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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 February 2007 (22.02.2007)

PCT

(10) International Publication Number
WO 2007/021574 A1

(51) International Patent Classification:
C07D 471/04 (2006.01) *A61P 25/00* (2006.01)
C07D 487/04 (2006.01) *A61P 1/00* (2006.01)
A61K 31/4985 (2006.01)

(21) International Application Number:
PCT/US2006/030393

(22) International Filing Date: 4 August 2006 (04.08.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/707,945 15 August 2005 (15.08.2005) US

(71) Applicants *(for all designated States except US)*: **ASTRAZENECA AB** [SE/SE]; S-151 85 Sodertalje (SE). **NPS PHARMACEUTICALS, INC.** [US/US]; 383 Colorow Drive, Salt Lake City, UT 84108 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **EDWARDS, Louise** [CA/CA]; c/o NPS Allelix Corp., 101 College St. 8th Fl., Toronto, Ontario M5G 1L8 (CA). **ISAAC, Methvin** [CA/CA]; 101 College St., 8th Floor, Toronto, Ontario M5G 1L8 (CA). **SLASSI, Abdelmalik** [CA/CA]; 101 College St., 8th Floor, Toronto, Ontario M5G 1L8 (CA). **SUN, Guang-Ri** [CA/CA]; c/o NPS Allelix Corp., 101 College St. 8th Fl., Toronto, Ontario M5G 1L8 (CA). **XIN, Tao** [CA/CA]; c/o NPS Allelix Corp., 100 College St 8th Fl., Toronto, Ontario M5G 1L8 (CA). **MINIDIS, Alexander** [SE/SE]; c/o AstraZeneca AB, S-151 85 Sodertalje (SE). **DOVE, Peter** [CA/CA]; c/o NPS Allelix Corp., 101 College St. 8th Fl., Toronto, Ontario M5G 1L8 (CA).

(74) Agent: **MEIKLE, Andrew, D.**; c/o Birch, Stewart, Kolasch & Birch, LLP, P.O. Box 747, Falls Church, VA 22040-0747 (US).

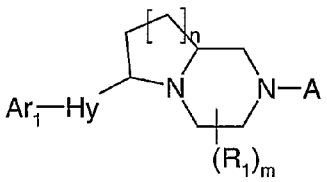
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ,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

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.

(54) Title: BICYCLIC PIPERAZINES AS METABOTROPIC GLUTAMATE RECEPTOR ANTAGONISTS



(I)

(57) Abstract: The invention relates to compounds of formula I or pharmaceutically acceptable salts or solvates thereof: where Ar_1, A Hy, R_1, m and n are as defined in the description. The invention also includes pharmaceutical compositions and uses of, and processes of making the compounds, as well as methods of medical treatment of mGluR5-mediated disorders.

WO 2007/021574 A1