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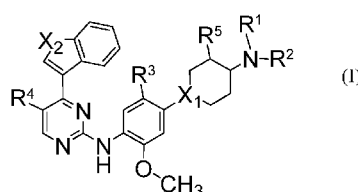
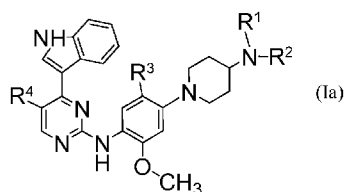
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(88) Date of publication of the international search report:

5 April 2012

(54) Title: 4-(1H-INDOL-3-YL)-PYRIMIDINES AS ALK INHIBITORS



(57) Abstract: The present invention relates to compounds of Formula (I) and/or Formula (Ia); and to their salts, pharmaceutical compositions, methods of use, and methods for their preparation. These compounds inhibit ALK kinase activity, and thus may be used for the treatment of cancer.

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2011/051465

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D401/14 C07F9/6568 A61K31/506 A61P35/00
ADD.

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 C07F 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, WPI Data, BIOSIS, EMBASE, 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.
Y	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 104, no. 1, January 2007 (2007-01), pages 270-275, XP002661293, ISSN: 0027-8424, DOI: DOI:10.1073/PNAS.0609412103 page 270 - page 271; figure 1; compound A / TAE684	1-17
X	----- WO 2007/149427 A2 (MERCK & CO INC [US]; KOZINA EKATERINA S [US]; SIU TONY [US]) 27 December 2007 (2007-12-27)	18
Y	abstract; claims 3,5-12; table 1 scheme A and example 1, step 2 and 3 ----- -/-	1-17

☒ 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.

"&" document member of the same patent family

Date of the actual completion of the international search

14 February 2012

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23/02/2012

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INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2011/051465

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2010/049731 A1 (ASTRAZENECA AB [SE]; ASTRAZENECA UK LTD [GB]; DUCRAY RICHARD [FR]; JON) 6 May 2010 (2010-05-06) the whole document in particular claim 16	1-17
X	----- EMMITTE K A ET AL: "Discovery and optimization of imidazo[1,2-a]pyridine inhibitors of insulin-like growth factor-1 receptor (IGF-1R)", BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, PERGAMON, ELSEVIER SCIENCE, GB, vol. 19, no. 3, 1 February 2009 (2009-02-01), pages 1004-1008, XP025893617, ISSN: 0960-894X, DOI: 10.1016/J.BMCL.2008.11.058 [retrieved on 2008-11-20]	19
Y	the whole document in particular Tables 3 and 4 Scheme 2	1-17
X	----- ALAM ET AL: "Synthesis and SAR of aminopyrimidines as novel c-Jun N-terminal kinase (JNK) inhibitors", BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, PERGAMON, ELSEVIER SCIENCE, GB, vol. 17, no. 12, 15 June 2007 (2007-06-15) , pages 3463-3467, XP022097804, ISSN: 0960-894X, DOI: 10.1016/J.BMCL.2007.03.078	18
A	page 3466; figure 1; compounds 31,32	1-17
X	----- HUANG ET AL: "Synthesis and biological study of 2-amino-4-aryl-5-chloropyrimidine analogues as inhibitors of VEGFR-2 and cyclin dependent kinase 1 (CDK1)", BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, PERGAMON, ELSEVIER SCIENCE, GB, vol. 17, no. 8, 30 March 2007 (2007-03-30) , pages 2179-2183, XP022009228, ISSN: 0960-894X, DOI: 10.1016/J.BMCL.2007.01.086 figure 3; table 2; compound 8c ----- -/--	18

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2011/051465

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LUTH A ET AL: "Syntheses of 4-(indole-3-yl)quinazolines - A new class of epidermal growth factor receptor tyrosine kinase inhibitors", EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 43, no. 7, 1 July 2008 (2008-07-01), pages 1478-1488, XP022795993, ISSN: 0223-5234, DOI: 10.1016/J.EJMECH.2007.09.018 [retrieved on 2008-06-28] page 1480; figure 3; compounds 14, 19 page 1484, paragraph 4.12; compound 19 -----	18
X	WO 2009/024824 A1 (ASTRAZENECA AB [SE]; ASTRAZENECA UK LTD [GB]; ANDREWS DAVID MICHAEL [G] 26 February 2009 (2009-02-26) page 88; examples 20,21 -----	19
X	US 2008/300242 A1 (KUNTZ KEVIN [US] ET AL) 4 December 2008 (2008-12-04) examples 22B, 22C, 57E, 57F, 104C, 104D -----	19

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2011/051465

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 all searchable 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.:

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: 1-17

Compounds of the formula (I) suitable as ALK inhibitors, their pharmaceutical compositions, uses, methods of treatment comprising their administration and a process for their preparation.

2. claim: 18

A process for the preparation of the starting material of the formula (a).

3. claim: 19

A process for the preparation of the starting material of the formula (b).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2011/051465

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2007149427 A2	27-12-2007	AU 2007261440 A1 CA 2659582 A1 EP 2040546 A2 JP 2009541318 A US 2010267707 A1 WO 2007149427 A2	27-12-2007 27-12-2007 01-04-2009 26-11-2009 21-10-2010 27-12-2007
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US 2008300242 A1	04-12-2008	AR 066781 A1 CN 101932580 A EP 2162454 A1 JP 2010529029 A US 2008300242 A1 US 2010216779 A1 WO 2008150799 A1	09-09-2009 29-12-2010 17-03-2010 26-08-2010 04-12-2008 26-08-2010 11-12-2008