

Clarke, Modet & C<sup>o</sup>  
COLOMBIA

ESCOBAR - URIBE ASOCIADOS  
Intellectual Property

148

As. 3035/PCT.

**SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO  
DIVISIÓN DE NUEVAS CREACIONES**

**E. S. D.**

Ref.: Expediente No. **07-028.506**  
Solicitud de Patente a nombre de  
**Janssen Pharmaceutica N.V.**

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-028506- -00002-0000

Fecha: 2008-01-21 16:35:02 Dep. 2020 NUECREACIONES  
Tra 11 PATENTE Y... Eje: 378 FASE NACIONAL I  
Act: 538 PETICION Folios: 2

Yo, **JIMENA ESCOBAR URIBE**, identificada como aparece al pie de mi firma, domiciliada en Bogotá, en la Carrera 11 No. 86-53, piso 6, obrando como apoderada de la sociedad **Janssen Pharmaceutica N.V.**, con domicilio en Beerse, Bélgica, solicitante de la patente de la referencia, pido a usted que se proceda a examinar si la invención, cuya patente se tramita en el expediente de la referencia, es patentable.

Adjunto al presente memorial el recibo No. 08 - 1,895 de 8 de enero de 2008, por la suma de \$420.000.00, con lo cual queda cubierta la tasa oficial correspondiente a dicho estudio.

Señor Superintendente,

  
**JIMENA ESCOBAR URIBE**  
C.C.39.779.452 de Usaquén  
T.P. 68.228

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 08 - 1,895  
FECHA : ENERO 8 DE 2008

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-028506- -00002-0000

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Act. 538 PETICION Folios: 2

\*\*\*\*\* CONSIGNACION \*\*\*\*\*

| DEPOSITANTE               | TIPO PAGO    | BANCO           | CUENTA    | Nº. PAGO | FECHA PGO  | Vr. PAGO      |
|---------------------------|--------------|-----------------|-----------|----------|------------|---------------|
| CLARKE MODET Y CO. COLOMB | CONSIGNACION | BANCO DE BOGOTA | 062754387 | 2662954  | 08/01/2008 | 40,235,000.00 |

\*\*\*\*\* CONCEPTO \*\*\*\*\*

| CANT. | RENTISTICO  | CONCEPTO                             | TOTAL CONCEPTO |
|-------|-------------|--------------------------------------|----------------|
| 1     | 50005-01-01 | SOLICITUDES                          |                |
|       |             | 85 EXAMEN DE PATENTABILIDAD DE INVEN | 420,000.00     |
|       |             | TOTAL :                              | \$ 420,000.00  |

SON: CUATROCIENTOS VEINTE MIL PESOS

RESPONSABLE : \_\_\_\_\_

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

3035

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

PA 150

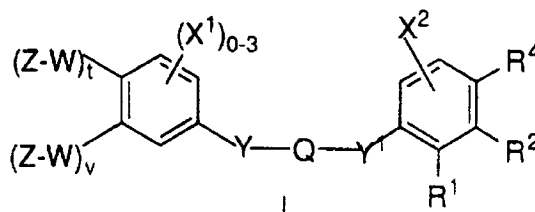
## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |  |           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>(51) International Patent Classification <sup>6</sup> :</b><br><b>C07C 63/06, 65/30, 65/32, 65/38, 65/40, 65/42, 69/12, 69/14, 69/612, 233/65, 251/10, 251/24, 257/06, C07D 257/06</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |  | <b>A1</b> | <b>(11) International Publication Number:</b> <b>WO 97/28115</b><br><b>(43) International Publication Date:</b> 7 August 1997 (07.08.97)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <b>(21) International Application Number:</b> PCT/US97/01689<br><b>(22) International Filing Date:</b> 31 January 1997 (31.01.97)<br><b>(30) Priority Data:</b><br>60/011,093 2 February 1996 (02.02.96) US<br>9604231.2 28 February 1996 (28.02.96) GB<br>60/034,435 23 December 1996 (23.12.96) US<br><b>(71) Applicant (for all designated States except US):</b> MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).<br><b>(72) Inventors; and</b><br><b>(75) Inventors/Applicants (for US only):</b> ADAMS, Alan, D. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). DOEBBER, Thomas, W. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). BERGER, Joel, P. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). BERGER, Gregory, D. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). JONES, Anthony, B. [GB/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). VON LANGEN, Derek [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). LEIBOWITZ, Mark, D. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). |  |           | <b>(US).</b> MOLLER, David, E. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). OLSON, John, T. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). PATCHETT, Arthur, A. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). SAHOO, Soumya, P. [IN/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). TOLMAN, Richard, L. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). TOUPENCE, Richard, B. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). WALSH, Thomas, F. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).<br><b>(74) Common Representative:</b> MERCK & CO., INC.; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).<br><b>(81) Designated States:</b> AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).<br><b>Published</b><br><i>With international search report.</i><br><i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> |
| <b>(54) Title:</b> ANTIDIABETIC AGENTS<br><b>(57) Abstract</b><br><p>The instant invention is concerned with acetylphenols which are useful as antiobesity and antidiabetic compounds. Compositions and methods for the use of the compounds in the treatment of diabetes and obesity and for lowering or modulating triglyceride levels and cholesterol levels or raising high density lipoprotein levels or for increasing gut motility or for treating atherosclerosis are also disclosed.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |  |           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |

- 152 -

WHAT IS CLAIMED IS:

1. A compound having the formula I:



or a pharmaceutically acceptable salt thereof, wherein:

R is selected from the group consisting of H, C<sub>1-6</sub> alkyl, C<sub>5-10</sub> aryl, and C<sub>5-10</sub> heteroaryl, said alkyl, aryl and heteroaryl optionally substituted with 1 to 3 groups of R<sup>a</sup>;

R<sup>1</sup> is selected from a group consisting of: H, C<sub>1-15</sub> alkyl, C<sub>2-15</sub> alkenyl, C<sub>2-15</sub> alkynyl and C<sub>3-10</sub> cycloalkyl, said alkyl, alkenyl, alkynyl, and cycloalkyl optionally substituted with 1 to 3 groups of R<sup>a</sup>;

R<sup>2</sup> is selected from a group consisting of: H, C<sub>1-15</sub> alkyl, acyl, C<sub>2-15</sub> alkenyl, OR<sup>3</sup>, CO<sub>2</sub>alkyl, C(O)R<sup>3</sup>, OH, -OC(O)R<sup>3</sup>, C<sub>2-15</sub> alkynyl, C<sub>5-10</sub> aryl, C<sub>5-10</sub> heteroaryl, said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 groups of R<sup>a</sup>;

R<sup>3</sup> is selected from a group consisting of: H, NHR<sup>1</sup>, NHacyl, C<sub>1-15</sub> alkyl, C<sub>2-15</sub> alkenyl, C<sub>1-15</sub> alkoxy, CO<sub>2</sub>alkyl, OH, C<sub>2-15</sub> alkynyl, C<sub>5-10</sub> aryl, C<sub>5-10</sub> heteroaryl said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 groups of R<sup>a</sup>;

R<sup>4</sup> is selected from the group consisting of: R<sup>2</sup>, -B-R<sup>5</sup> or  $\overset{\text{R}^3}{\sim}\text{C}=\text{Y}^2$ , with the proviso that when (Z-W-) is Z-CR<sup>6</sup>R<sup>7</sup>, Y is O and R<sup>4</sup> is R<sup>2</sup>, then R<sup>2</sup> is not acetyl, H, alkyl, alkoxy or aryl; or when (Z-W-) is Z-

CR<sup>6</sup>R<sup>7</sup>, Y is O and R<sup>4</sup> is  $\overset{\text{R}^3}{\sim}\text{C}=\text{Y}^2$  then Y<sup>2</sup> is not O, or when

152

- 154 -

$Y^1$  is selected from the group consisting of: O, NR and C;

$Y^2$  is selected from the group consisting of: O, N(C<sub>1-15</sub>) alkyl, N(CO<sub>2</sub>)alkyl, N-Oalkyl, N-Oacyl and N-OH, with the proviso that if  $Y^2$  is O and  $R^3$  is CH<sub>3</sub> then n is 2;

Z is selected from the group consisting of: CO<sub>2</sub>R<sup>3</sup>, R<sup>3</sup>CO<sub>2</sub>R<sup>3</sup>, CONHSO<sub>2</sub>R, CONH<sub>2</sub> and 5-(1H-tetrazole);

t and v are independently 0 or 1 such that  $t + v = 1$

Q is a saturated or unsaturated straight chain hydrocarbon containing 2-4 carbon atoms and

p is 0-2.

2. A compound of Claim 1 where  $X^1$  &  $X^2$  are independently H or halo.

3. A compound of Claim 1 where Y is O.

4. A compound of Claim 1 where Y is S(O)<sub>p</sub>, wherein p is 0-2.

5. A compound of Claim 1 where Y is -CH<sub>2</sub>-.

6. A compound of Claim 1 where Y is -CO-.

7. A compound of Claim 1 where Y is -NH-.

8. A compound of Claim 1 where Y is NHSO<sub>2</sub> or SO<sub>2</sub>NH.

9. A compound of Claim 1 where Y is C(O)NH.

- 153 -

(Z-W-) is  $Z-CR^6R^7-$ , or  $Z-\overset{\overset{R^6}{\diagup}}{\underset{\diagdown}{C}}-R^8-$ , where  $R^8$  is O, Y is S or O and  $R^4$  is -B- $R^5$ , then B is not O or S;

$R^5$  is selected from the group consisting of: C5-10 aryl and C5-10 heteroaryl, said aryl and heteroaryl optionally substituted with 1 to 3 groups of  $R^a$ ;

B is selected from the group consisting of: O, S(O)<sub>p</sub> and NR<sup>1</sup>;

(Z-W-) is  $Z-CR^6R^7-$ ,  $Z-CH=CH-$ , or  $Z-\overset{\overset{R^6}{\diagup}}{\underset{\diagdown}{C}}-R^8-$ ;

$R^8$  is selected from the group consisting of  $CR^6R^7$ , O, NR<sup>6</sup>, and S(O)<sub>p</sub>;

$R^6$  and  $R^7$  are independently selected from the group consisting of H, C<sub>1-6</sub> alkyl;

X<sup>1</sup> and X<sup>2</sup> are independently selected from a group consisting of: H, OH, C<sub>1-15</sub> alkyl, C<sub>2-15</sub> alkenyl, C<sub>2-15</sub> alkynyl, halo, OR<sup>3</sup>, C<sub>5-10</sub> aryl, C<sub>5-10</sub> aralkyl, C<sub>5-10</sub> heteroaryl and C<sub>1-10</sub> acyl, said alkyl, alkenyl, alkynyl, aryl and heteroaryl optionally substituted with 1 to 3 groups of  $R^a$ ;

$R^a$  represents a member selected from the group consisting of: halo, aryl, acyl, heteroaryl, CF<sub>3</sub>, OCF<sub>3</sub>, -O-, CN, NO<sub>2</sub>, R<sup>3</sup>, OR<sup>3</sup>, SR<sup>3</sup>, S(O)R<sup>3</sup>, SO<sub>2</sub>R<sup>3</sup>, NR<sup>3</sup>R<sup>3</sup>, NR<sup>3</sup>COR<sup>3</sup>, NR<sup>3</sup>CO<sub>2</sub>R<sup>3</sup>, NR<sup>3</sup>CON(R<sup>3</sup>)<sub>2</sub>, NR<sup>3</sup>SO<sub>2</sub>R<sup>3</sup>, COR<sup>3</sup>, CO<sub>2</sub>R<sup>3</sup>, CON(R<sup>3</sup>)<sub>2</sub>, SO<sub>2</sub>N(R<sup>3</sup>)<sub>2</sub>, OCON(R<sup>3</sup>)<sub>2</sub> said aryl and heteroaryl optionally substituted with 1 to 3 groups of halo or C<sub>1-6</sub> alkyl;

Y is selected from the group consisting of: S(O)<sub>p</sub>, -CH<sub>2</sub>-, -C(O)-, -C(O)NH-, -NR-, -O-, -SO<sub>2</sub>NH-, -NHSO<sub>2</sub>;

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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau(43) International Publication Date  
15 August 2002 (15.08.2002)

PCT

(10) International Publication Number  
WO 02/062774 A1(51) International Patent Classification<sup>7</sup>: C07D 277/26,  
A61K 31/10, A61P 3/10, 3/04, 3/06, C07D 277/24

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(21) International Application Number: PCT/US01/49230

(22) International Filing Date:  
19 December 2001 (19.12.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0031107.6 20 December 2000 (20.12.2000) GB

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

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

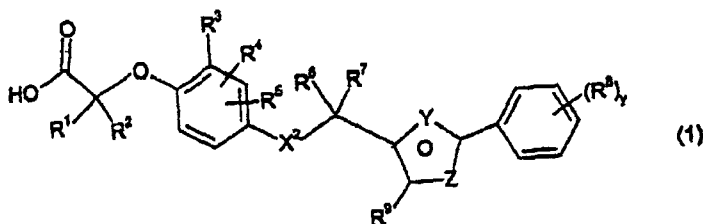
## Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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

WO 02/062774 A1

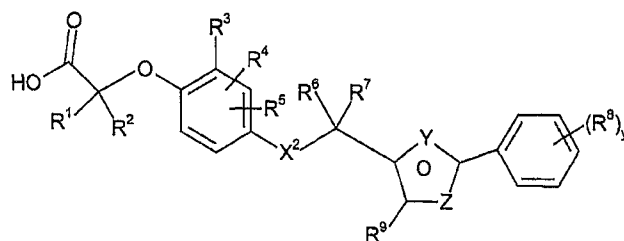
(54) Title: THIAZOLE DERIVATIVES FOR TREATING PPAR RELATED DISORDERS



(57) Abstract: The present invention provides compounds of formula (I). These compounds are used for the treatment of PPAR related diseases.

What is claimed is:

1. A compound of formula (I) or a pharmaceutically acceptable salt, solvate, or hydrolysable ester thereof, wherein:



(1)

$R^1$  and  $R^2$  are independently H or  $C_{1-3}$  alkyl, or  $R^1$  and  $R^2$  which are bonded to the same carbon atom may together with the carbon atom to which they are bonded form a 3-6 membered cycloalkyl ring, and at least one of  $R^1$  and  $R^2$  must be other than H;

$X^2$  is O, S, or  $(CR^{10}R^{11})_n$  where n is 1 or 2;

$R^3$ ,  $R^4$ , and  $R^5$  are independently H,  $C_{1-3}$ alkyl,  $OCH_3$ ,  $CF_3$ , allyl, or halogen;

$R^{10}$  and  $R^{11}$  are independently H, fluorine, or  $C_{1-6}$ alkyl;

one of Y and Z is N, the other is S or O;

$R^6$  and  $R^7$  are independently H, phenyl, benzyl, fluorine OH,  $C_{1-6}$  alkyl, allyl,  $R^6$  and  $R^7$  may, together with the carbon atom to which they are bonded, represent a carbonyl group;

$R^8$  is H,  $CF_3$  or  $CH_3$ ;

Each  $R^9$  is independently  $CF_3$ ,  $C_{1-3}$ alkyl,  $OCH_3$  or halogen;

y is 0, 1, 2, 3, 4, or 5.

2. A compound according to claim 1 wherein at least one of  $R^1$  and  $R^2$  is  $CH_3$ .

3. A compound according to claim 2 wherein  $R^1$  and  $R^2$  are both  $CH_3$ .

4. A compound according to any of claims 1-3 wherein  $X^2$  is O, S, or  $C(R^{10}R^{11})$ .

5. A compound according to claim 4 wherein  $X^2$  is O or S.

6. A compound according to any of claims 1-5 wherein Z is N.

7. A compound according to any of claims 1-6 wherein Y is S.