



(43) International Publication Date
24 May 2012 (24.05.2012)

(10) International Publication Number
WO 2012/068468 A1

(51) International Patent Classification:

A61K 31/44 (2006.01) *C07D 417/14* (2006.01)
C07D 401/00 (2006.01) *C12Q 1/68* (2006.01)
C07D 417/00 (2006.01) *G01N 33/53* (2006.01)

(21) International Application Number:

PCT/US2011/061408

(22) International Filing Date:

18 November 2011 (18.11.2011)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/415,620 19 November 2010 (19.11.2010) US
61/559,072 12 November 2011 (12.11.2011) US

(71) Applicant (for all designated States except US): **GLAXO-SMITHKLINE LLC** [US/US]; One Franklin Plaza, 200 North 16th Street, Philadelphia, PA 19102 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BLEAM, Maureen** [US/US]; 1250 South Collegeville Road, Collegeville, PA 19426 (US). **GILMER, Tona, M.** [US/US]; Five Moore Drive, Research Triangle Park, NC 27709 (US). **GREGER, James, G., Jr.** [US/US]; 1250 South Collegeville Road, Collegeville, PA 19426 (US). **LAQUERRE, Sylvie, G.** [US/US]; 709 Swedeland Road, King of Prussia, PA 19406 (US). **LIU, Li** [US/US]; 1250 South Collegeville Road, Collegeville, PA 19426 (US).

(74) Agents: **TOMASKA, Margaret M.** et al.; Glaxosmithkline, Global Patents-US, UW2220, 709 Swedeland Road, P.O. Box 1539, King of Prussia, PA 19406-0939 (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).

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))
- with sequence listing part of description (Rule 5.2(a))

(54) Title: METHOD OF TREATMENT WITH BRAF INHIBITOR

(57) Abstract: The disclosure is directed to a method of treating humans suffering from V600 mutant melanoma that incorporates the detection of the presence or absence of at least one mutation in at least one NRAS protein and/or at least one MEK1 protein, or a gene encoding said protein, and subsequently initiating treatment, modifying treatment, or discontinuing treatment with a chemotherapeutic agent selected from a BRAf inhibitor or other suitable agent based upon the presence or absence of said mutation.



WO 2012/068468 A1