

Doctor

José Luis Salazar

Director de División de Nuevas Creaciones (C)

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

E. _____ S. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



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Solicitud de Patente de Invención titulada: "Aryl dihidropiridinona y piperidinona como inhibidores de monoacilglicerol aciltransferasa (MGAT2)"

Solicitante: Bristol Myers Squibb Company

RESPUESTA AL AUTO NOTIFICADO POR FIJACIÓN EN LISTA NO. 21
DEL 26 DE MAYO DE 2015, OFICIO NO.5335 (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. Respuesta a las objeciones del Examinador

1.1 Modificación a una solicitud en trámite

Con el objeto de atender a las observaciones del examinador y de conformidad con el artículo 34 de la Decisión 486 presento un nuevo pliego reivindicatorio modificado conformado por 15 reivindicaciones.

Las modificaciones efectuadas al pliego reivindicatorio se encuentran totalmente sustentadas en la memoria descriptiva originalmente presentada.

1.2 Reivindicaciones relativas a un uso o a un segundo uso

Su Despacho establece que el uso de las reivindicaciones 21-23 no es patentable.

Con el propósito de atender a la anterior observación, informamos a su Despacho que las reivindicaciones 21-23 fueron canceladas del pliego reivindicatorio.

Por lo tanto, se da por superada esta observación.

1.3 Reivindicación 1

Su Despacho considera que el pliego reivindicatorio presenta inconsistencias e incoherencias pues en la reivindicación 1, la definición de R¹ no contempla en ningún momento que sea un fenilo.

Con el objeto de atender a la anterior observación, aclaramos a su Despacho que el grupo fenilo si aparece en la definición de R¹ de la reivindicación 1, el cual aparece con la sigla Ph.

Hacemos notar a su Despacho que en la descripción en la página 75 se menciona que la sigla Ph es fenilo.

Sin embargo, para mayor claridad la sigla ph se cambió en todo el pliego reivindicatorio por fenilo.

Respetuosamente mi representada considera que la reivindicación 1 es clara y concisa. Es decir cumple a cabalidad con el artículo 30 de la Decisión 486 y se encuentra limitada a una razonable generalización.

De esta forma se da por superada esta observación.

1.4 Reivindicación 4

Su Despacho menciona que la reivindicación 4 no es clara porque no se menciona los sustituyentes en cada caso particular.

Con el objeto de atender a la anterior observación se presenta una nueva reivindicación 4 en la cual se incluyeron los sustituyentes de la reivindicación 5 y la reivindicación 5 fue cancelada.

1.5 Reivindicación 17

Su Despacho establece que la reivindicación 17 reclama, una sal farmacéuticamente aceptable de los compuestos precedentes a ella, lo que se considera una divulgación implícita y no ofrece ninguna característica técnica o esencial que le otorgue dicha caracterización.

Con el objeto de atender a esta observación, informamos a su Despacho que dicha reivindicación fue cancelada.

1.6 Reivindicaciones 18-20

Su Despacho establece que las reivindicaciones 18-20 no son concisas porque con todo el universo reclamado se pueden presentar múltiples opciones de posibles composiciones farmacéuticas que no permiten distinguir el objeto reclamado o de interés ya que no define de manera específica los otros agentes terapéuticos que pueden ir en la composición sino que delimitan por acción terapéutica, más no por compuestos específicos lo que tampoco se encuentra sustentado en la descripción.

Con el propósito de atender a esta observación informamos a su Despacho que las reivindicaciones 18-20 se han cancelado del pliego reivindicatorio que ahora se presenta.

1.7 Novedad

El Examinador plantea que, después de realizada la búsqueda de anterioridades, encontró los documentos D1 (NIPPON KAGAKU ZASSHI), D2 (AKIO SAKURAI ET AL) y D3 (S.M.MCELVAIN ET AL) afectan la novedad de las reivindicaciones 1,2,4,5,6,8,10 de la presente solicitud.

Particularmente, el Examinador afirma que después de comparar las características técnicas de las reivindicaciones 1 y 2 con los documentos D1-D3, se puede observar que tal como están, la materia reclamada ya se encuentra totalmente revelada en dichos documentos del estado del arte. Por lo tanto, las reivindicaciones 1 y 2 no son nuevas o carecen de novedad.

Puesto que las reivindicaciones dependientes 4,5,6,8 y 10 no mencionan alguna característica que haga nueva la invención, tampoco cumplen con el requisito de novedad.

1.7.1 Argumentos en favor de la novedad de la presente invención con relación a los documentos D1, D2 y D3.

La novedad de una solicitud está legalmente definida en el Artículo 16 de la Decisión 486 así: *“una invención se considerará nueva, cuando no está comprendida en el estado de la técnica. El estado de la técnica comprenderá todo lo que haya sido accesible al público por una descripción escrita u oral, utilización, comercialización o cualquier otro medio antes de la fecha de presentación de la solicitud de patente o, en su caso de la prioridad reconocida...”*

En virtud de la anterior definición, consideramos que los documentos D1, D2, y D3 no constituyen documentos del arte previo que afecten la novedad de la presente solicitud por las siguientes razones:

Mi representada nota que los documentos D1, D2 y D3 citados por su Despacho fueron también citados en la opinión escrita de la búsqueda internacional para la solicitud PCT/US2012/067173.

Por otro lado, hacemos notar a su Despacho que en la solicitud de patente europea equivalente a la presente invención se efectuaron modificaciones a las reivindicaciones y la oficina Europea de Patentes notificó su intención de otorgamiento.

Las modificaciones efectuadas en Europa son las que ahora se presentan en el capítulo reivindicatorio de la solicitud colombiana.

El examinador podrá notar que las reivindicaciones modificadas no permiten que R⁶ sea - CN.

De esta forma es claro que las reivindicaciones modificadas son novedosas con relación al arte previo citado.

En este orden de ideas, tenemos que la invención propuesta por el solicitante si cumple con los requisitos de patentabilidad y de esta manera es susceptible de ostentar el título de patente de invención.

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

A manera informativa, y como se cito anteriormente la Oficina de Patentes Europea tiene intención de otorgar la patente Europea de la solicitud EP No. 12 821 212.3, equivalente a la presente solicitud colombiana. Anexo copia de la comunicación de la Oficina de Patentes Europea donde se menciona la intención de otorgar la presente invención.

Por otro lado, la patente US 8,791,091 equivalente a la presente solicitud colombiana ha sido otorgada. Aún cuando entiendo que estas decisiones de ninguna manera obligan al Despacho para decidir de igual forma, considero que por tratarse de una pregunta fáctica la determinación de la existencia de novedad, nivel inventivo y aplicación industrial, las decisiones de otras oficinas de patentes constituyen un antecedente persuasivo en la materia.

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

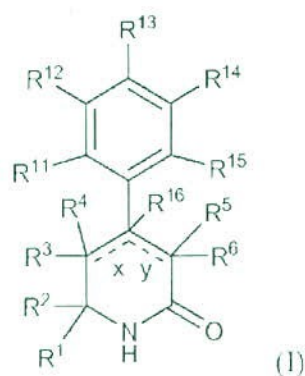
Anexos: - Capítulo reivindicatorio modificado conformado por 15 reivindicaciones
- Copia de la carátula y reivindicaciones de la Patente US 8,791,091
- Copia de la notificación de la Oficina de Patentes Europea comunicando la intención de otorgamiento de la solicitud EP 12 821 212.3 junto con las reivindicaciones aceptadas.

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Reivindicaciones modificadas para la solicitud de patente No.

14.133.538

1. Un compuesto de la Fórmula (I):



o un estereoisómero, un tautómero, una sal aceptable desde el punto de vista farmacéutico o un solvato de aquel, caracterizado porque:

--- indica un enlace simple o doble;

x e y pueden ser ambos un enlace simple; en donde x es un enlace doble, y es un enlace simple, y R^4 y R^{16} están ausentes; cuando y es un enlace doble, x es un enlace simple, y R^5 y R^{16} están ausentes;

R^1 se selecciona independientemente del grupo que consiste en: $-\text{CONH}(\text{C}_{4-18} \text{ alquilo})$, $-\text{CONHC}_{2-8} \text{ haloalquilo}$, $-\text{CONH}(\text{CH}_2)_{1-8} \text{ fenilo}$, $-\text{CONHCH}_2\text{COC}_{2-8} \text{ alquilo}$, $-(\text{CH}_2)_m-(\text{C}_{3-10} \text{ carbociclo sustituido con 0-2 } R^b \text{ y 0-2 } R^g)$, $-(\text{CH}_2)_m-(\text{heteroarilo de 5 a 6 miembros que comprende átomos de carbono y 1-4 heteroátomos seleccionados de N, NR}^e, \text{O y S; en donde el heteroarilo se sustituye con 0-1 } R^b \text{ y 0-2 } R^g)$, y una

cadena de hidrocarburos C_{1-12} sustituida con 0-3 R^a ; en donde la cadena de hidrocarburos puede ser lineal o ramificada, saturada o insaturada;

R^2 se selecciona independientemente del grupo que consiste en: C_{1-4} alquilo, C_{3-4} cicloalquilo y C_{1-4} haloalquilo;

R^3 se selecciona independientemente del grupo que consiste en: H, F, Cl, C_{1-4} alquilo y CN;

R^4 y R^5 se seleccionan independientemente del grupo que consiste en: H, F, Cl y C_{1-4} alquilo;

cuando x es un enlace simple, R^3 y R^4 se pueden combinar con el átomo de carbono al que están unidos para formar un carbociclo de 3 a 6 miembros;

R^6 se selecciona independientemente del grupo que consiste en: H, halo, C_{1-4} alquilo, NO_2 , R^c , $(CH_2)_n-(X)_t-$ $(CH_2)_mR^c$, NH_2 , $-CONH(C_{1-6}$ alquilo), $-NHCOX_1SO_2R^j$, $-NHCOCH_2PO(OEt)_2$, $-NHCOCOR^j$, $-NHCOCH(OH)R^j$, $-NHCOCH_2COR^j$, $-NHCONHR^j$ y $-OCONR^fR^j$;

X se selecciona independientemente del grupo que consiste en: O, S, NH, $-CONH$ y $NHCO$;

X_1 es independientemente una cadena de hidrocarburos C_{1-4} opcionalmente sustituida con C_{1-4} alquilo o C_{3-4} cicloalquilo;

cuando y es un enlace simple, R^5 y R^6 se pueden combinar con el átomo de carbono al que están unidos para formar un carbociclo de 3 a 6 miembros;

R^{11} , R^{12} , R^{13} , R^{14} y R^{15} se seleccionan independientemente del grupo que consiste en: H, halo, C_{1-4} alquilo sustituido con 0-2 R^i , C_{1-4} alcoxi, C_{1-4} haloalquilo, C_{1-4} haloalcoxi, C_{3-6} cicloalquilo- $(CH_2)_m$, CN, NR^fR^j , OR^j , SR^j , $NHCO_2(C_{1-4} \text{ alquilo})$, $NHSO_2(C_{1-4} \text{ alquilo})$ y un heterociclo de 4 a 6 miembros que comprende átomos de carbono y 1-4 heteroátomos seleccionados de N, NR^e , O y S;

de manera alternativa, R^{11} y R^{12} , junto con los átomos de carbono a los que están unidos, se combinan para formar un anillo carbocíclico de 5 a 6 miembros o un anillo heterocíclico de 5 a 6 miembros, que comprende átomos de carbono y 1-3 heteroátomos seleccionados de N, NR^e , O y S;

de manera alternativa, R^{12} y R^{13} , junto con los átomos de carbono a los que están unidos, se combinan para formar un anillo carbocíclico de 5 a 6 miembros o un anillo heterocíclico de 5 a 6 miembros, que comprende átomos de carbono y 1-3 heteroátomos seleccionados de N, NR^e , O y S;

R^{16} se selecciona independientemente del grupo que consiste en: H y C_{1-4} alquilo;

R^a , en cada caso, se selecciona independientemente del grupo que consiste en halo, OH, C_{1-6} alcoxi, C_{1-6} haloalquilo, C_{1-6} haloalcoxi, $N(C_{1-4} \text{ alquil})_2$, $-(CH_2)_n-(X)_t-$ $(CH_2)_mR^c$ y $-(CH_2)_n-(CH_2O)_m-(CH_2)_nR^f$;

R^b , en cada caso, se selecciona independientemente del grupo que consiste en halo, OH, C_{1-10} alquilo, C_{1-10} alcoxi,

C₁₋₁₀ haloalquilo, C₁₋₁₀ haloalcoxi, C₁₋₁₀ alquiltio, C₁₋₁₀ haloalquiltio, N(C₁₋₄ alquil)₂, -CONH(CH₂)₄₋₂₀H, O(CH₂)₅O(C₁₋₆ alquilo), R^c, -(CH₂)_n-(X)_t-(CH₂)_mR^c y -(CH₂)_n-(CH₂O)_m-(CH₂)_nR^f;

R^c, en cada caso, se selecciona independientemente del grupo que consiste en: C₃₋₆ cicloalquilo sustituido con 0-2 R^d, C₃₋₆ cicloalqueno sustituido con 0-2 R^d, -(CH₂)_m-(fenilo sustituido con 0-3 R^d) y un heterociclo de 5 a 6 miembros que comprende átomos de carbono y 1-4 heteroátomos seleccionados de N, NR^e, O y S; en donde el heterociclo se sustituye con 0-2 R^d;

R^d, en cada caso, se selecciona independientemente del grupo que consiste en halo, OH, CN, NO₂, C₁₋₄ alquilo, C₁₋₄ alcoxi, C₁₋₄ haloalquilo, C₁₋₄ haloalcoxi, tetrazolilo, OBn y fenilo sustituido con 0-2 R^h;

R^e, en cada caso, se selecciona independientemente del grupo que consiste en: H, C₁₋₈ alquilo, C₁₋₈ haloalquilo, bencilo opcionalmente sustituido con C₁₋₄ alcoxi, CO(C₁₋₄ alquilo) y COBn;

R^f, en cada caso, se selecciona independientemente del grupo que consiste en: H y C₁₋₄ alquilo;

R^g, R^h y Rⁱ, en cada caso, se seleccionan independientemente del grupo que consiste en halo, C₁₋₄ alquilo, C₁₋₄ alcoxi, C₁₋₄ haloalquilo y C₁₋₄ haloalcoxi;

R^j, en cada caso, se selecciona independientemente del grupo que consiste en: C₁₋₄ alquilo, C₃₋₄ cicloalquilo y

fenilo;

n, en cada caso, es independientemente 0 ó 1;

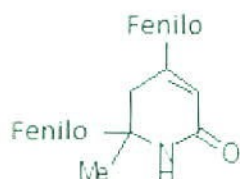
m, en cada caso, es independientemente 0, 1, 2, 3 ó

4;

s, en cada caso, es independientemente 1, 2 ó 3; y

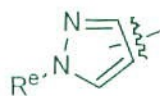
t, en cada caso, es independientemente 0 ó 1;

siempre que se excluya el siguiente compuesto:



2. El compuesto de conformidad con la reivindicación 1, caracterizado porque:

R^1 se selecciona independientemente del grupo que consiste en: $-\text{CONHC}_{4-18}$ alquilo, $-\text{CONH}(\text{CH}_2)_{1-8}$ fenilo, C_{1-12} alquilo sustituido con 0-2 R^a , C_{1-12} alquenilo sustituido con 0-2 R^a , C_{1-12} alquinilo sustituido con 0-2 R^a , $-(\text{CH}_2)_m$ -(fenilo sustituido con 0-1 R^b y 0-2 R^g), $-(\text{CH}_2)_m$ -(C_{3-6} cicloalquilo sustituido con 0-1 R^b) y $-(\text{CH}_2)_m$ -(heteroarilo de 5 a 6 miembros sustituido con 0-1 R^b y 0-2 R^g), en donde el heteroarilo se selecciona de piridilo, oxazolilo, tiazolilo y



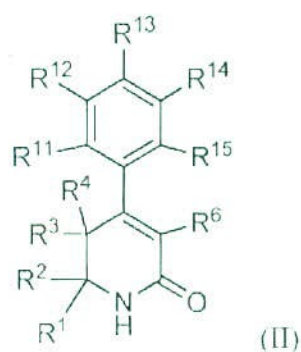
3. El compuesto de conformidad con la reivindicación 1 o la reivindicación 2, caracterizado porque:

R^{11} y R^{15} se seleccionan independientemente del grupo que consiste en: H, C_{1-4} alquilo y halo;

R^{12} y R^{14} se seleccionan independientemente del grupo que consiste en: H, halo, C_{1-4} alquilo y C_{1-4} alcoxi; y

R^{13} se selecciona independientemente del grupo que consiste en: H, halo, C_{1-4} alquilo sustituido con 0-1 R^i , C_{1-4} alcoxi, C_{1-4} haloalquilo, C_{1-4} haloalcoxi, $-(CH_2)_m-C_{3-4}$ cicloalquilo, CN, NR^fR^j , SR^j , $NHCO_2(C_{1-4}$ alquilo), $NHSO_2(C_{1-4}$ alquilo) y un heterociclo de 4 a 6 miembros que comprende átomos de carbono y 1-4 heteroátomos seleccionados de N, NR^e , O y S.

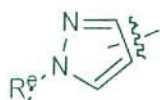
4. El compuesto de conformidad con cualquiera de las reivindicaciones 1 a 3, caracterizado porque tiene la Fórmula (II):



o un estereoisómero, un tautómero, una sal aceptable desde el punto de vista farmacéutica,

R^1 se selecciona independientemente del grupo que consiste en: C_{1-6} alquilo, C_{3-6} cicloalquilo, $-CONHC_{4-18}$ alquilo, $-CONHC_{2-8}$

haloalquilo, $-\text{CONH}(\text{CH}_2)_{1-8}\text{fenilo}$, $(\text{CH}_2)_m$ -(fenilo sustituido con 1 R^b y 0-2 R^g) y un heteroarilo de 5 a 6 miembros sustituido con 0-1 R^b y 0-2 R^g , en donde el heteroarilo se selecciona de piridilo, oxazolilo, tiazolilo y



R^2 se selecciona independientemente del grupo que consiste en: C_{1-4} alquilo y C_{1-4} haloalquilo;

R^3 se selecciona independientemente del grupo que consiste en: H y F;

R^4 se selecciona independientemente del grupo que consiste en: H y F;

R^6 se selecciona independientemente del grupo que consiste en: NH_2 , $-\text{CONH}(\text{C}_{1-6}\text{ alquilo})$, R^c , $(\text{CH}_2)_n-(\text{X})_t-(\text{CH}_2)_m\text{R}^c$, $-\text{NHCO}(\text{CH}_2)\text{SO}_2(\text{C}_{1-4}\text{ alquilo})$, $-\text{NHCOCH}_2\text{PO}(\text{OEt})_2$, $-\text{NHCOCO}(\text{C}_{1-4}\text{ alquilo})$, $-\text{NHCOCH}(\text{OH})(\text{C}_{1-4}\text{ alquilo})$, $-\text{NHCOCH}_2\text{CO}(\text{C}_{1-4}\text{ alquilo})$, $-\text{NHCONH}(\text{C}_{1-4}\text{ alquilo})$ y $-\text{OCONH}(\text{C}_{1-4}\text{ alquilo})$;

R^{11} y R^{15} se seleccionan independientemente del grupo que consiste en: H, C_{1-4} alquilo y halo;

R^{12} y R^{14} se seleccionan independientemente del grupo que consiste en: H, halo, C_{1-4} alquilo y C_{1-4} alcoxi;

R^{13} se selecciona independientemente del grupo que consiste en: H, halo, C_{1-4} alquilo sustituido con 0-1 C_{1-4} alcoxi, C_{1-4} alcoxi, C_{1-4} haloalquilo, C_{1-4} haloalcoxi, $-(\text{CH}_2)_m-\text{C}_{3-4}$ cicloalquilo, CN, $\text{N}(\text{C}_{1-4}\text{ alquilo})_2$, $\text{NHCO}_2(\text{C}_{1-4}$

alquilo), $\text{NHSO}_2(\text{C}_{1-4} \text{ alquilo})$, pirazolilo y morfolinilo;

de manera alternativa, R^{12} y R^{13} , junto con los átomos de carbono a los que están unidos, se combinan para formar un anillo carbocíclico de 5 a 6 miembros o un anillo heterocíclico de 5 a 6 miembros, que comprende átomos de carbono y 1-3 heteroátomos seleccionados de N, NR^e , O y S;

R^b , en cada caso, se selecciona independientemente del grupo que consiste en halo, OH, C_{1-8} alquilo, C_{1-8} alcoxi, C_{1-8} haloalquilo, C_{1-10} haloalcoxi, $\text{O}(\text{CH}_2)_s\text{O}(\text{C}_{1-6} \text{ alquilo})$, $\text{N}(\text{C}_{1-4} \text{ alquilo})_2$, $-\text{CONH}(\text{CH}_2)_{6-20}\text{H}$, $(\text{CH}_2)_m(\text{C}_{3-6} \text{ cicloalquilo})$, $(\text{CH}_2)_m(\text{C}_{4-6} \text{ cicloalquenilo})$, $\text{O}(\text{CH}_2)_m(\text{C}_{3-6} \text{ cicloalquilo})$, 4- C_{1-4} alcoxi-fenilo, $\text{O}(\text{CH}_2)_m$ fenilo, morfolinilo, piridilo, 2- C_{1-4} alcoxi-piridin-5-ilo, pirimidinilo, pirazinilo y -O-pirimidinilo;

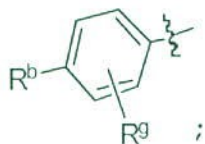
R^g , en cada caso, se selecciona independientemente del grupo que consiste en halo, C_{1-4} alquilo, C_{1-4} alcoxi, C_{1-4} haloalquilo y C_{1-4} haloalcoxi;

m, en cada caso, es independientemente 0, 1, 2 ó 3; y

s, en cada caso, es independientemente 1, 2 ó 3.

5. El compuesto de conformidad con cualquiera de las reivindicaciones 1 a 4, caracterizado porque:

R^1 se selecciona independientemente del grupo que consiste en: C_{1-6} alquilo, $-\text{CONHC}_{4-18} \text{ alquilo}$, $-\text{CONH}(\text{CH}_2)_{1-8}$ fenilo y



R^6 se selecciona independientemente del grupo que consiste en: NH_2 , $-CONH(C_{1-6}$ alquilo), $-NHCOCH_2PO(OEt)_2$, $-NHCO(CH_2)SO_2(C_{1-4}$ alquilo), R^c , OR^c , $-CONHR^c$ y $-NHCOR^c$;

R^{12} se selecciona independientemente del grupo que consiste en: H, halo, C_{1-4} alquilo y C_{1-4} alcoxi;

R^{13} se selecciona independientemente del grupo que consiste en: H, halo, C_{1-4} alquilo sustituido con 0-1 C_{1-4} alcoxi, C_{1-4} alcoxi, C_{1-4} haloalquilo, C_{1-4} haloalcoxi, $-(CH_2)_m-C_{3-4}$ cicloalquilo, CN, $N(C_{1-4}$ alquilo) $_2$, $NHCO_2(C_{1-4}$ alquilo), $NHSO_2(C_{1-4}$ alquilo), pirazolilo y morfolinilo;

de manera alternativa, R^{12} y R^{13} , junto con los átomos de carbono a los que están unidos, se combinan para formar un anillo carbocíclico de 5 a 6 miembros o un anillo heterocíclico saturado de 5 a 6 miembros, que comprende átomos de carbono y 1-2 átomos de oxígeno;

R^{14} se selecciona independientemente del grupo que consiste en: H y C_{1-4} alcoxi;

R^b , en cada caso, se selecciona independientemente del grupo que consiste en halo, C_{1-6} alquilo, C_{1-6} alcoxi, C_{1-6} haloalquilo, C_{1-10} haloalcoxi, $O(CH_2)_5O(C_{1-6}$ alquilo), $-CONH(CH_2)_{6-20}H$, $-(CH_2)_m(C_{3-6}$ cicloalquilo), $(CH_2)_m(C_{4-6}$

cicloalquenilo), $-O(CH_2)_m(C_{3-6}$ cicloalquilo), fenoxi, benzoxi, morfolinilo, 2- C_{1-4} alcoxi-piridin-5-ilo, pirimidin-5-ilo, pirazin-2-ilo y -O-pirimidinilo; y

R^c , en cada caso, se selecciona independientemente del grupo que consiste en: C_{3-6} cicloalquilo sustituido con 0-2 R^d , $-(CH_2)_m$ -(fenilo sustituido con 0-3 R^d) y un heteroarilo seleccionado de oxazolilo, isoxazolilo, tiazolilo, pirazolilo, imidazolilo, oxadiazolilo, triazolilo, tetrazolilo, piridilo y pirazinilo; en donde el heteroarilo se sustituye con 0-2 R^d .

6. El compuesto de conformidad con cualquiera de las reivindicaciones 1 a 5, caracterizado porque:

R^2 se selecciona independientemente del grupo que consiste en: CF_3 y Me;

R^3 se selecciona independientemente del grupo que consiste en: H y F;

R^4 se selecciona independientemente del grupo que consiste en: H y F;

R^6 se selecciona independientemente del grupo que consiste en: NH_2 , $-CONHMe$, Ofenilo, $-CONH$ (ciclopropilo), $-CONH$ (ciclobutilo), $-CONH$ (ciclopentilo), $-CONH$ (ciclohexilo), $-CONH$ fenilo, $-CONH$ (4-F-fenilo), $-CONH$ (2-Cl-fenilo), $-CONH$ (4-Cl-fenilo), $-CONH$ (4-Me-fenilo), $-CONH$ (4-OH-fenilo), $-CONH$ (3-OMe-fenilo), $-CONH$ (4-OMe-fenilo), $-CONH$ (4- CF_3 -fenilo), $-CONH$ (4-OCF₃-fenilo), $-CONH$ (1-Me-pirazol-3-ilo), $-CONH$ (4-(1H-

tetrazol-2-il)-fenilo), -CONH(4-(2H-tetrazol-5-il)-fenilo), -CONH(3-F-4-Me-fenilo), -CONH(3-F-4-OMe-fenilo), -CONH(CH₂)₂fenilo, -CONH(5-OMe-pirid-2-ilo), -CONH(6-OMe-pirid-3-ilo), -CONH(5-OMe-pirazin-2-ilo), -CONH(6-OMe-piridazin-3-ilo), -NHCO(CH₂)SO₂Me, -NHCOfenilo, -NHCO(2-Me-fenilo), -NHCO(3-Me-fenilo), -NHCO(4-Me-fenilo), -NHCO(2-Cl-fenilo), -NHCO(3-Cl-fenilo), -NHCO(2-Cl-4-F-fenilo), -NHCO(2-Cl-5-F-fenilo), -NHCO(isoxazol-5-ilo), -NHCO(3-Me-isoxazol-5-ilo), -NHCO(4-Me-isoxazol-5-ilo), -NHCO(3-OMe-isoxazol-5-ilo), -NHCO(3-Br-isoxazol-5-ilo), -NHCO(3-(2-Cl-fenilo)-isoxazol-5-ilo), -NHCO(3-(3-F-fenilo)-isoxazol-5-ilo), -NHCO(3-OBn-isoxazol-5-ilo), 1H-imidazol-1-ilo, -NHCO(5-Me-1,3,4-oxadiazol-2-ilo), -NHCO(1-Me-1,2,3-triazol-4-ilo), -NHCO(6-OMe-pirid-3-ilo), -NHCO(6-Cl-piridazin-3-ilo), 5-CF₃-1,3,4-oxadiazol-2-ilo, 1H-tetrazol-1-ilo, 1H-tetrazol-3-ilo y 2H-tetrazol-5-ilo;

R¹¹ y R¹⁵ se seleccionan independientemente del grupo que consiste en: H, Me, F y Cl;

R¹² se selecciona independientemente del grupo que consiste en: H, F, Cl, Me y OMe;

R¹³ se selecciona independientemente del grupo que consiste en: H, F, Cl, Br, Me, OMe, OEt, CH₂OMe, CF₃, CH₂CF₃, OCHF₂, OCF₃, CN, N(Me)₂, ciclopropilo y ciclopropilmetilo;

de manera alternativa, R¹² y R¹³, junto con los átomos de carbono a los que están unidos, se combinan para

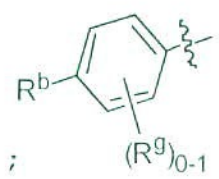
formar un anillo carbocíclico de 5 a 6 miembros o un anillo heterocíclico saturado de 5 a 6 miembros que comprende: átomos de carbono y 1-2 átomos de oxígeno;

R^{14} es H;

R^b , en cada caso, se selecciona independientemente del grupo que consiste en n pentilo, metoxi, n-butoxi, i-butoxi, i-pentoxi, $O(CH_2)_{1-6}CF_3$, $O(CH_2)_{1-4}CF_2CF_3$, $-CONH(CH_2)_{6-20}H$, ciclopropilo, ciclopent-1-en-1-ilo, ciclohex-1-en-1-ilo, $-O(CH_2)_2$ (ciclopentilo), fenoxi, benzoxi, pirimidin-5-ilo, pirazin-2-ilo y -O-pirimidin-2-ilo; y

R^g es F.

7. El compuesto de conformidad con la reivindicación 4, caracterizado porque:



R^1 es ;

R^2 se selecciona independientemente de CF_3 y CH_3 ;

R^6 se selecciona independientemente de: R^c , $-CONHR^c$, $-NHCOR^c$ y $-NHCOCH_2SO_2$ (C_{1-4} alquilo);

R^b se selecciona independientemente de: $-O(CH_2)_{1-6}CF_3$, $O(CH_2)_{1-4}CF_2CF_3$, $-CONH(CH_2)_{6-20}H$, ciclopent-1-en-1-ilo, ciclohex-1-en-1-ilo, $O(CH_2)_2$ (ciclopentilo), fenoxi, benzoxi, pirimidin-5-ilo, pirazin-2-ilo y -O-pirimidin-2-ilo;

R^c , en cada caso, se selecciona independientemente del grupo que consiste en: $-(CH_2)_m$ -(fenilo sustituido con 0-3

R^d), y un heteroarilo seleccionado de oxazolilo, isoxazolilo, pirazolilo, imidazolilo, oxadiazolilo, triazolilo, tetrazolilo, piridilo y pirazinilo; en donde el heteroarilo se sustituye con 0-2 R^d ; y

R^d , en cada caso, se selecciona independientemente del grupo que consiste en halo, OH, CN, C_{1-4} alquilo, C_{1-4} alcoxi, C_{1-4} haloalquilo, C_{1-4} haloalcoxi, tetrazolilo y OBn.

8. El compuesto de conformidad con cualquiera de las reivindicaciones 1 a 5 u 7, caracterizado porque:

R^{13} se selecciona independientemente del grupo que consiste en: H, halo, C_{1-4} alquilo sustituido con 0-1 C_{1-4} alcoxi, C_{1-4} alcoxi, C_{1-4} haloalquilo, C_{1-4} haloalcoxi, CN o C_{3-4} cicloalquilo.

9. El compuesto de conformidad con cualquiera de las reivindicaciones 1-4, 7 ó 8, caracterizado porque:



10. El compuesto de conformidad con cualquiera de las reivindicaciones 1-9, caracterizado porque:

R^b se selecciona independientemente de: $-C(CH_2)_{1-6}CF_3$ y $-O(CH_2)_{1-4}CF_2CF_3$.

11. El compuesto de conformidad con cualquiera de las reivindicaciones 1-4, caracterizado porque:

R^6 es independientemente heteroarilo de nitrógeno de 5 miembros.

12. El compuesto de conformidad con cualquiera de las reivindicaciones 1-11, caracterizado porque:

R⁶ es independientemente: 1*H*-imidazol-1-ilo, 1*H*-tetrazol-1-ilo, 1*H*-tetrazol-3-ilo o 2*H*-tetrazol-5-ilo.

13. El compuesto de conformidad con la reivindicación 1, caracterizado porque se selecciona de:

(*S*)-3-(1*H*-tetrazol-5-il)-4-(*p*-tolil)-6-(4-(4,4,4-trifluorobutoxi)fenil)-6-(trifluorometil)-5,6-dihidropiridin-2(1*H*)-ona,

(*S*)-N-(4-metoxifenil)-2-oxo-4-(*p*-tolil)-6-(4-(4,4,4-trifluorobutoxi)fenil)-6-(trifluorometil)-1,2,5,6-tetrahidropiridin-3-carboxamida,

(*S*)-3-(2*H*-tetrazol-5-il)-4-(*p*-tolil)-6-(4-((6,6,6-trifluorohexil)oxi)fenil)-6-(trifluorometil)-5,6-dihidropiridin-2(1*H*)-ona,

(*S*)-2-oxo-4-(*p*-tolil)-6-(4-(4,4,4-trifluorobutoxi)fenil)-N-(4-(trifluorometoxi)fenil)-6-(trifluorometil)-1,2,5,6-tetrahidropiridin-3-carboxamida,

(*S*)-N-(6-metoxipiridin-3-il)-2-oxo-4-(*p*-tolil)-6-(4-(4,4,4-trifluorobutoxi)fenil)-6-(trifluorometil)-1,2,5,6-tetrahidropiridin-3-carboxamida,

(*S*)-N-ciclopropil-2-oxo-4-(*p*-tolil)-6-(4-(4,4,4-trifluorobutoxi)fenil)-6-(trifluorometil)-1,2,5,6-tetrahidropiridin-3-carboxamida,

(*S*)-N-(4-hidroxifenil)-2-oxo-4-(*p*-tolil)-6-(4-

(4,4,4-trifluorobutoxi)fenil)-6-(trifluorometil)-1,2,5,6-tetrahidropiridin-3-carboxamida,

(S)-4-(4-(difluorometoxi)fenil)-3-(1H-tetrazol-1-il)-6-(4-(4,4,4-trifluorobutoxi)fenil)-6-(trifluorometil)-5,6-dihidropiridin-2(1H)-ona,

(S)-3-metil-N-(2-oxo-4-(p-tolil)-6-(4-(4,4,4-trifluorobutoxi)fenil)-6-(trifluorometil)-1,2,5,6-tetrahidropiridin-3-il)isoxazol-5-carboxamida,

(S)-5-metil-N-(2-oxo-4-(p-tolil)-6-(4-(4,4,4-trifluorobutoxi)fenil)-6-(trifluorometil)-1,2,5,6-tetrahidropiridin-3-il)-1,3,4-oxadiazol-2-carboxamida,

N²-heptil-N⁵-(4-metoxifenil)-2-metil-6-oxo-4-(p-tolil)-1,2,3,6-tetrahidropiridin-2,5-dicarboxamida,

(S)-3-(1H-tetrazol-1-il)-4-(p-tolil)-6-(4-(6,6,6-trifluorohexil)oksi)fenil)-6-(trifluorometil)-5,6-dihidropiridin-2(1H)-ona,

(S)-4-(5,6,7,8-tetrahidronaftalen-2-il)-3-(1H-tetrazol-5-il)-6-(4-(4,4,4-trifluorobutoxi)fenil)-6-(trifluorometil)-5,6-dihidropiridin-2(1H)-ona,

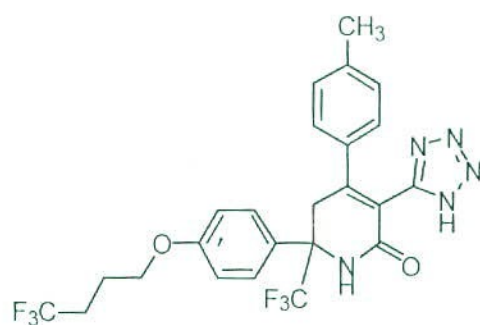
(S)-2-(metilsulfonil)-N-(2-oxo-4-(p-tolil)-6-(4-(4,4,4-trifluorobutoxi)fenil)-6-(trifluorometil)-1,2,5,6-tetrahidropiridin-3-il)acetamida,

(S)-3-(1H-tetrazol-5-il)-6-(4-(4,4,4-trifluorobutoxi)fenil)-4-(4-(2,2,2-trifluoroetil)fenil)-6-(trifluorometil)-5,6-dihidropiridin-2(1H)-ona, y

(S)-N-(5-metoxipirazin-2-il)-2-oxo-4-(p-tolil)-6-(4-(4,4,4-trifluorobutoxi)fenil)-6-(trifluorometil)-1,2,5,6-tetrahidropiridin-3-carboxamida;

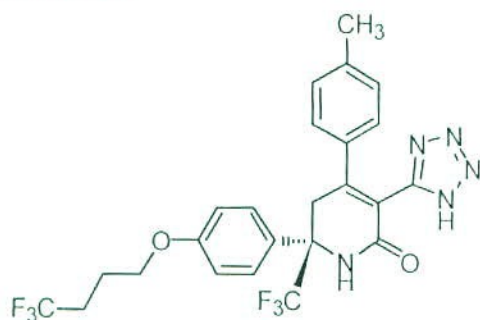
o un tautómero o una sal del mismo aceptable desde el punto de vista farmacéutico.

14. El compuesto de conformidad con la reivindicación 1, caracterizado porque tiene la siguiente fórmula:



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

15. El compuesto de conformidad con la reivindicación 14, caracterizado porque tiene la siguiente fórmula:



o un tautómero o una sal farmacéuticamente aceptable del mismo.



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

(10) **Patent No.:** **US 8,791,091 B2**
(45) **Date of Patent:** **Jul. 29, 2014**

(54) **ARYL DIHYDROPYRIDINONE AND
PIPERIDINONE MGAT2 INHIBITORS**

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C07D 413/04 (2006.01)
C07D 413/14 (2006.01)
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C07D 401/14 (2006.01)
C07D 211/90 (2006.01)
C07D 221/20 (2006.01)

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USPC **514/89; 514/232.2; 514/278; 514/340;**
514/341; 514/344; 544/82; 546/16; 546/24;
546/268.4; 546/269.4; 546/275.4; 546/288

(58) **Field of Classification Search**

None
See application file for complete search history.

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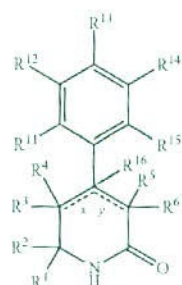
Primary Examiner — Janet L. Andres

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(57) **ABSTRACT**

The present invention provides compounds of Formula (I):



or a stereoisomer, or a pharmaceutically acceptable salt
thereof, wherein all of the variables are as defined herein.
These compounds are monoacylglycerol acyltransferase type
2 (MGAT2) inhibitors which may be used as medicaments.

103 Claims, No Drawings

(56)

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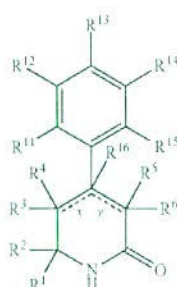
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What is claimed is:

1. A compound of Formula (I):



or a stereoisomer, a tautomer, or a pharmaceutically acceptable salt thereof, wherein:

--- designates a single or double bond;

x and y can be both a single bond; when x is a double bond, then y is a single bond and R⁴ and R¹⁶ are absent; when y is a double bond, then x is a single bond and R⁵ and R¹⁶ are absent;

R¹ is independently selected from the group consisting of: —CONH(C₄₋₁₈ alkyl), —CONH(C₂₋₈ haloalkyl), —CONH(CH₂)₁₋₈Ph, —CONHCH₂COC₂₋₈ alkyl, —(CH₂)_m—(C₃₋₁₀ carbocycle substituted with 0-2 R^b and 0-2 R^s), —(CH₂)_m—(5- to 6-membered heteroaryl comprising: carbon atoms and 1-4 heteroatoms selected from N, NR^e, O and S; wherein said heteroaryl is substituted with 0-1 R^b and 0-2 R^s), and a C₁₋₁₂ hydrocarbon chain substituted with 0-3 R^a; wherein said hydrocarbon chain may be straight or branched, saturated or unsaturated;

R² is independently selected from the group consisting of: C₁₋₄ alkyl, C₃₋₄ cycloalkyl, and C₁₋₄ haloalkyl;

R³ is independently selected from the group consisting of: H, F, Cl, C₁₋₄ alkyl and CN;

R⁴ and R⁵ are independently selected from the group consisting of: H, F, Cl, and C₁₋₄ alkyl;

when x is a single bond, R³ and R⁴ may be combined with the carbon atom to which they are attached to form a 3- to 6-membered carbocycle;

R⁶ is independently selected from the group consisting of: H, halo, C₁₋₄ alkyl, NO₂, R^c, (CH₂)_n—(X)_t, (CH₂)_mR^c, NH₂, —CONH(C₁₋₆ alkyl), —NHCOX, SO₂R^d, —NHCOCH₂PO(OEt)₂, —NHCO—COR^e, —NHCOCH(OH)R^e, —NHCOCH₂COR^e, —NHCONHR^e, and —OCONR^eR^e;

X is independently selected from the group consisting of: O, S, NH, CONH, and NHCO;

X₁ is independently C₁₋₄ hydrocarbon chain optionally substituted with C₁₋₄ alkyl or C₃₋₄ cycloalkyl;

when y is a single bond, R⁵ and R⁶ may be combined with the carbon atom to which they are attached to form a 3- to 6-membered carbocycle;

R¹¹, R¹², R¹³, R¹⁴ and R¹⁵ are independently selected from the group consisting of: H, halo, C₁₋₄ alkyl substituted with 0-2 R^f, C₁₋₄ haloalkyl, C₁₋₄ haloalkoxy, —(CH₂)_m—C₃₋₆ cycloalkyl, CN, NR^gR^g, OR^g, SR^g, NHCO₂(C₁₋₄ alkyl), NHSO₂(C₁₋₄ alkyl), and a 4- to 6-membered heterocycle comprising: carbon atoms and 1-4 heteroatoms selected from N, NR^e, O, and S;

alternatively, R¹¹ and R¹², together with the carbon atoms to which they are attached, combine to form a 5- to

6-membered carbocyclic ring or a 5- to 6-membered heterocyclic ring comprising: carbon atoms and 1-3 heteroatoms selected from N, NR^e, O, and S;

alternatively, R¹² and R¹³, together with the carbon atoms to which they are attached, combine to form a 5- to 6-membered carbocyclic ring or a 5- to 6-membered heterocyclic ring comprising: carbon atoms and 1-3 heteroatoms selected from N, NR^e, O, and S;

R¹⁶ is independently selected from the group consisting of: H and C₁₋₄ alkyl;

R^a is, at each occurrence, independently selected from the group consisting of: halo, OH, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, N(C₁₋₄ alkyl)₂, —(CH₂)_n(X)_t—(CH₂)_mR^c, and —(CH₂)_n—(CH₂O)_m—(CH₂)_nR^c;

R^b is, at each occurrence, independently selected from the group consisting of: halo, OH, C₁₋₁₀ alkyl, C₁₋₁₀ alkoxy, C₁₋₁₀ haloalkyl, C₁₋₁₀ haloalkoxy, C₁₋₁₀ alkylthio, C₁₋₁₀ haloalkylthio, N(C₁₋₄ alkyl)₂, —CONH(CH₂)₃₋₂₀Ph, —O(CH₂)_nO(C₁₋₆ alkyl), R^c, —(CH₂)_n—(X)_t—(CH₂)_mR^c, and —(CH₂)_n—(CH₂O)_m—(CH₂)_nR^c;

R^c is, at each occurrence, independently selected from the group consisting of: C₃₋₆ cycloalkyl substituted with 0-2 R^d, C₃₋₆ cycloalkenyl substituted with 0-2 R^d, —(CH₂)_m—(phenyl substituted with 0-3 R^d), and a 5- to 6-membered heterocycle comprising: carbon atoms and 1-4 heteroatoms selected from N, NR^e, O, and S; wherein said heterocycle is substituted with 0-2 R^d;

R^d is, at each occurrence, independently selected from the group consisting of: halo, OH, CN, NO₂, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkyl, C₁₋₄ haloalkoxy, tetrazolyl, OBn and phenyl substituted with 0-2 R^b;

R^e is, at each occurrence, independently selected from the group consisting of: H, C₁₋₈ alkyl, C₁₋₈ haloalkyl, benzyl optionally substituted with C₁₋₄ alkoxy, CO(C₁₋₄ alkyl) and COBn;

R^f is, at each occurrence, independently selected from the group consisting of: H and C₁₋₄ alkyl;

R^g, R^h and Rⁱ are, at each occurrence, independently selected from the group consisting of: halo, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkyl, and C₁₋₄ haloalkoxy;

R^j is, at each occurrence, independently selected from the group consisting of: C₁₋₄ alkyl, C₃₋₄ cycloalkyl and phenyl;

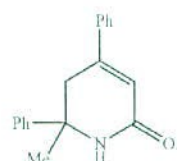
n, at each occurrence, is independently 0 or 1;

m, at each occurrence, is independently 0, 1, 2, 3, or 4

s, at each occurrence, is independently 1, 2, or 3; and

t, at each occurrence, is independently 0 or 1;

provided that the following compound is excluded:

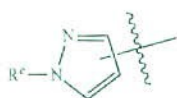


2. A compound according to claim 1, wherein:

R¹ is independently selected from the group consisting of: —CONH(C₄₋₁₈ alkyl), —CONH(CH₂)₁₋₈Ph, C₁₋₁₂ alkyl substituted with 0-2 R^a, C₁₋₁₂ alkenyl substituted with 0-2 R^a, C₁₋₁₂ alkynyl substituted with 0-2 R^a, —(CH₂)_m—(phenyl substituted with 0-1 R^b and 0-2 R^s), —(CH₂)_m—(C₃₋₆ cycloalkyl substituted with 0-1 R^b), and —(CH₂)_m—(5- to 6-membered heteroaryl substituted

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with 0-1 R^b and 0-2 R^c), wherein said heteroaryl is selected from: pyridyl, oxazolyl, thiazolyl and



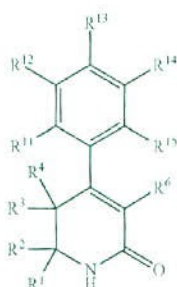
3. A compound according to claim 2, wherein:

R^{11} and R^{15} are independently selected from the group consisting of: H, C_{1-4} alkyl and halo;

R^{12} and R^{14} are independently selected from the group consisting of: H, halo, C_{1-4} alkyl and C_{1-4} alkoxy; and

R^{13} is independently selected from the group consisting of: H, halo, C_{1-4} alkyl substituted with 0-1 R^1 , C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, $-(CH_2)_m-C_{3-4}$ cycloalkyl, CN , NR^2R^3 , SR^2 , $NHCO_2(C_{1-4}$ alkyl), $NHSO_2(C_{1-4}$ alkyl), and a 4- to 6-membered heterocycle comprising: carbon atoms and 1-4 heteroatoms selected from N, NR^c , O, and S.

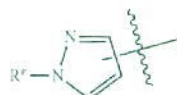
4. A compound according to claim 3, wherein the compound is of Formula (II):



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

5. A compound according to claim 4, wherein:

R^1 is independently selected from the group consisting of: C_{1-6} alkyl, C_{3-6} cycloalkyl, $—CONHC_{4-18}$ alkyl, $—CONHC_{2-8}$ haloalkyl, $—CONH(CH_2)_{1-8}Ph$, $—(CH_2)_m$ -(phenyl substituted with 1 R^b and 0-2 R^c), and a 5- to 6-membered heteroaryl substituted with 0-1 R^b and 0-2 R^c , wherein said heteroaryl is selected from: pyridyl, oxazolyl, thiazolyl and



R^2 is independently selected from the group consisting of: C_{1-4} alkyl and C_{1-4} haloalkyl;

R^3 is independently selected from the group consisting of: H and F;

R^4 is independently selected from the group consisting of: H and F;

R^6 is independently selected from the group consisting of: NH_2 , $—CONH(C_{1-6}$ alkyl), R^c , $—(CH_2)_m$ -(X), $(CH_2)_mR^c$, $—NHCO(CH_2)SO_2(C_{1-4}$ alkyl), $—NHCOCH_2PO(OEt)_2$, $—NHCOCO(C_{1-4}$ alkyl),

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$—NHCOCH(OH)(C_{1-4}$ alkyl), $—NHCOCH_2CO(C_{1-4}$ alkyl), $—NHCONH(C_{1-4}$ alkyl), and $—OCONH(C_{1-4}$ alkyl);

R^{11} and R^{15} are independently selected from the group consisting of: H, C_{1-4} alkyl and halo;

R^{12} and R^{14} are independently selected from the group consisting of: H, halo, C_{1-4} alkyl and C_{1-4} alkoxy;

R^{13} is independently selected from the group consisting of: H, halo, C_{1-4} alkyl substituted with 0-1 C_{1-4} alkoxy, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, $—(CH_2)_m$ — C_{3-4} cycloalkyl, CN , $N(C_{1-4}$ alkyl) $_2$, $NHCO_2(C_{1-4}$ alkyl), $NHSO_2(C_{1-4}$ alkyl), pyrazolyl, and morpholinyl; alternatively, R^{12} and R^{13} , together with the carbon atoms to which they are attached, combine to form a 5- to 6-membered carbocyclic ring or a 5- to 6-membered heterocyclic ring comprising: carbon atoms and 1-3 heteroatoms selected from N, NR^c , O, and S;

R^b is, at each occurrence, independently selected from the group consisting of: halo, OH, C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} haloalkyl, C_{1-10} haloalkoxy, $—O(CH_2)_nO(C_{1-6}$ alkyl), $N(C_{1-4}$ alkyl) $_2$, $—CONH(CH_2)_{6-20}H$, $—(CH_2)_m$ (C_{1-6} cycloalkyl), $—(CH_2)_m$ (C_{3-6} cycloalkenyl), $—O(CH_2)_m$ (C_{3-6} cycloalkyl), 4- C_{1-4} alkoxy-Ph, $O(CH_2)_m$ Ph, morpholinyl, pyridyl, 2- C_{1-4} alkoxy-pyridin-5-yl, pyrimidinyl, pyrazinyl, and $—O$ -pyrimidinyl;

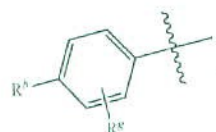
R^c is, at each occurrence, independently selected from the group consisting of: halo, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, and C_{1-4} haloalkoxy;

m, at each occurrence, is independently 0, 1, 2 or 3; and

s, at each occurrence, is independently 1, 2, or 3.

6. A compound according to claim 5, wherein:

R^1 is independently selected from the group consisting of: C_{1-6} alkyl, $—CONHC_{4-18}$ alkyl, $—CONH(CH_2)_{1-8}Ph$, and



R^6 is independently selected from the group consisting of: NH_2 , $—CONH(C_{1-6}$ alkyl), $—NHCOCH_2PO(OEt)_2$, $—NHCO(CH_2)SO_2(C_{1-4}$ alkyl), R^c , OR^c , $—CONHR^c$, and $—NHCOR^c$;

R^{12} is independently selected from the group consisting of: H, halo, C_{1-4} alkyl and C_{1-4} alkoxy;

R^{13} is independently selected from the group consisting of: H, halo, C_{1-4} alkyl substituted with 0-1 C_{1-4} alkoxy, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, $—(CH_2)_m$ — C_{3-4} cycloalkyl, CN , $N(C_{1-4}$ alkyl) $_2$, $NHCO_2(C_{1-4}$ alkyl), $NHSO_2(C_{1-4}$ alkyl), pyrazolyl, and morpholinyl; alternatively, R^{12} and R^{13} , together with the carbon atoms to which they are attached, combine to form a 5- to 6-membered carbocyclic ring or a 5- to 6-membered saturated heterocyclic ring comprising: carbon atoms and 1-2 oxygen atoms;

R^{14} is independently selected from the group consisting of: H and C_{1-4} alkoxy;

R^b is, at each occurrence, independently selected from the group consisting of: halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-10} haloalkoxy, $—O(CH_2)_nO(C_{1-6}$ alkyl), $—CONH(CH_2)_{6-20}H$, $—(CH_2)_m$ (C_{3-6} cycloalkyl), $—(CH_2)_m$ (C_{4-6} cycloalkenyl), $—O(CH_2)_m$ (C_{3-6}

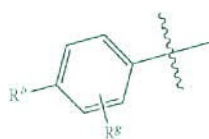
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cycloalkyl), phenoxy, benzoxy, morpholinyl, 2- C_{1-4} alkoxy-pyridin-5-yl, pyrimidin-5-yl, pyrazin-2-yl and —O-pyrimidinyl; and

R^c is, at each occurrence, independently selected from the group consisting of: C_{3-6} cycloalkyl substituted with 0-2 R^d , — $(CH_2)_m$ -(phenyl substituted with 0-3 R^d), and a heteroaryl selected from: oxazolyl, isoxazolyl, thiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, and pyrazinyl; wherein said heteroaryl is substituted with 0-2 R^d .

7. A compound according to claim 6, wherein:

R^1 is



R^6 is independently selected from the group consisting of:

NH_2 , — $CONH(C_{1-4}$ alkyl), OPh , — $CONH(C_{3-6}$ cycloalkyl), — $CONHPh$, — $CONH(2-halo-Ph)$, — $CONH(3-halo-Ph)$, — $CONH(4-halo-Ph)$, — $CONH(4-C_{1-4}$ alkyl- Ph), — $CONH(4-OH-Ph)$, — $CONH(3-C_{1-4}$ alkoxy- Ph), — $CONH(4-C_{1-4}$ alkoxy- Ph), — $CONH(4-C_{1-4}$ haloalkyl- Ph), — $CONH(4-C_{1-4}$ haloalkoxy- Ph), — $CONH(4-CN-Ph)$, — $CONH(4-tetrazolyl-Ph)$, — $CONH(3-halo-4-C_{1-4}$ alkyl- Ph), — $CONH(3-halo-4-C_{1-4}$ alkoxy- Ph), — $CONH(CH_2)_2Ph$, — $CONH(4-(4-C_{1-4}$ alkoxy- Ph)-thiazol-2-yl), — $CONH(1-C_{1-4}$ alkyl-pyrazol-3-yl), — $CONH(5-C_{1-4}$ alkoxy-pyrid-2-yl), — $CONH(6-C_{1-4}$ alkoxy-pyrid-3-yl), — $CONH(5-C_{1-4}$ alkoxy-pyrazin-2-yl), — $CONH(6-C_{1-4}$ alkoxy-pyridazin-3-yl), — $NHCO(CH_2)SO_2(C_{1-4}$ alkyl), — $NHCOPh$, — $NHCO(2-C_{1-4}$ alkyl- Ph), — $NHCO(3-C_{1-4}$ alkyl- Ph), — $NHCO(4-C_{1-4}$ alkyl- Ph), — $NHCO(2-halo-Ph)$, — $NHCO(3-halo-Ph)$, — $NHCO(2-C_{1-4}$ haloalkyl- Ph), — $NHCO(2-C_{1-4}$ haloalkoxy- Ph), — $NHCO(2-halo-4-halo-Ph)$, — $NHCO(2-halo-5-halo-Ph)$, — $NHCO(oxazolyl)$, — $NHCO(isoxazolyl)$, — $NHCO(3-C_{1-4}$ alkyl-isoxazol-5-yl), — $NHCO(4-C_{1-4}$ alkyl-isoxazol-5-yl), — $NHCO(3-C_{1-4}$ alkoxy-isoxazol-5-yl), — $NHCO(4-C_{1-4}$ alkoxy-isoxazol-5-yl), — $NHCO(3-halo-isoxazol-5-yl)$, — $NHCO(3-OBn-isoxazol-5-yl)$, — $NHCO(3-(2-halo-Ph)-isoxazol-5-yl)$, — $NHCO(3-(3-halo-Ph)-isoxazol-5-yl)$, — $NHCO(5-C_{1-4}$ alkyl-1H-pyrazol-3-yl), imidazolyl, — $NHCO(5-C_{1-4}$ alkyl-1,3,4-oxadiazol-2-yl), — $NHCO(1-C_{1-4}$ alkyl-1,2,3-triazol-4-yl), — $NHCO(6-C_{1-4}$ alkoxy-pyrid-3-yl), — $NHCO(pyrazinyl)$, — $NHCO(6-halo-pyridazin-3-yl)$, 5- C_{1-4} haloalkyl-1,3,4-oxadiazol-2-yl, 3- NO_2 -1H-1,2,4-triazol-1-yl, tetrazolyl and 5- C_{1-4} alkyl-tetrazol-1-yl;

R^b is independently selected from the group consisting of:

halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-8} haloalkoxy, — $CONH(CH_2)_{6-20}H$, C_{3-6} cycloalkyl, C_{4-6} cycloalkenyl, — $O(CH_2)_m(C_{3-6}$ cycloalkyl), phenoxy, benzoxy, pyrimidinyl, pyrazinyl and —O-pyrimidinyl; and

R^8 is independently selected from the group consisting of: halo and C_{1-4} alkyl.

8. A compound according to claim 7, wherein:

R^2 is independently selected from the group consisting of: CF_3 and Me;

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R^3 is independently selected from the group consisting of: H and F;

R^4 is independently selected from the group consisting of: H and F;

R^6 is independently selected from the group consisting of: NH_2 , — $CONHMe$, OPh , — $CONH(cyclopropyl)$, — $CONH(cyclobutyl)$, — $CONH(cyclopentyl)$, — $CONH(cyclohexyl)$, — $CONHPh$, — $CONH(4-F-Ph)$, — $CONH(2-Cl-Ph)$, — $CONH(4-Cl-Ph)$, — $CONH(4-Me-Ph)$, — $CONH(4-OH-Ph)$, — $CONH(3-OMe-Ph)$, — $CONH(4-OMe-Ph)$, — $CONH(4- CF_3 - Ph)$, — $CONH(4- OCF_3 - Ph)$, — $CONH(1-Me-pyrazol-3-yl)$, — $CONH(4-(1H-tetrazol-2-yl)-Ph)$, — $CONH(4-(2H-tetrazol-5-yl)-Ph)$, — $CONH(3-F-4-Me-Ph)$, — $CONH(3-F-4-OMe-Ph)$, — $CONH(CH_2)_2Ph$, — $CONH(5-OMe-pyrid-2-yl)$, — $CONH(6-OMe-pyrid-3-yl)$, — $CONH(5-OMe-pyrazin-2-yl)$, — $CONH(6-OMe-pyridazin-3-yl)$, — $NHCO(CH_2)SO_2Me$, — $NHCOPh$, — $NHCO(2-Me-Ph)$, — $NHCO(3-Me-Ph)$, — $NHCO(4-Me-Ph)$, — $NHCO(2-Cl-Ph)$, — $NHCO(3-Cl-Ph)$, — $NHCO(2-Cl-4-F-Ph)$, — $NHCO(2-Cl-5-F-Ph)$, — $NHCO(isoxazol-5-yl)$, — $NHCO(3-Me-isoxazol-5-yl)$, — $NHCO(4-Me-isoxazol-5-yl)$, — $NHCO(3-OMe-isoxazol-5-yl)$, — $NHCO(3-Br-isoxazol-5-yl)$, — $NHCO(3-(2-Cl-Ph)-isoxazol-5-yl)$, — $NHCO(3-(3-F-Ph)-isoxazol-5-yl)$, — $NHCO(3-OBn-isoxazol-5-yl)$, 1H-imidazol-1-yl, — $NHCO(5-Me-1,3,4-oxadiazol-2-yl)$, — $NHCO(1-Me-1,2,3-triazol-4-yl)$, — $NHCO(6-OMe-pyrid-3-yl)$, — $NHCO(6-Cl-pyridazin-3-yl)$, 5- CF_3 -1,3,4-oxadiazol-2-yl, 1H-tetrazol-1-yl, 1H-tetrazol-3-yl, and 2H-tetrazol-5-yl;

R^{11} and R^{15} are independently selected from the group consisting of: H, Me, F, and Cl;

R^{12} is independently selected from the group consisting of: H, F, Cl, Me and OMe;

R^{13} is independently selected from the group consisting of: H, F, Cl, Br, Me, OMe, OPh , CH_2OMe , CF_3 , CH_2CF_3 , OCF_3 , OCF_3 , CN, $N(Me)_2$, cyclopropyl and cyclopropylmethyl;

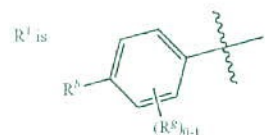
alternatively, R^{12} and R^{13} , together with the carbon atoms to which they are attached, combine to form a 5- to 6-membered carbocyclic ring or a 5- to 6-membered saturated heterocyclic ring comprising: carbon atoms and 1-2 oxygen atoms;

R^{14} is H;

R^b is, at each occurrence, independently selected from the group consisting of: n-pentyl, methoxy, n-butoxy, i-butoxy, i-pentoxy, $O(CH_2)_{1-6}CF_3$, $O(CH_2)_1-4CF_2CF_3$, — $CONH(CH_2)_{6-20}H$, cyclopropyl, cyclopent-1-en-1-yl, cyclohex-1-en-1-yl, — $O(CH_2)_2$ (cyclopentyl), phenoxy, benzoxy, pyrimidin-5-yl, pyrazin-2-yl and —O-pyrimidin-2-yl; and

R^8 is F;

9. A compound according to claim 5, wherein:



R^2 is independently selected from CF_3 and CH_3 ;

R^6 is independently selected from: R^c , — $CONHR^c$, — $NH-COR^c$, and — $NHCOCH_2SO_2(C_{1-4}$ alkyl);

R^b is independently selected from: $O(CH_2)_{1-6}CF_3$, $-O(CH_2)_{1-4}CF_2CF_3$, $-CONH(CH_2)_{6-20}H$, cyclopent-1-en-1-yl, cyclohex-1-en-1-yl, $-O(CH_2)_3$ (cyclopentyl), phenoxy, benzoxy, pyrimidin-5-yl, pyrazin-2-yl and $-O$ -pyrimidin-2-yl;

R^c is, at each occurrence, independently selected from the group consisting of: $-(CH_2)_m$ -(phenyl substituted with 0-3 R^d), and a heteroaryl selected from: oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, and pyrazinyl; wherein said heteroaryl is substituted with 0-2 R^d ; and

R^d is, at each occurrence, independently selected from the group consisting of: halo, OH, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, tetrazolyl and OBn.

10. A compound according to claim 1, wherein the compound is selected from:

(S)-3-(1H-tetrazol-5-yl)-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1H)-one,

(S)-N-(4-methoxyphenyl)-2-oxo-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide,

(S)-3-(2H-tetrazol-5-yl)-4-(p-tolyl)-6-(4-(6,6,6-trifluorohexyloxy)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1H)-one,

(S)-2-oxo-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-N-(4-(trifluoromethoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide,

(S)-N-(6-methoxypyridin-3-yl)-2-oxo-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide,

(S)-N-cyclopropyl-2-oxo-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide,

(S)-N-(4-hydroxyphenyl)-2-oxo-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide,

(S)-4-(4-(difluoromethoxy)phenyl)-3-(1H-tetrazol-1-yl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1H)-one,

(S)-3-methyl-N-(2-oxo-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridin-3-yl)isoxazole-5-carboxamide,

(S)-5-methyl-N-(2-oxo-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridin-3-yl)-1,3,4-oxadiazole-2-carboxamide,

N²-heptyl-N⁵-(4-methoxyphenyl)-2-methyl-6-oxo-4-(p-tolyl)-1,2,3,6-tetrahydropyridine-2,5-dicarboxamide,

(S)-3-(1H-tetrazol-1-yl)-4-(p-tolyl)-6-(4-(6,6,6-trifluorohexyloxy)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1H)-one,

(S)-4-(5,6,7,8-tetrahydronaphthalen-2-yl)-3-(1H-tetrazol-5-yl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1H)-one,

(S)-2-(methylsulfonyl)-N-(2-oxo-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridin-3-yl)acetamide,

(S)-3-(1H-tetrazol-5-yl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-4-(4-(2,2,2-trifluoroethyl)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1H)-one; and

(S)-N-(5-methoxypyrazin-2-yl)-2-oxo-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide;

or a tautomer, or a pharmaceutically acceptable salt thereof.

11. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a compound of claim 1, or a stereoisomer, a tautomer, or a pharmaceutically acceptable salt thereof.

12. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a compound of claim 9, or a stereoisomer, a tautomer, or a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a compound of claim 10, or a stereoisomer, a tautomer, or a pharmaceutically acceptable salt thereof.

14. The pharmaceutical composition according to claim 11, further comprising one or more other suitable therapeutic agents selected from: anti-diabetic agents, anti-hyperglycemic agents, anti-hyperinsulinemic agents, anti-retinopathic agents, anti-neuropathic agents, anti-nephropathic agents, anti-atherosclerotic agents, anti-ischemic agents, anti-hypertensive agents, anti-obesity agents, anti-dyslipidemic agents, anti-hyperlipidemic agents, anti-hypertriglyceridemic agents, anti-hypercholesterolemic agents, anti-restenotic agents, lipid lowering agents, anorectic agents, and appetite suppressants.

15. The pharmaceutical composition according to claim 11, further comprising a dipeptidyl peptidase-IV inhibitor.

16. A method for the treatment of diabetes, hyperglycemia, gestational diabetes, obesity, dyslipidemia, hypertension, nonalcoholic fatty liver disease and nonalcoholic steatohepatitis, comprising administering to a patient in need of such treatment a therapeutically effective amount of at least a compound of claim 1.

17. A method for the treatment of diabetes, hyperglycemia, gestational diabetes, obesity, dyslipidemia, hypertension, nonalcoholic fatty liver disease and nonalcoholic steatohepatitis, comprising administering to a patient in need of such treatment a therapeutically effective amount of at least a compound of claim 9.

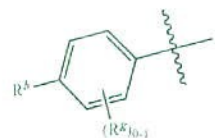
18. A method for the treatment of diabetes, hyperglycemia, gestational diabetes, obesity, dyslipidemia, hypertension, nonalcoholic fatty liver disease and nonalcoholic steatohepatitis, comprising administering to a patient in need of such treatment a therapeutically effective amount of at least a compound of claim 10.

19. The pharmaceutical composition according to claim 11, further comprising one or more other suitable therapeutic agents selected from: a dipeptidyl peptidase-IV inhibitor, a sodium-glucose transporter-2 inhibitor and a 11b-HSD-1 inhibitor.

20. The pharmaceutical composition according to claim 11, further comprising a sodium-glucose transporter-2 inhibitor.

21. A compound according to claim 5, wherein:

R^1 is independently selected from the group consisting of: C_{1-6} alkyl, $-CONHC_{4-18}$ alkyl, $-CONH(CH_2)_{1-8}Ph$, and



R^b is independently selected from the group consisting of: NH_2 , $-CONH(C_{1-6}$ alkyl), $-NHCOCH_2PO(OEt)_2$, $-NHCO(CH_2)_2SO_2(C_{1-4}$ alkyl), R^c , OR^c , $-CONHR^c$, and $-NHCOR^c$;

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R¹² is independently selected from the group consisting of:
H, halo, C₁₋₄ alkyl and C₁₋₄ alkoxy;

R¹³ is independently selected from the group consisting of:

H, halo, C₁₋₄ alkyl substituted with 0-1 C₁₋₄ alkoxy, C₁₋₄ alkoxy, C₁₋₄ haloalkyl, C₁₋₄ haloalkoxy, —(CH₂)_m—, C₃₋₄ cycloalkyl, CN, N(C₁₋₄ alkyl)₂, NHCO₂(C₁₋₄ alkyl), NHSO₂(C₁₋₄ alkyl), pyrazolyl, and morpholiny; alternatively, R¹² and R¹³, together with the carbon atoms to which they are attached, combine to form a 5- to 6-membered carbocyclic ring or a 5- to 6-membered saturated heterocyclic ring comprising: carbon atoms and 1-2 oxygen atoms;

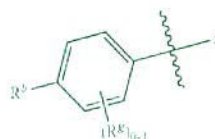
R¹⁴ is independently selected from the group consisting of:
H and C₁₋₄ alkoxy;

R^b is, at each occurrence, independently selected from the group consisting of: halo, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₁₀ haloalkoxy, —O(CH₂)_nO(C₁₋₆ alkyl), —CONH(CH₂)₆₋₂₀H, —(CH₂)_m(C₃₋₆ cycloalkyl), —(CH₂)_m(C₄₋₆ cycloalkenyl), —O(CH₂)_m(C₃₋₆ cycloalkenyl), phenoxy, benzoxy, morpholiny, 2-C₁₋₄ alkoxy-pyridin-5-yl, pyrimidin-5-yl, pyrazin-2-yl and O-pyrimidinyl; and

R^c is, at each occurrence, independently selected from the group consisting of: C₃₋₆ cycloalkyl substituted with 0-2 R^d, —(CH₂)_m-(phenyl substituted with 0-3 R^d), and a heteroaryl selected from: oxazolyl, isoxazolyl, thiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, and pyrazinyl; wherein said heteroaryl is substituted with 0-2 R^d.

22. A compound according to claim 21, wherein:

R¹ is



R⁶ is independently selected from the group consisting of:
NH₂, —CONH(C₁₋₄ alkyl), OPh, —CONH(C₃₋₆ cycloalkyl), —CONHPh, —CONH(2-halo-Ph), —CONH(3-halo-Ph), —CONH(4-halo-Ph), —CONH(4-C₁₋₄ alkyl-Ph), —CONH(4-OH-Ph), —CONH(3-C₁₋₄ alkoxy-Ph), —CONH(4-C₁₋₄ haloalkyl-Ph), —CONH(4-C₁₋₄ haloalkoxy-Ph), —CONH(4-CN-Ph), —CONH(4-tetrazolyl-Ph), —CONH(3-halo-4-C₁₋₄ alkyl-Ph), —CONH(3-halo-4-C₁₋₄ alkoxy-Ph), —CONH(CH₂)₂Ph, —CONH(4-(4-C₁₋₄ alkoxy-Ph)-thiazol-2-yl), —CONH(1-C₁₋₄ alkyl-pyrazol-3-yl), —CONH(5-C₁₋₄ alkoxy-pyrid-2-yl), —CONH(6-C₁₋₄ alkoxy-pyrid-3-yl), —CONH(5-C₁₋₄ alkoxy-pyrazin-2-yl), —CONH(6-C₁₋₄ alkoxy-pyridazin-3-yl), —NHCO(CH₂)SO₂(C₁₋₄ alkyl), —NHCOPh, —NHCO(2-C₁₋₄ alkyl-Ph), —NHCO(3-C₁₋₄ alkyl-Ph), —NHCO(4-C₁₋₄ alkyl-Ph), —NHCO(2-halo-Ph), —NHCO(3-halo-Ph), —NHCO(2-C₁₋₄ haloalkyl-Ph), —NHCO(2-C₁₋₄ haloalkoxy-Ph), —NHCO(2-halo-4-halo-Ph), —NHCO(2-halo-5-halo-Ph), —NHCO(oxazolyl), —NHCO(isoxazolyl), —NHCO(3-C₁₋₄ alkyl-isoxazol-5-yl), —NHCO(4-C₁₋₄ alkyl-isoxazol-5-yl), —NHCO(3-C₁₋₄ alkoxy-isoxazol-5-yl), —NHCO(4-C₁₋₄ alkoxy-isoxazol-5-yl), —NHCO(3-halo-isoxazol-5-yl), —NHCO(3-OBn-isoxazol-5-yl), —NHCO(3-(2-halo-Ph)-isoxazol-5-yl), —NHCO(3-(3-halo-Ph)-isoxazol-

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5-yl), —NHCO(5-C₁₋₄ alkyl-1H-pyrazol-3-yl), imidazolyl, —NHCO(5-C₁₋₄ alkyl-1,3,4-oxadiazol-2-yl), —NHCO(1-C₁₋₄ alkyl-1,2,3-triazol-4-yl), —NHCO(6-C₁₋₄ alkoxy-pyrid-3-yl), —NHCO(pyrazinyl), —NHCO(6-halo-pyridazin-3-yl), 5-C₁₋₄ haloalkyl-1,3,4-oxadiazol-2-yl, 3-NO₂-1H-1,2,4-triazol-1-yl, tetrazolyl and 5-C₁₋₄ alkyl-tetrazol-1-yl;

R^b is independently selected from the group consisting of:
halo, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₈ haloalkoxy, —CONH(CH₂)₆₋₂₀H, C₃₋₆ cycloalkyl, C₄₋₆ cycloalkenyl, —O(CH₂)_m(C₃₋₆ cycloalkyl), phenoxy, benzoxy, pyrimidinyl, pyrazinyl and —O-pyrimidinyl; and

R⁸ is independently selected from the group consisting of:
halo and C₁₋₄ alkyl.

23. A compound according to claim 22, wherein:

R² is independently selected from the group consisting of:
CF₃ and Me;

R³ is independently selected from the group consisting of:
H and F;

R⁴ is independently selected from the group consisting of:
H and F;

R⁶ is independently selected from the group consisting of:

NH₂, —CONHMe, OPh, —CONH(cyclopropyl), —CONH(cyclobutyl), —CONH(cyclopentyl), —CONH(cyclohexyl), —CONHPh, —CONH(4-F-Ph), —CONH(2-Cl-Ph), —CONH(4-Cl-Ph), —CONH(4-Me-Ph), —CONH(4-OH-Ph), —CONH(3-OMe-Ph), —CONH(4-OMe-Ph), —CONH(4-CF₃-Ph), —CONH(4-OCF₃-Ph), —CONH(1-Me-pyrazol-3-yl), —CONH(4-(1H-tetrazol-2-yl)-Ph), —CONH(4-(2H-tetrazol-5-yl)-Ph), —CONH(3-F-4-Me-Ph), —CONH(3-F-4-OMe-Ph), —CONH(CH₂)₂Ph, —CONH(5-OMe-pyrid-2-yl), —CONH(6-OMe-pyrid-3-yl), —CONH(5-OMe-pyrazin-2-yl), —CONH(6-OMe-pyridazin-3-yl), —NHCO(CH₂)SO₂Me, —NHCOPh, —NHCO(2-Me-Ph), —NHCO(3-Me-Ph), —NHCO(4-Me-Ph), —NHCO(2-Cl-Ph), —NHCO(3-Cl-Ph), —NHCO(2-Cl-4-F-Ph), —NHCO(2-Cl-5-F-Ph), —NHCO(isoxazol-5-yl), —NHCO(3-Me-isoxazol-5-yl), —NHCO(4-Me-isoxazol-5-yl), —NHCO(3-OMe-isoxazol-5-yl), —NHCO(3-Br-isoxazol-5-yl), —NHCO(3-(2-Cl-Ph)-isoxazol-5-yl), —NHCO(3-(3-F-Ph)-isoxazol-5-yl), —NHCO(3-OBn-isoxazol-5-yl), 1H-imidazol-1-yl, —NHCO(5-Me-1,3,4-oxadiazol-2-yl), —NHCO(1-Me-1,2,3-triazol-4-yl), —NHCO(6-OMe-pyrid-3-yl), —NHCO(6-Cl-pyridazin-3-yl), 5-CF₃-1,3,4-oxadiazol-2-yl, 1H-tetrazol-1-yl, 1H-tetrazol-3-yl, and 2H-tetrazol-5-yl;

R¹¹ and R¹⁵ are independently selected from the group consisting of: H, Me, F, and Cl;

R¹² is independently selected from the group consisting of:
H, F, Cl, Me and OMe;

R¹³ is independently selected from the group consisting of:
H, F, Cl, Br, Me, OMe, OEt, CH₂OMe, CF₃, CH₂CF₃, OCHF₂, OCF₃, CN, N(Me)₂, cyclopropyl and cyclopropylmethyl;

alternatively, R¹² and R¹³, together with the carbon atoms to which they are attached, combine to form a 5- to 6-membered carbocyclic ring or a 5- to 6-membered saturated heterocyclic ring comprising: carbon atoms and 1-2 oxygen atoms;

R¹⁴ is H;

R^b is, at each occurrence, independently selected from the group consisting of: n-pentyl, methoxy, n-butoxy, i-butoxy, i-pentoxy, —O(CH₂)₁₋₆CF₃, —O(CH₂)₁₋₄CF₂CF₃, —CONH(CH₂)₆₋₂₀H, cyclopropyl, cyclo-

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pent-1-en-1-yl, cyclohex-1-en-1-yl, $-\text{O}(\text{CH}_2)_2$ (cyclopentyl), phenoxy, benzyloxy, pyrimidin-5-yl, pyrazin-2-yl and $-\text{O}$ -pyrimidin-2-yl; and

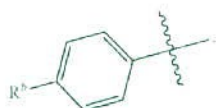
R^5 is F;

24. A compound according to claim 9, wherein:

R^{13} is independently selected from the group consisting of: H, halo, C_{1-4} alkyl substituted with 0-1 C_{1-4} alkoxy, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, CN or C_{3-4} cycloalkyl.

25. A compound according to claim 23, wherein:

R^1 is independently



26. A compound according to claim 25, wherein:

R^b is independently selected from: $-\text{O}(\text{CH}_2)_{1-6}\text{CF}_3$, and $-\text{O}(\text{CH}_2)_{1-4}\text{CF}_2\text{CF}_3$.

27. A compound according to claim 26, wherein:

R^6 is independently 5-membered nitrogen heteroaryl.

28. A compound according to claim 27, wherein:

R^6 is independently: 1H-imidazol-1-yl, 1H-tetrazol-1-yl, 1H-tetrazol-3-yl, or 2H-tetrazol-5-yl.

29. A compound according to claim 1, wherein the compound is selected from:

(S)-3-(1H-tetrazol-5-yl)-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1H)-one,

(S)-3-(2H-tetrazol-5-yl)-4-(p-tolyl)-6-(4-(4,4,4-trifluorohexyloxy)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1H)-one,

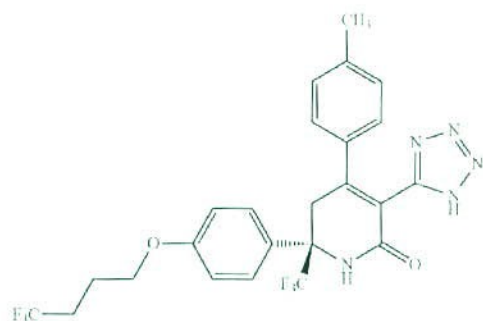
(S)-2-oxo-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-N-(4-(trifluoromethoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide,

(S)-4-(4-(difluoromethoxy)phenyl)-3-(1H-tetrazol-1-yl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1H)-one, and

(S)-2-(methylsulfonyl)-N-(2-oxo-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridin-3-yl)acetamide;

or a tautomer, or a pharmaceutically acceptable salt thereof.

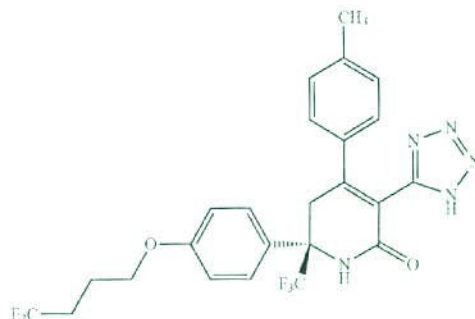
30. A racemic mixture of a compound having the following formula:



and its enantiomer, or a tautomer, or a pharmaceutically acceptable salt thereof.

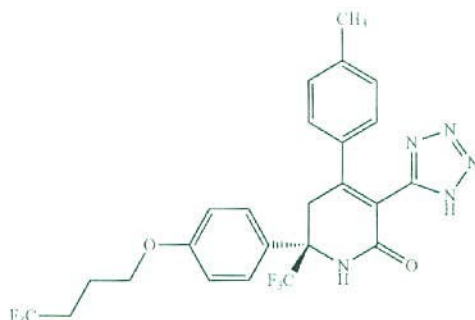
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31. A compound having the following formula:

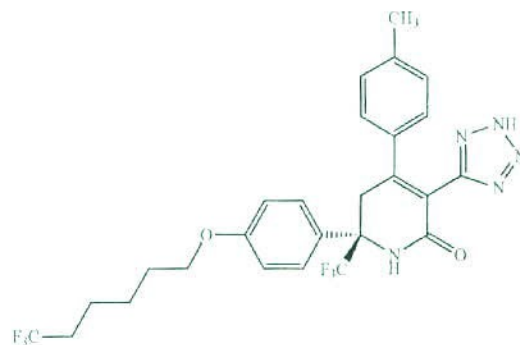


or a tautomer, or a pharmaceutically acceptable salt thereof.

32. A compound according to claim 31, wherein the compound has the following formula:



33. A compound according to claim 1, wherein the compound is a racemic mixture of a compound having the following formula:

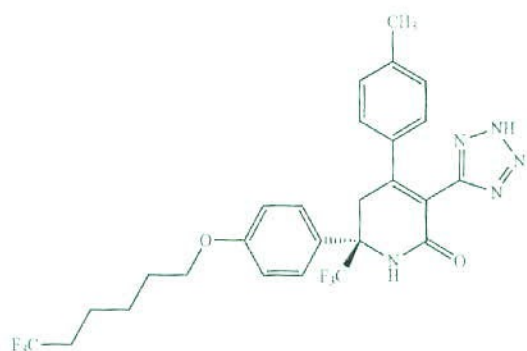


and its enantiomer, or a tautomer, or a pharmaceutically acceptable salt thereof.

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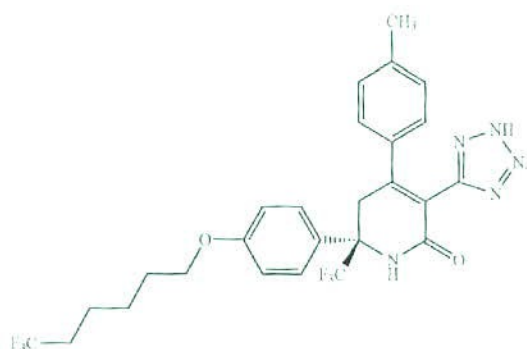
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34. A compound according to claim 33, wherein the compound has the following formula:

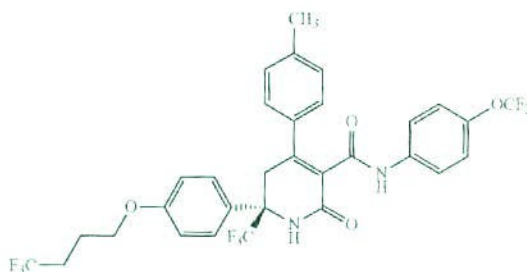


or a tautomer, or a pharmaceutically acceptable salt thereof.

35. A compound according to claim 34, wherein the compound has the following formula:



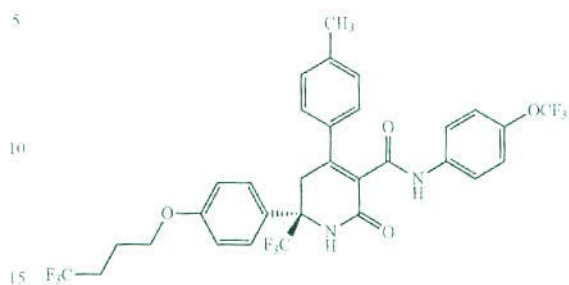
36. A compound according to claim 1, wherein the compound is a racemic mixture of a compound having the following formula:



and its enantiomer, or a tautomer, or a pharmaceutically acceptable salt thereof.

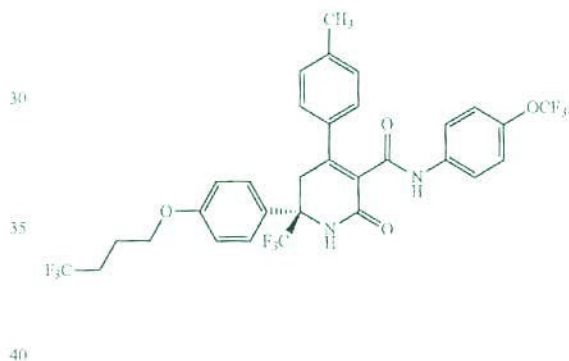
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37. A compound according to claim 36, wherein the compound has the following formula:

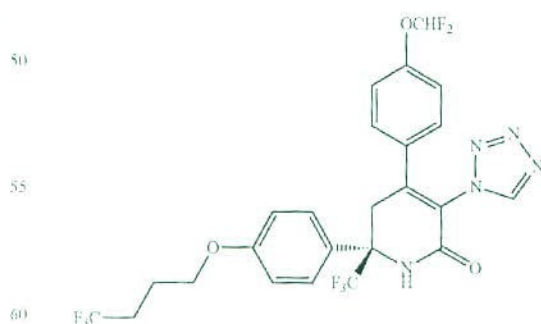


or a tautomer, or a pharmaceutically acceptable salt thereof.

38. A compound according to claim 37, wherein the compound has the following formula:



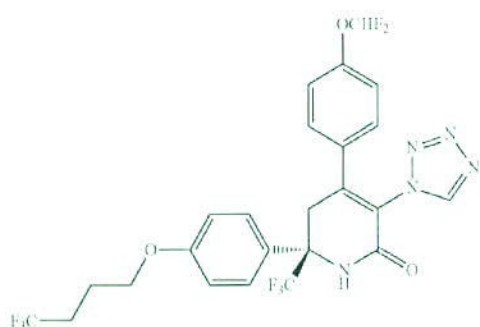
39. A compound according to claim 1, wherein the compound is a racemic mixture of a compound having the following formula:



and its enantiomer, or a tautomer, or a pharmaceutically acceptable salt thereof.

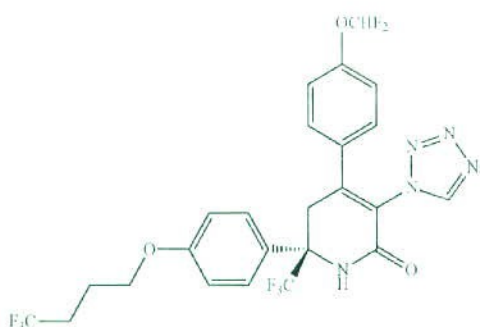
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40. A compound according to claim 39, wherein the compound has the following formula:

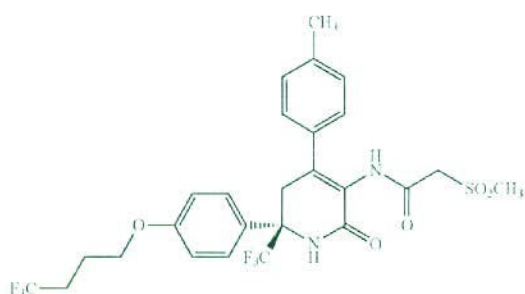


or a tautomer, or a pharmaceutically acceptable salt thereof.

41. A compound according to claim 40, wherein the compound has the following formula:



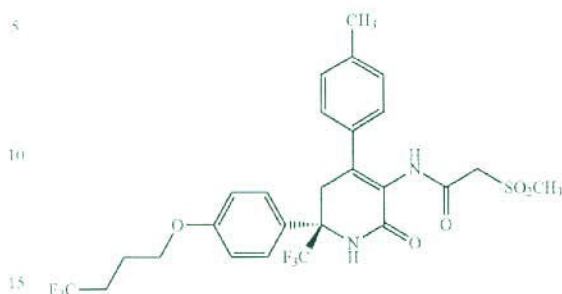
42. A compound according to claim 1, wherein the compound is a racemic mixture of a compound having the following formula:



and its enantiomer, or a tautomer, or a pharmaceutically acceptable salt thereof.

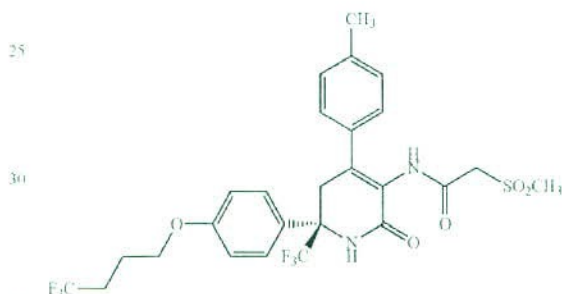
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43. A compound according to claim 42, wherein the compound has the following formula:



or a tautomer, or a pharmaceutically acceptable salt thereof.

44. A compound according to claim 43, wherein the compound has the following formula:



45. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a compound of claim 21, or a stereoisomer, a tautomer, or a pharmaceutically acceptable salt thereof.

46. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a compound of claim 28, or a stereoisomer, a tautomer, or a pharmaceutically acceptable salt thereof.

47. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a compound of claim 29.

48. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a compound of claim 30.

49. The pharmaceutical composition according to claim 48, further comprising one or more other suitable therapeutic agents selected from: anti-diabetic agents, anti-hyperglycemic agents, anti-hyperinsulinemic agents, anti-retinopathic agents, anti-neuropathic agents, anti-nephropathic agents, anti-atherosclerotic agents, anti-ischemic agents, anti-hypertensive agents, anti-obesity agents, anti-dyslipidemic agents, anti-hyperlipidemic agents, anti-hypertriglyceridemic agents, anti-hypercholesterolemic agents, anti-restenotic agents, lipid lowering agents, anorectic agents, and appetite suppressants.

50. The pharmaceutical composition according to claim 48, further comprising one or more other suitable therapeutic agents selected from: a dipeptidyl peptidase-IV inhibitor, a sodium-glucose transporter-2 inhibitor and a 11b-HSD-1 inhibitor.

51. The pharmaceutical composition according to claim 48, further comprising a dipeptidyl peptidase-IV inhibitor.

52. The pharmaceutical composition according to claim 48, further comprising a sodium-glucose transporter-2 inhibitor.

53. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a compound of claim 31.

54. The pharmaceutical composition according to claim 53, further comprising one or more other suitable therapeutic agents selected from: anti-diabetic agents, anti-hyperglycemic agents, anti-hyperinsulinemic agents, anti-retinopathic agents, anti-neuropathic agents, anti-nephropathic agents, anti-atherosclerotic agents, anti-ischemic agents, anti-hypertensive agents, anti-obesity agents, anti-dyslipidemic agents, anti-hyperlipidemic agents, anti-hypertriglyceridemic agents, anti-hypercholesterolemic agents, anti-restenotic agents, lipid lowering agents, anorectic agents, and appetite suppressants.

55. The pharmaceutical composition according to claim 53, further comprising one or more other suitable therapeutic agents selected from: a dipeptidyl peptidase-IV inhibitor, a sodium-glucose transporter-2 inhibitor and a 11b-HSD-1 inhibitor.

56. The pharmaceutical composition according to claim 53, further comprising a dipeptidyl peptidase-IV inhibitor.

57. The pharmaceutical composition according to claim 54, further comprising a sodium-glucose transporter-2 inhibitor.

58. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a compound of claim 32.

59. The pharmaceutical composition according to claim 58, further comprising one or more other suitable therapeutic agents selected from: anti-diabetic agents, anti-hyperglycemic agents, anti-hyperinsulinemic agents, anti-retinopathic agents, anti-neuropathic agents, anti-nephropathic agents, anti-atherosclerotic agents, anti-ischemic agents, anti-hypertensive agents, anti-obesity agents, anti-dyslipidemic agents, anti-hyperlipidemic agents, anti-hypertriglyceridemic agents, anti-hypercholesterolemic agents, anti-restenotic agents, lipid lowering agents, anorectic agents, and appetite suppressants.

60. The pharmaceutical composition according to claim 58, further comprising one or more other suitable therapeutic agents selected from: a dipeptidyl peptidase-IV inhibitor, a sodium-glucose transporter-2 inhibitor and a 11b-HSD-1 inhibitor.

61. The pharmaceutical composition according to claim 58, further comprising a dipeptidyl peptidase-IV inhibitor.

62. The pharmaceutical composition according to claim 58, further comprising a sodium-glucose transporter-2 inhibitor.

63. A method for the treatment of diabetes, hyperglycemia, gestational diabetes, obesity, dyslipidemia, hypertension, nonalcoholic fatty liver disease and nonalcoholic steatohepatitis, comprising administering to a patient in need of such treatment a therapeutically effective amount of at least a compound of claim 21.

64. A method for the treatment of diabetes, hyperglycemia, gestational diabetes, obesity, dyslipidemia, hypertension, nonalcoholic fatty liver disease and nonalcoholic steatohepatitis, comprising administering to a patient in need of such treatment a therapeutically effective amount of at least a compound of claim 28.

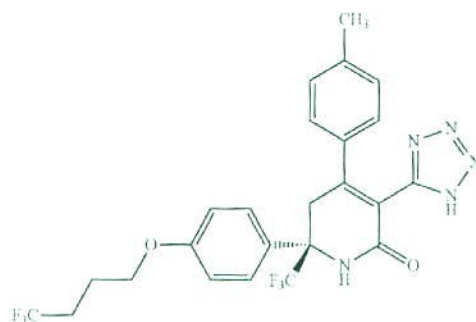
65. A method for the treatment of diabetes, hyperglycemia, gestational diabetes, obesity, dyslipidemia, hypertension, nonalcoholic fatty liver disease and nonalcoholic steatohepatitis, comprising administering to a patient in need of such treatment a therapeutically effective amount of at least a compound of claim 29.

66. A method for the treatment of diabetes, hyperglycemia, gestational diabetes, obesity, dyslipidemia, hypertension, nonalcoholic fatty liver disease and nonalcoholic steatohepatitis, comprising administering to a patient in need of such treatment a therapeutically effective amount of at least a compound of claim 30.

67. A method for the treatment of diabetes, hyperglycemia, gestational diabetes, obesity, dyslipidemia, hypertension, nonalcoholic fatty liver disease and nonalcoholic steatohepatitis, comprising administering to a patient in need of such treatment a therapeutically effective amount of at least a compound of claim 31.

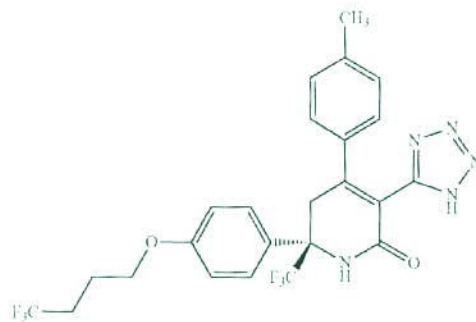
68. A method for the treatment of diabetes, hyperglycemia, gestational diabetes, obesity, dyslipidemia, hypertension, nonalcoholic fatty liver disease and nonalcoholic steatohepatitis, comprising administering to a patient in need of such treatment a therapeutically effective amount of at least a compound of claim 32.

69. A compound according to claim 30, where the compound is a racemic mixture of the compound having the following formula:



and its enantiomer, or a pharmaceutically acceptable salt thereof.

70. A compound according to claim 31, where the compound has the following formula:



or a pharmaceutically acceptable salt thereof.

71. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a compound of claim 69.

72. The pharmaceutical composition according to claim 69, further comprising one or more other suitable therapeutic agents selected from: anti-diabetic agents, anti-hyperglycemic agents, anti-hyperinsulinemic agents, anti-retinopathic agents, anti-neuropathic agents, anti-nephropathic agents, anti-atherosclerotic agents, anti-ischemic agents, anti-hypertensive agents, anti-obesity agents, anti-dyslipidemic agents,

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anti-hyperlipidemic agents, anti-hypertriglyceridemic agents, anti-hypercholesterolemic agents, anti-restenotic agents, lipid lowering agents, anorectic agents, and appetite suppressants.

73. The pharmaceutical composition according to claim 69, further comprising one or more other suitable therapeutic agents selected from: a dipeptidyl peptidase-IV inhibitor, a sodium-glucose transporter-2 inhibitor and a 11b-HSD-1 inhibitor.

74. The pharmaceutical composition according to claim 69, further comprising a dipeptidyl peptidase-IV inhibitor.

75. The pharmaceutical composition according to claim 72, further comprising a sodium-glucose transporter-2 inhibitor.

76. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a compound of claim 70.

77. The pharmaceutical composition according to claim 76, further comprising one or more other suitable therapeutic agents selected from: anti-diabetic agents, anti-hyperglycemic agents, anti-hyperinsulinemic agents, anti-retinopathic agents, anti-neuropathic agents, anti-nephropathic agents, anti-atherosclerotic agents, anti-ischemic agents, anti-hypertensive agents, anti-obesity agents, anti-dyslipidemic agents, anti-hyperlipidemic agents, anti-hypertriglyceridemic agents, anti-hypercholesterolemic agents, anti-restenotic agents, lipid lowering agents, anorectic agents, and appetite suppressants.

78. The pharmaceutical composition according to claim 76, further comprising one or more other suitable therapeutic agents selected from: a dipeptidyl peptidase-IV inhibitor, a sodium-glucose transporter-2 inhibitor and a 11b-HSD-1 inhibitor.

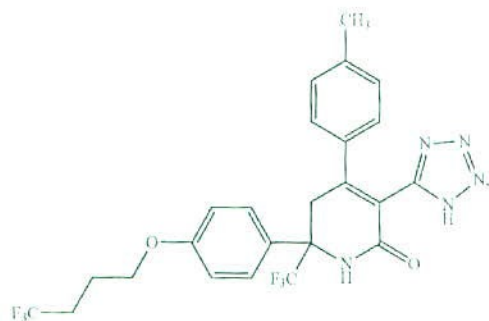
79. The pharmaceutical composition according to claim 76, further comprising a dipeptidyl peptidase-IV inhibitor.

80. The pharmaceutical composition according to claim 76, further comprising a sodium-glucose transporter-2 inhibitor.

81. A method for the treatment of diabetes, hyperglycemia, gestational diabetes, obesity, dyslipidemia, hypertension, nonalcoholic fatty liver disease and nonalcoholic steatohepatitis, comprising administering to a patient in need of such treatment a therapeutically effective amount of at least a compound of claim 69.

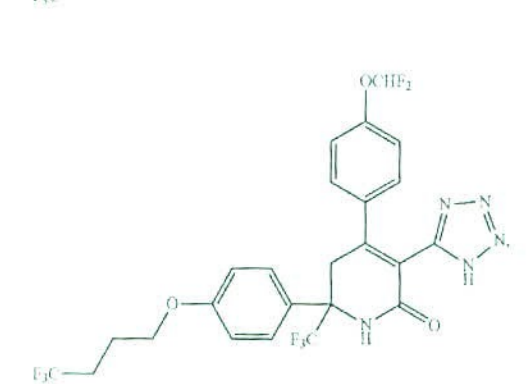
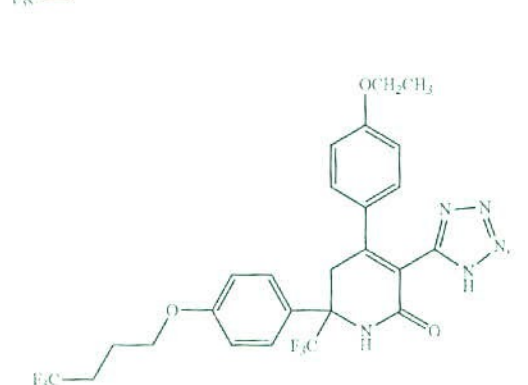
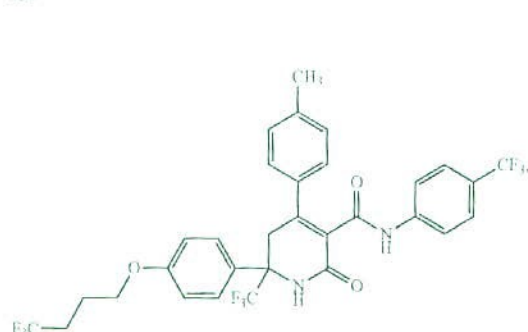
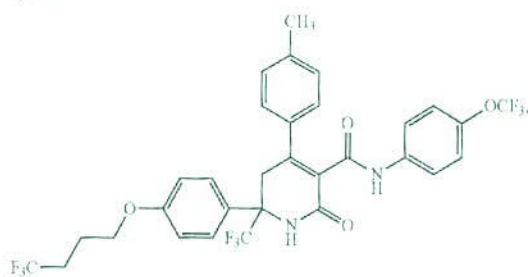
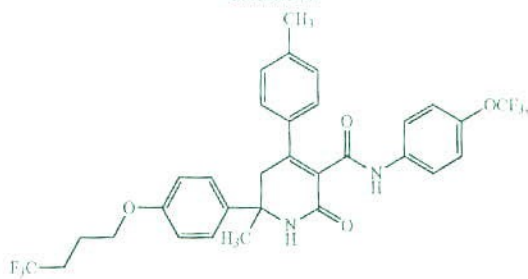
82. A method for the treatment of diabetes, hyperglycemia, gestational diabetes, obesity, dyslipidemia, hypertension, nonalcoholic fatty liver disease and nonalcoholic steatohepatitis, comprising administering to a patient in need of such treatment a therapeutically effective amount of at least a compound of claim 70.

83. A compound selected from:



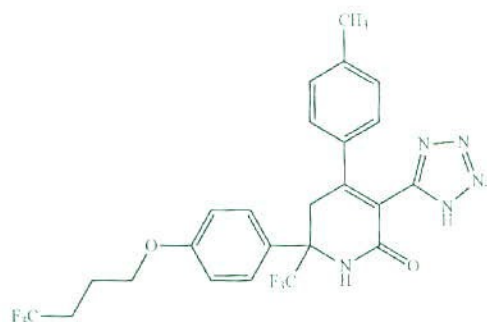
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97. A compound according to claim 90, wherein the compound has the following formula:



98. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier and a compound of claim 97.

99. The pharmaceutical composition according to claim 98, further comprising one or more other suitable therapeutic agents selected from: anti-diabetic agents, anti-hyperglycemic agents, anti-hyperinsulinemic agents, anti-retinopathic

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agents, anti-neuropathic agents, anti-nephropathic agents, anti-atherosclerotic agents, anti-ischemic agents, anti-hypertensive agents, anti-obesity agents, anti-dyslipidemic agents, anti-hyperlipidemic agents, anti-hypertriglyceridemic agents, anti-hypercholesterolemic agents, anti-restenotic agents, lipid lowering agents, anorectic agents, and appetite suppressants.

100. The pharmaceutical composition according to claim 98, further comprising one or more other suitable therapeutic agents selected from: a dipeptidyl peptidase-IV inhibitor, a sodium-glucose transporter-2 inhibitor and a 11b-HSD-1 inhibitor.

101. The pharmaceutical composition according to claim 98, further comprising a dipeptidyl peptidase-IV inhibitor.

102. The pharmaceutical composition according to claim 98, further comprising a sodium-glucose transporter-2 inhibitor.

103. A method for the treatment of diabetes, hyperglycemia, gestational diabetes, obesity, dyslipidemia, hypertension, nonalcoholic fatty liver disease and nonalcoholic steatohepatitis, comprising administering to a patient in need of such treatment a therapeutically effective amount of at least a compound of claim 97.

* * * * *

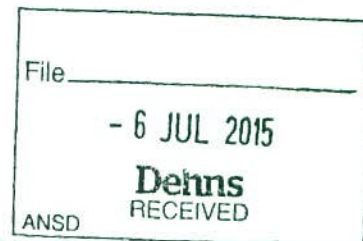


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Application No. 12 821 212.3 - 1462	Ref. 61.84.117315.01	Date 30.06.2015
Applicant Bristol-Myers Squibb Company		

Communication under Rule 71(3) EPC

1. Intention to grant

You are informed that the Examining Division intends to grant a European patent on the basis of the above application with the text and drawings and the related bibliographic data as indicated below.

A copy of the relevant documents is enclosed.

1.1 In the text for the Contracting States:

AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT
RO RS SE SI SK SM TR

Description, Pages

1-198 filed in electronic form on 10-12-2014

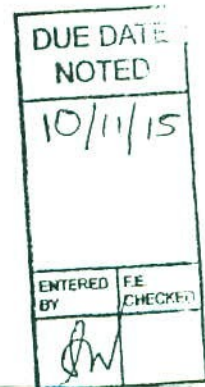
Claims, Numbers

1-22 filed in electronic form on 10-12-2014

With the following amendments to the above-mentioned documents according to your request dated 10-12-2014: (2)

Description, Pages

Delete Previous: 199-259



Registered letter

EPO Form 2004C 03.14CSXP

1.2 Bibliographic data

The title of the invention in the three official languages of the European Patent Office, the international patent classification, the designated Contracting States, the registered name(s) of the applicant(s) and the other bibliographic data are shown on the **enclosed EPO Form 2056**.

2. Invitation

You are invited, **within a non-extendable period of four months** of notification of this communication,

2.1 to EITHER approve the text communicated above and verify the bibliographic data (R. 71(5) EPC)

- (1) by filing a translation of the claim(s) in the other two official languages of the EPO

	Fee code	EUR
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- (2a) by paying the fee for grant including the fee for publication:
minus any amount already paid (R. 71a(5) EPC):

007	915.00
	0.00

Total amount:	915.00
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- (3) by paying additional claims fees under Rule 71(4) EPC;
number of claims fees payable: 0
minus any amount already paid (R. 71a(5) EPC):

016	0.00
	0.00

Total amount:	0.00
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Important: If the translations of the claims and fees have already been filed and paid respectively in reply to a previous communication under Rule 71(3) EPC, e.g. in the case of resumption of examination after approval (see Guidelines C-V, 6), **agreement as to the text to be granted** (R. 71a(1) EPC) must be expressed within the same time limit (e.g. by approving the text and verifying the bibliographic data, by confirming that grant proceedings can go ahead with the documents on file and/or by stating which translations of the claims already on file are to be used).

Note 1: See "Important notes concerning fee payments" below.

Note 2: Any overpaid "minus" amounts will be refunded when the decision to grant (EPO Form 2006A) has been issued.

Note 3: For the calculation of the grant fee under Art. 2(2), No. 7, RFees (old fee structure), the number of pages is determined on the basis of a clean copy of the application documents, in which text deleted as a result of any amendments by the Examining Division is not shown. Such clean copy is made available via on-line file inspection only.

2.2 OR, in the case of disapproval, to request reasoned amendments or corrections to the text communicated above or keep to the latest text submitted by you (R. 71(6) EPC).

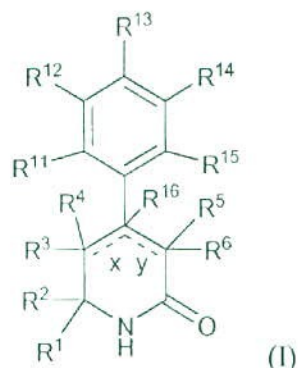
In this case the translations of the claims and fee payments mentioned under point 2.1 above are NOT due.

The terms "amendment(s)" and "correction(s)" refer only to amendments or corrections of the application documents and not of other documents (e.g. bibliographic data, the designation of the inventor, etc.).

If filing amendments, you must identify them and indicate the basis for them in the application as filed. Failure to meet either requirement may lead to a communication from the Examining Division requesting that you correct this deficiency (R. 137(4) EPC).

Claims:

1. A compound of Formula (I):



5 or a stereoisomer, a tautomer, or a pharmaceutically acceptable salt thereof, wherein:

--- designates a single or double bond;

x and y can be both a single bond; when x is a double bond, then y is a single bond and R^4 and R^{16} are absent; when y is a double bond, then x is a single bond and R^5 and R^{16} are absent;

10 R^1 is independently selected from the group consisting of: $-\text{CONH}(\text{C}_{4-18} \text{ alkyl})$, $-\text{CONHC}_{2-8} \text{ haloalkyl}$, $-\text{CONH}(\text{CH}_2)_{1-8} \text{Ph}$, $-\text{CONHCH}_2\text{COC}_{2-8} \text{ alkyl}$, $-(\text{CH}_2)_m-(\text{C}_{3-10} \text{ carbocycle substituted with 0-2 } R^b \text{ and 0-2 } R^g)$, $-(\text{CH}_2)_m-(5\text{- to } 6\text{-membered heteroaryl comprising: carbon atoms and 1-4 heteroatoms selected from N, NR}^c, \text{O and S; wherein said heteroaryl is substituted with 0-1 } R^b \text{ and 0-2 } R^g)$, and a

15 $\text{C}_{1-12} \text{ hydrocarbon chain substituted with 0-3 } R^a$; wherein said hydrocarbon chain may be straight or branched, saturated or unsaturated;

R^2 is independently selected from the group consisting of: $\text{C}_{1-4} \text{ alkyl}$, $\text{C}_{3-4} \text{ cycloalkyl}$, and $\text{C}_{1-4} \text{ haloalkyl}$;

R^3 is independently selected from the group consisting of: H, F, Cl, $\text{C}_{1-4} \text{ alkyl}$ and

20 CN;

R^4 and R^5 are independently selected from the group consisting of: H, F, Cl, and $\text{C}_{1-4} \text{ alkyl}$;

when x is a single bond, R^3 and R^4 may be combined with the carbon atom to which they are attached to form a 3- to 6-membered carbocycle;

R^6 is independently selected from the group consisting of: H, halo, C_{1-4} alkyl, NO_2 , R^c , $-(CH_2)_n-(X)_l-(CH_2)_m R^c$, NH_2 , $-CONH(C_{1-6}$ alkyl), $-NHCOX_1SO_2R^j$, $-NHCOCH_2PO(OEt)_2$, $-NHCOCOR^j$, $-NHCOCH(OH)R^j$, $-NHCOCH_2COR^j$, $-NHCONHR^j$, and $-OCONR^fR^j$;

- 5 X is independently selected from the group consisting of: O, S, NH, CONH, and NHCO;

X_1 is independently C_{1-4} hydrocarbon chain optionally substituted with C_{1-4} alkyl or C_{3-4} cycloalkyl;

- 10 when y is a single bond, R^5 and R^6 may be combined with the carbon atom to which they are attached to form a 3- to 6-membered carbocycle;

R^{11} , R^{12} , R^{13} , R^{14} and R^{15} are independently selected from the group consisting of: H, halo, C_{1-4} alkyl substituted with 0-2 R^i , C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, $-(CH_2)_m-C_{3-6}$ cycloalkyl, CN, NR^fR^j , OR^j , SR^j , $NHCO_2(C_{1-4}$ alkyl), $NHSO_2(C_{1-4}$ alkyl), and a 4- to 6-membered heterocycle comprising: carbon atoms and

- 15 1-4 heteroatoms selected from N, NR^c , O, and S;

alternatively, R^{11} and R^{12} , together with the carbon atoms to which they are attached, combine to form a 5- to 6-membered carbocyclic ring or a 5- to 6-membered heterocyclic ring comprising: carbon atoms and 1-3 heteroatoms selected from N, NR^c , O, and S;

- 20 alternatively, R^{12} and R^{13} , together with the carbon atoms to which they are attached, combine to form a 5- to 6-membered carbocyclic ring or a 5- to 6-membered heterocyclic ring comprising: carbon atoms and 1-3 heteroatoms selected from N, NR^c , O, and S;

R^{16} is independently selected from the group consisting of: H and C_{1-4} alkyl;

- 25 R^a is, at each occurrence, independently selected from the group consisting of: halo, OH, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, $N(C_{1-4}$ alkyl) $_2$, $-(CH_2)_n-(X)_l-(CH_2)_m R^c$, and $-(CH_2)_n-(CH_2O)_m-(CH_2)_n R^f$;

R^b is, at each occurrence, independently selected from the group consisting of: halo, OH, C_{1-10} alkyl, C_{1-10} alkoxy, C_{1-10} haloalkyl, C_{1-10} haloalkoxy, C_{1-10} alkylthio,

C_{1-10} haloalkylthio, $N(C_{1-4} \text{ alkyl})_2$, $-CONH(CH_2)_{4-20}H$, $-O(CH_2)_sO(C_{1-6} \text{ alkyl})$, R^c ,
 $-(CH_2)_n-(X)_t-(CH_2)_mR^c$, and $-(CH_2)_n-(CH_2O)_m-(CH_2)_nR^f$;

R^c is, at each occurrence, independently selected from the group consisting of:
 C_{3-6} cycloalkyl substituted with 0-2 R^d , C_{3-6} cycloalkenyl substituted with 0-2 R^d ,

- 5 $-(CH_2)_m$ -(phenyl substituted with 0-3 R^d), and a 5- to 6-membered heterocycle comprising: carbon atoms and 1-4 heteroatoms selected from N, NR^c , O, and S; wherein said heterocycle is substituted with 0-2 R^d ;

R^d is, at each occurrence, independently selected from the group consisting of:
halo, OH, CN, NO_2 , C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, tetrazolyl,

- 10 OBn and phenyl substituted with 0-2 R^h ;

R^e is, at each occurrence, independently selected from the group consisting of: H, C_{1-8} alkyl, C_{1-8} haloalkyl, benzyl optionally substituted with C_{1-4} alkoxy, $CO(C_{1-4} \text{ alkyl})$ and COBn;

R^f is, at each occurrence, independently selected from the group consisting of: H

- 15 and

C_{1-4} alkyl;

R^g , R^h and R^i are, at each occurrence, independently selected from the group consisting of: halo, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, and C_{1-4} haloalkoxy;

R^j is, at each occurrence, independently selected from the group consisting of:

- 20 C_{1-4} alkyl,

C_{3-4} cycloalkyl and phenyl;

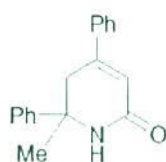
n , at each occurrence, is independently 0 or 1;

m , at each occurrence, is independently 0, 1, 2, 3, or 4

s , at each occurrence, is independently 1, 2, or 3; and

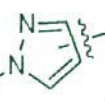
- 25 t , at each occurrence, is independently 0 or 1;

provided that the following compound is excluded:



2. A compound according to claim 1, wherein:

R^1 is independently selected from the group consisting of: $-\text{CONHC}_{4-18}$ alkyl, $-\text{CONH}(\text{CH}_2)_{1-8}$ Ph, C_{1-12} alkyl substituted with 0-2 R^a , C_{1-12} alkenyl substituted with 0-2 R^a , C_{1-12} alkynyl substituted with 0-2 R^a , $-(\text{CH}_2)_m$ -(phenyl substituted with 0-1 R^b and 0-2 R^g), $-(\text{CH}_2)_m$ -(C_{3-6} cycloalkyl substituted with 0-1 R^b), and $-(\text{CH}_2)_m$ -(5- to 6-membered heteroaryl substituted with 0-1 R^b and 0-2 R^g), wherein said heteroaryl is

selected from: pyridyl, oxazolyl, thiazolyl and $\text{Re}-\text{N}$ 

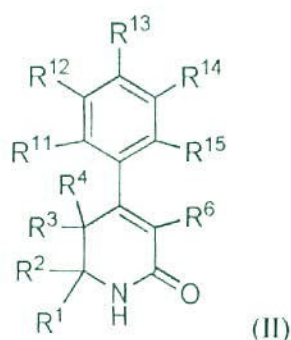
3. A compound according to claim 1 or claim 2, wherein:

10 R^{11} and R^{15} are independently selected from the group consisting of: H, C_{1-4} alkyl and halo;

R^{12} and R^{14} are independently selected from the group consisting of: H, halo, C_{1-4} alkyl and C_{1-4} alkoxy; and

15 R^{13} is independently selected from the group consisting of: H, halo, C_{1-4} alkyl substituted with 0-1 R^i , C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, $-(\text{CH}_2)_m$ - C_{3-4} cycloalkyl, CN, NR^fR^j , SR^j , $\text{NHCO}_2(\text{C}_{1-4}$ alkyl), $\text{NHSO}_2(\text{C}_{1-4}$ alkyl), and a 4- to 6-membered heterocycle comprising: carbon atoms and 1-4 heteroatoms selected from N, NR^e , O, and S.

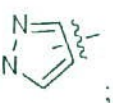
20 4. A compound according to any one of claims 1 to 3, wherein the compound is of Formula (II):



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

5. A compound according to any one of claims 1 to 4, wherein:

R^1 is independently selected from the group consisting of: C_{1-6} alkyl, C_{3-6} cycloalkyl, $-\text{CONHC}_{4-18}$ alkyl, $-\text{CONHC}_{2-8}$ haloalkyl, $-\text{CONH}(\text{CH}_2)_{1-8}$ Ph, $-(\text{CH}_2)_m$ -(phenyl substituted with 1 R^b and 0-2 R^g), and a 5- to 6-membered heteroaryl substituted with 0-1 R^b and 0-2 R^g , wherein said heteroaryl is selected from: pyridyl,

oxazolyl, thiazolyl and R^e -;

R^2 is independently selected from the group consisting of: C_{1-4} alkyl and C_{1-4} haloalkyl;

R^3 is independently selected from the group consisting of: H and F;

10 R^4 is independently selected from the group consisting of: H and F;

R^6 is independently selected from the group consisting of: NH_2 , $-\text{CONH}(C_{1-6}$ alkyl), R^c , $-(\text{CH}_2)_n$ -(X)- $(\text{CH}_2)_m R^c$, $-\text{NHCO}(\text{CH}_2)\text{SO}_2(C_{1-4}$ alkyl), $-\text{NHCOCH}_2\text{PO}(\text{OEt})_2$, $-\text{NHCOCO}(C_{1-4}$ alkyl), $-\text{NHCOCH}(\text{OH})(C_{1-4}$ alkyl), $-\text{NHCOCH}_2\text{CO}(C_{1-4}$ alkyl), $-\text{NHCONH}(C_{1-4}$ alkyl), and $-\text{OCONH}(C_{1-4}$ alkyl);

15 R^{11} and R^{15} are independently selected from the group consisting of: H, C_{1-4} alkyl and halo;

R^{12} and R^{14} are independently selected from the group consisting of: H, halo, C_{1-4} alkyl and C_{1-4} alkoxy;

20 R^{13} is independently selected from the group consisting of: H, halo, C_{1-4} alkyl substituted with 0-1 C_{1-4} alkoxy, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, $-(\text{CH}_2)_m$ - C_{3-4} cycloalkyl, CN, $\text{N}(C_{1-4}$ alkyl) $_2$, $\text{NHCO}_2(C_{1-4}$ alkyl), $\text{NH}\text{SO}_2(C_{1-4}$ alkyl), pyrazolyl, and morpholinyl;

alternatively, R^{12} and R^{13} , together with the carbon atoms to which they are attached, combine to form a 5- to 6-membered carbocyclic ring or a 5- to 6-membered heterocyclic ring comprising: carbon atoms and 1-3 heteroatoms selected from N, NR^e , O, and S;

25 R^b is, at each occurrence, independently selected from the group consisting of: halo, OH, C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} haloalkyl, C_{1-10} haloalkoxy, $-\text{O}(\text{CH}_2)_s\text{O}(C_{1-6}$ alkyl),

$N(C_{1-4} \text{ alkyl})_2$, $-\text{CONH}(\text{CH}_2)_{6-20}\text{H}$, $-(\text{CH}_2)_m(\text{C}_{3-6} \text{ cycloalkyl})$, $-(\text{CH}_2)_m(\text{C}_{4-6} \text{ cycloalkenyl})$, $-\text{O}(\text{CH}_2)_m(\text{C}_{3-6} \text{ cycloalkyl})$, 4- C_{1-4} alkoxy-Ph, $-\text{O}(\text{CH}_2)_m\text{Ph}$, morpholinyl, pyridyl, 2- C_{1-4} alkoxy-pyridin-5-yl, pyrimidinyl, pyrazinyl, and -O-pyrimidinyl;

R^g is, at each occurrence, independently selected from the group consisting of:

5 halo,

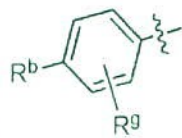
C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, and C_{1-4} haloalkoxy;

m , at each occurrence, is independently 0, 1, 2 or 3; and

s , at each occurrence, is independently 1, 2, or 3.

10 6. A compound according to any one of claims 1 to 5, wherein:

R^1 is independently selected from the group consisting of: C_{1-6} alkyl,



$-\text{CONHC}_{4-18} \text{ alkyl}$, $-\text{CONH}(\text{CH}_2)_{1-8}\text{Ph}$, and

R^6 is independently selected from the group consisting of: NH_2 , $-\text{CONH}(C_{1-6} \text{ alkyl})$,

$-\text{NHCOCH}_2\text{PO}(\text{OEt})_2$, $-\text{NHCO}(\text{CH}_2)\text{SO}_2(C_{1-4} \text{ alkyl})$, R^c , OR^c , $-\text{CONHR}^c$, and

15 $-\text{NHCOR}^c$;

R^{12} is independently selected from the group consisting of: H, halo, C_{1-4} alkyl and C_{1-4} alkoxy;

R^{13} is independently selected from the group consisting of: H, halo, C_{1-4} alkyl substituted with 0-1 C_{1-4} alkoxy, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy,

20 $-(\text{CH}_2)_m-\text{C}_{3-4} \text{ cycloalkyl}$, CN, $N(C_{1-4} \text{ alkyl})_2$, $\text{NHCO}_2(C_{1-4} \text{ alkyl})$, $\text{NHISO}_2(C_{1-4} \text{ alkyl})$, pyrazolyl, and morpholinyl;

alternatively, R^{12} and R^{13} , together with the carbon atoms to which they are attached, combine to form a 5- to 6-membered carbocyclic ring or a 5- to 6-membered saturated heterocyclic ring comprising: carbon atoms and 1-2 oxygen atoms;

25 R^{14} is independently selected from the group consisting of: H and C_{1-4} alkoxy;

R^b is, at each occurrence, independently selected from the group consisting of: halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-10} haloalkoxy, $-\text{O}(\text{CH}_2)_s\text{O}(C_{1-6} \text{ alkyl})$, $-\text{CONH}(\text{CH}_2)_{6-20}\text{H}$, $-(\text{CH}_2)_m(\text{C}_{3-6} \text{ cycloalkyl})$, $-(\text{CH}_2)_m(\text{C}_{4-6} \text{ cycloalkenyl})$,

-O(CH₂)_m(C₃₋₆ cycloalkyl), phenoxy, benzoxy, morpholinyl, 2-C₁₋₄ alkoxy-pyridin-5-yl, pyrimidin-5-yl, pyrazin-2-yl and -O-pyrimidinyl; and

- R^c is, at each occurrence, independently selected from the group consisting of: C₃₋₆ cycloalkyl substituted with 0-2 R^d, -(CH₂)_m-(phenyl substituted with 0-3 R^d), and a
5 heteroaryl selected from: oxazolyl, isoxazolyl, thiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, and pyrazinyl; wherein said heteroaryl is substituted with 0-2 R^d.

7. A compound according to any one of claims 1-6, wherein:
- 10 R² is independently selected from the group consisting of: CF₃ and Me;
R³ is independently selected from the group consisting of: H and F;
R⁴ is independently selected from the group consisting of: H and F;
R⁶ is independently selected from the group consisting of: NH₂, -CONHMe, OPh,
-CONH(cyclopropyl), -CONH(cyclobutyl), -CONH(cyclopentyl), -CONH(cyclohexyl),
15 -CONHPh, -CONH(4-F-Ph), -CONH(2-Cl-Ph), -CONH(4-Cl-Ph), -CONH(4-Me-Ph),
-CONH(4-OH-Ph), -CONH(3-OMe-Ph), -CONH(4-OMe-Ph), -CONH(4-CF₃-Ph),
-CONH(4-OCF₃-Ph), -CONH(1-Me-pyrazol-3-yl), -CONH(4-(1H-tetrazol-2-yl)-Ph),
-CONH(4-(2H-tetrazol-5-yl)-Ph), -CONH(3-F-4-Me-Ph), -CONH(3-F-4-OMe-Ph),
-CONH(CH₂)₂Ph, -CONH(5-OMe-pyrid-2-yl), -CONH(6-OMe-pyrid-3-yl),
20 -CONH(5-OMe-pyrazin-2-yl), -CONH(6-OMe-pyridazin-3-yl), -NHCO(CH₂)SO₂Me,
-NHCOPh, -NHCO(2-Me-Ph), -NHCO(3-Me-Ph), -NHCO(4-Me-Ph), -NHCO(2-Cl-Ph),
-NHCO(3-Cl-Ph), -NHCO(2-Cl-4-F-Ph), -NHCO(2-Cl-5-F-Ph), -NHCO(isoxazol-5-yl),
-NHCO(3-Me-isoxazol-5-yl), -NHCO(4-Me-isoxazol-5-yl),
-NHCO(3-OMe-isoxazol-5-yl), -NHCO(3-Br-isoxazol-5-yl),
25 -NHCO(3-(2-Cl-Ph)-isoxazol-5-yl), -NHCO(3-(3-F-Ph)-isoxazol-5-yl),
-NHCO(3-OBn-isoxazol-5-yl), 1H-imidazol-1-yl, -NHCO(5-Me-1,3,4-oxadiazol-2-yl),
-NHCO(1-Me-1,2,3-triazol-4-yl), -NHCO(6-OMe-pyrid-3-yl),
-NHCO(6-Cl-pyridazin-3-yl), 5-CF₃-1,3,4-oxadiazol-2-yl, 1H-tetrazol-1-yl,
1H-tetrazol-3-yl, and 2H-tetrazol-5-yl;
- 30 R¹¹ and R¹⁵ are independently selected from the group consisting of: H, Me, F, and Cl;

R^{12} is independently selected from the group consisting of: H, F, Cl, Me and OMe;

R^{13} is independently selected from the group consisting of: H, F, Cl, Br, Me, OMe, OEt, CH_2OMe , CF_3 , CH_2CF_3 , $OCHF_2$, OCF_3 , CN, $N(Me)_2$, cyclopropyl and
5 cyclopropylmethyl;

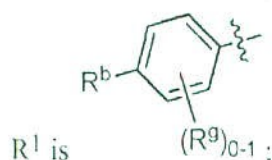
alternatively, R^{12} and R^{13} , together with the carbon atoms to which they are attached, combine to form a 5- to 6-membered carbocyclic ring or a 5- to 6-membered saturated heterocyclic ring comprising: carbon atoms and 1-2 oxygen atoms;

R^{14} is H;

10 R^b is, at each occurrence, independently selected from the group consisting of: n-pentyl, methoxy, n-butoxy, i-butoxy, i-pentoxo, $-O(CH_2)_{1-6}CF_3$, $-O(CH_2)_{1-4}CF_2CF_3$, $-CONH(CH_2)_{6-20}H$, cyclopropyl, cyclopent-1-en-1-yl, cyclohex-1-en-1-yl, $-O(CH_2)_2$ (cyclopentyl), phenoxy, benzoxy, pyrimidin-5-yl, pyrazin-2-yl and -O-pyrimidin-2-yl; and

15 R^g is F.

8. A compound according to Claim 4 or Claim 5, wherein:



R^2 is independently selected from CF_3 and CH_3 ;

20 R^6 is independently selected from: R^c , $-CONHR^c$, $-NHCOR^c$, and $-NHCOCH_2SO_2(C_{1-4} \text{ alkyl})$;

R^b is independently selected from: $-O(CH_2)_{1-6}CF_3$, $-O(CH_2)_{1-4}CF_2CF_3$, $-CONH(CH_2)_{6-20}H$, cyclopent-1-en-1-yl, cyclohex-1-en-1-yl, $-O(CH_2)_2$ (cyclopentyl), phenoxy, benzoxy, pyrimidin-5-yl, pyrazin-2-yl and -O-pyrimidin-2-yl;

25 R^c is, at each occurrence, independently selected from the group consisting of: $-(CH_2)_m$ -(phenyl substituted with 0-3 R^d), and a heteroaryl selected from: oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, and pyrazinyl; wherein said heteroaryl is substituted with 0-2 R^d ; and

R^d is, at each occurrence, independently selected from the group consisting of: halo, OH, CN, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, tetrazolyl and OBn.

- 5 9. A compound according to any of claims 1-6 or 8, wherein:

R^{13} is independently selected from the group consisting of: H, halo, C_{1-4} alkyl substituted with 0-1 C_{1-4} alkoxy, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, CN or C_{3-4} cycloalkyl.

- 10 10. A compound according to any one of claims 1-5, 8 or 9 wherein:



11. A compound according to any one of claims 1-10, wherein:

R^b is independently selected from: $-O(CH_2)_{1-6}CF_3$, and $-O(CH_2)_{1-4}CF_2CF_3$.

15

12. A compound according to any one of claims 1-5, wherein:

R^6 is independently 5-membered nitrogen heteroaryl.

13. A compound according to any one of claims 1-12, wherein:

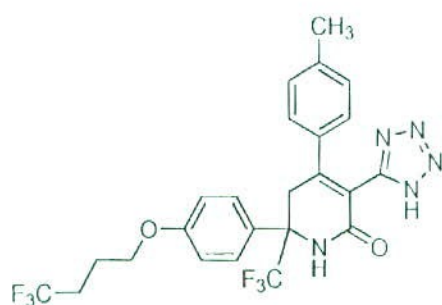
- 20 R^6 is independently: 1*H*-imidazol-1-yl, 1*H*-tetrazol-1-yl, 1*H*-tetrazol-3-yl, or 2*H*-tetrazol-5-yl.

14. A compound according to claim 1, wherein the compound is selected from:

- 25 (S)-3-(1*H*-tetrazol-5-yl)-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1*H*)-one,
(S)-N-(4-methoxyphenyl)-2-oxo-4-(p-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide,
(S)-3-(2*H*-tetrazol-5-yl)-4-(p-tolyl)-6-(4-((6,6,6-trifluorohexyl)oxy)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1*H*)-one,

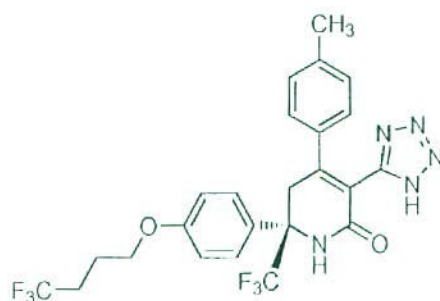
- (*S*)-2-oxo-4-(*p*-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-*N*-(4-(trifluoromethoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide,
(*S*)-*N*-(6-methoxypyridin-3-yl)-2-oxo-4-(*p*-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide,
5 (*S*)-*N*-cyclopropyl-2-oxo-4-(*p*-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide,
(*S*)-*N*-(4-hydroxyphenyl)-2-oxo-4-(*p*-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide,
(*S*)-4-(4-(difluoromethoxy)phenyl)-3-(1*H*-tetrazol-1-yl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1*H*)-one,
10 (*S*)-3-methyl-*N*-(2-oxo-4-(*p*-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridin-3-yl)isoxazole-5-carboxamide,
(*S*)-5-methyl-*N*-(2-oxo-4-(*p*-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridin-3-yl)-1,3,4-oxadiazole-2-carboxamide,
15 *N*²-heptyl-*N*⁵-(4-methoxyphenyl)-2-methyl-6-oxo-4-(*p*-tolyl)-1,2,3,6-tetrahydropyridine-2,5-dicarboxamide,
(*S*)-3-(1*H*-tetrazol-1-yl)-4-(*p*-tolyl)-6-(4-((6,6,6-trifluorohexyl)oxy)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1*H*)-one,
(*S*)-4-(5,6,7,8-tetrahydronaphthalen-2-yl)-3-(1*H*-tetrazol-5-yl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1*H*)-one,
20 (*S*)-2-(methylsulfonyl)-*N*-(2-oxo-4-(*p*-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridin-3-yl)acetamide,
(*S*)-3-(1*H*-tetrazol-5-yl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-4-(4-(2,2,2-trifluoroethyl)phenyl)-6-(trifluoromethyl)-5,6-dihydropyridin-2(1*H*)-one, and
25 (*S*)-*N*-(5-methoxypyrazin-2-yl)-2-oxo-4-(*p*-tolyl)-6-(4-(4,4,4-trifluorobutoxy)phenyl)-6-(trifluoromethyl)-1,2,5,6-tetrahydropyridine-3-carboxamide;
or a tautomer, or a pharmaceutically acceptable salt thereof.

15. A compound according to claim 1, wherein the compound has the following
30 formula:



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

16. A compound according to claim 15, wherein the compound has the following
5 formula:



or a tautomer, or a pharmaceutically acceptable salt thereof.

17. A pharmaceutically acceptable salt of the compound according to claim 15 or
10 claim 16.
18. A pharmaceutical composition, comprising: a pharmaceutically acceptable carrier
and a compound of any one of claims 1 to 17, or a stereoisomer, a tautomer, or a
pharmaceutically acceptable salt thereof, and optionally one or more additional
15 therapeutic agents.
19. The pharmaceutical composition according to claim 18, further comprising one or
more other suitable therapeutic agents selected from: anti-diabetic agents,
anti-hyperglycemic agents, anti-hyperinsulinemic agents, anti-retinopathic agents,
20 anti-neuropathic agents, anti-nephropathic agents, anti-atherosclerotic agents,
anti-ischemic agents, anti-hypertensive agents, anti-obesity agents, anti-dyslipidemic
agents, anti-hyperlipidemic agents, anti-hypertriglyceridemic agents,

anti-hypercholesterolemic agents, anti-restenotic agents, lipid lowering agents, anorectic agents, and appetite suppressants.

- 5 20. The pharmaceutical composition according to claim 18, further comprising one or more other suitable therapeutic agents selected from: a dipeptidyl peptidase-IV inhibitor, a sodium-glucose transporter-2 inhibitor and a 11b-HSD-1 inhibitor.

- 10 21. A compound of any one of claims 1-17, or a stereoisomer, a tautomer, a pharmaceutically acceptable salt or a solvate thereof, or a composition according to any of claims 18-20, for use in therapy, optionally simultaneously, separately or sequentially with one or more additional therapeutic agents.

- 15 22. A compound of any one of claims 1 to 17, or a stereoisomer, a tautomer, a pharmaceutically acceptable salt or a solvate thereof, or a composition according to any of claims 18-20, for use in preventing, modulating or treating diabetes, hyperglycemia, impaired glucose tolerance, gestational diabetes, insulin resistance, hyperinsulinemia, nonalcoholic fatty liver disease (NAFLD) including nonalcoholic steatohepatitis (NASH), retinopathy, neuropathy, nephropathy, delayed wound healing, atherosclerosis and its
20 sequelae, abnormal heart function, myocardial ischemia, stroke, Metabolic Syndrome, hypertension, obesity, dyslipidemia, dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low high-density lipoprotein (HDL), high low-density lipoprotein (LDL), non-cardiac ischemia, lipid disorders, and glaucoma, optionally for use simultaneously, separately or sequentially with one or more additional therapeutic agents.