

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
20 March 2008 (20.03.2008)

PCT

(10) International Publication Number
WO 2008/031772 A1

(51) International Patent Classification:

C07D 221/04 (2006.01) A61P 25/00 (2006.01)
A61K 31/435 (2006.01)

(21) International Application Number:

PCT/EP2007/059381

(22) International Filing Date:

7 September 2007 (07.09.2007)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

0617863.6 11 September 2006 (11.09.2006) GB
0617868.5 11 September 2006 (11.09.2006) GB
0716371.0 22 August 2007 (22.08.2007) GB(71) Applicant (for all designated States except US): **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

(72) Inventors; and

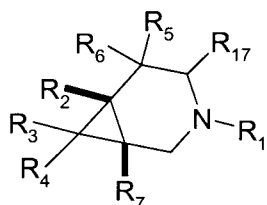
(75) Inventors/Applicants (for US only): **BERTANI, Barbara** [IT/IT]; GlaxoSmithKline SpA, Via Alessandro Fleming, 2, I-37135 Verona (IT). **DI FABIO, Romano** [IT/IT]; GlaxoSmithKline SpA, Via Alessandro Fleming,2, I-37135 Verona (IT). **MICHELLI, Fabrizio** [IT/IT]; GlaxoSmithKline SpA, Via Alessandro Fleming, 2, I-37135 Verona (IT). **TEDESCO, Giovanna** [IT/IT]; GlaxoSmithKline SpA, Via Alessandro Fleming, 2, I-37135 Verona (IT). **TERRENI, Silvia** [IT/IT]; GlaxoSmithKline SpA, Via Alessandro Fleming, 2, I-37135 Verona (IT).(74) Agents: **DOLTON, Peter, I.** et al.; GlaxoSmithKline, Corporate Intellectual Property CN925.1, 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

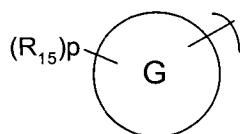
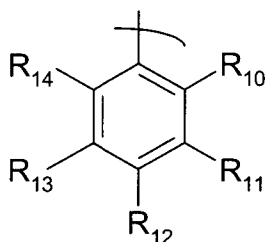
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH,

[Continued on next page]

(54) Title: AZABICYCLIC COMPOUNDS AS INHIBITORS OF MONOAMINES REUPTAKE



(I')



(57) Abstract: The present invention relates to novel compounds of formula (I'), pharmaceutically acceptable salts, prodrugs or solvates thereof: wherein R_1 is hydrogen or C_{1-4} alkyl; R_2 is a group A, K or W wherein A is (II) K is an α or β naphthyl group, optionally substituted by 1 or 2 groups R_{18} , each of them being the same or different; and W is (III) and wherein G is a 5,6-membered monocyclic heteroaryl, or a 8- to 11-membered heteroaryl bicyclic group; such G may be substituted by $(R_{15})_p$, which can be the same or different; p is an integer from 0 to 5; R_3 is selected in the group consisting of: hydrogen, fluorine, and C_{1-4} alkyl; or corresponds to a group X or X_1 ; R_4 is selected in the group consisting of: hydrogen, fluorine, and C_{1-4} alkyl; or corresponds to a group X or X_1 ; R_5 is hydrogen or C_{1-4} alkyl; R_7 is hydrogen or C_{1-4} alkyl; or is a group X, X_1 , X_2 or X_3 ; wherein X is (IV) X_1 is (V) X_2 is (VI) and X_3 is (VII) R_6 is hydrogen or C_{1-4} alkyl; or is a group X or X_1 ; R_9 is C_{1-4} alkyl; R_{10} is selected from a group consisting of: hydrogen, halogen, hydroxy, cyano, C_{1-4} alkyl, halo C_{1-4} alkyl, C_{1-4} alkoxy, halo C_{1-4} alkoxy, C_{1-4} alkanoyl and SF_5 ; or corresponds to a group R_8 ; R_8 is a 5-6 membered heterocycle group, which may be substituted by one or two substituents selected from a group consisting of: halogen, cyano, C_{1-4} alkyl, halo C_{1-4} alkyl, C_{1-4} alkoxy and C_{1-4} alkanoyl; R_{11} is selected from a group consisting of: hydrogen, halogen, hydroxy, cyano, C_{1-4} alkyl, halo C_{1-4} alkyl, C_{1-4} alkoxy, halo C_{1-4} alkoxy, C_{1-4} alkanoyl and SF_5 ; or corresponds to a group R_8 ; R_{12} is selected from a group consisting of: hydrogen, halogen, hydroxy, cyano, C_{1-4} alkyl, halo C_{1-4} alkyl, C_{1-4} alkoxy, halo C_{1-4} alkoxy, C_{1-4} alkanoyl and SF_5 ; or corresponds to a group R_8 ; R_{13} is selected from a group consisting of: hydrogen, halogen, hydroxy, cyano, C_{1-4} alkyl, halo C_{1-4} alkyl, C_{1-4} alkoxy, halo C_{1-4} alkoxy, C_{1-4} alkanoyl and SF_5 ; or corresponds to a group R_8 ; R_{14} is selected from a group consisting of: hydrogen, halogen, hydroxy, cyano, C_{1-4} alkyl, halo C_{1-4} alkyl, C_{1-4} alkoxy, halo C_{1-4} alkoxy, C_{1-4} alkanoyl and SF_5 ; or corresponds to a group R_8 ; R_{15} is selected from a group consisting of: halogen, hydroxy, cyano, C_{1-4} alkyl, halo C_{1-4} alkyl, C_{1-4} alkoxy, halo C_{1-4} alkoxy, C_{1-4} alkanoyl and SF_5 ; or corresponds to a group R_8 ; R_{16} is hydrogen, C_{1-4} alkyl, C_{3-6} cycloalkyl or C_{3-6} cycloalkyl C_{1-3} alkyl; R_{17} is hydrogen or C_{1-4} alkyl; R_{18} is selected from a group consisting of: halog

WO 2008/031772 A1



GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

- *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*

Declarations under Rule 4.17:

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