

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
05 April 2018 (05.04.2018)



(10) International Publication Number
WO 2018/064632 A1

(51) International Patent Classification:

C07D 401/14 (2006.01) A61K 31/4439 (2006.01)
C07D 471/14 (2006.01) A61P 11/12 (2006.01)
C07D 498/14 (2006.01)

(21) International Application Number:

PCT/US2017/054611

(22) International Filing Date:

29 September 2017 (29.09.2017)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/402,838	30 September 2016 (30.09.2016)	US
62/410,353	19 October 2016 (19.10.2016)	US
62/415,409	31 October 2016 (31.10.2016)	US
62/419,935	09 November 2016 (09.11.2016)	US

(71) Applicant: VERTEX PHARMACEUTICALS INCORPORATED [US/US]; 50 Northern Avenue, Boston, MA 02210 (US).

(72) Inventors: ALCACIO, Timothy; 50 Northern Avenue, Boston, MA 02210 (US). BAEK, Minson; 50 Northern Avenue, Boston, MA 02210 (US). GROOTENHUIS, Peter; 50 Northern Avenue, Boston, MA 02210 (US). HADI-DA RUAH, Sara, Sabina; 50 Northern Avenue, Boston, MA 02210 (US). HUGHES, Robert, M.; 50 Northern Avenue, Boston, MA 02210 (US). KESHAVARZ-SHOKRI, Ali; 50 Northern Avenue, Boston, MA 02210 (US). MCAULEY-AOKI, Rachel; 50 Northern Avenue, Boston, MA 02210 (US). MCCARTNEY, Jason; 50 Northern Avenue, Boston, MA 02210 (US). MILLER, Mark, Thomas; 50 Northern Avenue, Boston, MA 02210 (US). VAN GOOR, Fredrick; 50 Northern Avenue, Boston, MA 02210 (US). ZHANG, Beili; 50 Northern Avenue, Boston, MA 02210 (US). ANDRESON, Corey; 50 Northern Av-

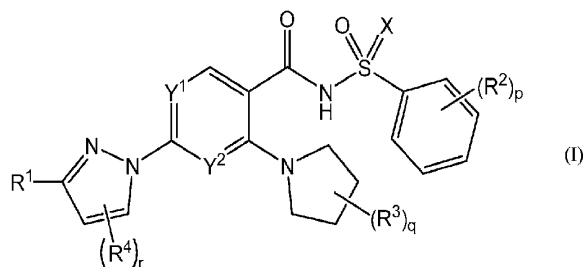
enue, Boston, MA 02210 (US). CLEVELAND, Thomas; 50 Northern Avenue, Boston, MA 02210 (US). FRIEMAN, Bryan, A.; 50 Northern Avenue, Boston, MA 02210 (US). KHATUYA, Haripada; 50 Northern Avenue, Boston, MA 02210 (US). JOSHI, Pramod, Virupax; 13023 Old West Avenue, San Diego, CA 92129 (US). KRENITSKY, Paul, John; 50 Northern Avenue, Boston, MA 02210 (US). MELILLO, Vito; 50 Northern Avenue, Boston, MA 02210 (US). PIERRE, Fabrice, Jean Denis; 50 Northern Avenue, Boston, MA 02210 (US). TERMIN, Andreas, P.; 50 Northern Avenue, Boston, MA 02210 (US). UY, Johnny; 50 Northern Avenue, Boston, MA 02210 (US). ZHOU, Jinglan; 50 Northern Avenue, Boston, MA 02210 (US). ABELA, Alexander, Russell; 50 Northern Avenue, Boston, MA 02210 (US). BUSCH, Brett, Bradley; 50 Northern Avenue, Boston, MA 02210 (US). PARASELLI, Prasuna; 50 Northern Avenue, Boston, MA 02210 (US). SIESEL, David, Andrew; 50 Northern Avenue, Boston, MA 02210 (US).

(74) Agent: MACALPINE, Jill, K. et al.; Finnegan, Henderson, Farabow, Garrett & Dunner, LLP, 901 New York Avenue, NW, Washington, DC 20001 (US).

(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, 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, 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,

(54) Title: MODULATOR OF CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR, PHARMACEUTICAL COMPOSITIONS, METHODS OF TREATMENT, AND PROCESS FOR MAKING THE MODULATOR



(57) Abstract: Compounds of Formula (I), pharmaceutically acceptable salts thereof, deuterated derivatives of any of the foregoing, and metabolites of any of the foregoing are disclosed. Pharmaceutical compositions comprising the same, methods of treating cystic fibrosis using the same, and methods for making the same are also disclosed.

[Continued on next page]

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).

Published:

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