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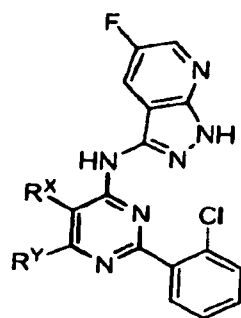
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(54) Title: AMINOPYRIMIDINES USEFUL AS INHIBITORS OF PROTEIN KINASES



(I)

(57) Abstract: The present invention relates to compounds (I) useful as inhibitors of protein kinases. The invention also provides pharmaceutically acceptable compositions comprising those compounds and methods of using the compounds and compositions in the treatment of various disease, conditions, and disorders. The invention also provides processes for preparing compounds of the invention.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/056433

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D471/04 A61K31/506 A61P3/10 A61P9/00 A61P25/00

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

EPO-Internal , WPI Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 2008/057940 A (VERTEX PHARMA [US]; JIMENEZ JUAN-MIGUEL [GB]; COLLIER PHILIP [GB]; MIL) 15 May 2008 (2008-05-15) claims 1,35; examples 3,9-11; table 1 -----	1-26
Y	WO 2004/013140 A (VERTEX PHARMA [US]; FORSTER CORNELIA J [US]; PARK LARRY C [US]; WANNAM) 12 February 2004 (2004-02-12) claims 1,15 -----	1-26
A	WO 02/50065 A (VERTEX PHARMA [US]; BEBBINGTON DAVID [GB]; CHARRIER JEAN-DAMIEN [GB];) 27 June 2002 (2002-06-27) claims 1,26 ----- -/-	1-26

☒ 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

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'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

23 September 2008

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01/10/2008

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International application No

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication where appropriate of the relevant passages	Relevant to claim No
x, Y	US 2003/078166 A1 (DAVIES ROBERT [US] ET AL) 24 April 2003 (2003-04-24) claims 1-13 -----	1-26

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/056433

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 claims 10-26 are 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 allsearchable 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 reportcovers 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/US2008/056433

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
wo 2008057940	A	15-05-2008	NONE	
wo 2004013140	A	12-02-2004	AT 339419 T	15-10-2006
			AU 2003257078 AI	23-02-2004
			BR 0313176 A	14-06-2005
			CA 2494100 AI	12-02-2004
			CN 1681815 A	12-10-2005
			CN 101037438 A	19-09-2007
			DE 60308387 T2	20-09-2007
			DK 1532145 T3	15-01-2007
			EP 1532145 AI	25-05-2005
			ES 2273043 T3	01-05-2007
			HK 1081186 AI	25-01-2008
			JP 2005539012 T	22-12-2005
			JP 2006273872 A	12-10-2006
			KR 20050032105 A	06-04-2005
			MX PA05001367 A	28-04-2005
			NZ 538426 A	31-05-2007
			NZ 550883 A	30-06-2008
wo 0250065	A	27-06-2002	AT 327989 T	15-06-2006
			AT 354573 T	15-03-2007
			AT 326460 T	15-06-2006
			AT 353890 T	15-03-2007
			AT 326461 T	15-06-2006
			AT 340172 T	15-10-2006
			AT 326463 T	15-06-2006
			AT 326462 T	15-06-2006
			AU 3116602 A	01-07-2002
			AU 3404702 A	01-07-2002
			AU 2001297619 B2	08-06-2006
			AU 2002231166 B2	21-02-2008
			AU 2002246754 B2	08-06-2006
			AU 2002255452 B2	08-06-2006
			BR 0116411 A	11-11-2003
			BR 0116493 A	30-09-2003
			CA 2432129 AI	25-07-2002
			CA 2432131 AI	01-08-2002
			CA 2432132 AI	01-08-2002
			CA 2432222 AI	15-08-2002
			CA 2432223 AI	06-09-2002
			CA 2432303 AI	29-08-2002
			CA 2432799 AI	27-06-2002
			CA 2432872 AI	27-06-2002
			CN 1487933 A	07-04-2004
			CN 1486310 A	31-03-2004
			CN 1549812 A	24-11-2004
			CN 1486311 A	31-03-2004
			CN 1486312 A	31-03-2004
			DE 60119774 T2	16-05-2007
			DE 60119775 T2	10-05-2007
			DE 60119776 T2	16-05-2007
			DE 60119777 T2	03-05-2007
			DE 60120219 T2	12-04-2007
			DE 60123283 T2	12-04-2007
			DE 60126658 T2	22-11-2007
			DE 60126828 T2	08-11-2007
			DK 1345922 T3	18-09-2006

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2008/056433

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0250065	A	DK 1355905 T3	18-06--2007
		DK 1353916 T3	29-01--2007
		EP 1345922 A1	24-09--2003
		EP 1355905 A1	29-10--2003
		EP 1345925 A2	24-09-- 2003
		EP 1345928 A2	24-09--2003
		EP 1345926 A2	24-09--2003
		EP 1353916 A2	22-10--2003
		EP 1345929 A2	24-09--2003
		EP 1345927 A1	24-09--2003
		ES 2266095 T3	01-03--2007
US 2003078166	A1	24-04-2003	US 2004116454 A1
			17-06-2004