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

(19) World Intellectual Property Organization

International Bureau





(10) International Publication Number WO 2016/172134 A3

(43) International Publication Date 27 October 2016 (27.10.2016)

(51) International Patent Classification: **C07D 239/86** (2006.01) C07D 207/09 (2006.01) C07D 403/12 (2006.01)

(21) International Application Number:

PCT/US2016/028332

(22) International Filing Date:

20 April 2016 (20.04.2016)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 1506872.9

22 April 2015 (22.04.2015)

GB

- (71) Applicant: GLAXOSMITHKLINE INTELLECTUAL PROPERTY DEVELOPMENT LIMITED [GB/GB]; 980 Great West Road, Brentford Middlesex TW8 9GS (GB).
- (71) Applicant (for PG only): GLAXOSMITHKLINE LLC [US/US]; Corporation Service Company, 2711 Centerville Road, Suite 400, Wilmington, Delaware 19808 (US).
- (72) Inventors: CASILLAS, Linda, N.; GlaxoSmithKline, Global Patents, 1250 South Collegeville Road, Collegeville, Pennsylvania 19426 (US). HARLING, John, David; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). MIAH, Afjal, Hussain; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). RACKHAM, Mark, David; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB). SMITH, Ian, Edward, David; GlaxoSmithKline, Gunnels Wood Road, Stevenage Hertfordshire SG1 2NY (GB).
- Agent: BRINK, Robert, H.; GlaxoSmithKline, Global Patents, Five Moore Drive - P. O. Box 13398, Research Triangle Park, North Carolina 27709 (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, 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, 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, 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, ST, 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).

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))

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: 1 December 2016



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 16/28332

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:					
Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such extent that no meaningful international search can be carried out, specifically:	an				
Claims Nos.: 5-6 and 8-18 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 searchab claims.	le				
2. As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment additional fees.	of				
3. As only some of the required additional search fees were timely paid by the applicant, this international search report cover only those claims for which fees were paid, specifically claims Nos.:	rs				
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report restricted to the invention first mentioned in the claims; it is covered by claims Nos.:	is				
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/US 16/28332

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - C07D 239/86; C07D 403/12; C07D 207/09 (2016.01) CPC - C07D239/86; C07D403/12; C07D207/09; A61K38/06 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): C07D 239/86; C07D 403/12; C07D 207/09 (2016.01) CPC: C07D239/86; C07D403/12; C07D207/09; A61K38/06					
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC: 514/266.2; 544/293; 514/18.9; 530/331					
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PatBase, Google Scholar, PubWEST PROTAC, Receptor Interacting Protein-2 kinase, RIP2 kinase inhibitor, 4-aminoquinazoline, IAP binding, tripeptide, linker, targeted ubiquitination					
C. DOCUMENTS CONSIDERED TO BE RELEVANT					
Category*	Citation of document, with indication, where a	ppropriate, of the relevant passages	Relevant to claim No.		
	WO 2014/043437 A1 (GLAXOSMITHKLINE LLC.) 20 1; pg 57, ln 10-14	March 2014 (20.03.2014) pg 39, Example	1-4, 7		
A	US 2010/0273812 A1 (WANG et al.) 28 October 2010	1-4, 7			
A	US 2006/0128632 A1 (SHARMA et al.) 15 June 2006	1-4, 7			
	US 2014/0356322 A1 (CREWS et al.) 04 December 2 6 to Fig 12	1-4, 7			
Α	BUCKLEY et al. 'Small Molecule Control of Intracellula of the Ubiquitin Proteasome System', Angew Chem Inpg 29, Fig 6; pg 35, Fig 11		1-4, 7		
A	PENG et al. 'Bivalent Smac Mimetics with a Diazabicyclic Core as Highly Potent Antagonists of XIAP and cIAP1/2 and Novel Anticancer Agents', Journal of Medicinal Chemistry, 2012, Vol.55, pages 106-114 [Published Online: December 2011]; pg 107, Fig 1; Table 1; pg 108, Fig 3				
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 "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 considered novel or cannot be considered to involve an inverse when the document is taken alone					
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 "O" document of particular relevance; the claimed invention cannot considered to involve an inventive step when the document combined with one or more other such documents, such combination being obvious to a person skilled in the art.					
"P" documen	comb do trous to a person strined in the art				
Date of the actual completion of the international search Date of mailing of the international search report					
26 September 2016 2 4 0 CT 2016					
Name and mailing address of the ISA/US Authorized officer:					
P.O. Box 1450	, Attn: ISA/US, Commissioner for Patents , Alexandria, Virginia 22313-1450 . 571-273-8300	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774			

Form PCT/ISA/210 (second sheet) (January 2015)