



(51) International Patent Classification:

C07D 401/14 (2006.01) A61K 31/4725 (2006.01)
C07D 487/04 (2006.01) A61P 19/02 (2006.01)

(21) International Application Number:

PCT/EP2012/065844

(22) International Filing Date:

14 August 2012 (14.08.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/524,374 17 August 2011 (17.08.2011) US
61/649,991 22 May 2012 (22.05.2012) US

(71) Applicant (for all designated States except US): **F. HOFFMANN-LA ROCHE AG** [CH/CH]; Grenzacherstrasse 124, CH-4070 Basel (CH).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BROTHERTON-PLEISS, Christine** [US/US]; 848 Stella Court, Sunnyvale, California 94087 (US). **JAIME-FIGUEROA, Saul** [US/US]; 45 Gatheringhill Court, Morris Plains, New Jersey 07950 (US). **LOPEZ-TAPIA, Francisco Javier** [US/US]; 9 Country Lane, Mahwah, New Jersey 07430 (US). **LOU, Yan** [US/US]; 254 Forest Avenue, Glen Ridge, New Jersey 07028 (US). **OWENS, Timothy D.** [US/US]; 5 Pyxie Lane, San Carlos, California 94070 (US).

(74) Agent: **SAUER, Frank**; Grenzacherstrasse 124, CH-4070 Basel (CH).

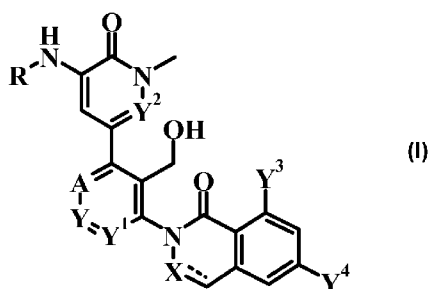
(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, 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, 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).

Published:

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

(54) Title: INHIBITORS OF BRUTON'S TYROSINE KINASE



(57) Abstract: This application discloses compounds according to generic Formula I: wherein the variables are defined as described herein, and which inhibit Btk. The compounds disclosed herein are useful to modulate the activity of Btk and treat diseases associated with excessive Btk activity. The compounds are further useful to treat inflammatory and auto immune diseases associated with aberrant B-cell proliferation, such as rheumatoid arthritis. Also disclosed are compositions containing compounds of Formula I and at least one carrier, diluent or excipient.