(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 March 2006 (02.03.2006)

(10) International Publication Number
WO 2006/021881 A3

(51) International Patent Classification:
C07D 401/14 (2006.01) A61K 31/4439 (2006.01)
C07D 401/04 (2006.01) A61P 35/00 (2006.01)

(21) International Application Number:
PCT/IB2005/002695

(22) International Filing Date: 15 August 2005 (15.08.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/605,244 26 August 2004 (26.08.2004) US
60/690,803 14 June 2005 (14.06.2005) US


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(84) Designated States (unless otherwise indicated, for every kind of regional protection available): AI, ARA (AR); BHR, BH, BG, CH, CN, CO, CZ, DE, DK, DM, DM, DZ, EC, EE, EG, ES, FI, FR, GB, GR, HU, HR, ID, IL, IN, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BI, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published: with international search report

(88) Date of publication of the international search report: 18 May 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PYRAZONE-SUBSTITUTED AMINOHETEROARYL COMPOUNDS AS PROTEIN KINASE INHIBITORS

(57) Abstract: Compounds of formula (1) are provided, as well as methods for their synthesis and use. Preferred compounds are potent inhibitors of the c-Met protein kinase, and are useful in the treatment of abnormal cell growth disorders, such as cancers.

(1)
**INTERNATIONAL SEARCH REPORT**

A. CLASSIFICATION OF SUBJECT MATTER

C07D401/14  C07D401/04  A61K31/4439  A61P35/00

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 database consulted during the international search (name of database and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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Further documents are listed in the continuation of Box C.

X 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.

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Date of the actual completion of the international search

3 February 2006

Date of mailing of the international search report

13/02/2006

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel: (+31-70) 340-2040, Tx: 31 651 epi nl,
Fax: (+31-70) 340-3016

Authorized officer

Hoepfner, W
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<td>WO 03/066608 A (YISSUM RESEARCH DEVELOPMENT COMPANY OF THE HEBREW; GAZIT, AVIV; LEVITZ) 14 August 2003 (2003-08-14) page 1, lines 5-7 page 3, Formula 1 page 4, Formulae 2-4 page 5, Formula 5 pages 6,7, Formulae page 27, line 1 - page 28, line 24</td>
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INTERNATIONAL SEARCH REPORT

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:
   Although claim 24 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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:

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 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.

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2005)
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<td>14-12-2005</td>
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