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3590 Diepenbeek (BE). BOURIN, Arnaud, Pierre, Jean [FR/BE]; Life Sciences Incubator, Agoralaan A bis, B-3590 Diepenbeek (BE).

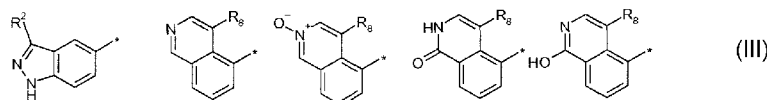
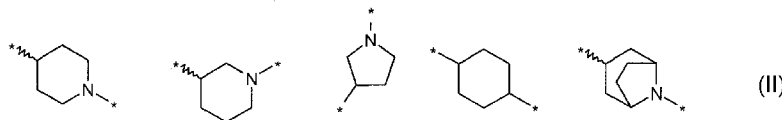
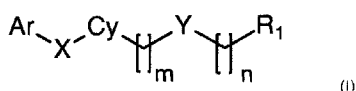
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[Continued on next page]

(54) Title: NOVEL ROCK INHIBITORS



(57) Abstract: The present invention relates to new kinase inhibitors of Formula (I), wherein X is oxygen, -NH-, or a direct bond; Y is -NH- or a direct bond; n is an integer from 0 to 4; m is an integer from 0 to 4; Cy represents a bivalent radical consisting of a saturated (poly)cycle, including fused, bi-, spiro or bridged carbocycles and heterocycles; in particular selected from the group consisting of: Formula (II), Ar is selected from the group comprising: Formula (III), R² is hydrogen or methyl; R⁸ is hydrogen, methyl, halogen, or alkynyl; R¹ is an aryl or heteroaryl more specifically ROCK inhibitors, compositions, in particular pharmaceuticals, comprising such inhibitors, and to uses of such inhibitors in the treatment and prophylaxis of disease. In particular, the present invention relates to new ROCK inhibitors, compositions, in particular pharmaceuticals, comprising such inhibitors, and to uses of such inhibitors in the treatment and prophylaxis of disease. In addition, the invention relates to methods of treatment and use of said compounds in the manufacture of a medicament for the application to a number of therapeutic indications including sexual dysfunction, inflammatory diseases, ophthalmic diseases and Respiratory diseases.

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*
- *of inventorship (Rule 4.17(iv))*

Published:

- *with international search report (Art. 21(3))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(88) Date of publication of the international search report:

17 January 2013

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2012/057785

A. CLASSIFICATION OF SUBJECT MATTER					
INV.	C07D401/12	C07D401/14	C07D405/14	C07D409/14	C07D451/04
	A61K31/4725	A61K31/439	A61K31/4468	A61P9/00	A61P11/00
	A61P15/00	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 A61K A61P

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) EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2010/022517 A1 (RICHARDS LORI A [US] ET AL) 28 January 2010 (2010-01-28) claims; examples 1.112, 1.126, 1.209, 1.216 -----	1-24
A	WO 2008/049919 A2 (DEVGEN NV [BE]; DEFERT OLIVIER [FR]; LEYSEN DIRK [BE]; VAN ROMPAEY PHI) 2 May 2008 (2008-05-02) claims; examples -----	1-24
A	WO 2007/133622 A2 (VERTEX PHARMA [US]; GREEN JEREMY [US]; CAO JINGRONG [US]; BANDARAGE UP) 22 November 2007 (2007-11-22) the whole document -----	1-24
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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	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 13 September 2012	Date of mailing of the international search report 23/11/2012
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	Authorized officer Bosma, Peter

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2012/057785

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 2012/015760 A1 (INSPIRE PHARMACEUTICALS INC [US]; LAMPE JOHN W [US]; SHAVER SAMMY R [U] 2 February 2012 (2012-02-02) claims; examples -----	1-24
X	US 2008/214614 A1 (LAMPE JOHN W [US] ET AL) 4 September 2008 (2008-09-04) claims; example 1.112 -----	1-24
X	WO 2008/077057 A2 (INSPIRE PHARMACEUTICALS, INC., USA) 26 June 2008 (2008-06-26) the whole document -----	1-24
X	WO 2010/065782 A1 (INSPIRE PHARMACEUTICALS, INC., USA) 10 June 2010 (2010-06-10) the whole document -----	1-24

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2012/057785

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:

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

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 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 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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-24(partially)

Compounds according the formula (I) in claim 1, wherein R1 is an aryl or heteroaryl optionally substituted with halo or C1-6alkyl; wherein said aryl or heteroaryl is substituted with a substituent consisting of $-(CH_2)_p-C(=O)-OR_{21}$

2. claims: 1-24(partially)

Compounds according the formula (I) in claim 1, wherein R1 is an aryl or heteroaryl optionally substituted with halo or C1-6alkyl; wherein said aryl or heteroaryl is substituted with a substituent consisting of $-(CH_2)_p-C(=O)-NR_{3R4}$

3. claims: 1-24(partially)

Compounds according the formula (I) in claim 1, wherein R1 is an aryl or heteroaryl optionally substituted with halo or C1-6alkyl; wherein said aryl or heteroaryl is substituted with a substituent consisting of $-(CH_2)_p-C(=O)-SR_{22}$

4. claims: 1-24(partially)

Compounds according the formula (I) in claim 1, wherein R1 is an aryl or heteroaryl optionally substituted with halo or C1-6alkyl; wherein said aryl or heteroaryl is substituted with a substituent consisting of Het1, -OHet1, -NH-Het1, or -S-Het1

5. claims: 1-24(partially)

Compounds according the formula (I) in claim 1, wherein R1 is an aryl or heteroaryl optionally substituted with halo or C1-6alkyl; wherein said aryl or heteroaryl is substituted with a substituent consisting of -O-C1-6alkyl, -NH-C1-6alkyl, -S-C1-6alkyl, or -C1-6alkyl; wherein said -O-C1-6alkyl, -NH-C1-6alkyl, -S-C1-6alkyl, or -C1-6alkyl are each independently substituted with a substituent selected from the group consisting of $-C(=O)-OR_{21}$, $-C(=O)-NR_{3N4}$, Het1, -O-Het1, -NH-Het1, and -S-Het1.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2012/057785

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2010022517	A1	28-01-2010	NONE

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