(19) World Intellectual Property Organization

International Bureau



(43) International Publication Date 21 November 2002 (21.11.2002)

PCT

(10) International Publication Number WO 2002/092573 A3

(51) International Patent Classification⁷: C07D 403/04, 401/14, 405/14, 409/14, 417/14, 403/14, A61K 31/506, A61P 29/00

(21) International Application Number:

PCT/US2002/015606

(22) International Filing Date: 16 May 2002 (16.05.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data: 60/291,340 16 May 2001 (16.05.2001)

(71) Applicant (for all designated States except US): VERTEX PHARMACEUTICALS INCORPORATED [US/US]; Patent Department, 130 Waverly Street, Cambridge, MA 02139-4242 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): MOON, Young-Choon [KR/US]; 1 Great Rock Road, Lexington, MA 02173 (US).

(74) Agents: ROBIDOUX, Andrea et al.; Vertex Pharmaceuticals Inc., 130 Waverly Street, Cambridge, MA 02139-4242 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG,

SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

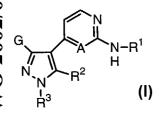
Published:

- with international search report
- with sequence listing part of description published separately in electronic form and available upon request from the International Bureau

(88) Date of publication of the international search report: 22 January 2004

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: HETEROCYCLIC SUBSTITUTED PYRAZOLES AS INHIBITORS OF SRC AND OTHER PROTEIN KINASES



(57) Abstract: The present invention provides compounds of formula I:wherein A is N or CR, and G, R_1 , R_2 , and R_3 are as described in the specification. These compounds are inhibitors of protein kinase, particularly inhibitors of Src mammalian protein kinase involved in cell proliferation, cell death and response to extracellular stimuli. The invention also relates to methods for producing these inhibitors. The invention also provides pharmaceutical compositions comprising the inhibitors of the invention and methods of utilizing those compositions in the treatment and prevention of various disorders.



INTERNATIONAL SEARCH REPORT

Internati Application No PCT/US 02/15606

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07D403/04 C07D401/14 CO7D409/14 CO7D417/14 CO7D405/14 C07D403/14 A61K31/506 A61P29/00

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) IPC 7 A61K A61F 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, PAJ, BIOSIS, MEDLINE, BEILSTEIN Data, CHEM ABS Data

C. DOCUME	ENTS CONSIDERED TO BE RELEVANT				
Category °	Citation of document, with indication, where appropriate, of	the relevant passages	Relevant to claim No.		
A	ZIMMERMANN J ET AL: "PHENYLAMINO-PYRIMIDINE (PAP) A NEW CLASS OF POTENT ANDSELE INHIBITORS OF PROTEIN KINASE ARCHIV DER PHARMAZIE, VCH VERLAGSGESELLSCHAFT MBH, WEIN vol. 329, no. 7, July 1996 (1) pages 371-376, XP000885618 ISSN: 0365-6233 abstract page 372; table I	1-32			
P,A	WO 02 22601 A (KAY DAVID ;BIN (GB); GOLEC JULIAN (GB); KNEG (G) 21 March 2002 (2002-03-21 abstract examples claims	TEL RONALD	1-32		
X Furth	ner documents are listed in the continuation of box C.	Patent family members are listed	in annex.		
"A" docume consid "E" earlier of filing of "L" docume which citation "O" docume other r"P" docume later th	ent defining the general state of the art which is not dered to be of particular relevance document but published on or after the international date ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another no rother special reason (as specified) ent referring to an oral disclosure, use, exhibition or means ent published prior to the international filling date but and the priority date claimed	or priority date and not in conflict with cited to understand the principle or th invention "X" document of particular relevance; the cannot be considered novel or cannot involve an inventive step when the document of particular relevance; the cannot be considered to involve an in document is combined with one or ments, such combination being obvio in the art. "&" document member of the same patent	 "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 		
2	9 October 2003	05/11/2003	05/11/2003		
Name and r	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 epo nl, Fax: (+31–70) 340–3016	Authorized officer Stix-Malaun, E			

International application No. PCT/US 02/15606

INTERNATIONAL SEARCH REPORT

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. χ	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
	Although claims 16-30 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 II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This inte	ernational 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.:
, []	No control of difficulty and according to the standard of the
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	The additional search fees were accompanied by the applicant's protest.
	No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internation Application No
PCT/US 02/15606

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
•			A ! !		
WO 0222601	Α	21-03-2002	AU	9091201 A	26-03-2002 26-03-2002
			ΑU	9091401 A	
			AU	9094401 A	26-03-2002
			AU	9101301 A	26-03-2002
			AU	9267001 A	26-03-2002
			AU	9455801 A	26-03-2002
			AU	9687101 A	26-03-2002
			AU	9687501 A	26-03-2002
			BR	0114088 A	17-06-2003
			CA	2422299 A1	21-03-2002
			CA	2422354 A1	21-03-2002
			CA	2422367 A1	21-03-2002
			CA	2422371 A1	21-03-2002
			CA	2422377 A1	21-03-2002
			CA	2422378 A1	21-03-2002
			CA	2422379 A1	21-03-2002
			CA	2422380 A1	21-03-2002
			EP	1317447 A1	11-06-2003
			EP	1317444 A1	11-06-2003
			ĒΡ	1317448 A1	11-06-2003
			ĒΡ	1318997 A1	18-06-2003
			EP	1317449 A1	11-06-2003
			EP	1317450 A1	11-06-2003
			EP	1317450 A1 1317452 A1	11-06-2003
			EP	1318814 A2	18-06-2003
			HU	0302172 A2	29-09-2003
			HU	0302172 A2	29-09-2003
			NO	20031188 A	13-05-2003
					13-05-2003
			NO NO	20031189 A	
			NO	20031190 A	13-05-2003
			NO	20031191 A	13-05-2003
			MO	0222603 A1	21-03-2002
			WO	0222601 A1	21-03-2002
			WO	0222604 A1	21-03-2002
			MO	0222605 A1	21-03-2002
			WO	0222606 A1	21-03-2002
			WO	0222607 A1	21-03-2002
			WO	0222608 A1	21-03-2002
			WO	0222602 A2	21-03-2002
			US	2003073687 A1	17-04-2003
			US	2003083327 A1	01-05-2003
			US	2003064981 A1	03-04-2003
			US	2003064982 A1	03-04-2003
			US	2003055044 A1	20-03-2003
			US	2003078166 A1	24-04-2003
			ΑŪ	3116602 A	01-07-2002
			AU	3404702 A	01-07-2002
			BR	0116493 A	30-09-2003
			CA	2432129 A1	25-07-2002
W0 0246184	Α	13-06-2002	 AU	2878302 A	18-06-2002
JE IOZOT		10 00 E00E	CA	2430539 A1	13-06-2002
			EP	1343781 A1	17-09-2003
			ÜS	2002111353 A1	15-08-2002
			WO	0246184 A1	13-06-2002
			1/11()		

INTERNATIONAL SEARCH REPORT

Internation Application No
PCT/US 02/15606

C.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	101/03 02/13000
Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
E	WO 02 46184 A (LEDEBOER MARK ;VERTEX PHARMA (US); MOON YOUNG CHOON (US); SALITURO) 13 June 2002 (2002-06-13) abstract claims examples	1-32