

(43) International Publication Date  
24 September 2009 (24.09.2009)(10) International Publication Number  
**WO 2009/115874 A3**

## (51) International Patent Classification:

C07D 209/08 (2006.01) C07D 413/04 (2006.01)  
 C07D 209/88 (2006.01) A61K 31/403 (2006.01)  
 C07D 307/91 (2006.01) A61K 31/404 (2006.01)  
 C07D 403/04 (2006.01) A61K 31/343 (2006.01)  
 C07D 405/04 (2006.01) A61P 29/00 (2006.01)

## (21) International Application Number:

PCT/IB2009/000190

## (22) International Filing Date:

29 January 2009 (29.01.2009)

## (25) Filing Language:

English

## (26) Publication Language:

English

## (30) Priority Data:

656/CHE/2008 17 March 2008 (17.03.2008) IN  
 2228/CHE/2008 12 September 2008 (12.09.2008) IN

(71) Applicant (for all designated States except US): **MA-TRIX LABORATORIES LTD.** [IN/IN]; 1-1-151/1, IV Floor, Sairam Towers, Alexander Road, Secunderabad 500 003 (IN).

## (72) Inventors; and

(75) Inventors/Applicants (for US only): **GOPALAN, Bala-subramanian** [IN/IN]; Plot No. 476/14, Old Mahabalipuram Road, Sholinganallur, 600 119 Chennai (IN). **MANO-JIT, Pal** [IN/IN]; Plot 17, Flat 203, Maruti Majestic, Miyapur, Hyderabad 500049 (IN). **SHRIKANT, Hanu-mantappa, Havale** [IN/IN]; Flat No. 106, Bhanu's Cherukanti Enclave, Jayanagar Main Road, Kukatpally Housing Board, Hyderabad 500072 (IN). **ARUMUGAM,**

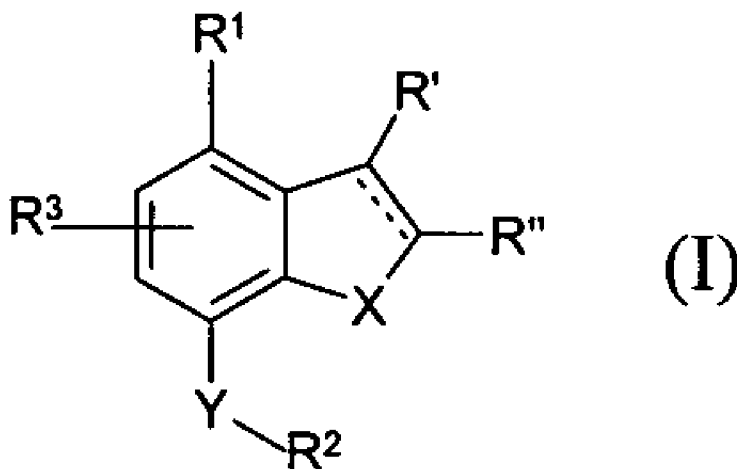
**Kodimuthali** [IN/IN]; H. No. 5-117, Flat No. 202, Sai Guru Nivas, Road No. 1, Adarsh Nagar, Serilingampally, Hyderabad 500 019 (IN). **SANTOSH, Kumar Singh** [IN/IN]; Flat No. 302, Plot No. 29, santosh Residential Apt., Bhagya Nagar Colony, Kukatpally, Hyderabad 500072 (IN). **RAJESH, Vidyawant Gupta** [IN/IN]; G6 Vaishna Vi Residency, Near More Shop, Brindavan Colony Road, Nizampet Road, Kukatpally, Hyderabad 500072 (IN). **RANJEET, Kumar, Tokala** [IN/IN]; 8-2703/4/1, Banjara Hills, Road No. 12, Hyderabad, PIN 500033 (IN). **ANITHA, Mungara** [IN/IN]; H. No. 5-117, Flat No. 202, Sai Guru Nivas, Road No. 2, Adarsh Nagar Colony, Serilingampally, Hyderabad 500019 (IN). **BATHOJU, Chandra Chary** [IN/IN]; Plot No. 92, Jaya Prakash Narayan Nagar, Miyapur, Hyderabad 500049 (IN). **SUG-IN, Lal Jabaris Sobhana George** [IN/IN]; Block No. 12, Flat No. 20, Kendriya Vihar, Opp B.B.U., Bollaram Road, Andra Pradesh, Miyapur 500050 (IN).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, 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, ST, 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,

[Continued on next page]

(54) Title: NOVEL HETEROCYCLIC COMPOUNDS, PHARMACEUTICAL COMPOSITIONS CONTAINING THEM AND PROCESSES FOR THEIR PREPARATION



(57) Abstract: The present invention relates to novel heterocyclic compounds of general formula (I) that are phosphodiesterase inhibitors (PDEs), in particular phosphodiesterase type 4 inhibitors. These novel PDEs are useful in the treatment of inflammatory diseases (such as asthma, COPD, allergic rhinitis, allergic conjunctivitis, respiratory distress syndrome, chronic bronchitis, nephritis, rheumatoid spondylitis, osteoarthritis, atopic dermatitis, eosinophilic granuloma, psoriasis, rheumatoid septic shock, ulcerative colitis, multiple sclerosis, chronic inflammation, Crohn's syndrome and central nervous system(CNS) disorders) as well as disorders or conditions generally characterized by or associated with an excessive secretion of TNF- $\alpha$  and Phosphodiesterase 4 (PDE IV).



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, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

— of inventorship (Rule 4.17(iv))

**Published:**

— with international search report (Art. 21(3))

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

**Declarations under Rule 4.17:**

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

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

12 November 2009

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/IB2009/000190

## A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D209/08 C07D209/88 C07D307/91 C07D403/04 C07D405/04  
C07D413/04 A61K31/403 A61K31/404 A61K31/343 A61P29/00

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

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

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                            | Relevant to claim No. |
|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| A         | WO 2006/011024 A (GLENMARK PHARMACEUTICALS LTD [IN]; BALASUBRAMANIAN GOPALAN [IN]; GHARA) 2 February 2006 (2006-02-02) cited in the application example 65    | 1-18                  |
| P,X       | WO 2008/032171 A (MATRIX LAB LTD [IN]; GOPALAN BALASUBRAMANIAN [IN]; RAVI DHAMJEWAR [IN]) 20 March 2008 (2008-03-20) cited in the application examples 4,7-23 | 1-18                  |

☐ 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
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- \*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.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

18 May 2009

Date of mailing of the international search report

18/09/2009

Name and mailing address of the ISA/

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

Authorized officer

Bakboord, Joan

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB2009/000190

## Box No. 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:
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 No. 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:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
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.:

see annex

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-18 (all part)

compounds of formula I in which R1 is the cyclohexyl group substituted with X1, X2 and X3  
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2. claims: 1-18 (all part)

compounds of formula I in which R1 is the cyclohexyl group substituted with X1, X3 and X4  
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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2009/000190

| Patent document<br>cited in search report |   | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|-------------------------------------------|---|---------------------|----------------------------|---------------------|
| WO 2006011024                             | A | 02-02-2006          | NONE                       |                     |
| WO 2008032171                             | A | 20-03-2008          | AU 2007297221 A1           | 20-03-2008          |
|                                           |   |                     | CA 2663178 A1              | 20-03-2008          |
|                                           |   |                     | EP 2074106 A1              | 01-07-2009          |