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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
1 November 2012 (01.11.2012)

WIPO | PCT

(10) International Publication Number
WO 2012/148846 A1

(51) International Patent Classification:
A61K 31/436 (2006.01) *A61P 35/00* (2006.01)
A61K 31/4439 (2006.01)

(21) International Application Number:
PCT/US2012/034647

(22) International Filing Date:
23 April 2012 (23.04.2012)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/478,572 25 April 2011 (25.04.2011) US

(71) Applicant *(for all designated States except US)*: **NOVARTIS AG** [CH/CH]; Lichstrasse 35, CH-4056 Basel (CH).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **FRITSCH, Christine** [FR/CH]; c/o Novartis Pharma AG, Werk Klybeck, Klybeckstrasse 141, CH-4057 Basel (CH). **GARCIA-ECHEVERRIA, Carlos** [ES/FR]; 11 Boulevard de la Republique, F-92210 Saint-Cloud (FR). **HUANG, Xizhong** [US/US]; c/o Novartis Institutes for BioMedical Research, Inc., 250 Massachusetts Avenue, Cambridge, Massachusetts 02139 (US). **MAIRA, Sauveur-Michel** [FR/CH]; c/o Novartis Pharma AG, Werk Klybeck, Klybeckstrasse 141, CH-4057 Basel (CH).

(74) Agent: **RUECK, Sandra**; Novartis Pharmaceuticals Corporation, One Health Plaza, Building 101, East Hanover, New Jersey 07936-1080 (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 the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

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

WO 2012/148846 A1

(54) **Title**: COMBINATION OF A PHOSPHATIDYLINOSITOL-3-KINASE (PI3K) INHIBITOR AND A MTOR INHIBITOR

(57) **Abstract**: The present invention relates to a pharmaceutical combination comprising a phosphatidylinositol- 3-kinase (PI3K) inhibitor compound which is a 2-carboxamide cycloamino urea derivative or a pharmaceutically acceptable salt thereof and at least one mammalian target of rapamycin (mTOR) inhibitor or a pharmaceutically acceptable salt thereof; a pharmaceutical composition comprising such a combination; and the uses of such a combination in the treatment proliferative diseases, more specifically of mammalian target of rapamycin (mTOR) kinase dependent diseases.