

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
15 May 2008 (15.05.2008)

PCT

(10) International Publication Number
WO 2008/057862 A3

(51) International Patent Classification:

C07C 235/36 (2006.01) **C07D 277/56 (2006.01)**
C07D 213/75 (2006.01) **C07D 277/60 (2006.01)**
C07D 231/40 (2006.01) **C07D 277/82 (2006.01)**
C07D 233/88 (2006.01) **C07D 285/08 (2006.01)**
C07D 239/42 (2006.01) **C07D 417/04 (2006.01)**
C07D 241/20 (2006.01) **C07D 417/10 (2006.01)**
C07D 263/48 (2006.01) **C07D 417/12 (2006.01)**
C07D 277/46 (2006.01) **C07D 285/135 (2006.01)**

TORTOLANI, David R. [US/US]; c/o Bristol-Myers Squibb Co., Route 206 & Province Line Road, Princeton, New Jersey 08543 (US). **DHAR, T.g. Murali** [US/US]; c/o Bristol-Myers Squibb Co., Route 206 & Province Line Road, Princeton, New Jersey 08543 (US).

(74) **Agents: DUNCAN, Laurelee A.** et al.; Bristol-Myers Squibb Company, P.O. Box 4000, Princeton, New Jersey 08543-4000 (US).

(21) International Application Number:

PCT/US2007/083094

(22) International Filing Date: 31 October 2007 (31.10.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/855,950 1 November 2006 (01.11.2006) US

(71) **Applicant (for all designated States except US): BRIS-TOL-MYERS SQUIBB COMPANY** [US/US]; Route 206 and Province Line Road, Princeton, New Jersey 08543-4000 (US).

(72) Inventors; and

(75) **Inventors/Applicants (for US only): YANG, Bingwei Vera** [US/US]; c/o Bristol-Myers Squibb Co., Route 206 & Province Line Road, Princeton, New Jersey 08543 (US). **DOWEYKO, Lidia M.** [US/US]; c/o Bristol-Myers Squibb Co., Route 206 & Province Line Road, Princeton, New Jersey 08543 (US). **VACCARO, Wayne** [US/US]; c/o Bristol-Myers Squibb Co., Route 206 & Province Line Road, Princeton, New Jersey 08543 (US). **HUYNH, Tram N.** [US/US]; c/o Bristol-Myers Squibb Co., Route 206 & Province Line Road, Princeton, New Jersey 08543 (US).

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

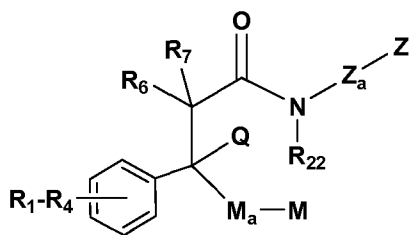
(84) **Designated States (unless otherwise indicated, for every kind of regional protection available):** ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

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

(88) Date of publication of the international search report:

16 October 2008

(54) **Title:** MODULATORS OF GLUCOCORTICOID RECEPTOR, AP-I, AND/OR NF-KB ACTIVITY AND USE THEREOF

(57) **Abstract:** Novel non-steroidal compounds are provided which are useful in treating diseases associated with modulation of the glucocorticoid receptor, AP-I, and/or NF-KB activity including inflammatory and immune diseases, obesity and diabetes having the structure of formula (I) an enantiomer, diastereomer, tautomer, solvate (e.g. a hydrate), or a pharmaceutically-acceptable salt, thereof, wherein: M is selected from alkyl, substituted alkyl, cycloalkyl, aryl, heterocyclo, and heteroaryl, provided that if M is alkyl then R₆ and R₇ taken together with the carbon atom to which they are both attached are selected from a group other than cycloalkyl; Q is selected from (i) hydrogen, C₁-C₄ alkyl, and substituted C₁-C₄ alkyl; or (ii) Q and R₆ are combined with the carbon atoms to which they

are attached to form a 3- to 6-membered cycloalkyl; or (iii) Q and M_aM are combined with the carbon atom(s) to which they are attached to form a 3- to 7-membered ring containing 1-2 heteroatoms which are independently selected from the group consisting of O, S, SO₂, and N which ring may be optionally substituted with 0-2 R₅ groups or carbonyl; Z is selected from cycloalkyl, heterocyclo, aryl, or heteroaryl; and M_a, Z, R₁, R₂, R₃, R₄, R₆, R₇, and R₂₂ are as defined herein. Also provided are pharmaceutical compositions and methods of treating metabolic and inflammatory- or immune-associated diseases or disorders using said compounds.



WO 2008/057862 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/083094

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07C235/36	C07D213/75	C07D231/40	C07D233/88	C07D239/42
C07D241/20	C07D263/48	C07D277/46	C07D277/56	C07D277/60
C07D277/82	C07D285/08	C07D417/04	C07D417/10	C07D417/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07C C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/005261 A (SANKYO AGRO COMPANY LTD [JP]; ITO HIROYUKI [JP]; IMAI CHIAKI [JP]; KAW) 15 January 2004 (2004-01-15) page 35 - page 42; compounds 1-667 TO 1-888	1-9
A	DE 103 46 939 A1 (SCHERING AG [DE]) 19 May 2005 (2005-05-19) paragraph [0001]; claim 1	1-15

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- ¹E¹ earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- ¹T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- ¹Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

20 August 2008

Date of mailing of the international search report

26/08/2008

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Moriggi, J

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/083094

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/083094

Patent document cited, in search report		Publication date	Patent family member(s)	Publication date
WO 2004005261	A	15-01-2004	AU 2003281366 A1	23-01-2004
DE 10346939	A1	19-05-2005	NONE	