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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 April 2011 (21.04.2011)

PCT

(10) International Publication Number
WO 2011/046894 A1

(51) International Patent Classification:
A61K 31/54 (2006.01)

(21) International Application Number:
PCT/US2010/052242

(22) International Filing Date:
12 October 2010 (12.10.2010)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/250,635 12 October 2009 (12.10.2009) US

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

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **AUGER, Kurt** [US/US]; 1250 South Collegeville Road, Collegeville, PA 19426 (US). **BACHMAN, Kurtis, Earl** [US/US]; 1250 South Collegeville Road, Collegeville, PA 19426 (US). **GRESHOCK, Joel, David** [US/US]; 1250 South Collegeville Road, Collegeville, PA 19426 (US). **GILMER, Tona** [US/US]; Five Moore Drive, Research Triangle Park, NC 27709 (US). **LAQUERRE, Sylvie** [US/US]; 709 Swedeland Road, King Of Prussia, PA 19406 (US). **MORRIS, Shannon, Renae** [US/US]; Five Moore Drive, Research Triangle Park, NC 27709 (US).

(74) Agents: **PENG, Tony, W.** et al.; Glaxosmithkline, Corporate Intellectual Property, UW2220, 709 Swedeland Road, P.O. Box 1539, King Of Prussia, PA 19406-09039 (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, RO, RS, RU, 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, 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).

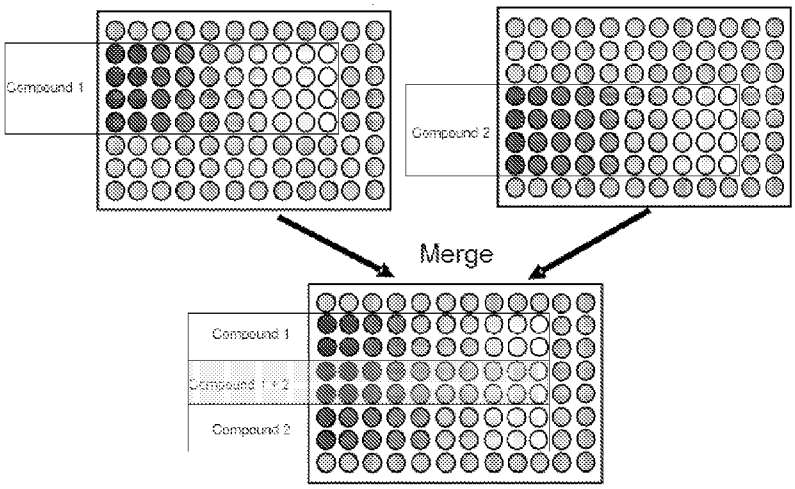
Declarations under Rule 4.17:

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

[Continued on next page]

(54) Title: COMBINATION

Figure 1. Representation of plate arrangements for Fixed concentration dosing in a 96 well plate.



(57) Abstract: The present invention relates to a method of treating cancer in a mammal and to pharmaceutical combinations useful in such treatment. In particular, the method relates to a novel combination comprising the MEK inhibitor: N-{3-[3-cyclopropyl-5-(2-fluoro-4- iodo-phenylamino)6,8-dimethy;-2,4,7-trioxo-3,4,6,7-tetrahydro-2H-pyrido[4,3-d]pyrimidin- 1-yl]phenyl}acetamide, or a pharmaceutically acceptable salt or solvate thereof, and the PI3 kinase inhibitor: 2,4-difluoro-Λ/-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3- pyridinyl}benzenesulfonamide, or a pharmaceutically acceptable salt thereof, pharmaceutical compositions comprising the same, and methods of using such combinations in the treatment of cancer.

WO 2011/046894 A1

— *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))*