} cycloalkyl, C_3 - C_{12} heterocyclyl, C_6 - C_{19} aryl and C_1 - C_{12} heteroaryl and where some or all of the rings may be fused to each other;

R^4 and R^5 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or $-N(R^{12})_2$;

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

or R^6 and R^{6a} together, or R^7 and R^{7a} together, or R^8 and R^{8a} together, or R^9 and R^{9a} together are an oxo group, provided that when V is $-C(O)-$, R^7 and R^{7a} together or R^8 and R^{8a} together do not form an oxo group, while the remaining R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

or one of R^6 , R^{6a} , R^7 , and R^{7a} together with one of R^8 , R^{8a} , R^9 and R^{9a} form an alkylene bridge, while the remaining R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

R^{10} is hydrogen or C_1 - C_3 alkyl; and

each R^{12} is independently selected from hydrogen or C_1 - C_6 alkyl;

wherein each of C_1 - C_6 alkyl, C_2 - C_6 alkyl, C_1 - C_{12} alkyl, and each alkyl part of each C_2 - C_{12} hydroxyalkyl, C_1 - C_{12} alkoxy, C_2 - C_{12} alkoxyalkyl, C_4 - C_{12} cycloalkylalkyl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclalkyl and C_3 - C_{12} heteroarylalkyl are unsubstituted or substituted by one or more of the following groups: C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, halo, C_2 - C_{12} haloalkenyl, cyano, nitro, C_6 - C_{19} aryl, C_3 - C_{12} cycloalkyl, C_3 - C_{12} heterocyclyl, C_1 - C_{12} heteroaryl, $-OR^{14}$, $-OC(O)R^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)OR^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)OR^{16}$, $-N(R^{14})C(O)R^{16}$, $-N(R^{14})(S(O)_tR^{16})$ (where t is 1 to 2), $-S(O)_tOR^{16}$ (where t is 1 to 2), $-S(O)_tR^{16}$ (where t is 0 to 2), and $-S(O)_tN(R^{14})_2$ (where t is 1 to 2), where each R^{14} is independently hydrogen, C_1 - C_{12} alkyl, halo C_1 - C_{12} alkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl (unsubstituted or substituted with one or more halo groups), C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl; and each R^{16} is C_1 - C_{12} alkyl, halo C_1 - C_{12} alkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each C_2 - C_{12} alkenyl and each alkenyl part of each C_2 - C_{12} hydroxyalkenyl are unsubstituted or substituted by one of the following groups: C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, halo, C_1 - C_{12} haloalkyl, C_2 - C_{12} haloalkenyl, cyano, nitro, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl, C_3 - C_{12} heteroarylalkyl, $-OR^{14}$, $-OC(O)R^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)OR^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)OR^{16}$, $-N(R^{14})C(O)R^{16}$, $-N(R^{14})(S(O)_tR^{16})$ (where t is 1 to 2), $-S(O)_tOR^{16}$ (where t is 1 to 2), $-S(O)_tR^{16}$ (where t is 0 to 2), and $-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, C_1 - C_{12} alkyl, halo C_1 - C_{12} alkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl,

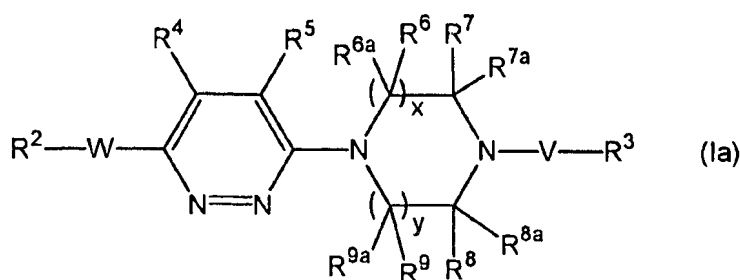
C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; and each R¹⁶ is C₁-C₁₂alkyl, haloC₁-C₁₂alkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each C₃-C₁₂cycloalkyl, each cycloalkyl part of each C₄-C₁₂cycloalkylalkyl, each C₆-C₁₉aryl and each aryl part of each C₇-C₁₂aralkyl are unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each C₃-C₁₂heterocyclyl, each heterocyclyl part of each C₃-C₁₂heterocyclylalkyl, each C₁-C₁₂heteroaryl and each heteroaryl part of C₃-C₁₂heteroarylalkyl are unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, oxo, thioxo, nitro, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

a stereoisomer, enantiomer or tautomer thereof, a pharmaceutically acceptable salt thereof, or a pharmaceutical composition thereof.

2. A compound of formula (Ia):



wherein:

x and y are each independently 1, 2 or 3;

W is $-\text{OC(O)N(R}^1\text{)}-$, $-\text{N(R}^1\text{)S(O)}_p-$ (where p is 1), $-\text{S(O)}_p\text{N(R}^1\text{)}-$ (where p is 1 or 2), $-\text{OS(O)}_2\text{N(R}^1\text{)}-$, $-\text{N(R}^1\text{)C(O)O}-$, $-\text{N(R}^1\text{)C(=NR}^{1a}\text{)N(R}^1\text{)}-$, $-\text{N(R}^1\text{)C(=S)N(R}^1\text{)}-$, $-\text{N(R}^1\text{)C(=NR}^{1a}\text{)}-$, or $-\text{C(=NR}^{1a}\text{)N(R}^1\text{)}-$;

V is $-\text{C(O)}-$, $-\text{C(O)O}-$, $-\text{C(S)}-$, $-\text{C(O)N(R}^1\text{)}-$, $-\text{S(O)}_t-$ (where t is 0, 1 or 2), $-\text{S(O)}_p\text{N(R}^1\text{)}-$ (where p is 1 or 2), $-\text{C(R}^{10}\text{)H}-$, or $-\text{C(=NR}^{1a}\text{)}-$;

each R^1 is independently selected from the group consisting of hydrogen; C_1 - C_6 alkyl optionally substituted with one or more substituents selected from the group consisting of halo, methyl or trifluoromethyl; and C_2 - C_6 alkyl optionally substituted with one or more substituents selected from the group consisting of methoxy and hydroxyl;

R^{1a} is selected from the group consisting of hydrogen, $-\text{OR}^1$, cyano, C_1 - C_6 alkyl and C_4 - C_{12} cycloalkylalkyl;

R^2 is selected from the group consisting of C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} hydroxyalkyl, C_2 - C_{12} hydroxyalkenyl, C_1 - C_{12} alkoxy, C_2 - C_{12} alkoxyalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclylalkyl, C_1 - C_{12} heteroaryl, and C_3 - C_{12} heteroarylalkyl;

or R^2 is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of C_3 - C_{12} cycloalkyl, C_3 - C_{12} heterocyclyl, C_6 - C_{19} aryl and C_1 - C_{12} heteroaryl and where some or all of the rings may be fused to each other;

R^3 is selected from the group consisting of C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} hydroxyalkyl, C_2 - C_{12} hydroxyalkenyl, C_1 - C_{12} alkoxy, C_2 - C_{12} alkoxyalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclylalkyl, C_1 - C_{12} heteroaryl and C_3 - C_{12} heteroarylalkyl;

or R^3 is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of C_3 - C_{12} cycloalkyl, C_3 - C_{12} heterocyclyl, C_6 - C_{19} aryl and C_1 - C_{12} heteroaryl and where some or all of the rings may be fused to each other;

R^4 and R^5 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or $-\text{N(R}^{12}\text{)}_2$;

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

or R^6 and R^{6a} together, or R^7 and R^{7a} together, or R^8 and R^{8a} together, or R^9 and R^{9a} together are an oxo group, provided that when V is -C(O)-, R^7 and R^{7a} together or R^8 and R^{8a} together do not form an oxo group, while the remaining R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

or one of R^6 , R^{6a} , R^7 , and R^{7a} together with one of R^8 , R^{8a} , R^9 and R^{9a} form an alkylene bridge, while the remaining R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

R^{10} is hydrogen or C_1 - C_3 alkyl; and

each R^{12} is independently selected from hydrogen or C_1 - C_6 alkyl;

wherein each of C_1 - C_6 alkyl, C_2 - C_6 alkyl, C_1 - C_{12} alkyl, and each alkyl part of each C_2 - C_{12} hydroxyalkyl, C_1 - C_{12} alkoxy, C_2 - C_{12} alkoxyalkyl, C_4 - C_{12} cycloalkylalkyl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclalkyl and C_3 - C_{12} heteroarylalkyl are unsubstituted or substituted by one or more of the following groups: C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, halo, C_2 - C_{12} haloalkenyl, cyano, nitro, C_6 - C_{19} aryl, C_3 - C_{12} cycloalkyl, C_3 - C_{12} heterocycl, C_1 - C_{12} heteroaryl, -OR¹⁴, -OC(O)-R¹⁴, -N(R¹⁴)₂, -C(O)R¹⁴, -C(O)OR¹⁴, -C(O)N(R¹⁴)₂, -N(R¹⁴)C(O)OR¹⁶, -N(R¹⁴)C(O)R¹⁶, -N(R¹⁴)(S(O)_t)R¹⁶ (where t is 1 to 2), -S(O)_tOR¹⁶ (where t is 1 to 2), -S(O)_tR¹⁶ (where t is 0 to 2), and -S(O)_tN(R¹⁴)₂ (where t is 1 to 2), where each R¹⁴ is independently hydrogen, C_1 - C_{12} alkyl, halo C_1 - C_{12} alkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl (unsubstituted or substituted with one or more halo groups), C_7 - C_{12} aralkyl, C_3 - C_{12} heterocycl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl; and each R¹⁶ is C_1 - C_{12} alkyl, halo C_1 - C_{12} alkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocycl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each C_2 - C_{12} alkenyl and each alkenyl part of each C_2 - C_{12} hydroxyalkenyl are unsubstituted or substituted by one of the following groups: C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, halo, C_1 - C_{12} haloalkyl, C_2 - C_{12} haloalkenyl, cyano, nitro, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_3 - C_{12} heterocycl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl, C_3 - C_{12} heteroarylalkyl, -OR¹⁴, -OC(O)-R¹⁴, -N(R¹⁴)₂, -C(O)R¹⁴, -C(O)OR¹⁴, -C(O)N(R¹⁴)₂, -N(R¹⁴)C(O)OR¹⁶, -N(R¹⁴)C(O)R¹⁶, -N(R¹⁴)(S(O)_t)R¹⁶ (where t is 1 to 2), -S(O)_tOR¹⁶ (where t is 1 to 2), -S(O)_tR¹⁶ (where t is 0 to 2), and -S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C_1 - C_{12} alkyl, halo C_1 - C_{12} alkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocycl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl; and each R¹⁶ is C_1 - C_{12} alkyl, halo C_1 - C_{12} alkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocycl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each C_3 - C_{12} cycloalkyl, each cycloalkyl part of each C_4 - C_{12} cycloalkylalkyl, each C_6 -

C₁₉aryl and each aryl part of each C₇-C₁₂aralkyl are unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each C₃-C₁₂heterocyclyl, each heterocyclyl part of each C₃-C₁₂heterocyclylalkyl, each C₁-C₁₂heteroaryl and each heteroaryl part of C₃-C₁₂heteroarylalkyl are unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, oxo, thioxo, nitro, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

a stereoisomer, enantiomer or tautomer thereof, a pharmaceutically acceptable salt thereof, or a pharmaceutical composition thereof.

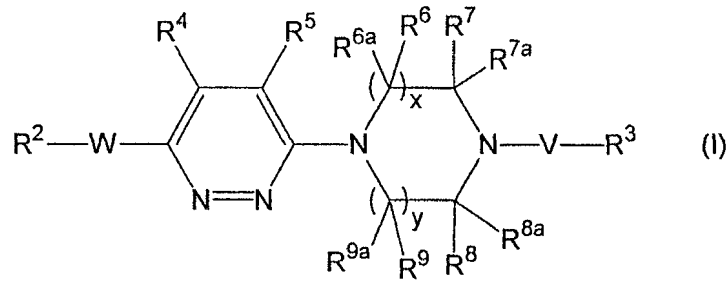
3. The compound of Claim 2, wherein W is -N(R¹)C(=NR^{1a})-.

4. The compound of Claim 2, wherein W is -N(R¹)C(=NR^{1a})N(R¹)- or -N(R¹)C(=S)N(R¹)-.

5. The compound of claim 2 for the treatment of a disease or condition mediated by stearyl-CoA desaturase (SCD) in a mammal.
6. The compound of Claim 5, wherein the mammal is a human.
7. The compound of Claim 6, wherein the disease or condition is selected from the group consisting of Type II diabetes, impaired glucose tolerance, insulin resistance, obesity, fatty liver, non-alcoholic steatohepatitis, dyslipidemia, acne and metabolic syndrome and any combination of these.
8. The compound of Claim 7, wherein the disease or condition is Type II diabetes.
9. The compound of Claim 7, wherein the disease or condition is obesity.
10. The compound of Claim 7, wherein the disease or condition is metabolic syndrome.
11. The compound of Claim 7, wherein the disease or condition is fatty liver.
12. The compound of Claim 7, wherein the disease or condition is non-alcoholic steatohepatitis.
13. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of Claim 2.

English Translation of Amended Japanese Claims (June 22, 2011)

1. A compound of formula (I):



wherein:

x and y are each independently 1, 2 or 3;

W is -C(O)N(R¹)-, -C(O)N[C(O)R^{1a}]-, -N(R¹)C(O)N(R¹)- or -N(R¹)C(O)-;

V is -C(O)-, -C(S)-, or -C(R¹⁰)H;

each R¹ is independently selected from the group consisting of hydrogen; C₁-C₆alkyl unsubstituted or substituted with one or more substituents selected from the group consisting of halo, methyl or trifluoromethyl; and C₂-C₆alkyl unsubstituted or substituted with one or more substituents selected from the group consisting of methoxy and hydroxyl, provided that when W is -C(O)N(R¹)- and V is -C(O)-, R¹ is not hydrogen;

R^{1a} is selected from the group consisting of hydrogen, C₁-C₆alkyl and C₃-C₁₂cycloalkyl;

R² is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl, and C₃-C₁₂heteroarylalkyl;

or R² is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl, C₆-C₁₉aryl and C₁-C₁₂heteroaryl and where some or all of the rings may be fused to each other;

R³ is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl and C₃-C₁₂heteroarylalkyl;

or R³ is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl, C₆-C₁₉aryl and C₁-C₁₂heteroaryl and where some or all of the rings may be fused to each other;

R⁴ and R⁵ are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or -N(R¹²)₂;

Your Ref: 17243/005JP1
Our Ref: P206144

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

or R^6 and R^{6a} together, or R^7 and R^{7a} together, or R^8 and R^{8a} together, or R^9 and R^{9a} together are an oxo group, provided that when V is $-C(O)-$, R^7 and R^{7a} together or R^8 and R^{8a} together do not form an oxo group, while the remaining R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

or one of R^6 , R^{6a} , R^7 , and R^{7a} together with one of R^8 , R^{8a} , R^9 and R^{9a} form an alkylene bridge, while the remaining R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

R^{10} is hydrogen or C_1 - C_3 alkyl; and

each R^{12} is independently selected from hydrogen or C_1 - C_6 alkyl;

wherein each of C_1 - C_3 alkyl, C_1 - C_6 alkyl, C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} hydroxyalkyl, C_2 - C_{12} hydroxyalkenyl, C_1 - C_{12} alkoxy, and C_2 - C_{12} alkoxyalkyl is unsubstituted or substituted by one or more of the following groups: halo, cyano, nitro, $-OR^{14}$, $-OC(O)-R^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)OR^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)OR^{16}$, $-N(R^{14})C(O)R^{16}$, $-N(R^{14})(S(O)_t)R^{16}$ (where t is 1 to 2), $-S(O)_tOR^{16}$ (where t is 1 to 2), $-S(O)_tR^{16}$ (where t is 0 to 2), and $-S(O)_tN(R^{14})_2$ (where t is 1 to 2), where each R^{14} is independently hydrogen, C_1 - C_{12} alkyl, C_1 - C_{12} haloalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl (unsubstituted or substituted with one or more halo groups), C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl; and each R^{16} is C_1 - C_{12} alkyl, C_1 - C_{12} haloalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl, and where each of the above substituents in R^{14} or R^{16} is unsubstituted;

wherein each of C_3 - C_{12} cycloalkyl and C_4 - C_{12} cycloalkylalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, halo, C_1 - C_{12} haloalkyl, C_2 - C_{12} haloalkenyl, cyano, nitro, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl, C_3 - C_{12} heteroarylalkyl, $-R^{15}-OR^{14}$, $-R^{15}-OC(O)-R^{14}$, $-R^{15}-N(R^{14})_2$, $-R^{15}-C(O)R^{14}$, $-R^{15}-C(O)OR^{14}$, $-R^{15}-C(O)N(R^{14})_2$, $-R^{15}-N(R^{14})C(O)OR^{16}$, $-R^{15}-N(R^{14})C(O)R^{16}$, $-R^{15}-N(R^{14})(S(O)_t)R^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tOR^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tR^{16}$ (where t is 0 to 2), and $-R^{15}-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, C_1 - C_{12} alkyl, C_1 - C_{12} haloalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl; each R^{15} is independently a direct bond or a straight or branched C_1 - C_{12} alkylene or C_2 - C_{12} alkenylene chain; and each R^{16} is C_1 - C_{12} alkyl, C_1 - C_{12} haloalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₆-C₁₉aryl or C₇-C₁₂aralkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₃-C₁₂heterocyclyl or C₃-C₁₂heterocyclalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, oxo, thioxo, nitro, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₃-C₁₂cycloalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

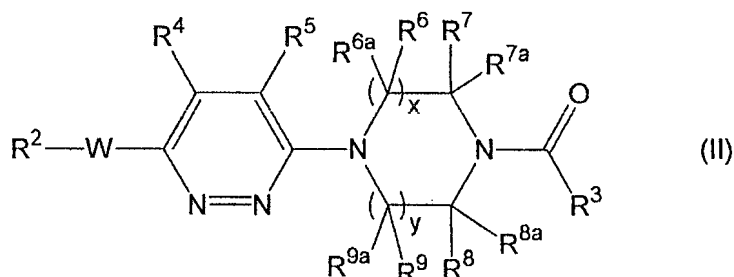
Your Ref: 17243/005JP1

Our Ref: P206144

C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted; and

a stereoisomer, enantiomer thereof, or a pharmaceutically acceptable salt thereof.

2. A compound of formula (II):



wherein:

x and y are each independently 1, 2 or 3;

W is selected from -C(O)N(R¹)- and -N(R¹)C(O)-;

each R¹ is independently selected from the group consisting of hydrogen; C₁-C₆alkyl unsubstituted or substituted with one or more substituents selected from the group consisting of halo, methyl or trifluoromethyl; and C₂-C₆alkyl unsubstituted or substituted with one or more substituents selected from the group consisting of methoxy and hydroxy, provided that when W is -C(O)N(R¹)-, then R¹ is not hydrogen;

R² is selected from the group consisting of C₇-C₁₂alkyl, C₃-C₁₂alkenyl, C₇-C₁₂hydroxyalkyl, C₂-C₁₂alkoxyalkyl, C₃-C₁₂hydroxyalkenyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₁₃-C₁₉aralkyl, C₃-C₁₂heterocyclalkyl, and C₃-C₁₂heteroarylalkyl;

or R² is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl, C₆-C₁₉aryl and C₁-C₁₂heteroaryl, where some or all of the rings may be fused to each other;

R³ is selected from the group consisting of C₃-C₁₂alkyl, C₃-C₁₂alkenyl, C₃-C₁₂hydroxyalkyl, C₃-C₁₂hydroxyalkenyl, C₃-C₁₂alkoxy, C₃-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₅-C₁₂heteroaryl and C₃-C₁₂heteroarylalkyl;

or R³ is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl, C₆-C₁₉aryl and C₁-C₁₂heteroaryl and where some or all of the rings may be fused to each other;

Your Ref: 17243/005JP1
Our Ref: P206144

R^4 and R^5 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy or trifluoromethyl; and

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

or R^6 and R^{6a} together, or R^9 and R^{9a} together are an oxo group, while the remaining R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

or one of R^6 , R^{6a} , R^7 , and R^{7a} together with one of R^8 , R^{8a} , R^9 and R^{9a} form an alkylene bridge, while the remaining R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

wherein each of C_1 - C_3 alkyl, C_1 - C_6 alkyl, C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} hydroxyalkyl, C_2 - C_{12} hydroxyalkenyl, C_1 - C_{12} alkoxy, and C_2 - C_{12} alkoxyalkyl is unsubstituted or substituted by one or more of the following groups: halo, cyano, nitro, $-OR^{14}$, $-OC(O)R^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)OR^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)OR^{16}$, $-N(R^{14})C(O)R^{16}$, $-N(R^{14})(S(O)_tR^{16})$ (where t is 1 to 2), $-S(O)_tOR^{16}$ (where t is 1 to 2), $-S(O)_tR^{16}$ (where t is 0 to 2), and $-S(O)_tN(R^{14})_2$ (where t is 1 to 2), where each R^{14} is independently hydrogen, C_1 - C_{12} alkyl, C_1 - C_{12} haloalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl (unsubstituted or substituted with one or more halo groups), C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclylalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl; and each R^{16} is C_1 - C_{12} alkyl, C_1 - C_{12} haloalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclylalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl, and where each of the above substituents in R^{14} or R^{16} is unsubstituted;

wherein each of C_3 - C_{12} cycloalkyl and C_4 - C_{12} cycloalkylalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, halo, C_1 - C_{12} haloalkyl, C_2 - C_{12} haloalkenyl, cyano, nitro, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclylalkyl, C_1 - C_{12} heteroaryl, C_3 - C_{12} heteroarylalkyl, $-R^{15}-OR^{14}$, $-R^{15}-OC(O)R^{14}$, $-R^{15}-N(R^{14})_2$, $-R^{15}-C(O)R^{14}$, $-R^{15}-C(O)OR^{14}$, $-R^{15}-C(O)N(R^{14})_2$, $-R^{15}-N(R^{14})C(O)OR^{16}$, $-R^{15}-N(R^{14})C(O)R^{16}$, $-R^{15}-N(R^{14})(S(O)_tR^{16})$ (where t is 1 to 2), $-R^{15}-S(O)_tOR^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tR^{16}$ (where t is 0 to 2), and $-R^{15}-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, C_1 - C_{12} alkyl, C_1 - C_{12} haloalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclylalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl; each R^{15} is independently a direct bond or a straight or branched C_1 - C_{12} alkylene or C_2 - C_{12} alkenylene chain; and each R^{16} is C_1 - C_{12} alkyl, C_1 - C_{12} haloalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclylalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C_6 - C_{19} aryl or C_7 - C_{12} aralkyl is unsubstituted or substituted by one or

Your Ref: 17243/005JP1
Our Ref: P206144

more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₃-C₁₂heterocyclyl or C₃-C₁₂heterocyclalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, oxo, thioxo, nitro, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₃-C₁₂cycloalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-

Your Ref: 17243/005JP1
Our Ref: P206144

C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted; and

a stereoisomer, enantiomer thereof, or a pharmaceutically acceptable salt thereof.

3. The compound of Claim 2 wherein:

x and y are each 1;

W is selected from -C(O)N(R¹)- and -N(R¹)C(O)-;

each R¹ is independently selected from hydrogen or C₁-C₆alkyl, provided that when W is -C(O)N(R¹)-, then R¹ is not hydrogen;

R² is selected from the group consisting of C₇-C₁₂alkyl, C₃-C₁₂alkenyl, C₇-C₁₂hydroxyalkyl, C₂-C₁₂alkoxyalkyl, C₃-C₁₂hydroxyalkenyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₁₃-C₁₉aralkyl, C₃-C₁₂heterocyclalkyl, and C₃-C₁₂heteroarylalkyl;

each R² is unsubstituted or substituted by one or more substituents selected from the group consisting of halo, C₁-C₃alkyl, -OR¹¹, -C(O)OR¹¹, C₁-C₆trihaloalkyl, C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl, C₆-C₁₉aryl, C₁-C₁₂heteroaryl and C₁-C₁₂heteroarylC₃-C₁₂cycloalkyl;

R³ is selected from the group consisting of C₃-C₁₂alkyl, C₃-C₁₂alkenyl, C₃-C₁₂hydroxyalkyl, C₃-C₁₂hydroxyalkenyl, C₃-C₁₂alkoxy, C₃-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₅-C₁₂heteroaryl and C₃-C₁₂heteroarylalkyl;

each R³ is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₆alkyl, C₁-C₆trihaloalkyl, C₁-C₆trihaloalkoxy, C₁-C₆alkoxy, C₁-C₆alkylsulfonyl, halo, cyano, nitro, hydroxy, -N(R¹²)₂, -C(O)OR¹¹, -S(O)₂N(R¹²)₂, C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₁-C₁₂heteroaryl and C₁-C₁₂heteroarylC₃-C₁₂cycloalkyl;

R⁴ and R⁵ are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy or trifluoromethyl;

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₆-C₁₉aryl or C₇-C₁₂aralkyl; and

each R¹² is independently selected from hydrogen or C₁-C₆alkyl.

4. The compound of Claim 3 wherein:

Your Ref: 17243/005JP1
Our Ref: P206144

W is -N(R¹)C(O)-;

R¹ is hydrogen;

R² is C₄-C₁₂cycloalkylalkyl;

R³ is C₃-C₁₂alkyl or C₃-C₁₂alkenyl, each unsubstituted or substituted with one or more halo groups;

R⁴ and R⁵ are each hydrogen; and

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each hydrogen.

5. The compound of Claim 4 selected from the group selected from the following:

6-[4-(2-Ethylbutyryl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(3,3,3-Trifluoro-2-methyl-2-trifluoromethylpropionyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(2,2-Dimethylpropionyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(2,2-Dimethylbutyryl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(2,2-Dimethylpentanoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(4,4,4-Trifluorobut-2-enoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide; and

6-[4-(4,4,4-Trifluoro-3-trifluoromethylbut-2-enoyl)-piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropyl-ethyl)amide.

6. The compound of Claim 3 wherein:

W is -N(R¹)C(O)-;

R¹ is hydrogen;

R² is C₄-C₁₂cycloalkylalkyl;

R³ is C₃-C₁₂cycloalkyl unsubstituted or substituted with one or more substituents selected from hydroxy, C₁-C₆trihaloalkyl or C₁-C₆alkyl;

R⁴ and R⁵ are each hydrogen; and

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each hydrogen.

7. The compound of Claim 6 selected from the group consisting of the following:

6-[4-(1-Hydroxycyclopropanecarbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-(4-Cyclobutanecarbonylpiperazin-1-yl)pyridazine-3-carboxylic acid (2-

Your Ref: 17243/005JP1

Our Ref: P206144

cyclopropylethyl)amide;

6-[4-(2-Trifluoromethylcyclopropanecarbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-(4-Cyclohexanecarbonylpiperazin-1-yl)pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(2-Methylcyclohexanecarbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(3-Methylcyclohexanecarbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(4-Methylcyclohexanecarbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(2-Methylcyclopropanecarbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide; and

6-[4-(2,2,3,3-Tetramethylcyclopropanecarbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide.

8. The compound of Claim 3 wherein:

W is $-N(R^1)C(O)-$;

R^2 is C_4-C_{12} cycloalkylalkyl and

R^3 is C_3-C_{12} hydroxyalkyl unsubstituted or substituted with one or more halo

groups;

R^4 and R^5 are each hydrogen; and

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each hydrogen.

9. The compound of Claim 8 selected from the following:

6-[4-(4,4,4-Trifluoro-3-hydroxy-3-trifluoromethylbutyryl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(4,4,4-Trifluoro-3-hydroxy-3-methylbutyryl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide; and

6-[4-(3,3,3-Trifluoro-2-hydroxy-2-methylpropionyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide.

10. The compound of Claim 3 wherein:

W is $-N(R^1)C(O)-$;

R^1 is hydrogen;

R^2 is C_4-C_{12} cycloalkylalkyl;

R^3 is C_3-C_{12} alkoxy;

Your Ref: 17243/005JP1
Our Ref: P206144

R^4 and R^5 are each hydrogen; and
 R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each hydrogen.

11. The compound of Claim 10 selected from the group consisting of the following:
4-[6-(3-Methylbutylcarbamoyl)pyridazin-3-yl]piperazine-1-carboxylic acid *t*-butyl ester; and
4-[6-(2-Cyclopropylethylcarbamoyl)pyridazin-3-yl]piperazine-1-carboxylic acid *t*-butyl ester.

12. The compound of Claim 3 wherein:
W is $-N(R^1)C(O)-$;
 R^1 is hydrogen;
 R^2 is C_4-C_{12} cycloalkylalkyl;
 R^3 is C_7-C_{12} aralkyl unsubstituted or substituted with one or more substituents independently selected from halo or C_1-C_6 trihaloalkyl;
 R^4 and R^5 are each hydrogen; and
 R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each hydrogen.

13. The compound of Claim 12, namely, 6-{4-[2-(2-Trifluoromethylphenyl)acetyl]piperazin-1-yl}pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide.

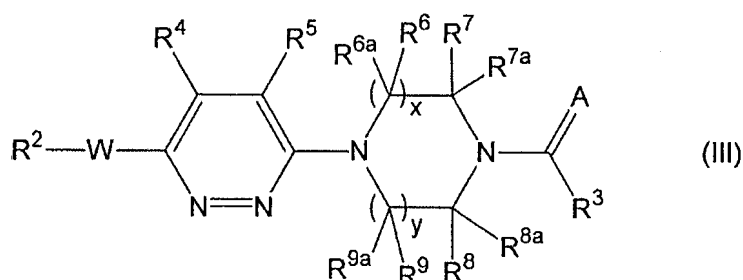
14. The compound of Claim 3 wherein:
W is $-N(R^1)C(O)-$;
 R^1 is hydrogen;
 R^2 is C_4-C_{12} cycloalkylalkyl;
 R^3 is C_3-C_{12} heterocyclyl or C_5-C_{12} heteroaryl, each unsubstituted or substituted with one or more substituents independently selected from halo, C_1-C_6 alkyl, C_1-C_6 trihaloalkyl or C_7-C_{12} aralkyl;
 R^4 and R^5 are each hydrogen; and
 R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each hydrogen.

15. The compound of Claim 14 selected from the group consisting of the following:
6-[4-(Pyridine-2-carbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
6-[4-(2-Trifluoromethylfuran-3-carbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

Your Ref: 17243/005JP1
Our Ref: P206144

- 6-[4-(2-Chloro-4-trifluoromethylpyrimidine-5-carbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(5-Methyl-2-trifluoromethylfuran-3-carbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(2-Chloropyridine-3-carbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(2-Methyl-5-trifluoromethyloxazole-4-carbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(2,6-Dichloropyridine-3-carbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(Pyrrolidine-1-carbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(1-Methyl-1*H*-pyrrole-2-carbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide; and
- 6-[4-(Tetrahydrofuran-2-carbonyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide.

16. A compound of formula (III):



wherein:

x and y are each independently 1, 2 or 3;

A is oxygen or sulfur;

W is selected from -C(O)N(R¹)- and -N(R¹)C(O)-;

each R¹ is independently selected from the group consisting of hydrogen; C₁-C₆alkyl unsubstituted or substituted with one or more substituents selected from the group consisting of halo, methyl or trifluoromethyl; and C₂-C₆alkyl unsubstituted or substituted with one or more substituents selected from the group consisting of methoxy and hydroxy, provided that when W is -C(O)N(R¹)- and A is oxygen, then R¹ is not hydrogen;

R² is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₆alkoxy, C₃-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-

Your Ref: 17243/005JP1

Our Ref: P206144

C₁₂heteroaryl and C₃-C₁₂heteroarylalkyl;

or R² is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl, C₆-C₁₉aryl and C₁-C₁₂heteroaryl, where some or all of the rings may be fused to each other;

R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C₁-C₆alkyl, C₁-C₆trihaloalkyl, C₁-C₆trihaloalkoxy, C₁-C₆alkylsulfonyl, -N(R¹¹)₂, -OC(O)R¹¹, -C(O)OR¹¹, -S(O)₂N(R¹¹)₂, C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl, C₁-C₁₂heteroaryl and C₁-C₁₂heteroarylC₃-C₁₂cycloalkyl, provided that R³ is not phenyl substituted with unsubstituted or substituted thienyl;

R⁴ and R⁵ are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy or trifluoromethyl;

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

or R⁶ and R^{6a} together, or R⁷ and R^{7a} together, or R⁸ and R^{8a} together, or R⁹ and R^{9a} together are an oxo group, provided that when A is oxygen, R⁷ and R^{7a} together or R⁸ and R^{8a} together do not form an oxo group, while the remaining R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

or one of R⁶, R^{6a}, R⁷, and R^{7a} together with one of R⁸, R^{8a}, R⁹ and R^{9a} form an alkylene bridge, while the remaining R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl; and

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, C₆-C₁₉aryl or C₇-C₁₂aralkyl;

wherein each of C₁-C₃alkyl, C₁-C₆alkyl, C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, and C₂-C₁₂alkoxyalkyl is unsubstituted or substituted by one or more of the following groups: halo, cyano, nitro, -OR¹⁴, -OC(O)-R¹⁴, -N(R¹⁴)₂, -C(O)R¹⁴, -C(O)OR¹⁴, -C(O)N(R¹⁴)₂, -N(R¹⁴)C(O)OR¹⁶, -N(R¹⁴)C(O)R¹⁶, -N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -S(O)_tOR¹⁶ (where t is 1 to 2), -S(O)_tR¹⁶ (where t is 0 to 2), and -S(O)_tN(R¹⁴)₂ (where t is 1 to 2), where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl (unsubstituted or substituted with one or more halo groups), C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents in R¹⁴ or R¹⁶ is unsubstituted;

wherein each of C₃-C₁₂cycloalkyl and C₄-C₁₂cycloalkylalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₇-C₁₂aralkyl, C₃-

Your Ref: 17243/005JP1

Our Ref: P206144

C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₆-C₁₉aryl or C₇-C₁₂aralkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₃-C₁₂heterocyclyl or C₃-C₁₂heterocyclalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, oxo, thioxo, nitro, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl,

Your Ref: 17243/005JP1
Our Ref: P206144

C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₃-C₁₂cycloalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted; and

a stereoisomer, enantiomer thereof, or a pharmaceutically acceptable salt thereof.

17. The compound of Claim 16 wherein:

x and y are each 1;

A is oxygen or sulfur;

W is selected from -C(O)N(R¹)- and -N(R¹)C(O)-;

each R¹ is independently selected from hydrogen or C₁-C₆alkyl, provided that when W is -C(O)N(R¹)- and A is oxygen, then R¹ is not hydrogen;

R² is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₆alkoxy, C₃-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl and C₃-C₁₂heteroarylalkyl;

each R² is unsubstituted or substituted by one or more substituents selected from the group consisting of halo, cyano, oxo, thioxo, C₁-C₃alkyl, -OR¹¹, -C(O)R¹¹, -OC(O)R¹¹, -C(O)OR¹¹, -C(O)N(R¹²)₂, -N(R¹²)₂, C₁-C₆trihaloalkyl, C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl, C₆-C₁₉aryl, C₁-C₁₂heteroaryl and C₁-C₁₂heteroaryl(C₃-C₁₂cycloalkyl);

R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C₁-C₆alkyl, C₁-C₆trihaloalkyl, C₁-C₆trihaloalkoxy, C₁-C₆alkylsulfonyl, -N(R¹²)₂, -OC(O)R¹¹, -C(O)OR¹¹, -S(O)₂N(R¹²)₂, C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl and C₁-C₁₂heteroaryl(C₃-C₁₂cycloalkyl);

Your Ref: 17243/005JP1
Our Ref: P206144

R^4 and R^5 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy or trifluoromethyl;

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

or R^6 and R^{6a} together or R^9 and R^{9a} together are an oxo group, while the remaining R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

each R^{11} is independently selected from hydrogen, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, C_6 - C_{19} aryl or C_7 - C_{12} aralkyl; and

each R^{12} is independently selected from hydrogen or C_1 - C_6 alkyl.

18. The compound of Claim 17 wherein:

x and y are each 1;

A is oxygen or sulfur;

W is $-N(R^1)C(O)-$;

R^1 is hydrogen, methyl or ethyl;

R^4 and R^5 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy or trifluoromethyl; and

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl.

19. The compound of Claim 18 wherein:

R^2 is C_4 - C_{12} cycloalkylalkyl unsubstituted or substituted by one or more substituents selected from the group consisting of $-OR^{11}$, C_1 - C_3 alkyl and C_6 - C_{19} aryl;

R^3 is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C_1 - C_6 alkyl, C_1 - C_6 trihaloalkyl, C_1 - C_6 trihaloalkoxy, C_1 - C_6 alkylsulfonyl, $-N(R^{12})_2$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-S(O)_2N(R^{12})_2$ and C_3 - C_{12} cycloalkyl;

each R^{11} is independently selected from hydrogen, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, C_6 - C_{19} aryl or C_7 - C_{12} aralkyl; and

each R^{12} is independently selected from hydrogen or C_1 - C_6 alkyl.

20. The compound of Claim 19 selected from the group consisting of the following:

6-(4-Benzoylpiperazin-1-yl)pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(2-Chloro-5-fluorobenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

Your Ref: 17243/005JP1

Our Ref: P206144

- 6-[4-(5-Chloro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(2,6-Difluorobenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(2,5-Bis-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide
- 6-[4-(2,4-Bis-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(2,5-Difluorobenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(5-Fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-cyclopropylpropyl)amide;
- 6-[4-(2-Fluorobenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(3-Fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(4-Fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-cyclopropylpropyl)amide;
- 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-methylcyclopropylmethyl)amide;
- 6-[4-(5-Fluoro-2-methoxybenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(2-Dimethylaminobenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(2-Chloro-5-dimethylaminobenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(2,5-Dimethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(2,5-Dichlorobenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
- 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid cyclobutylmethylamide;
- Acetic acid 2-{4-[6-(2-cyclopropylethylcarbamoyl)-pyridazin-3-yl]piperazine-1-carbonyl}phenyl ester;
- 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropyl-2-hydroxyethyl)amide;
- 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-phenylcyclopropylmethyl)amide;

Your Ref: 17243/005JP1

Our Ref: P206144

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-cyclopropylpropyl)amide;
 6-[4-(2-Cyanobenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
 6-{4-[2-(2-Trifluoromethylphenyl)acetyl]piperazin-1-yl}pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
 6-[4-(4-Fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
 6-[4-(5-Chloro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-cyclopropylpropyl)amide;
 6-[3,5-Dimethyl-4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
 2-{4-[6-(2-Cyclopropylethylcarbamoyl)pyridazin-3-yl]piperazine-1-carbonyl}benzoic acid methyl ester;
 6-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid (2-cyclobutyl-ethyl)-amide;
 2-{4-[6-(2-Cyclopropyl-ethylcarbamoyl)-pyridazin-3-yl]-piperazine-1-carbonyl}-benzoic acid;
 6-[4-(5-Chloro-2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid (2-cyclobutyl-ethyl)-amide;
 6-[4-(5-Fluoro-2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid (2-cyclobutyl-ethyl)-amide;
 6-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid (3-cyclobutyl-propyl)-amide;
 6-[4-(5-Fluoro-2-trifluoromethyl-benzoyl)-[1,4]diazepan-1-yl]-pyridazine-3-carboxylic acid (2-cyclopropyl-ethyl)-amide;
 6-[4-(2-Trifluoromethyl-thiobenzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid (2-cyclopropyl-ethyl)-amide;
 6-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid (4-cyclopropyl-butyl)-amide; and
 6-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid (2,2-dimethyl-cyclopropylmethyl)-amide.

21. The compound of Claim 18 wherein:

A is oxygen;

R² is C₁-C₁₂alkyl or C₂-C₁₂alkenyl, each unsubstituted or substituted by one or more substituents selected from the group consisting of halo, C₆-C₁₀aryloxy, -C(O)R¹¹, -OC(O)R¹¹ or -C(O)OR¹¹;

R³ is phenyl unsubstituted or substituted by one or more substituents selected

Your Ref: 17243/005JP1

Our Ref: P206144

from the group consisting of halo, cyano, nitro, hydroxy, C₁-C₆alkyl, C₁-C₆trihaloalkyl, C₁-C₆trihaloalkoxy, C₁-C₆alkylsulfonyl, -N(R¹²)₂, -OC(O)R¹¹, -C(O)OR¹¹, -S(O)₂N(R¹²)₂ and C₃-C₁₂cycloalkyl;

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, C₇-C₁₂aralkyl or C₆-C₁₉aryl (unsubstituted or substituted with one or more halo groups); and

each R¹² is independently selected from hydrogen or C₁-C₆alkyl.

22. The compound of Claim 21 selected from the group consisting of the following:

- 6-[4-(2-Nitrobenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-methylbutyl)amide;
- 6-[4-(2-Chlorobenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-methylbutyl)amide;
- 6-[4-(2,4-Dichlorobenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-methylbutyl)amide;
- 6-[4-(2-Aminobenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-methylbutyl)amide;
- 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid [2-(4-chlorophenoxy)ethyl]amide;
- 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid [2-(4-fluorophenoxy)ethyl]amide;
- 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3,3-dimethylbutyl)amide;
- 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid pentylamide;
- 4-({6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carbonyl}amino)butyric acid ethyl ester;
- 6-[4-(5-Fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid pentylamide;
- 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (4-methylpentyl)amide;
- 6-[4-(2-Fluoro-6-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-methylbutyl)amide;
- 6-[4-(2,6-Difluorobenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-methylbutyl)amide;
- 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-oxo-2-phenylethyl)amide;
- Acetic acid 1,1-dimethyl-3-({6-[4-(2-trifluoromethyl-benzoyl)piperazin-1-yl]pyridazine-3-carbonyl}amino)propyl ester;
- 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid hexylamide;
- 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (4-methylpentyl)amide;
- 6-[4-(5-Fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (4-

Your Ref: 17243/005JP1
Our Ref: P206144

methypentyl)amide;
6-[2,5-Dimethyl-4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid
pentylamide;
6-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid heptylamide;
6-[4-(2-Sulfamoyl-benzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid (3-methyl-butyl)-
amide;
6-[4-(5-Chloro-2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid
hexylamide;
6-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid (2-cyclopropyl-2-
oxo-ethyl)-amide;
4-Trifluoromethyl-6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid
(3-methyl-butyl)-amide; and
6-[4-(5-Fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid pentyl-4-
enylamide.

23. The compound of Claim 18 wherein:

A is oxygen;

R^2 is C_2 - C_{12} hydroxyalkyl, or C_2 - C_{12} hydroxyalkenyl, each unsubstituted or
substituted by one or more halo groups;

R^3 is phenyl unsubstituted or substituted by one or more substituents selected
from the group consisting of halo, cyano, nitro, hydroxy, C_1 - C_6 alkyl, C_1 - C_6 trihaloalkyl, C_1 -
 C_6 trihaloalkoxy, C_1 - C_6 alkylsulfonyl, $-N(R^{12})_2$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-S(O)_2N(R^{12})_2$ and C_3 -
 C_{12} cycloalkyl;

each R^{11} is independently selected from hydrogen, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl,
 C_7 - C_{12} aralkyl or C_6 - C_{19} aryl (unsubstituted or substituted with one or more halo groups); and

each R^{12} is independently selected from hydrogen or C_1 - C_6 alkyl.

24. The compound of Claim 23 selected from the group consisting of the
following:

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (4-
hydroxybutyl)amide;
6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-hydroxy-4,4-
dimethylpentyl)amide;
6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-hydroxy-3-
methylbutyl)amide;
6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-hydroxy-3,3-
dimethylbutyl)amide; and

Your Ref: 17243/005JP1
Our Ref: P206144

6-[4-(5-Fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-hydroxy-3,3-dimethylbutyl)amide.

25. The compound of Claim 18 wherein:

A is oxygen;

R^2 is C_7 - C_{12} aralkyl, where the aryl part of the C_7 - C_{12} aralkyl group is unsubstituted or substituted by one or more substituents independently selected from halo, C_1 - C_3 alkyl, $-OR^{11}$, $-C(O)OR^{11}$, C_1 - C_6 trihaloalkyl, C_3 - C_{12} cycloalkyl or C_6 - C_{19} aryl, and the alkyl part of the C_7 - C_{12} aralkyl group is unsubstituted or substituted by one or more substituents independently selected from halo, $-OR^{11}$ or $-OC(O)R^{11}$;

R^3 is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C_1 - C_6 alkyl, C_1 - C_6 trihaloalkyl, C_1 - C_6 trihaloalkoxy, C_1 - C_6 alkylsulfonyl, $-N(R^{12})_2$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-S(O)_2N(R^{12})_2$ and C_3 - C_{12} cycloalkyl;

each R^{11} is independently selected from hydrogen, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, C_7 - C_{12} aralkyl or C_6 - C_{19} aryl (unsubstituted or substituted with one or more halo groups); and

each R^{12} is independently selected from hydrogen or C_1 - C_6 alkyl.

26. The compound of Claim 25 selected from the group consisting of the following:

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid [2-(2,4-fluorophenyl)ethyl]amide;

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid [2-(2-fluorophenyl)ethyl]amide;

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid [2-(4-chlorophenyl)ethyl]amide;

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid [2-(3-chlorophenyl)ethyl]amide;

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-phenylpropyl)amide;

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-biphenyl-4-ylethyl)amide;

(*R*)-6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-hydroxy-2-phenylethyl)-amide;

(*S*)-6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-hydroxy-2-phenylethyl)-amide;

Acetic acid 1-phenyl-2-({6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]pyridazine-3-

Your Ref: 17243/005JP1
Our Ref: P206144

carbonyl}amino)ethyl ester;

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2,2-difluoro-2-phenylethyl)amide; and

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid [2-(3-fluorophenyl)-2-hydroxyethyl]amide.

27. The compound of Claim 18 wherein:

A is oxygen;

R^2 is C_1 - C_6 alkoxy or C_3 - C_{12} alkoxyalkyl, each unsubstituted or substituted with one or more substituents independently selected from halo or C_3 - C_6 cycloalkyl;

R^3 is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C_1 - C_6 alkyl, C_1 - C_6 trihaloalkyl, C_1 - C_6 trihaloalkoxy, C_1 - C_6 alkylsulfonyl, $-N(R^{12})_2$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-S(O)_2N(R^{12})_2$ and C_3 - C_{12} cycloalkyl;

each R^{11} is independently selected from hydrogen, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, C_7 - C_{12} aralkyl or C_6 - C_{19} aryl (unsubstituted or substituted with one or more halo groups); and

each R^{12} is independently selected from hydrogen or C_1 - C_6 alkyl.

28. The compound of Claim 27 selected from the group consisting of the following:

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-ethoxyethyl)amide;

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-methoxy-3,3-dimethylbutyl)amide; and

2-(2-Cyclopropyl-ethoxy)-N-{6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazin-3-yl}-acetamide.

29. The compound of Claim 18 wherein:

A is oxygen;

R^2 is C_6 - C_{19} aryl unsubstituted or substituted with one or more substituents independently selected from halo, cyano, C_1 - C_3 alkyl, $-OR^{11}$, $-C(O)R^{11}$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-C(O)N(R^{12})_2$, C_1 - C_6 trihaloalkyl, C_3 - C_{12} cycloalkyl, C_3 - C_{12} heterocyclyl, C_6 - C_{19} aryl, C_1 - C_{12} heteroaryl or C_1 - C_{12} heteroaryl- C_3 - C_{12} cycloalkyl;

R^3 is phenyl unsubstituted or substituted by C_1 - C_6 trihaloalkyl or C_1 - C_6 trihaloalkoxy;

each R^{11} is independently selected from hydrogen, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, C_7 - C_{12} aralkyl or C_6 - C_{19} aryl (unsubstituted or substituted with one or more halo groups); and

Your Ref: 17243/005JP1
Our Ref: P206144

each R^{12} is independently selected from hydrogen or C_1 - C_6 alkyl.

30. The compound of Claim 29 which is:

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (4-chloro-phenyl)amide.

31. The compound of Claim 18 wherein:

A is oxygen;

R^2 is C_1 - C_{12} heteroaryl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, cyano, oxo, thioxo, C_1 - C_3 alkyl, $-OR^{11}$, $-C(O)R^{11}$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-C(O)N(R^{12})_2$ and C_1 - C_6 trihaloalkyl;

R^3 is phenyl unsubstituted or substituted by C_1 - C_6 trihaloalkyl or C_1 - C_6 trihaloalkoxy;

each R^{11} is independently selected from hydrogen, C_1 - C_6 alkyl, C_3 - C_6 cycloalkyl, C_7 - C_{12} aralkyl or C_6 - C_{19} aryl (unsubstituted or substituted with one or more halo groups); and

each R^{12} is independently selected from hydrogen or C_1 - C_6 alkyl.

32. The compound of Claim 31 wherein C_1 - C_{12} heteroaryl is selected from the group consisting of pyridinyl, purinyl, pyrazinyl, indolyl, indazolyl, benzoimidazolyl, imidazolyl, tetrazolyl, triazolyl, isoxazolyl, pyrazolyl, pyrimidinyl, thiadiazolyl, thiazolyl and pyridazinyl.

33. The compound of Claim 32 selected from the group consisting of the following:

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (5-chloro-pyridin-2-yl)amide;

6-[4-(2-Trifluoromethyl-benzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid pyridazin-3-ylamide;

6-[4-(2-Trifluoromethylbenzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid (6-chloro-pyridazin-3-yl)-amide.

34. The compound of Claim 18 wherein:

A is oxygen;

R^2 is C_3 - C_{12} C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclylalkyl or C_3 - C_{12} heteroarylalkyl, each unsubstituted or substituted by one or more substituents selected from the group consisting of halo, cyano, oxo, thioxo, C_1 - C_3 alkyl, $-OR^{11}$, $-C(O)R^{11}$, $-OC(O)R^{11}$, $-C(O)OR^{11}$, $-C(O)N(R^{12})_2$ and C_1 - C_6 trihaloalkyl;

R^3 is phenyl unsubstituted or substituted by halo, C_1 - C_6 trihaloalkyl or C_1 -

Your Ref: 17243/005JP1

Our Ref: P206144

C₆trihaloalkoxy;

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, C₇-C₁₂aralkyl or C₆-C₁₉aryl (unsubstituted or substituted with one or more halo groups); and
each R¹² is independently selected from hydrogen or C₁-C₆alkyl.

35. The compound of Claim 34 selected from the group consisting of the following:

5-[1,2]Dithiolan-3-yl-pentanoic acid {6-[4-(2-trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazin-3-yl}-amide;
6-[4-(2-Trifluoromethyl-benzoyl)-piperazin-1-yl]-pyridazine-3-carboxylic acid (2-thiophen-2-ylethyl)-amide;
6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-benzo[1,3]dioxol-5-yl-ethyl)amide;
6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2,2-difluoro-2-pyridin-2-ylethyl)amide;
6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-pyridin-2-ylethyl)amide, and
6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (pyridin-2-yl-methyl)amide.

36. The compound of Claim 17 wherein:

x and y are each 1;

A is oxygen;

W is -C(O)N(R¹)-;

R¹ is methyl or ethyl;

R⁴ and R⁵ are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy or trifluoromethyl; and

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl.

37. The compound of Claim 36 wherein:

R² is C₃-C₁₂cycloalkyl or C₄-C₁₂cycloalkylalkyl, each unsubstituted or substituted by one or more substituents selected from the group consisting of -OR¹¹, C₁-C₃alkyl, C₁-C₆trihaloalkyl or C₆-C₁₉aryl;

R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, C₁-C₆trihaloalkyl and C₁-C₆trihaloalkoxy; and

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl,

Your Ref: 17243/005JP1

Our Ref: P206144

C₆-C₁₉aryl or C₇-C₁₂aralkyl.

38. The compound of Claim 36 wherein:

R² is C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₁-C₆alkoxy or C₃-C₁₂alkoxyalkyl, each of which is unsubstituted or substituted by one or more substituents selected from the group consisting of halo, cyano, oxo, thioxo, C₁-C₃alkyl, -OR¹¹, -C(O)R¹¹, -OC(O)R¹¹, -C(O)OR¹¹, -C(O)N(R¹²)₂, -N(R¹²)₂, C₁-C₆trihaloalkyl, C₃-C₁₂cycloalkyl and C₆-C₁₉aryl;

R³ is phenyl unsubstituted or substituted by halo, C₁-C₆trihaloalkyl or C₁-C₆trihaloalkoxy;

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, C₇-C₁₂aralkyl or C₆-C₁₉aryl (unsubstituted or substituted with one or more halo groups); and

each R¹² is independently selected from hydrogen or C₁-C₆alkyl.

39. The compound of Claim 38 selected from the group consisting of the following:

2-Methyl-1-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-

ylcarbamoyl}propylamine;

{6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}carbamic acid butyl ester;

{6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}carbamic acid propyl ester;

{6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}carbamic acid isobutyl ester;

{6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}carbamic acid ethyl ester;

4-Fluoro-N-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]-pyridazin-3-yl}benzamide;

{6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}carbamic acid 3,3-dimethylbutyl ester; and

{6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}carbamic acid 2-cyclopropylethyl ester.

40. The compound of Claim 36 wherein:

R² is C₇-C₁₂aralkyl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, cyano, oxo, thioxo, C₁-C₃alkyl, -OR¹¹, -C(O)R¹¹, -OC(O)R¹¹, -C(O)OR¹¹, -C(O)N(R¹²)₂, -N(R¹²)₂, C₁-C₆trihaloalkyl, C₃-C₁₂cycloalkyl and C₆-C₁₉aryl;

R³ is phenyl unsubstituted or substituted by halo, C₁-C₆trihaloalkyl or C₁-C₆trihaloalkoxy;

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, C₇-C₁₂aralkyl or C₆-C₁₉aryl (unsubstituted or substituted with one or more halo groups); and

each R¹² is independently selected from hydrogen or C₁-C₆alkyl.

Your Ref: 17243/005JP1
Our Ref: P206144

41. The compound of Claim 19 wherein:
 x and y are each 1;
 A is oxygen;
 W is -N(R¹)C(O)-;
 R¹ is hydrogen, methyl or ethyl;
 R² is cyclopropylethyl or cyclopropylmethyl;
 R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of fluoro, chloro and trifluoromethyl;
 R⁴ and R⁵ are each hydrogen; and
 R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each hydrogen.
42. The compound of Claim 41 selected from the group consisting of the following:
 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;
 6-[4-(5-Fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide; and
 6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid cyclopropylmethylamide.
43. The compound of Claim 21 wherein:
 x and y are each 1;
 A is oxygen;
 W is -N(R¹)C(O)-;
 R¹ is hydrogen, methyl or ethyl;
 R² is C₁-C₆alkyl unsubstituted or substituted by -C(O)OR¹¹;
 R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of fluoro, chloro and trifluoromethyl;
 R⁴ and R⁵ are each hydrogen;
 R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each hydrogen; and
 R¹¹ is hydrogen, methyl, ethyl or 1,1-dimethylethyl.
44. The compound of Claim 43 selected from the group consisting of the following:
 4-Methyl-2-({6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]-pyridazine-3-carbonyl}amino)pentanoic acid methyl ester;

Your Ref: 17243/005JP1

Our Ref: P206144

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-methylbutyl)amide;

6-[4-(5-Fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-methylbutyl)amide;

6-[4-(4-Fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-methylbutyl)amide; and

4-Methyl-2-({6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carbonyl}amino)pentanoic acid.

45. The compound of Claim 25 wherein:

x and y are each 1;

A is oxygen;

W is -N(R¹)C(O)-;

R¹ is hydrogen, methyl or ethyl;

R² is 2-phenylethyl or 3-phenylpropyl where the phenyl group is unsubstituted or substituted by one or more substituents independently selected from chloro, fluoro or -OR¹¹;

R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of fluoro, chloro and trifluoromethyl;

R⁴ and R⁵ are each hydrogen;

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each hydrogen; and

R¹¹ is hydrogen, methyl, ethyl or 1,1-dimethylethyl.

46. The compound of Claim 45 selected from the group consisting of the following:

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid [2-(4-methoxyphenyl)ethyl]amide;

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid [2-(3-fluorophenyl)ethyl]amide;

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-phenylpropyl)amide; and

6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]pyridazine-3-carboxylic acid [2-(4-fluorophenyl)ethyl]amide.

47. The compound of Claim 37 wherein:

x and y are each 1;

A is oxygen;

Your Ref: 17243/005JP1
Our Ref: P206144

W is -C(O)N(R¹)-;

R¹ is methyl or ethyl;

R² is cyclopropylethyl, cyclopropylmethyl or cyclopentylethyl;

R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of fluoro, chloro and trifluoromethyl;

R⁴ and R⁵ are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy or trifluoromethyl; and

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each hydrogen.

48. The compound of Claim 38 wherein:

x and y are each 1;

A is oxygen;

W is -C(O)N(R¹)-;

R¹ is methyl or ethyl;

R² is C₁-C₆alkyl;

R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of fluoro, chloro and trifluoromethyl;

R⁴ and R⁵ are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy or trifluoromethyl; and

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each hydrogen.

49. The compound of Claim 40 wherein:

x and y are each 1;

A is oxygen;

W is -C(O)N(R¹)-;

R¹ is methyl or ethyl;

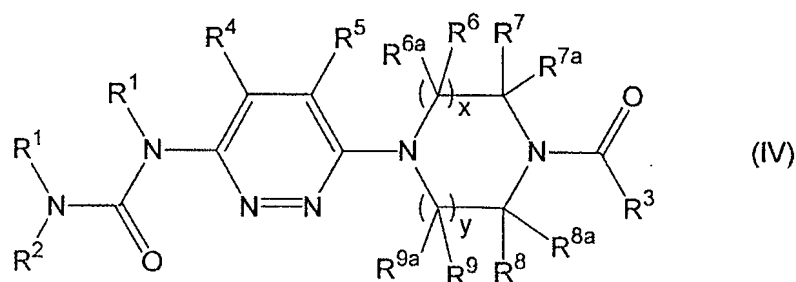
R² is 3-phenylpropyl;

R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of fluoro, chloro and trifluoromethyl;

R⁴ and R⁵ are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy or trifluoromethyl; and

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each hydrogen.

50. A compound of formula (IV):



wherein:

x and y are each independently 1, 2 or 3;

each R^1 is independently selected from the group consisting of hydrogen; C_1 - C_6 alkyl unsubstituted or substituted with one or more substituents selected from the group consisting of halo, methyl or trifluoromethyl; and C_2 - C_6 alkyl unsubstituted or substituted with one or more substituents selected from the group consisting of methoxy and hydroxy;

R^2 is selected from the group consisting of C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} hydroxyalkyl, C_2 - C_{12} hydroxyalkenyl, C_2 - C_{12} alkoxyalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_1 - C_{12} heteroaryl, and C_3 - C_{12} heteroarylalkyl;

or R^2 is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of C_3 - C_{12} cycloalkyl, C_3 - C_{12} heterocyclyl, C_6 - C_{19} aryl and C_1 - C_{12} heteroaryl and where some or all of the rings may be fused to each other;

R^3 is selected from the group consisting of C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} hydroxyalkyl, C_2 - C_{12} hydroxyalkenyl, C_1 - C_{12} alkoxy, C_2 - C_{12} alkoxyalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl and C_3 - C_{12} heteroarylalkyl;

or R^3 is a multi-ring structure having 2 to 4 rings wherein the rings are independently selected from the group consisting of C_3 - C_{12} cycloalkyl, C_3 - C_{12} heterocyclyl, C_6 - C_{19} aryl and C_1 - C_{12} heteroaryl and where some or all of the rings may be fused to each other;

R^4 and R^5 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy or trifluoromethyl; and

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

or R^6 and R^{6a} together, or R^9 and R^{9a} together are an oxo group, while the remaining R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

or one of R^6 , R^{6a} , R^7 , and R^{7a} together with one of R^8 , R^{8a} , R^9 and R^{9a} form an alkylene bridge, while the remaining R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each independently selected from hydrogen or C_1 - C_3 alkyl;

wherein each of C_1 - C_3 alkyl, C_1 - C_6 alkyl, C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} hydroxyalkyl,

Your Ref: 17243/005JP1

Our Ref: P206144

C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, and C₂-C₁₂alkoxyalkyl is unsubstituted or substituted by one or more of the following groups: halo, cyano, nitro, -OR¹⁴, -OC(O)-R¹⁴, -N(R¹⁴)₂, -C(O)R¹⁴, -C(O)OR¹⁴, -C(O)N(R¹⁴)₂, -N(R¹⁴)C(O)OR¹⁶, -N(R¹⁴)C(O)R¹⁶, -N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -S(O)_tOR¹⁶ (where t is 1 to 2), -S(O)_tR¹⁶ (where t is 0 to 2), and -S(O)_tN(R¹⁴)₂ (where t is 1 to 2), where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl (unsubstituted or substituted with one or more halo groups), C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents in R¹⁴ or R¹⁶ is unsubstituted;

wherein each of C₃-C₁₂cycloalkyl and C₄-C₁₂cycloalkylalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₆-C₁₉aryl or C₇-C₁₂aralkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-

Your Ref: 17243/005JP1

Our Ref: P206144

C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₃-C₁₂heterocyclyl or C₃-C₁₂heterocyclalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, oxo, thioxo, nitro, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₃-C₁₂cycloalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted; and

a stereoisomer, enantiomer thereof, or a pharmaceutically acceptable salt thereof.

51. The compound of Claim 50 wherein:

x and y are each 1;

each R¹ is hydrogen or C₁-C₆alkyl;

R² is selected from the group consisting of C₃-C₁₂alkyl, C₃-C₁₂alkenyl, C₃-

Your Ref: 17243/005JP1
Our Ref: P206144

C₁₂hydroxyalkyl, C₃-C₁₂hydroxyalkenyl, C₃-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₁-C₁₂heteroaryl, and C₃-C₁₂heteroarylalkyl;

each R² is unsubstituted or substituted by one or more substituents selected from the group consisting of halo, oxo, thioxo, C₁-C₃alkyl, -OR¹¹, -C(O)OR¹¹, C₁-C₆trihaloalkyl, C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl, C₆-C₁₉aryl, C₁-C₁₂heteroaryl and C₁-C₁₂heteroarylC₃-C₁₂cycloalkyl;

R³ is selected from the group consisting of C₃-C₁₂alkyl, C₃-C₁₂alkenyl, C₃-C₁₂hydroxyalkyl, C₃-C₁₂hydroxyalkenyl, C₃-C₁₂alkoxy, C₃-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl and C₃-C₁₂heteroarylalkyl;

where each of the above R³ groups are unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₆alkyl, C₁-C₆trihaloalkyl, C₁-C₆trihaloalkoxy, C₁-C₆alkoxy, C₁-C₆alkylsulfonyl, halo, cyano, nitro, hydroxy, -N(R¹²)₂, -C(O)OR¹¹, -S(O)₂N(R¹²)₂, C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl, C₆-C₁₉aryl, C₁-C₁₂heteroaryl and C₁-C₁₂heteroarylC₃-C₁₂cycloalkyl;

R⁴ and R⁵ are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy or trifluoromethyl;

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

or R⁶ and R^{6a} together or R⁹ and R^{9a} together are an oxo group while the remaining R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

or one of R⁶, R^{6a}, R⁷, and R^{7a} together with one of R⁸, R^{8a}, R⁹ and R^{9a} form an alkylene bridge, while the remaining R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, C₆-C₁₉aryl or C₇-C₁₂aralkyl; and

each R¹² is independently selected from hydrogen or C₁-C₆alkyl.

52. The compound of Claim 51 wherein:

R² is C₃-C₁₂cycloalkyl or C₄-C₁₂cycloalkylalkyl, each unsubstituted or substituted by one or more substituents selected from the group consisting of -OR¹¹, C₁-C₃alkyl or C₆-C₁₉aryl;

R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, C₁-C₆trihaloalkyl and C₁-C₆trihaloalkoxy; and

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl,

Your Ref: 17243/005JP1

Our Ref: P206144

C₆-C₁₉aryl or C₇-C₁₂alkyl.

53. The compound of Claim 52 selected from the group consisting of the following:

1-(2-Phenylcyclopropyl)-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea;
 1-Cyclopentyl-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]-pyridazin-3-yl}urea;
 1-(3-Cyclopropylpropyl)-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea;
 1-Cyclopropylmethyl-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea;
 1-(2-Cyclopropylethyl)-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea;
 1-(2-Cyclopropylethyl)-3-{6-[4-(2-fluoro-6-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea;
 1-(2-Cyclopropylethyl)-3-{6-[4-(5-fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea;
 1-Cyclohexyl-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea
 1-(2-Cyclopropylethyl)-3-{6-[4-(2,6-difluorobenzoyl)piperazin-1-yl]pyridazin-3-yl}urea; and
 1-(3-Cyclopropylpropyl)-3-{6-[4-(5-fluoro-2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea.

54. The compound of Claim 51 wherein:

R² is C₇-C₁₂alkyl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, -OR¹¹ or C₁-C₃alkyl;

R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, C₁-C₆trihaloalkyl and C₁-C₆trihaloalkoxy; and

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, C₆-C₁₉aryl or C₇-C₁₂alkyl.

55. The compound of Claim 54 selected from the group consisting of the following:

1-Phenethyl-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]-pyridazin-3-yl}urea;
 1-(4-Fluorobenzyl)-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea; and
 1-(3,4-Dichlorobenzyl)-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea.

56. The compound of Claim 51 wherein:

R² is C₆-C₁₉aryl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, -OR¹¹ or C₁-C₃alkyl;

R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, C₁-C₆trihaloalkyl and C₁-C₆trihaloalkoxy; and

Your Ref: 17243/005JP1
Our Ref: P206144

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, C₆-C₁₉aryl or C₇-C₁₂aralkyl.

57. The compound of Claim 56 selected from the group consisting of the following:

1-(4-Fluorophenyl)-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]-pyridazin-3-yl}urea; and
1-(2-Fluorophenyl)-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea.

58. The compound of Claim 51 wherein:

R² is C₃-C₁₂alkyl, C₃-C₁₂hydroxyalkyl or C₃-C₁₂alkoxyalkyl, each unsubstituted or substituted by one or more substituents selected from the group consisting of halo, -OR¹¹ or -C(O)OR¹¹;

R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, C₁-C₆trihaloalkyl and C₁-C₆trihaloalkoxy; and

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, C₆-C₁₉aryl or C₇-C₁₂aralkyl.

59. The compound of Claim 58 selected from the group consisting of the following:

3-(3-{6-[4-(2-Trifluoromethylbenzoyl)piperazin-1-yl]-pyridazin-3-yl}ureido)propionic acid ethyl ester;

1-Butyl-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea;

1-(2-chloroethyl)-3-{6-[4-(2-trifluoromethylbenzoyl)-piperazin-1-yl]pyridazin-3-yl}urea;

1-{6-[4-(2,6-Difluorobenzoyl)piperazin-1-yl]pyridazin-3-yl}-3-(3-methylbutyl)urea;

1-(3,3-Dimethylbutyl)-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea;

1-(2-Isopropoxyethyl)-3-{6-[4-(2-trifluoromethylbenzoyl)-piperazin-1-yl]pyridazin-3-yl}urea;

1-(3-Hydroxy-4,4-dimethylpentyl)-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea;

1-Hexyl-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea;

1-Heptyl-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea; and

1-(4-Methylpentyl)-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea

60. The compound of Claim 54 wherein:

x and y are each 1;

each R¹ is hydrogen, methyl or ethyl;

R² is benzyl;

R³ is phenyl unsubstituted or substituted by one or more substituents selected

Your Ref: 17243/005JP1
Our Ref: P206144

from the group consisting of fluoro, chloro and trifluoromethyl;

R^4 and R^5 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy or trifluoromethyl; and

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each hydrogen.

61. The compound of Claim 58, namely 1-Benzyl-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea.

62. The compound of Claim 58 wherein:

x and y are each 1;

each R^1 is hydrogen, methyl or ethyl;

R^2 is pentyl;

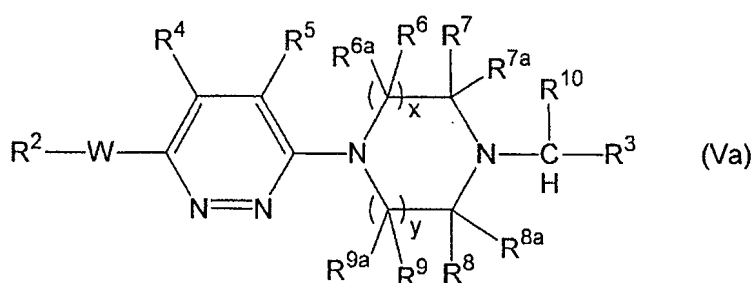
R^3 is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of fluoro, chloro and trifluoromethyl;

R^4 and R^5 are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy or trifluoromethyl; and

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 , and R^{9a} are each hydrogen.

63. The compound of Claim 62, namely 1-Pentyl-3-{6-[4-(2-trifluoromethylbenzoyl)piperazin-1-yl]pyridazin-3-yl}urea.

64. A compound of formula (Va):



wherein:

x and y are each independently 1, 2 or 3;

W is $-C(O)N(R^1)-$, $-N(R^1)C(O)N(R^1)-$ or $-N(R^1)C(O)-$;

each R^1 is independently selected from the group consisting of hydrogen; C_1 - C_6 alkyl unsubstituted or substituted with one or more substituents selected from the group consisting of halo, methyl and trifluoromethyl; and C_2 - C_6 alkyl unsubstituted or substituted with one or more substituents selected from the group consisting of methoxy and hydroxy;

R^2 is selected from the group consisting of C_7 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_7 -

Your Ref: 17243/005JP1
Our Ref: P206144

C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₁₃-C₁₉aryl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl, and C₃-C₁₂heteroarylalkyl;

R³ is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl and C₃-C₁₂heteroarylalkyl;

R⁴ and R⁵ are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or -N(R¹²)₂;

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

or R⁶ and R^{6a} together, or R⁷ and R^{7a} together, or R⁸ and R^{8a} together, or R⁹ and R^{9a} together are an oxo group, while the remaining R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

or one of R⁶, R^{6a}, R⁷, and R^{7a} together with one of R⁸, R^{8a}, R⁹ and R^{9a} form an alkylene bridge, while the remaining R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

R¹⁰ is hydrogen or C₁-C₃alkyl; and

each R¹² is independently selected from hydrogen or C₁-C₆alkyl;

provided, however, that R² can not be pyrazinyl, pyridinonyl, pyrrolidinonyl or imidazolyl;

wherein each of C₁-C₃alkyl, C₁-C₆alkyl, C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, and C₂-C₁₂alkoxyalkyl is unsubstituted or substituted by one or more of the following groups: halo, cyano, nitro, -OR¹⁴, -OC(O)-R¹⁴, -N(R¹⁴)₂, -C(O)R¹⁴, -C(O)OR¹⁴, -C(O)N(R¹⁴)₂, -N(R¹⁴)C(O)OR¹⁶, -N(R¹⁴)C(O)R¹⁶, -N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -S(O)_tOR¹⁶ (where t is 1 to 2), -S(O)_tR¹⁶ (where t is 0 to 2), and -S(O)_tN(R¹⁴)₂ (where t is 1 to 2), where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl (unsubstituted or substituted with one or more halo groups), C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents in R¹⁴ or R¹⁶ is unsubstituted;

wherein each of C₃-C₁₂cycloalkyl and C₄-C₁₂cycloalkylalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -

Your Ref: 17243/005JP1
Our Ref: P206144

$R^{15}-OC(O)-R^{14}$, $-R^{15}-N(R^{14})_2$, $-R^{15}-C(O)R^{14}$, $-R^{15}-C(O)OR^{14}$, $-R^{15}-C(O)N(R^{14})_2$, $-R^{15}-N(R^{14})C(O)OR^{16}$, $-R^{15}-N(R^{14})C(O)R^{16}$, $-R^{15}-N(R^{14})(S(O)_tR^{16})$ (where t is 1 to 2), $-R^{15}-S(O)_tOR^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tR^{16}$ (where t is 0 to 2), and $-R^{15}-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, C_1-C_{12} alkyl, C_1-C_{12} haloalkyl, C_3-C_{12} cycloalkyl, C_4-C_{12} cycloalkylalkyl, C_6-C_{19} aryl, C_7-C_{12} aralkyl, C_3-C_{12} heterocyclyl, C_3-C_{12} heterocyclylalkyl, C_1-C_{12} heteroaryl or C_3-C_{12} heteroarylalkyl; each R^{15} is independently a direct bond or a straight or branched C_1-C_{12} alkylene or C_2-C_{12} alkenylene chain; and each R^{16} is C_1-C_{12} alkyl, C_1-C_{12} haloalkyl, C_3-C_{12} cycloalkyl, C_4-C_{12} cycloalkylalkyl, C_6-C_{19} aryl, C_7-C_{12} aralkyl, C_3-C_{12} heterocyclyl, C_3-C_{12} heterocyclylalkyl, C_1-C_{12} heteroaryl or C_3-C_{12} heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C_6-C_{19} aryl or C_7-C_{12} aralkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C_1-C_{12} alkyl, C_2-C_{12} alkenyl, halo, C_1-C_{12} haloalkyl, C_2-C_{12} haloalkenyl, cyano, nitro, C_3-C_{12} cycloalkyl, C_4-C_{12} cycloalkylalkyl, C_3-C_{12} heterocyclyl, C_3-C_{12} heterocyclylalkyl, C_1-C_{12} heteroaryl, C_3-C_{12} heteroarylalkyl, $-R^{15}-OR^{14}$, $-R^{15}-OC(O)-R^{14}$, $-R^{15}-N(R^{14})_2$, $-R^{15}-C(O)R^{14}$, $-R^{15}-C(O)OR^{14}$, $-R^{15}-C(O)N(R^{14})_2$, $-R^{15}-N(R^{14})C(O)OR^{16}$, $-R^{15}-N(R^{14})C(O)R^{16}$, $-R^{15}-N(R^{14})(S(O)_tR^{16})$ (where t is 1 to 2), $-R^{15}-S(O)_tOR^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tR^{16}$ (where t is 0 to 2), and $-R^{15}-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, C_1-C_{12} alkyl, C_1-C_{12} haloalkyl, C_3-C_{12} cycloalkyl, C_4-C_{12} cycloalkylalkyl, C_6-C_{19} aryl, C_7-C_{12} aralkyl, C_3-C_{12} heterocyclyl, C_3-C_{12} heterocyclylalkyl, C_1-C_{12} heteroaryl or C_3-C_{12} heteroarylalkyl; each R^{15} is independently a direct bond or a straight or branched C_1-C_{12} alkylene or C_2-C_{12} alkenylene chain; and each R^{16} is C_1-C_{12} alkyl, C_1-C_{12} haloalkyl, C_3-C_{12} cycloalkyl, C_4-C_{12} cycloalkylalkyl, C_6-C_{19} aryl, C_7-C_{12} aralkyl, C_3-C_{12} heterocyclyl, C_3-C_{12} heterocyclylalkyl, C_1-C_{12} heteroaryl or C_3-C_{12} heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C_3-C_{12} heterocyclyl or C_3-C_{12} heterocyclylalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C_1-C_{12} alkyl, C_2-C_{12} alkenyl, halo, C_1-C_{12} haloalkyl, C_2-C_{12} haloalkenyl, cyano, oxo, thioxo, nitro, C_6-C_{19} aryl, C_7-C_{12} aralkyl, C_3-C_{12} cycloalkyl, C_4-C_{12} cycloalkylalkyl, C_1-C_{12} heteroaryl, C_3-C_{12} heteroarylalkyl, $-R^{15}-OR^{14}$, $-R^{15}-OC(O)-R^{14}$, $-R^{15}-N(R^{14})_2$, $-R^{15}-C(O)R^{14}$, $-R^{15}-C(O)OR^{14}$, $-R^{15}-C(O)N(R^{14})_2$, $-R^{15}-N(R^{14})C(O)OR^{16}$, $-R^{15}-N(R^{14})C(O)R^{16}$, $-R^{15}-N(R^{14})(S(O)_tR^{16})$ (where t is 1 to 2), $-R^{15}-S(O)_tOR^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tR^{16}$ (where t is 0 to 2), and $-R^{15}-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, C_1-C_{12} alkyl, C_2-C_{12} alkenyl, C_1-C_{12} haloalkyl, C_3-C_{12} cycloalkyl, C_4-C_{12} cycloalkylalkyl, C_6-C_{19} aryl, C_7-C_{12} aralkyl, C_3-C_{12} heterocyclyl, C_3-C_{12} heterocyclylalkyl, C_1-C_{12} heteroaryl or C_3-C_{12} heteroarylalkyl; each R^{15} is independently a direct bond or a straight or branched C_1-C_{12} alkylene or C_2-C_{12} alkenylene chain; and each R^{16} is C_1-C_{12} alkyl, C_1-C_{12} haloalkyl, C_3-C_{12} cycloalkyl, C_4-C_{12} cycloalkylalkyl, C_6-C_{19} aryl, C_7-C_{12} aralkyl, C_3-C_{12} heterocyclyl, C_3-C_{12} heterocyclylalkyl, C_1-C_{12} heteroaryl or C_3-C_{12} heteroarylalkyl, and where each of the above substituents is unsubstituted;

C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₃-C₁₂cycloalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted; and

a stereoisomer, enantiomer thereof, or a pharmaceutically acceptable salt thereof.

65. The compound of Claim 64 wherein:

x and y are each independently 1;

W is -N(R¹)C(O)-;

each R¹ is hydrogen or C₁-C₆alkyl;

R² is selected from the group consisting of C₇-C₁₂alkyl, C₂-C₁₂alkenyl, C₇-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₁₃-C₁₉aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl, and C₃-C₁₂heteroarylalkyl;

each R² is unsubstituted or substituted by one or more substituents selected from the group consisting of halo, cyano, oxo, thioxo, C₁-C₃alkyl, -OR¹¹, -C(O)R¹¹, -OC(O)R¹¹, -C(O)OR¹¹, -C(O)N(R¹²)₂, -N(R¹²)₂, C₁-C₆trihaloalkyl, C₃-C₁₂cycloalkyl, C₃-C₁₂heterocyclyl, C₆-C₁₉aryl, C₁-C₁₂heteroaryl and C₁-C₁₂heteroarylC₃-C₁₂cycloalkyl;

R³ is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl and C₃-C₁₂heteroarylalkyl;

each R³ is unsubstituted or substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C₁-C₆alkyl, C₁-C₆trihaloalkyl, C₁-C₆trihaloalkoxy, C₁-C₆alkylsulfonyl, -N(R¹²)₂, -OC(O)R¹¹, -C(O)OR¹¹, -S(O)₂N(R¹²)₂, C₃-

Your Ref: 17243/005JP1
Our Ref: P206144

C₁₂cycloalkyl, C₃-C₁₂heterocyclyl and C₁-C₁₂heteroarylC₃-C₁₂cycloalkyl;

R⁴ and R⁵ are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or -N(R¹²)₂;

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

R¹⁰ is hydrogen or C₁-C₃alkyl;

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, C₆-C₁₉aryl or C₇-C₁₂aralkyl; and

each R¹² is independently selected from hydrogen or C₁-C₆alkyl.

66. The compound of Claim 65 wherein:

R² is C₃-C₁₂cycloalkyl or C₄-C₁₂cycloalkylalkyl, each unsubstituted or substituted by one or more substituents selected from the group consisting of halo, C₁-C₆trihaloalkyl, -OR¹¹, C₁-C₃alkyl or C₆-C₁₉aryl;

R³ is phenyl unsubstituted or substituted by one or more substituents selected from the group consisting of halo, cyano, nitro, hydroxy, C₁-C₆alkyl, C₁-C₆trihaloalkyl, C₁-C₆trihaloalkoxy, C₁-C₆alkylsulfonyl, -N(R¹²)₂, -OC(O)R¹¹, -C(O)OR¹¹, -S(O)₂N(R¹²)₂ and C₃-C₁₂cycloalkyl;

each R¹¹ is independently selected from hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, C₆-C₁₉aryl or C₇-C₁₂aralkyl; and

each R¹² is independently selected from hydrogen or C₁-C₆alkyl.

67. The compound of Claim 66 selected from the group consisting of the following:

6-[4-(2-Trifluoromethylbenzyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(5-Fluoro-2-trifluoromethylbenzyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(4-Fluoro-2-trifluoromethylbenzyl)-piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(5-Chloro-2-trifluoromethylbenzyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(2-Chloro-4-fluorobenzyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(2,5-Dichlorobenzyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide;

6-[4-(2,4-Dichlorobenzyl)piperazin-1-yl]pyridazine-3-carboxylic acid (2-

Your Ref: 17243/005JP1

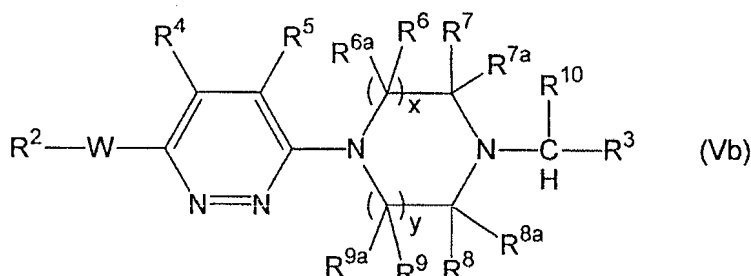
Our Ref: P206144

cyclopropylethyl)amide;

6-[4-(5-Fluoro-2-trifluoromethylbenzyl)piperazin-1-yl]pyridazine-3-carboxylic acid (3-cyclopropylpropyl)amide; and

6-{4-[1-(2-Trifluoromethylphenyl)ethyl]piperazin-1-yl}-pyridazine-3-carboxylic acid (2-cyclopropylethyl)amide.

68. A compound of formula (Vb):



wherein:

x and y are each independently 1, 2 or 3;

W is -C(O)N(R¹)-, -N(R¹)C(O)N(R¹)- or -N(R¹)C(O)-;

each R¹ is independently selected from the group consisting of hydrogen; C₁-C₆alkyl unsubstituted or substituted with one or more substituents selected from the group consisting of halo, methyl and trifluoromethyl; and C₂-C₆alkyl unsubstituted or substituted with one or more substituents selected from the group consisting of methoxy and hydroxy;

R² is selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy, C₂-C₁₂alkoxyalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocyclyl, C₃-C₁₂heterocyclylalkyl, C₁-C₁₂heteroaryl, and C₃-C₁₂heteroarylalkyl;

R³ is selected from the group consisting of C₇-C₁₂alkyl, C₂-C₁₂alkenyl, C₂-C₁₂hydroxyalkyl, C₂-C₁₂hydroxyalkenyl, C₁-C₁₂alkoxy and C₂-C₁₂alkoxyalkyl

R⁴ and R⁵ are each independently selected from hydrogen, fluoro, chloro, methyl, methoxy, trifluoromethyl, cyano, nitro or -N(R¹²)₂;

R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

or R⁶ and R^{6a} together, or R⁷ and R^{7a} together, or R⁸ and R^{8a} together, or R⁹ and R^{9a} together are an oxo group, while the remaining R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

or one of R⁶, R^{6a}, R⁷, and R^{7a} together with one of R⁸, R^{8a}, R⁹ and R^{9a} form an alkylene bridge, while the remaining R⁶, R^{6a}, R⁷, R^{7a}, R⁸, R^{8a}, R⁹, and R^{9a} are each independently selected from hydrogen or C₁-C₃alkyl;

R^{10} is hydrogen or C_1 - C_3 alkyl; and

each R^{12} is independently selected from hydrogen or C_1 - C_6 alkyl;

wherein each of C_1 - C_3 alkyl, C_1 - C_6 alkyl, C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} hydroxyalkyl, C_2 - C_{12} hydroxyalkenyl, C_1 - C_{12} alkoxy, and C_2 - C_{12} alkoxyalkyl is unsubstituted or substituted by one or more of the following groups: halo, cyano, nitro, $-OR^{14}$, $-OC(O)-R^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)OR^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)OR^{16}$, $-N(R^{14})C(O)R^{16}$, $-N(R^{14})(S(O)_t)R^{16}$ (where t is 1 to 2), $-S(O)_tOR^{16}$ (where t is 1 to 2), $-S(O)_tR^{16}$ (where t is 0 to 2), and $-S(O)_tN(R^{14})_2$ (where t is 1 to 2), where each R^{14} is independently hydrogen, C_1 - C_{12} alkyl, C_1 - C_{12} haloalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl (unsubstituted or substituted with one or more halo groups), C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl; and each R^{16} is C_1 - C_{12} alkyl, C_1 - C_{12} haloalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl, and where each of the above substituents in R^{14} or R^{16} is unsubstituted;

wherein each of C_3 - C_{12} cycloalkyl and C_4 - C_{12} cycloalkylalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, halo, C_1 - C_{12} haloalkyl, C_2 - C_{12} haloalkenyl, cyano, nitro, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl, C_3 - C_{12} heteroarylalkyl, $-R^{15}-OR^{14}$, $-R^{15}-OC(O)-R^{14}$, $-R^{15}-N(R^{14})_2$, $-R^{15}-C(O)R^{14}$, $-R^{15}-C(O)OR^{14}$, $-R^{15}-C(O)N(R^{14})_2$, $-R^{15}-N(R^{14})C(O)OR^{16}$, $-R^{15}-N(R^{14})C(O)R^{16}$, $-R^{15}-N(R^{14})(S(O)_t)R^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tOR^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tR^{16}$ (where t is 0 to 2), and $-R^{15}-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, C_1 - C_{12} alkyl, C_1 - C_{12} haloalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl; each R^{15} is independently a direct bond or a straight or branched C_1 - C_{12} alkylene or C_2 - C_{12} alkenylene chain; and each R^{16} is C_1 - C_{12} alkyl, C_1 - C_{12} haloalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl or C_3 - C_{12} heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C_6 - C_{19} aryl or C_7 - C_{12} aralkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, halo, C_1 - C_{12} haloalkyl, C_2 - C_{12} haloalkenyl, cyano, nitro, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, C_1 - C_{12} heteroaryl, C_3 - C_{12} heteroarylalkyl, $-R^{15}-OR^{14}$, $-R^{15}-OC(O)-R^{14}$, $-R^{15}-N(R^{14})_2$, $-R^{15}-C(O)R^{14}$, $-R^{15}-C(O)OR^{14}$, $-R^{15}-C(O)N(R^{14})_2$, $-R^{15}-N(R^{14})C(O)OR^{16}$, $-R^{15}-N(R^{14})C(O)R^{16}$, $-R^{15}-N(R^{14})(S(O)_t)R^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tOR^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tR^{16}$ (where t is 0 to 2), and $-R^{15}-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, C_1 - C_{12} alkyl, C_1 - C_{12} haloalkyl, C_3 - C_{12} cycloalkyl, C_4 - C_{12} cycloalkylalkyl, C_6 - C_{19} aryl, C_7 - C_{12} aralkyl, C_3 - C_{12} heterocyclyl, C_3 - C_{12} heterocyclalkyl, and where each of the above substituents is unsubstituted;

Your Ref: 17243/005JP1

Our Ref: P206144

C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocycl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₃-C₁₂heterocycl or C₃-C₁₂heterocyclalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, oxo, thioxo, nitro, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₁-C₁₂heteroaryl, C₃-C₁₂heteroarylalkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₂-C₁₂alkenyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocycl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocycl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted;

wherein each of C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl is unsubstituted or substituted by one or more substituents selected from the group consisting of C₁-C₁₂alkyl, C₂-C₁₂alkenyl, halo, C₁-C₁₂haloalkyl, C₂-C₁₂haloalkenyl, cyano, nitro, C₃-C₁₂cycloalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, -R¹⁵-OR¹⁴, -R¹⁵-OC(O)-R¹⁴, -R¹⁵-N(R¹⁴)₂, -R¹⁵-C(O)R¹⁴, -R¹⁵-C(O)OR¹⁴, -R¹⁵-C(O)N(R¹⁴)₂, -R¹⁵-N(R¹⁴)C(O)OR¹⁶, -R¹⁵-N(R¹⁴)C(O)R¹⁶, -R¹⁵-N(R¹⁴)(S(O)_tR¹⁶) (where t is 1 to 2), -R¹⁵-S(O)_tOR¹⁶ (where t is 1 to 2), -R¹⁵-S(O)_tR¹⁶ (where t is 0 to 2), and -R¹⁵-S(O)_tN(R¹⁴)₂ (where t is 1 to 2) where each R¹⁴ is independently hydrogen, C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocycl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl; each R¹⁵ is independently a direct bond or a straight or branched C₁-C₁₂alkylene or C₂-C₁₂alkenylene chain; and each R¹⁶ is C₁-C₁₂alkyl, C₁-C₁₂haloalkyl, C₃-C₁₂cycloalkyl, C₄-C₁₂cycloalkylalkyl, C₆-C₁₉aryl, C₇-C₁₂aralkyl, C₃-C₁₂heterocycl, C₃-C₁₂heterocyclalkyl, C₁-C₁₂heteroaryl or C₃-C₁₂heteroarylalkyl, and where each of the above substituents is unsubstituted; and

a stereoisomer, enantiomer thereof, or a pharmaceutically acceptable salt thereof.