



- (51) **International Patent Classification:**
C07D 239/48 (2006.01) A61K 31/506 (2006.01)
C07D 403/04 (2006.01) A61P 35/00 (2006.01)
- (21) **International Application Number:** PCT/US2012/031575
- (22) **International Filing Date:** 30 March 2012 (30.03.2012)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:** 61/469,482 30 March 2011 (30.03.2011) US
- (71) **Applicant (for all designated States except US):** H. LEE MOFFITT CANCER CENTER & RESEARCH INSTITUTE INC. [US/US]; 12902 Magnolia Dr., Tampa, FL 33612-9497 (US).
- (72) **Inventors; and**
- (75) **Inventors/Applicants (for US only):** LAWRENCE, Nicholas, J. [GB/US]; 16346 Heathrow Drive, Tampa, FL 33647 (US). SEBTL, Said, M. [US/US]; 8957 Magnolia Chase Circle, Tampa, FL 33647 (US). PIREDDU, Roberta [IT/US]; 13102 Thomasville Circle, Apt. C Bldg 52, Tampa, FL 33647 (US).
- (74) **Agents:** PACE, Doran, R. et al.; Saliwanchik, Lloyd & Eisenschenk, P.O. Box 142950, Gainesville, FL 32614-2950 (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, CL, 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, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, 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, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— with international search report (Art. 21(3))
- (88) **Date of publication of the international search report:**
17 January 2013



WO 2012/135697 A3

(54) **Title:** NOVEL RHO KINASE INHIBITORS AND METHODS OF USE

(57) **Abstract:** The subject invention concerns materials and methods for treating diseases and disorders associated with expression of Rho associated kinases (ROCKs). Examples of diseases and disorders contemplated within the scope of the invention include, but are not limited to, oncological disorders, cardiovascular diseases, CNS disorders, and inflammatory disorders. In one embodiment, a method of the invention comprises administering a therapeutically effective amount of one or more compounds of the present invention, or a composition comprising the compounds, to a person or animal in need of treatment. The subject invention also concerns compounds that inhibit ROCKs, and compositions that comprise the inhibitor compounds of the invention. Compounds contemplated within the scope of the invention include, but are not limited to, those compounds shown in Table (5).

A. CLASSIFICATION OF SUBJECT MATTER*C07D 239/48(2006.01)i, C07D 403/04(2006.01)i, A61K 31/506(2006.01)i, A61P 35/00(2006.01)i*

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 239/48; C07D 239/42; A61K 31/505; A61P 35/00

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 practicable, search terms used)

eKOMPASS (KIPO internal), NCBI (PubMed, MeSH), Google

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PubChemCompound, datasheet [online compound summary] Retrieved from the Internet: <URL: http://pubchem.ncbi.nlm.nih.gov/search/search.cgi>	1,8,10
A	See CID 459822, CID 437671, CID 31036, CID 35750, CID 459823.	2-4,9
X	US 3478030 A (JAMES HAROLD SHORT et al.) 11 November 1969 See column 1, lines 14-42; examples 2-3.	1,5,8,10
X	WO 2009-158011 A1 (AMGEN INC.) 30 December 2009 See compound A.95; examples 1-11, 18-31, 39-58, 93-103, 143-146 and 148-164, etc.; claims 1-25; abstract.	1-5,8-10
X	US 5223505 A (RODNEY B. HARGREAVES et al.) 29 June 1993 See formulas I and 3-5; examples 3-19, 21-43, 50, 55, 58-76, 110-112, etc.; abstract.	1-5,8-10
X	US 6924290 B2 (DHANAPALAN NAGARATHNAM et al.) 02 August 2005 See claims 1-17; abstract.	1,8,10

 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 application or patent 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 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

18 SEPTEMBER 2012 (18.09.2012)

Date of mailing of the international search report

19 SEPTEMBER 2012 (19.09.2012)

Name and mailing address of the ISA/KR

Korean Intellectual Property Office
189 Cheongsu-ro, Seo-gu, Daejeon Metropolitan
City, 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

SUNG Sun Young

Telephone No. 82-42-481-8405



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.: 6-7, 11-14
because they relate to subject matter not required to be searched by this Authority, namely:
The claims 6-7 and 11-14 pertain to methods for treatment of the human body by therapy, and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(I) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.
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 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.:
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/US2012/031575

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 3478030 A	11.11.1969	None	
WO 2009-158011 A1	30.12.2009	AU 2009-263037 B2 CA 2728767 A1 EP 2315751 A1 JP 2011-525915 A MX 2010013920 A US 2011-0086834 A1	06.10.2011 30.12.2009 04.05.2011 29.09.2011 21.02.2011 14.04.2011
US 5223505 A	29.06.1993	CN 1024793 C CN 1047080 A CN 1047080 CO EP 0422178 A1 EP 0422178 B1 KR 10-1992-0700203 A WO 90-12790 A1	01.06.1994 21.11.1990 11.03.1994 17.04.1991 05.10.1994 19.02.1992 01.11.1990
US 6924290 B2	02.08.2005	US 2004-0002508 A1 US 2005-0192304 A1	01.01.2004 01.09.2005