

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
23 December 2021 (23.12.2021)



(10) International Publication Number
WO 2021/255607 A1

(51) International Patent Classification:

C07D 491/048 (2006.01) A61K 31/4355 (2006.01)
C07D 221/04 (2006.01) A61P 25/00 (2006.01)

(21) International Application Number:

PCT/IB2021/055183

(22) International Filing Date:

11 June 2021 (11.06.2021)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

PCT/CN2020/096177

15 June 2020 (15.06.2020)

CN

(71) Applicant: **NOVARTIS AG** [CH/CH]; Lichtstrasse 35, 4056 Basel (CH).

(72) Inventors: **KIM, Sung David C.**; Novartis Institutes for Biomedical Research, Inc., 250 Massachusetts Avenue, Cambridge, Massachusetts 02139 (US). **LI, Zaixing**; Room 501, No. 47, Changhai Second Village, Yangpu District, Shanghai 200433 (CN). **LU, Chui**; China Novartis Institutes for BioMedical Research Co., Ltd., 4218 Jinke Road, ZhangJiang, Hi-Tech Park, Shanghai 201203 (CN). **LUBICKA, Danuta**; Novartis Institutes for Biomedical Research, Inc., 250 Massachusetts Avenue, Cambridge, Massachusetts 02139 (US). **NEEF, James**; Novartis Institutes for Biomedical Research, Inc., 250 Massachusetts Avenue, Cambridge, Massachusetts 02139 (US). **PARK, Hye-Yeon**; Novartis Institutes for Biomedical Research, Inc., 250 Massachusetts Avenue, Cambridge, Massachusetts 02139 (US). **PATHAK, Tejaskumar Pankajbhai**; Novartis Institutes for Biomedical Research, Inc., 250 Massachusetts Avenue, Cambridge, Massachusetts 02139 (US). **SADAGHIANI, Amir Masoud**; c/o Cygnal Therapeutics, 325 Vassar Street, Suite 2B, Cambridge, Massachusetts 02139 (US). **ZHOU, Xilin**; Novartis Institutes for Biomedical Research, Inc., 250 Massachusetts Avenue, Cambridge, Massachusetts 02139 (US).

(74) Agent: **NOVARTIS AG**; Lichtstrasse 35, 4056 Basel (CH).

(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, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, 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, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, 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, ST, 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, KM, ML, MR, NE, SN, TD, TG).

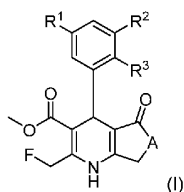
Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

Published:

- with international search report (Art. 21(3))

(54) Title: METHYL 2-(FLUOROMETHYL)-5-OXO-4-PHENYL-4,5,6,7-TETRAHYDRO-1H-CYCLOPENTA[B]PYRIDINE-3-CARBOXYLATES AND METHYL 2-(FLUOROMETHYL)-5-OXO-4-PHENYL-1,4,5,7-TETRAHYDROFURO[3,4-B]PYRIDINE-3-CARBOXYLATES AS CAV1.2 ACTIVATORS



(57) Abstract: The present disclosure provides for a compound according to formula (I) or a pharmaceutically acceptable salt thereof as Ca_v1.2 activators for the treatment of schizophrenia, bipolar disorder, major depressive disorder, substance use disorder, ADHD, Phelan-McDermid Syndrome, autism spectrum disorder, multiple sclerosis, frontotemporal dementia, Alzheimer's disease, Brugada Syndrome, Short QT syndrome, or early repolarization syndrome.

WO 2021/255607 A1