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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 June 2005 (02.06.2005)

PCT

(10) International Publication Number
WO 2005/049600 A1

(51) International Patent Classification[7]: C07D 401/04, A61P 25/00, A61K 31/4439

(21) International Application Number: PCT/EP2004/012772

(22) International Filing Date: 10 November 2004 (10.11.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0326407.4 12 November 2003 (12.11.2003) 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

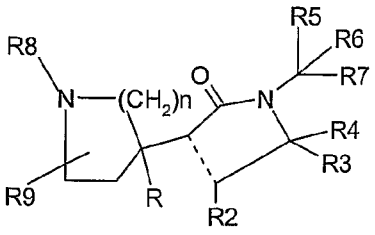
(75) Inventors/Applicants *(for US only)*: **ALVARO, Giuseppe** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **DI FABIO, Romano** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **GIOVANNINI, Riccardo** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **PAIO, Alfredo** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **TRANQUILLINI, Maria, Elvira** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **MATTIOLI, Lucia** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT).

(74) Agent: **GIDDINGS, Peter, John**; GlaxoSmithKline, 980 Great West Road (CN925.1), Brentford, Middlesex TW8 9GS (GB).

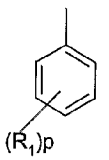
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,

[Continued on next page]

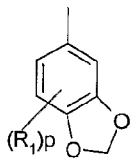
(54) Title: BETA-LACTAMS FOR TREATMENT OF CNS DISORDERS



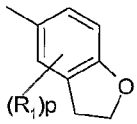
(I)



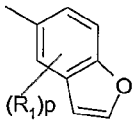
(i)



(ii)



(iii)



(iv)

(57) Abstract: The present invention relates to novel compounds of formula (I) wherein ---- represents a single or a double bond; R represents a radical selected from formulae i), ii), iii) and iv) in which R_1 is halogen, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, trifluoromethyl or trifluoromethoxy and p is zero or an integer from 1 to 3; R_2 represents hydrogen or C_{1-4} alkyl; R_3 represents hydrogen, hydroxy or C_{1-4} alkyl; R_4 represents hydrogen or R_4 together with R_3 represents =0 or $=CH_2$; R_5 represents phenyl, naphthyl, a 9 to 10 membered fused bicyclic heterocyclic group or a 5 or 6 membered heteroaryl group, wherein said groups are optionally substituted by 1 to 3 groups independently selected from trifluoromethyl, C_{1-4} alkyl, hydroxy, cyano, C_{1-4} alkoxy, trifluoromethoxy, halogen or $S(O)qC_{1-4}$ alkyl; R_6 and R_7 independently represent hydrogen, cyano, C_{1-4} alkyl; R_8 is $(CH_2)rR_{10}$; R_9 represents hydrogen, halogen, C_{3-7} cycloalkyl, hydroxy, nitro, cyano or C_{1-4} alkyl optionally substituted by one or two groups selected from halogen, cyano, hydroxy or C_{1-4} alkoxy; R_{10} represents hydrogen or C_{3-7} cycloalkyl; n represents 1 or 2; q is 0, 1 or 2; r is 0 or an integer from 1 to 4; or a pharmaceutically acceptable salt or a solvate thereof, process for their preparation and their use in the treatment of conditions mediated by tackykinins and/or by selective inhibition of the serotonin reuptake transporter protein.

WO 2005/049600 A1

TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

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

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (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)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)*

— *of inventorship (Rule 4.17(iv)) for US only*

Published:

— *with international search report*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.