

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
22 December 2005 (22.12.2005)

PCT

(10) International Publication Number
WO 2005/121121 A3

(51) International Patent Classification:

C07D 401/04 (2006.01) **C07D 409/14** (2006.01)
C07D 401/12 (2006.01) **C07D 413/14** (2006.01)
C07D 401/14 (2006.01) **C07D 417/14** (2006.01)
C07D 403/04 (2006.01) **A61K 31/506** (2006.01)
C07D 403/14 (2006.01) **A61P 3/10** (2006.01)
C07D 405/14 (2006.01)

Scripps Westview Way, N° 251, San Diego, CA 92131 (US).

(74) Agent: **GODDARD, Christine, A.**; Cozen O'Connor, 1900 Market Street, Philadelphia, PA 19103 (US).

(21) International Application Number:

PCT/US2005/019318

(22) International Filing Date: 2 June 2005 (02.06.2005)

(25) Filing Language: English

(26) Publication Language: English

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

(30) Priority Data:

60/577,354 4 June 2004 (04.06.2004) US

(71) Applicant (for all designated States except US): **ARENA PHARMACEUTICALS, INC.** [US/US]; 6166 Nancy Ridge Drive, San Diego, CA 92121 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **JONES, Robert, M.** [GB/US]; 10937 Corte luz del Sol, San Diego, CA 92130 (US). **SEMPLE, Graeme** [GB/US]; 15920 Camino Codorniz, San Diego, CA 92127 (US). **XIONG, Yifeng** [US/US]; 5036 Pearlman Way, San Diego, CA 92130 (US). **SHIN, Young-Jun** [KR/US]; 11051 Ice Skate Place, San Diego, CA 92126 (US). **REN, Albert, S.** [CN/US]; 4266 Corte de Sausalito, San Diego, CA 92130 (US). **LEHMANN, Juerg** [CH/US]; 9840 La Tortola Court, San Diego, CA 92129 (US). **FIORAVANTI, Beatriz** [BR/US]; 60 west Stone Loop, N° 327, Tucson, AR 85704 (US). **BRUCE, Marc, A.** [US/US]; 662 Corte Raquel, San Marcos, CA 92069 (US). **CHOI, Jin, Sun, Karoline** [US/US]; 9926

(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, MC, 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:

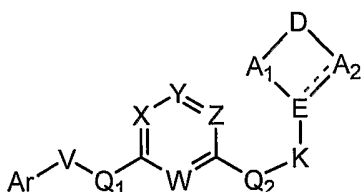
- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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

16 March 2006

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

(54) Title: SUBSTITUTED ARYL AND HETEROARYL DERIVATIVES AS MODULATORS OF METABOLISM AND THE PROPHYLAXIS AND TREATMENT OF DISORDERS RELATED THERETO



(I)

(57) Abstract: The present invention relates to certain substituted aryl and heteroaryl derivative of Formula (I) that are modulators of metabolism, especially of the activity of a GPCR, referred to herein as RUP3. Accordingly, compounds of the present invention are useful in the treatment of metabolic-related disorders and complications thereof, such as, diabetes and obesity.

INTERNATIONAL SEARCH REPORT

Inter-Application No
PC17DS2005/019318

A. CLASSIFICATION OF SUBJECT MATTER

C07D401/04 C07D401/12 C07D401/14 C07D403/04 C07D403/14
C07D405/14 C07D409/14 C07D413/14 C07D417/14 A61K31/506
A61P3/10

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)

C07D A61K

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, CHEM ABS Data, WPI 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 2004/041164 A (MERCK & CO., INC; HARTMAN, GEORGE, D; HOFFMAN, JACOB, M; SMITH, ANTHON) 21 May 2004 (2004-05-21) claims 1-9, 13-14, 22 and examples (e. g. compound 1-2). -----	1-3, 6, 8, 9, 12, 14-16, 19-21, 35-42
X	WO 03/002544 A (BRISTOL-MYERS SQUIBB COMPANY; PHARMACOEPIA, INC; AHMED, GULZAR; METZGE) 9 January 2003 (2003-01-09) page 47, line 25; claims 1, 14, 31 -----	1-20, 35-42
X	WO 02/45652 A (MERCK & CO., INC; BILODEAU, MARK, T; HARTMAN, GEORGE, D; HOFFMAN, JACO) 13 June 2002 (2002-06-13) claims and examples (e.g. compound 19-4 on scheme 19) -----	1-21, 25-32, 34-42
	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* 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

- *T* 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
- *Y* 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.
- *Z* document member of the same patent family

Date of the actual completion of the international search

17 January 2006

Date of mailing of the international search report

25/01/2006

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

Gregoire, A

INTERNATIONAL SEARCH REPORT

Int. Application No
PCT/US2005/019318

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/17995 A (MERCK & CO., INC; BILODEAU, MARK, T; HUNGATE, RANDALL, W; RODMAN, LEON) 15 March 2001 (2001-03-15) examples e.g. compound 6-6 claims 1,19 -----	25, 34-42
X	WO 03/000663 A (PFIZER PRODUCTS INC; CHIANG, YUAN-CHING, PHOEBE; NOVOMISLE, WILLIAM, A) 3 January 2003 (2003-01-03) claims 1-18 -----	25-28, 31, 35-42
X	WO 03/000687 A (MERCK & CO., INC; BILODEAU, MARK, T; HARTMAN, GEORGE, D) 3 January 2003 (2003-01-03) claims 1-9,16 -----	25,27, 29,31, 34-42
P,X	US 2005/070562 A1 (JONES, ROBERT M. ET AL) 31 March 2005 (2005-03-31) the whole document -----	1-42
P,X	WO 2004/078114 A (ENCYSIVE PHARMACEUTICALS INC; WU, CHENGDE; ANDERSON, C., ERIC; BUI, HU) 16 September 2004 (2004-09-16) claims and specific compounds see e.g. some of them in table 2 -----	1-42

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/019318

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 36-38 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2005/019318

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2004041164	A	21-05-2004	AU 2003285007 A1 CA 2503715 A1 EP 1558609 A2	07-06-2004 21-05-2004 03-08-2005
WO 03002544	A	09-01-2003	CA 2451128 A1 EP 1406875 A1 HU 0401711 A2 JP 2004535447 T	09-01-2003 14-04-2004 28-12-2004 25-11-2004
WO 0245652	A	13-06-2002	AU 3244102 A CA 2429728 A1 EP 1341540 A2 JP 2004524282 T	18-06-2002 13-06-2002 10-09-2003 12-08-2004
WO 0117995	A	15-03-2001	AT 309241 T AU 779908 B2 AU 7351700 A BG 106465 A BR 0013899 A CA 2384101 A1 CN 1390215 A CZ 20020861 A3 DE 60023926 D1 EE 200200123 A EP 1218376 A1 HU 0202682 A2 JP 2003509342 T MX PA02002559 A NO 20021166 A PL 355639 A1 SK 4772002 A3 ZA 200201898 A	15-11-2005 17-02-2005 10-04-2001 29-12-2002 08-07-2003 15-03-2001 08-01-2003 12-06-2002 15-12-2005 15-08-2003 03-07-2002 28-02-2003 11-03-2003 30-07-2002 25-04-2002 04-05-2004 06-11-2002 07-03-2003
WO 03000663	A	03-01-2003	BG 108491 A BG 108495 A BR 0210471 A BR 0210503 A CA 2450491 A1 CA 2455292 A1 CN 1630645 A CZ 20033431 A3 CZ 20033508 A3 EE 200400025 A EE 200400026 A EP 1401819 A1 EP 1401820 A1 HR 20031042 A2 HU 0400249 A2 HU 0400251 A2 WO 03000666 A1 JP 2004534823 T JP 2005501821 T MA 27035 A1 MA 27036 A1 MX PA03011940 A MX PA03011941 A NZ 529542 A NZ 529543 A	31-01-2005 31-08-2004 10-08-2004 18-05-2004 03-01-2003 03-01-2003 22-06-2005 14-07-2004 12-05-2004 15-06-2004 15-06-2004 31-03-2004 31-03-2004 31-10-2005 30-08-2004 30-08-2004 03-01-2003 18-11-2004 20-01-2005 20-12-2004 20-12-2004 26-03-2004 26-03-2004 19-12-2003 19-12-2003

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2005/019318

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03000663	A		SK 15672003 A3	04-05-2004
			SK 15712003 A3	08-06-2004
			ZA 200308842 A	23-11-2004
			ZA 200308843 A	23-11-2004
WO 03000687	A	03-01-2003	CA 2450562 A1	03-01-2003
			EP 1404672 A1	07-04-2004
			JP 2004535437 T	25-11-2004
US 2005070562	A1	31-03-2005	NONE	
WO 2004078114	A	16-09-2004	AU 2004218456 A1	16-09-2004
			CA 2517166 A1	16-09-2004
			EP 1603884 A2	14-12-2005