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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 December 2011 (15.12.2011)

PCT

(10) International Publication Number
WO 2011/154374 A1

(51) International Patent Classification:
C07D 401/10 (2006.01) ***A61K 31/496*** (2006.01)
C07D 401/12 (2006.01) ***A61P 25/28*** (2006.01)
C07D 403/10 (2006.01) ***A61P 25/16*** (2006.01)

(21) International Application Number:
PCT/EP2011/059330

(22) International Filing Date:
7 June 2011 (07.06.2011)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10165336.8 9 June 2010 (09.06.2010) EP

(71) Applicant *(for all designated States except US)*: **JANSSEN PHARMACEUTICA NV** [BE/BE]; Turnhoutseweg 30, B-2340 Beerse (BE).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **TRABANCO-SUÁREZ, Andrés, Avelino** [ES/ES]; c/o Janssen-Cilag S.A., Calle Jarama, 75, Poligono Industrial, E-45007 Toledo (ES). **TRESADERN, Gary, John** [GB/ES]; c/o Janssen-Cilag S.A., Calle Jarama, 75, Poligono Industrial, E-45007 Toledo (ES). **MACDONALD, Gregor, James** [GB/BE]; c/o Janssen Pharmaceutica NV, Turnhoutseweg 30, B-2340 Beerse (BE). **VEGA RAMIRO, Juan, Antonio** [ES/ES]; c/o Janssen-Cilag S.A., Calle Jarama, 75 , Poligono Industrial, E-45007 Toledo (ES).

(74) Common Representative: **JANSSEN PHARMACEUTICA NV**; Turnhoutseweg 30, B-2340 Beerse (BE).

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

— *of inventorship (Rule 4.17(iv))*

Published:

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

WO 2011/154374 A1

(54) **Title**: 5-AMINO-3,6-DIHYDRO-1*H*-PYRAZIN-2-ONE DERIVATIVES USEFUL AS INHIBITORS OF BETA-SECRETASE (BACE)

(57) **Abstract**: The present invention relates to novel 5-amino-3,6-dihydro-1H-pyrazin-2-one derivatives as inhibitors of beta-secretase, also known as beta-site amyloid cleaving enzyme, BACE, BACE1, Asp2, or memapsin2. The invention is also directed to pharmaceutical compositions comprising such compounds, to processes for preparing such compounds and compositions, and to the use of such compounds and compositions for the prevention and treatment of disorders in which beta-secretaseis involved, such as Alzheimer's disease (AD), mild cognitive impairment, senility, dementia, dementia with Lewy bodies, Down's syndrome, dementia associated with stroke, dementia associated with Parkinson's disease or dementia associated with beta-amyloid.