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## Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the  
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## (88) Date of publication of the international search report:

18 December 2014

(54) Title: HETEROCYCLIC COMPOUNDS USEFUL IN THE TREATMENT OF DISEASE

(57) Abstract: Heterocyclic compounds are described that are lysophosphatidic acid receptor ligands that are useful in the treatment of lysophosphatidic acid receptor-dependent diseases and conditions, including but not limited to diseases involving fibrosis, such as fibrosis of the heart, kidney, liver and lung, and scleroderma; inflammatory diseases such as diabetic nephropathy and inflammatory bowel disease; ocular diseases such as diseases involving retinal degeneration; nerve diseases such as pruritus and pain. Non-limiting examples of those compounds include (RS)-3-Cyclopropyl-2-{4-[3-methyl-4-((R)-1-phenyl-ethoxycarbonylamino)-isoxazol-5-yl]-benzyloxy}-propionic acid and (R)-1-(4'-{5-[1-(2-Chloro-phenyl)-ethoxycarbonylamino]-4-fluoro-pyrazol-1-yl]-2-fluoro-biphen-yl-4-yl)-cyclopropanecarboxylic acid.



WO 2014/145873 A3

## INTERNATIONAL SEARCH REPORT

International application No.  
**PCT/US2014/030712****A. CLASSIFICATION OF SUBJECT MATTER****A61K 31/42(2006.01)i, A61K 31/4152(2006.01)i, C07D 261/10(2006.01)i, C07D 231/10(2006.01)i**

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)

A61K 31/42; C07D 413/12; A61K 31/27; C07D 261/14; C07D 261/08; C07D 413/10; A61K 31/192; C07D 231/40; A61K 31/5377; C07D 413/04; C07D 249/06; A61K 31/4152; C07D 261/10; C07D 231/10

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

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

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

eKOMPASS(KIPO internal) &amp; Keywords: heterocyclic compound, lysophosphatidic acid receptor antagonist, isoxazole, pyrazole

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                   | Relevant to claim No.        |
|-----------|----------------------------------------------------------------------------------------------------------------------|------------------------------|
| X         | EP 1258484 B1 (KYOWA HAKKO KIRIN CO., LTD.) 14 January 2009<br>See page 62, lines 25-27; claims 1-14; and figure 11. | 1-3, 5-41, 44-48<br>, 50-52  |
| A         |                                                                                                                      | 4, 42, 43, 49                |
| X         | WO 2013-025733 A1 (INTERMUNE, INC.) 21 February 2013<br>See paragraph [0321]; and claim 1.                           | 1-5, 13-27, 33-43<br>, 49-52 |
| A         |                                                                                                                      | 6-12, 28-32, 44-48           |
| X         | US 2012-0289522 A1 (SEIDERS, T. J. et al.) 15 November 2012<br>See claims 1-16.                                      | 1-5, 13-27, 33-43<br>, 49-52 |
| X         | WO 2012-078593 A2 (AMIRA PHARMACEUTICALS, INC.) 14 June 2012<br>See claims 1-9.                                      | 1-5, 13-27, 33-43<br>, 49-52 |
| A         | WO 2012-138648 A1 (IRM LLC et al.) 11 October 2012<br>See claims 1-12.                                               | 1-52                         |
| A         | WO 2011-017350 A2 (AMIRA PHARMACEUTICALS, INC.) 10 February 2011<br>See claims 1-16.                                 | 1-52                         |



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 application or patent 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

"&amp;" document member of the same patent family

Date of the actual completion of the international search

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Name and mailing address of the ISA/KR

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# INTERNATIONAL SEARCH REPORT

International application No.  
**PCT/US2014/030712**

## 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.: 53  
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:

Group I, claims 1-3, 5, 13-27, 33-41, 50-53 (all in part); 6-12, 28-32, 44-48 related to a compound of Formula I, wherein Ring C is absent.

Group II, claims 1-3, 5, 13-27, 33-41, 50-53 (all in part); 4, 42, 43, 49 related to a compound of Formula I, wherein Ring C is present.

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 fees, this Authority did not invite payment of any 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.:

### 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.

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International application No.

**PCT/US2014/030712**

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|-------------------------------------------|---------------------|----------------------------|---------------------|
| EP 1258484 B1                             | 14/01/2009          | AT 420878 T                | 15/01/2009          |
|                                           |                     | AU 2001-32340 A1           | 27/08/2001          |
|                                           |                     | DE 60137405 D1             | 05/03/2009          |
|                                           |                     | DK 1258484 T3              | 20/04/2009          |
|                                           |                     | EP 1258484 A1              | 20/11/2002          |
|                                           |                     | EP 1258484 A4              | 23/04/2003          |
|                                           |                     | ES 2320320 T3              | 21/05/2009          |
|                                           |                     | PT 1258484 E               | 03/04/2009          |
|                                           |                     | TW 288136 A                | 11/10/2007          |
|                                           |                     | US 2003-0114505 A1         | 19/06/2003          |
|                                           |                     | US 6964975 B2              | 15/11/2005          |
|                                           |                     | WO 01-060819 A1            | 23/08/2001          |
| WO 2013-025733 A1                         | 21/02/2013          | AU 2012-296662 A1          | 27/03/2014          |
|                                           |                     | CA 2844982 A1              | 21/02/2013          |
|                                           |                     | EP 2744807 A1              | 25/06/2014          |
|                                           |                     | IL 230913 D                | 31/03/2014          |
|                                           |                     | KR 10-2014-0067048 A       | 03/06/2014          |
|                                           |                     | TW 201315717 A             | 16/04/2013          |
|                                           |                     | US 2013-072449 A1          | 21/03/2013          |
| US 2012-0289522 A1                        | 15/11/2012          | AR 078497 A1               | 09/11/2011          |
|                                           |                     | CN 102639515 A             | 15/08/2012          |
|                                           |                     | CN 102666504 A             | 12/09/2012          |
|                                           |                     | EP 2483252 A2              | 08/08/2012          |
|                                           |                     | EP 2483252 A4              | 03/04/2013          |
|                                           |                     | EP 2483253 A2              | 08/08/2012          |
|                                           |                     | EP 2483253 A4              | 03/04/2013          |
|                                           |                     | GB 201016314 D             | 10/11/2010          |
|                                           |                     | GB 2474120 A               | 06/04/2011          |
|                                           |                     | GB 2474120 B               | 21/12/2011          |
|                                           |                     | JP 2013-506694 A           | 28/02/2013          |
|                                           |                     | JP 2013-506695 A           | 28/02/2013          |
|                                           |                     | TW 201116278 A             | 16/05/2011          |
|                                           |                     | TW I401082 B               | 11/07/2013          |
|                                           |                     | US 2011-0082181 A1         | 07/04/2011          |
|                                           |                     | US 8217066 B2              | 10/07/2012          |
|                                           |                     | UY 32926 A                 | 30/11/2010          |
|                                           |                     | WO 2011-041694 A2          | 07/04/2011          |
|                                           |                     | WO 2011-041694 A3          | 18/08/2011          |
|                                           |                     | WO 2011-041729 A2          | 07/04/2011          |
|                                           |                     | WO 2011-041729 A3          | 04/08/2011          |
| WO 2012-078593 A2                         | 14/06/2012          | AU 2011-338561 A1          | 25/07/2013          |
|                                           |                     | CA 2820817 A1              | 14/06/2012          |
|                                           |                     | CN 103347510 A             | 09/10/2013          |
|                                           |                     | CO 6771417 A2              | 15/10/2013          |
|                                           |                     | EA 201390821 A1            | 30/10/2013          |
|                                           |                     | EP 2648714 A2              | 16/10/2013          |

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International application No.

**PCT/US2014/030712**

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|-------------------------------------------|---------------------|----------------------------|---------------------|
|                                           |                     | IL 226491 D                | 31/07/2013          |
|                                           |                     | JP 2014-508111 A           | 03/04/2014          |
|                                           |                     | KR 10-2013-0126659 A       | 20/11/2013          |
|                                           |                     | MA 34765 B1                | 03/12/2013          |
|                                           |                     | MX 2013006040 A            | 26/08/2013          |
|                                           |                     | SG 190417 A1               | 31/07/2013          |
|                                           |                     | US 2013-0253004 A1         | 26/09/2013          |
|                                           |                     | WO 2012-078593 A3          | 02/08/2012          |
| WO 2012-138648 A1                         | 11/10/2012          | None                       |                     |
| WO 2011-017350 A2                         | 10/02/2011          | CN 102574822 A             | 11/07/2012          |
|                                           |                     | EP 2462128 A2              | 13/06/2012          |
|                                           |                     | EP 2462128 A4              | 03/10/2012          |
|                                           |                     | JP 2013-501064 A           | 10/01/2013          |
|                                           |                     | US 2012-0196839 A1         | 02/08/2012          |
|                                           |                     | US 8592402 B2              | 26/11/2013          |
|                                           |                     | WO 2011-017350 A3          | 30/06/2011          |