(19) World Intellectual Property Organization

International Bureau





PCT

(43) International Publication Date 22 January 2009 (22.01.2009)

(51) International Patent Classification:

 C07D 401/12 (2006.01)
 A61P 11/00 (2006.01)

 C07D 405/12 (2006.01)
 A61P 17/00 (2006.01)

 C07D 207/44 (2006.01)
 A61P 19/00 (2006.01)

A61K 31/4409 (2006.01)

(21) International Application Number:

PCT/US2008/070312

(22) International Filing Date: 17 July 2008 (17.07.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/950,680 19 July 2007 (19.07.2007) US

(71) Applicant (for all designated States except US): WYETH [US/US]; Five Giralda Farms, Madison, New Jersey 07940 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): LOVERING, Frank Eldridge [US/US]; 2 Sutton Place, Acton, Massachusetts 01720 (US). KIRINCICH, Steven John [US/US]; 76 Channing Road, Concord, Massachusetts 01742 (US). WANG, Weiheng [US/US]; 33 Winterberry Way, Bedford, Massachusetts 01730 (US). TELLIEZ, Jean-baptiste [US/US]; 211 East Emerson Road, Lexington, MA 02420 (US). RESNICK, Lynn [US/US]; 5 Borelle Square, Parlin, New Jersey 08859 (US). SABALSKI, Joan E. [US/US]; 38 Elton Avenue, Hamilton, NJ 08620 (US). BANKER, Annette L. [US/US]; 707 Fox Run Drive, Plainsboro, NJ 08536 (US). BUTERA, John

WO 2009/012375 A3

[US/US]; 6 Lawrence Spring Drive, Clarksburg, NJ 08510
(US). MCFADYEN, Iain [GB/US]; 32 Maurice Street,

(10) International Publication Number

(74) Agent: GOODSON, Susanne H.; Fish & Richardson P.C., P.O. Box 1022, Minneapolis, Minnesota 55440-1022 (US).

Medford, MA 02155 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report: 2 July 2009

(54) Title: SQUARATE KINASE INHIBITORS

$$\begin{array}{c} O \\ O \\ Het - N \\ R^{10} \\ R^{9} \end{array} \qquad (I)$$

(57) Abstract: The present application provides compounds of Formula (I): and pharmaceutically acceptable salts thereof and pharmaceutical compositions thereof, wherein Het, R^4 , R^9 , and R^{10} are defined herein. Compounds of formula (I) are useful as inhibitors of MAP kinase activated protein kinase 2 (MK2).

INTERNATIONAL SEARCH REPORT

International application No PCT/US2008/070312

INV.	CO7D401/12 A61P17/00	C07D405/12 A61P19/00	C07D207/4	4 A61K31/4409	A61P11/00						
According to	o International Patent Cla	assification (IPC) or to bot	national classification	on and IPC							
	SEARCHED										
Minimum documentation searched (classification system followed by classification symbols) C07D											
				h documents are included in the f							
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, CHEM ABS Data, BEILSTEIN Data											
C. DOCUMENTS CONSIDERED TO BE RELEVANT											
Category*	Citation of document,	with indication, where app	propriate, of the releva	ant passages	Relevant to claim No.						
х .	WO 2004/01 PHARMACOPE 5 February page 89, 1 page 93	1-48									
X	SERGEY A I the Substi SYNTHETIC FRANCIS, F vol. 37, r 1 January 2527-2542, ISSN: 0039 page 2529,	1-48									
X Furti	her documents are listed	in the continuation of Bo	x 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 combined with one or more other such documents, such combination being obvious to a person skilled in the art. 'X' 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.											
Date of the actual completion of the international search Date of mailing of the international search report											
27 April 2009				14/05/2009							
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016			12	Authorized officer Beyss-Kahana, Ellen							

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/070312

:/Continua	tion). DOCUMENTS CONSIDERED TO BE RELEVANT	PCT/US2008/070312
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 464 867 A (ANTANE MADELENE M [US] ET AL) 7 November 1995 (1995-11-07)	1
(column 1, line 12; claim 1 ———— GRÜNEFELD, ET AL.: "Zur Reaktion von Quadratsäuredimethylester mit N,N-disubstituierten Hydrazin-Derivaten" ARCHIV DER PHARMAZIE, vol. 318, 1985, pages 984-988, XP002518747 page 985, compound 3	1-42
, X	WO 2007/140233 A (ABBOTT LAB [US]; DIEBOLD ROBERT B [US]; DJURIC STEVAN W [US]; GIRANDA) 6 December 2007 (2007-12-06) page 1, line 10; claim 1	1-48
		-

5

International application No. PCT/US2008/070312

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:
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
As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. X 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 2-39, 44 and partially 1, 40-43, 45-48

A compound according to present formula (I) wherein R4 = a cyclic moiety

2. claims: partially 1, 40-43, 45-48

A compound according to present formula (I) wherein $R4 = a \ CR1R2R3$

3. claims: partially 1, 40-43, 45-48

A compound according to present formula (I) wherein R4 = a carbon chain

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2008/070312

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 2004011418	A	05-02-2004	AU BR CA EP JP KR MX NZ US	2003259302 A1 0313109 A 2496676 A1 1539678 A1 2005534684 T 20050026060 A PA05001274 A 538521 A 2007021494 A1	16-02-2004 21-06-2005 05-02-2004 15-06-2005 17-11-2005 14-03-2005 08-09-2005 29-02-2008 25-01-2007
US 5464867	- —	07-11-1995	US US US US ZA	5536731 A 5536741 A 5512585 A 5530025 A 9509630 A	16-07-1996 16-07-1996 30-04-1996 25-06-1996 21-08-1997
WO 2007140233	Α	06-12-2007	CA EP US	2647592 A1 2021316 A1 2008015192 A1	06-12-2007 11-02-2009 17-01-2008