

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
8 June 2006 (08.06.2006)

PCT

(10) International Publication Number  
**WO 2006/060762 A3**

(51) International Patent Classification:

C07D 231/38 (2006.01) A61K 31/415 (2006.01)

C07D 401/12 (2006.01) A61P 25/00 (2006.01)

(21) International Application Number:

PCT/US2005/043893

(22) International Filing Date:

1 December 2005 (01.12.2005)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/633,157 3 December 2004 (03.12.2004) US

60/656,481 24 February 2005 (24.02.2005) US

(71) Applicant (for all designated States except US): **ARENA PHARMACEUTICALS, INC.** [US/US]; 6166 Nancy Ridge Drive, San Diego, 5 92121-3223 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **STRAHPLEYNET, Sonja** [SI/US]; 12542 Darkwood Road, San Diego, California 92129 (US). **TEEGARDEN, Bradley** [US/US]; 11933 Windom Peak Way, San Diego, California 92131 (US). **UNETT, David J.** [GB/US]; 11422 Cypress Terrace Place, San Diego, California 92131 (US).

(74) Agents: **SPRUCE, Lyle** et al.; ARENA PHARMACEUTICALS, INC., 6166 Nancy Ridge Drive, San Diego, California 92121-3223 (US).

(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, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, 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.

(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, 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

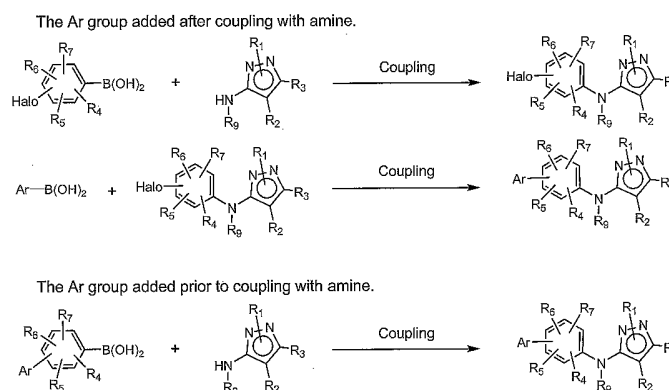
(88) Date of publication of the international search report:

20 July 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: PYRAZOLE DERIVATIVES AS MODULATORS OF THE 5-HT<sub>2A</sub> SEROTONIN RECEPTOR USEFUL FOR THE TREATMENT OF DISORDERS RELATED THERETO

General Methods for the preparation of compounds of the invention wherein Y is absent



(57) Abstract: The present invention relates to certain pyrazole derivatives of Formula (Ia) and pharmaceutical compositions thereof that modulate the activity of the 5-HT<sub>2A</sub> serotonin receptor. Compounds and pharmaceutical compositions thereof are directed to methods useful in the treatment of platelet aggregation, coronary artery disease, myocardial infarction, transient ischemic attack, angina, stroke, atrial fibrillation, reducing the risk of blood clot formation, asthma or symptoms thereof, agitation or a symptom, behavioral disorders, drug induced psychosis, excitative psychosis, Gilles de la Tourette's syndrome, manic disorder, organic or NOS psychosis, psychotic disorder, psychosis, acute schizophrenia, chronic schizophrenia, NOS schizophrenia and related disorders, sleep disorders, diabetic-related disorders, progressive multifocal leukoencephalopathy and the like. The present invention also relates to the methods for the treatment of 5-HT<sub>2A</sub> serotonin receptor mediated disorders in combination with other pharmaceutical agents administered separately or together.

WO 2006/060762 A3

# INTERNATIONAL SEARCH REPORT

Application No  
PCT/US2005/043893

## A. CLASSIFICATION OF SUBJECT MATTER

C07D231/38 C07D401/12 A61K31/415 A61P25/00

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 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, PAJ, WPI Data, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 295 233 A (MONSANTO COMPANY) 14 December 1988 (1988-12-14) compounds 200,201,280,181,291,292,345-354,357-365,36 9,371,373,376,378-380,386,389,422,425, 430,431,452,454,453,496,519,530,531,537,55 9,583,663,688,743,897 -----	1-7,9-11
X	EP 1 275 301 A (BAYER CROPS SCIENCE S.A) 15 January 2003 (2003-01-15) page 23, example C -----	1-5,7, 10,11
X	US 5 185 025 A (MOEDRITZER ET AL) 9 February 1993 (1993-02-09) example 83 ----- -/-	1,2,4,5, 10

☒ 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

\*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.

\*G\* document member of the same patent family

Date of the actual completion of the international search

6 April 2006

Date of mailing of the international search report

18/04/2006

Name and mailing address of the ISA/

European Patent Office, P.B. 5618 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Schmid, A

# INTERNATIONAL SEARCH REPORT

In **ational application No**  
PCT/US2005/043893

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>PARLOW JOHN J ET AL: "Utility of Complementary Molecular Reactivity and Molecular Recognition (CMR/R) Technology and Polymer -Supported Reagents in the Solution-Phase Synthesis of Heterocyclic Carboxamides"</p> <p>JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY. EASTON, US, vol. 62, 1997, pages 5908-5919, XP002213047</p> <p>ISSN: 0022-3263</p> <p>tables 1,4-7</p>	1,2,4-7, 10,11
A	<p>-----</p> <p>WO 03/062206 A (ARENA PHARMACEUTICALS, INC; TEEGARDEN, BRADLEY; DROUET, KEITH; JAYAKUM) 31 July 2003 (2003-07-31)</p> <p>compounds 1-164</p> <p>page 1, line 10 - page 1, line 21; claims 1-166</p>	1-55
A	<p>-----</p> <p>WO 2004/058722 A (ARENA PHARM INC [US]; TEEGARDEN BRADLEY [US]; JAYAKUMAR HONNAPPA [US];) 15 July 2004 (2004-07-15)</p> <p>page 1, "field of invention"; compounds 1-78; claims 1-89</p> <p>-----</p>	1-55

## INTERNATIONAL SEARCH REPORT

national application No.  
PCT/US2005/043893

### 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 18-29 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

International application No  
PCT/US2005/043893

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0295233	A	14-12-1988	AU 607225 B2	28-02-1991
			AU 1745088 A	08-12-1988
			BR 8802760 A	27-12-1988
			DK 308688 A	09-12-1988
			FI 882680 A	09-12-1988
			HU 52063 A2	28-06-1990
			JP 1025764 A	27-01-1989
			JP 1856941 C	07-07-1994
			JP 5075746 B	21-10-1993
			NO 882509 A	09-12-1988
			NZ 224920 A	26-10-1990
			PT 87666 A	01-07-1988
			YU 110188 A1	31-08-1990
EP 1275301	A	15-01-2003	WO 03006454 A2	23-01-2003
			JP 2004538277 T	24-12-2004
			US 2004152698 A1	05-08-2004
US 5185025	A	09-02-1993	AU 619914 B2	06-02-1992
			AU 4479289 A	24-05-1990
			CA 2003362 A1	21-05-1990
			DK 581589 A	22-05-1990
			EP 0371947 A1	06-06-1990
			JP 2193976 A	31-07-1990
			NZ 231450 A	27-11-1990
WO 03062206	A	31-07-2003	EP 1509505 A2	02-03-2005
WO 2004058722	A	15-07-2004	AU 2003297441 A1	22-07-2004