

REVISED VERSION

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
4 December 2014 (04.12.2014)



(10) International Publication Number
WO 2014/194254 A9

(51) International Patent Classification:
A61K 31/4725 (2006.01)

(21) International Application Number:

PCT/US2014/040337

(22) International Filing Date:

30 May 2014 (30.05.2014)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/829,168	30 May 2013 (30.05.2013)	US
61/836,088	17 June 2013 (17.06.2013)	US
61/863,365	7 August 2013 (07.08.2013)	US
61/888,454	8 October 2013 (08.10.2013)	US
PCT/US2013/067929		
	1 November 2013 (01.11.2013)	US
61/991,414	9 May 2014 (09.05.2014)	US

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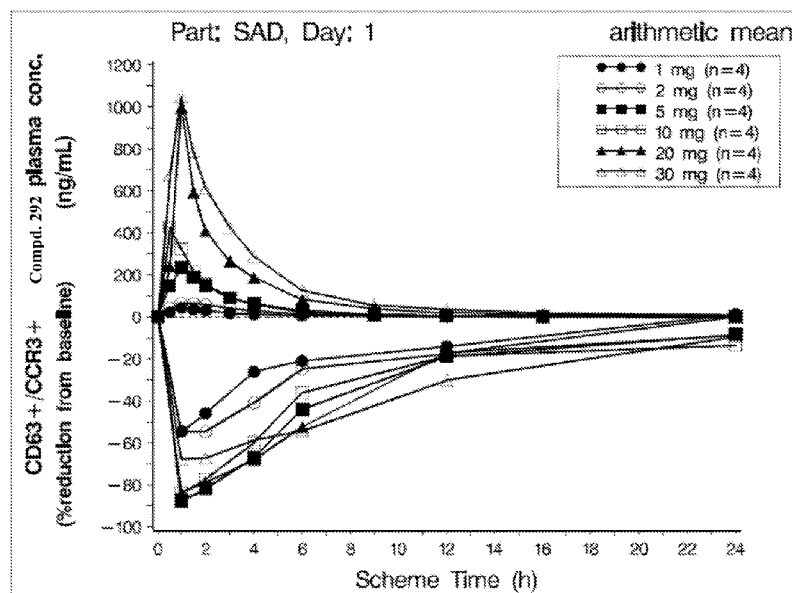
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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, 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, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM,

[Continued on next page]

(54) Title: TREATMENT OF CANCERS USING PI3 KINASE ISOFORM MODULATORS

FIG. 1



SAD part, single dose QD

(57) Abstract: Provided herein are methods, kits, and pharmaceutical compositions that include a PI3 kinase inhibitor for treating cancers or hematologic disorders. Provided herein are methods, compositions, and kits for treating or preventing cancers or diseases, such as hematologic malignancies, which have a high expression level of one or more isoform(s) of PI3K (e.g., PBK-8 and/or PI3K-y). In one embodiment, the methods, compositions, and kits provided herein relate to administering an isoform-selective PI3K modulator.



TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

Published:

— with international search report (Art. 21(3))

- (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, 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, KM, ML, MR, NE, SN, TD, TG).

- (88) Date of publication of the revised international search report:**

23 April 2015

- (15) Information about Correction:**
see Notice of 23 April 2015

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2014/040337

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.: 6, 13-30
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 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.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/040337

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61K 31/4725 (2014.01) CPC - A61K 45/06 (2014.09) 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(8) - A61K31/00, 31/4725, 31/506, 31/519, 31/52, 31/5377, 45/06; A61P 35/00, 35/02 (2014.01) USPC - 424/133.1, 94.6; 514/171, 234.2, 256, 262.1, 263.22, 265.1, 275, 300 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched CPC - A61K 31/00, 45/06; C07D 471/04, 473/00, 401/12; G01N 33/574 (2014.09) Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PatBase, Google Patents, Google, PubMed		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2012/0183535 A1 (BUGGY et al) 19 July 2012 (19.07.2012) entire document	1-3
Y		4, 5, 7-12
Y	WO 2013/059738 A2 (BUGGY et al) 23 April 2013 (23.04.2013) entire document	4, 5
Y	D'CRUZ et al. "Novel Bruton's tyrosine kinase inhibitors currently in development" OncoTargets and Therapy, 05 March 2013 (05.03.2013), Vol. 2013, No. 6, Pgs. 161-176. entire document	5
Y	PHARMACYCLICS INC Form 8-K filing. 16 May 2013 (16.05.2013). Article retrieved from the Internet: <http://www.sec.gov/Archives/edgar/data/949699/000092189513001115/0000921895-13-001115-index.htm> on 22 September 2014 (22.09.2014). entire document	7-12
T, X	CHIRON et al. "Cell-Cycle Reprogramming for PI3K Inhibition Overrides a Relapse-Specific C481S BTK Mutation Revealed by Longitudinal Functional Genomics in Mantle Cell Lymphoma," Cancer Discovery, 31 July 2014 (31.07.2014), Vol. 4, Pgs. 1022-1035. entire document	1-5, 7-12
P, X	WO 2014/018567 A1 (CHANG et al) 30 January 2014 (30.01.2014) entire document	1-5, 7-12
P, X	WO 2014/071109 A1 (STERN et al) 08 May 2014 (08.05.2014) entire document	1-5, 7-12
☐ Further documents are listed in the continuation of Box C. ☐		
* 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 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 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 22 September 2014		Date of mailing of the international search report 15 OCT 2014
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201		Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774