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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
13 June 2013 (13.06.2013)

WIPO | PCT

(10) International Publication Number
WO 2013/083557 A1

(51) International Patent Classification:
C07D 413/10 (2006.01) *A61P 25/16* (2006.01)
C07D 413/12 (2006.01) *A61P 25/28* (2006.01)
A61K 31/5377 (2006.01)

(21) International Application Number:
PCT/EP2012/074351

(22) International Filing Date:
4 December 2012 (04.12.2012)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
11191997.3 5 December 2011 (05.12.2011) EP

(71) Applicant: **JANSSEN PHARMACEUTICA NV** [BE/BE]; Turnhoutseweg 30, B-2340 Beerse (BE).

(72) Inventors: **TRABANCO-SUÁREZ, Andrés, Avelino**; c/o Janssen-Cilag S.A., Calle Jarama, 75, Poligono Industrial, E-45007 Toledo (ES). **GIJSEN, Henricus, Jacobus, Maria**; c/o Janssen Pharmaceutica NV, Turnhoutseweg 30, B-2340 Beerse (BE). **SURKYN, Michel**; c/o Janssen Pharmaceutica NV, Turnhoutseweg 30, B-2340 Beerse (BE). **PROKOPCOVÁ, Hana**; c/o 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, BN, 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, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, 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, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, 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 2013/083557 A1

(54) Title: 6-DIFLUOROMETHYL-5,6-DIHYDRO-2H-[1,4]OXAZIN-3-AMINE DERIVATIVES

(57) Abstract: The invention relates to novel 6-difluoromethyl-5,6-dihydro-2H-[1,4]oxazin-3- amine 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-secretase is involved, such as Alzheimer's disease (AD), mild cognitive impairment, senility, dementia, dementia with Lewy bodies, cerebral amyloid angiopathy, multi-infarct dementia, Down's syndrome, dementia associated with stroke, dementia associated with Parkinson's disease and dementia associated with beta-amyloid.