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(54) Title: PHOSPHOLIPASE A₂ INHIBITORS AND THEIR USE IN TREATING NEUROLOGICAL INJURY AND DISEASE

(57) Abstract: Phospholipase A₂ (PLA₂) forms are expressed in spinal cord whose inhibition induces a potent antihyperalgesia. PLA₂ inhibitor compounds are provided that include a common motif consisting of a 2-oxoamide with a hydrocarbon tail and a four carbon tether. The compounds block Group IVA calcium dependent PLA₂ (cPLA₂) and/or Group VIA calcium independent PLA₂ (iPLA₂) and/or Group V secreted PLA₂ (sPLA₂). Pharmaceutical compositions of compounds having cPLA₂ inhibitory activity (but not iPLA₂ or sPLA₂ inhibitory activity) are useful in treating multiple sclerosis, while compositions of compounds having sPLA₂ inhibitory activity (as well as iPLA₂ and cPLA₂ activity) are useful in treating spinal cord injuries (with related functional recovery).

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A. CLASSIFICATION OF SUBJECT MATTER*A61K 31/40(2006.01)i, A61K 31/27(2006.01)i, A61K 31/12(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)

IPC 8 AS ABOVE

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 practicable, search terms used)

eKIPASS(KIPO internal), STN(CA), "Keywords: 2-oxoamide* and PLA2 "

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	WO 2007/022443 A2 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 22 Feb 2007 See the table 1b (compound AX006, AX010)	1,6-7 2-5,10-11,13
X Y	US 2005/148549 A1 (DENNIS EDWARD) 07 Jul 2005 See the table 2-3, claims and para [0058]	1,6-7 2-5,10-11,13
A	KOKOTOS, G. et al., "Novel 2-oxoamide inhibitors of human group IVA phospholipase A2." J Med Chem. 07 Jun 2002, Vol.45, pp.2891-2893 See the abstract and pg 2891, col 2, para 3	1-7,10-11,13
A	WO 95/19959 A1 (TAKASE et al.) 27 July 1995 See the abstract and pg 1.	1-7,10-11,13



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 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

"&" document member of the same patent family

Date of the actual completion of the international search

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Telephone No. 82-42-481-5612



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2008/069257**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.: 14-15
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 14-15 pertain to methods for treatment (or screening) of the human or animal body by therapy/diagnostic methods, and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulation under the PCT, to search.
2. ☒ Claims Nos.: 9,12
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:
Claims 9,12 can not make meaningful search because they refer to multiple dependent claims not to be drafted in accordance with the second and third sentences of Rule 6.4(a).
3. ☒ Claims Nos.: 8
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:

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 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/US2008/069257

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2007-022443 A2	22.02.2007	AU 2006-279341 A1 EP 1937247 A2 KR 10-2008-0035011 WO 2007-022443 A3	22.02.2007 02.07.2008 22.04.2008 20.09.2007
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