(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 August 2012 (02.08.2012)

WIPO | PCT

(10) International Publication Number
WO 2012/101065 A3

(51) International Patent Classification:
C07D 401/04 (2006.01) *C07D 413/14* (2006.01)
C07D 401/14 (2006.01) *A61K 31/444* (2006.01)
C07D 403/04 (2006.01) *A61K 31/506* (2006.01)
C07D 405/14 (2006.01) *A61P 35/00* (2006.01)
C07D 409/14 (2006.01)

(21) International Application Number:
PCT/EP2012/050909

(22) International Filing Date:
20 January 2012 (20.01.2012)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/437,071 28 January 2011 (28.01.2011) US

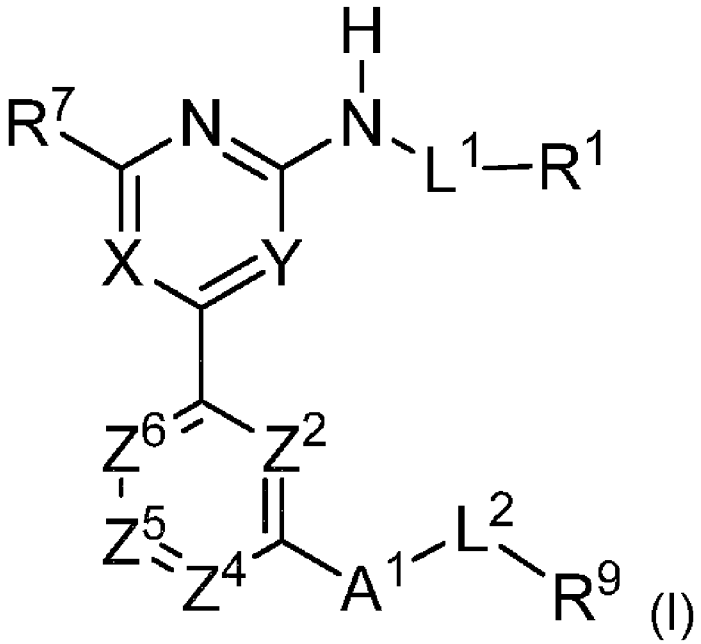
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[Continued on next page]

(54) Title: PYRIMIDINE BIARYL AMINE COMPOUNDS AND THEIR USE AS CDK9 INHIBITORS



(I)

(57) Abstract: The present invention provides a pyrimidine compound of formula (I): wherein one of X and Y but not both is N, and pharmaceutically acceptable salts, enantiomers, stereoisomers, rotamers, tautomers, diastereomers, deuterated versions, or racemates thereof. These compounds inhibit the activity of CDK9 and are thus useful as pharmaceuticals. Also provided are methods of treating a disease or condition mediated by CDK9 using the compounds of Formula I and isomers thereof, and pharmaceutical compositions comprising such compounds.

WO 2012/101065 A3

(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).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

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:
10 January 2013

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2012/050909

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D401/04 C07D401/14 C07D403/04 C07D405/14 C07D409/14
C07D413/14 A61K31/444 A61K31/506 A61P35/00
ADD.
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, WPI Data, CHEM ABS Data, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/061761 A2 (DU PONT [US]; CHEN YUZHONG [US]; SHARPE PAULA LOUISE [US]) 14 May 2009 (2009-05-14) examples; tables	1-3,5-32
X	WO 2008/079933 A2 (NOVARTIS AG [CH]; BECKWITH ROHAN ERIC JOHN [US]; CURTIS DANIEL TIM [US) 3 July 2008 (2008-07-03) claims; examples	1-3,5-32
X	WO 2008/148889 A1 (BAYER CROPSCIENCE SA [FR]; BEIER CHRISTIAN [FR]; COQUERON PIERRE-YVES) 11 December 2008 (2008-12-11) claims; examples	1-3,5-32

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[X] Further documents are listed in the continuation of Box 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

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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	Date of mailing of the international search report
9 May 2012	23/11/2012

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	

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Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/93682 A1 (SYNGENTA PARTICIPATIONS AG [CH]; EBERLE MARTIN [CH]; STIERLI DANIEL [C) 13 December 2001 (2001-12-13) examples	1-3,5-32
X	WO 95/09853 A1 (CIBA GEIGY AG [CH]; ZIMMERMANN JUERG [CH]) 13 April 1995 (1995-04-13) claims; examples	1-3,5-32
X	CHRISTIAN PILLONEL: "Evaluation of phenylaminopyrimidines as antifungal protein kinase inhibitors", PEST MANAGEMENT SCIENCE, WILEY & SONS, BOGNOR REGIS; GB, vol. 61, 13 June 2005 (2005-06-13), pages 1069-1076, XP002429106, ISSN: 1526-498X, DOI: 10.1002/PS.1080 page 1070; examples 6, 8, 13; table 1	1
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A	KUO G-H ET AL: "Synthesis and Identification of [1,3,5]Triazine-pyridine Biheteroaryl as a Novel Series of Potent Cyclin-Dependent Kinase Inhibitors", JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, US, vol. 48, no. 14, 27 May 2005 (2005-05-27), pages 4535-4546, XP002468199, ISSN: 0022-2623, DOI: 10.1021/JM040214H the whole document	1-40

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2012/050909

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.:

1-3, 10, 16-21(completely); 5-9, 11-15, 22-32(partially)

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: 1-3, 10, 16-21(completely); 5-9, 11-15, 22-32(partially)

   Compounds of formula (I)

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2. claims: 4(completely); 5-9, 11-15, 22-32(partially)

   Compounds of formula (IA)

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3. claims: 33-40

   Compounds of formula (IB)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2012/050909

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Information on patent family members

International application No
PCT/EP2012/050909

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