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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 September 2011 (22.09.2011)

PCT

(10) International Publication Number
WO 2011/115940 A1

(51) International Patent Classification:
C07D 403/04 (2006.01) *A61P 11/00* (2006.01)
A61K 31/505 (2006.01)

(21) International Application Number:
PCT/US2011/028427

(22) International Filing Date:
15 March 2011 (15.03.2011)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/314,428 16 March 2010 (16.03.2010) US

(71) Applicant *(for all designated States except US)*: **AVENTIS PHARMACEUTICALS INC.** [US/US]; 55 Corporate Drive, Bridgewater, New Jersey 08807 (US).

(72) Inventors; and

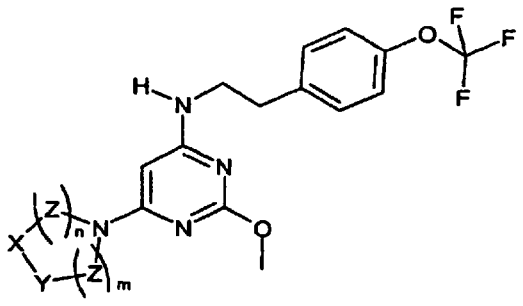
(75) Inventors/Applicants *(for US only)*: **HARRIS, Keith J.** [GB/US]; c/o sanofi-aventis U.S., 1041 Route 202-206, Mail Code: BWD-303A, Bridgewater, New Jersey 08807 (US). **AGUIAR, Joacy C.** [BR/US]; c/o sanofi-aventis U.S., 1041 Route 202-206, Mail Code: BWD-303A, Bridgewater, New Jersey 08807 (US). **SHUM, Patrick Wai-Kwok** [US/US]; c/o sanofi-aventis U.S., 1041 Route 202-206, Mail Code: BWD-303A, Bridgewater, New Jersey 08807 (US). **ZHAO, Zhicheng** [US/US]; c/o sanofi-aventis U.S., 1041 Route 202-206, Mail Code: BWD-303A, Bridgewater, New Jersey 08807 (US). **POLI, Gregory B.** [US/US]; c/o sanofi-aventis U.S., 1041 Route 202-206, Mail Code: BWD-303A, Bridgewater, New Jersey 08807 (US). **STOKLOSA, Gregory** [CA/US]; c/o sanofi-aventis U.S., 1041 Route 202-206, Mail Code: BWD-303A, Bridgewater, New Jersey 08807 (US). **CHOI-SLEDESKI, Yong-Mi** [US/US]; c/o sanofi-aventis U.S., 1041 Route 202-206, Mail Code: BWD-303A, Bridgewater, New Jersey 08807 (US). **REILING, Stephan** [DE/US]; c/o sanofi-aventis U.S., 1041 Route 202-206, Mail Code: BWD-303A, Bridgewater, New Jersey 08807 (US). **STEFANY, David** [US/US]; c/o sanofi-aventis U.S., 1041 Route 202-206, Mail Code: BWD-303A, Bridgewater, New Jersey 08807 (US). **GARDNER, Charles** [US/US]; c/o sanofi-aventis U.S., 1041 Route 202-206, Mail Code: BWD-303A, Bridgewater, New Jersey 08807 (US).

(74) Agents: **ORT, Ronald, G.** et al.; Sanofi-aventis U.S. Inc., 1041 Route 202-206, Mail Code: BWD-303A, Bridgewater, NJ 08807 (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,

[Continued on next page]

(54) Title: SUBSTITUTED PYRIMIDINES AS PROSTAGLANDIN D2 RECEPTOR ANTAGONISTS



(I)

(57) Abstract: The present invention is directed to a substituted pyrimidine compound of formula (I) as set forth herein, or an enantiomer thereof, or a prodrug or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising such a compound. The invention also includes a method of treatment of a patient by the administration of a pharmaceutically effective amount of such a compound. Formula (I), wherein m and n, independently of each other, are selected from the integers 0, 1, 2 or 3; X and Y, independently of each other, are selected from CR_1R_2, NR_1 or O, wherein X and Y cannot both be O; or X and Y, taken together with the bond between them, form a phenyl group optionally substituted by one to four R_3 groups; each Z, independently of each other, is CR_1R_2; R_1, R_2 and R_3, independently of each other, are selected from the group consisting of H, halogen, aryl, amino, optionally substituted alkyl, optionally substituted alkoxy, and carboxy; wherein optionally substituted alkyl, may be substituted by one to three of the same or different of halogen, carboxy, cyano, hydroxy, amino or aryl.

WO 2011/115940 A1

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 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))*