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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))*

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

28 February 2013

(54) Title: NECROPTOSIS INHIBITORS AND METHODS OF USE THEREFOR

(57) Abstract: Described herein are compositions that inhibit the production of TNF α downstream of CD40 activation. As such, also described are various methods of using compositions exhibiting this activity for the treatment or prevention of inflammatory diseases associated with TNF α production or CD40 activation.



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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2012/028747**A. CLASSIFICATION OF SUBJECT MATTER****C07D 487/04(2006.01)i, C07D 209/82(2006.01)i, C07D 417/12(2006.01)i, A61K 31/403(2006.01)i, A61P 29/00(2006.01)i, A61P 25/00(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)

C07D 487/04; A61K 31/4162; A61K; A61K 31/165; A61K 31/40

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) & Google Scholar & Keywords: pyrazolo[3,4-a]carbazole, benzofuro[3,2-g]indazole, necroptosis, inflammation, TNFa, CD40

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2007-0254877 A1 (TAKADA PHARMACEUTICAL COMPANY LIMITED) 01 November 2007 See abstract; paragraph [0006]; examples; claims	1-7,9-11,171
A	See the whole document.	8
A	WO 2004-071507 A1 (PHARMACIA ITALIA S.P.A. et al.) 26 August 2004 See abstract; formular A, formulars (I), A, B, (IA); pages 19-29; examples; claims	1,2-11,171
A	WO 00-06088 A2 (KIRKPATRICK, D., LYNN et al.) 10 February 2000 See the whole document	1,2-11,171
A	WO 97-12613 A1 (WARNER-LAMBERT COMPANY) 10 April 1997 See the whole document	1,2-11,171
A	BOTTIN, MARIE CLAIRE et al, "Genotoxic effects of bitumen fumes in Big Blue transgenic rat lung", Mutation Research 2006, Vol. 596, pp. 91-105. See the whole document	1,2-11,171

☐ 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

31 DECEMBER 2012 (31.12.2012)

Date of mailing of the international search report

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Name and mailing address of the ISA/KR

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2012/028747**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.: 172-177
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 172-177 pertain to methods for treatment of the human body by surgery or therapy, as well as 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 Regulations under the PCT, to search.
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.: 177
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 the extra sheet.

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.: claims 1(partial), 2-11, 171

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

International application No.

PCT/US2012/028747

(Continued on Box No. III)

The 13 inventions are as follows

Class I : The compounds of formula I (claims 1(partial), 2-11, 171(partial))

Class II : The compounds of formula II (claims 1(partial), 12-29, 171(partial))

Class III : The compounds of formula III and XII (claims 1(partial), 30-38, 135-143, 171(partial))

Class IV : The compounds of formula IV (claims 1(partial), 39-52, 171(partial))

Class V : The compounds of formula V (claims 1(partial), 53-66, 171(partial))

Class VI : The compounds of formula VI (claims 1(partial), 67-78, 171(partial))

Class VII : The compounds of formula VII (claims 1(partial), 79-87, 171(partial))

Class VIII : The compounds of formula VIII (claims 1(partial), 88-98, 171(partial))

Class IX : The compounds of formula IX (claims 1(partial), 99-110, 171(partial))

Class X : The compounds of formula X (claims 1(partial), 111-123, 171(partial))

Class XI : The compounds of formula XI (claims 1(partial), 124-134, 171(partial))

Class XII : The compounds of formula XIII (claims 1(partial), 144-157, 171(partial))

Class XIII : The compounds of formula XIV (claims 1(partial), 158-170, 171(partial))

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2012/028747

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2007-0254877 A1	01.11.2007	EP 1761539 A1 JP 2008-501628 A JP 2008-501628 T WO 2005-118587 A1	14.03.2007 24.01.2008 24.01.2008 15.12.2005
WO 2004-071507 A1	26.08.2004	BR P10407544A CA 2516254 A1 EP 1599202 A1 JP 2006-517949 A JP 2006-517949 T MX PA05008688A US 2006-0264493 A1	14.02.2006 26.08.2004 30.11.2005 03.08.2006 03.08.2006 05.10.2005 23.11.2006
WO 00-06088 A2	10.02.2000	AU 1999-54630 A1 CA 2339233 A1 MX PA01001255A US 6372772 B1 WO 00-06088 A3	21.02.2000 10.02.2000 29.11.2002 16.04.2002 10.02.2000
WO 97-12613 A1	10.04.1997	AU 6966696 A AU 7254196 A US 05958950A A US 05972980A A US 06001866A A WO 97-12613A1 WO 97-12615 A1 ZA9608332A ZA9608335A	28.04.1997 28.04.1997 28.09.1999 26.10.1999 14.12.1999 10.04.1997 10.04.1997 13.05.1997 13.05.1997