

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

(19) World Intellectual Property
Organization

International Bureau

(43) International Publication Date
06 June 2019 (06.06.2019)



(10) International Publication Number
WO 2019/109021 A1

(51) International Patent Classification:

C07D 215/56 (2006.01) C07B 59/00 (2006.01)

C07C 69/96 (2006.01) C07C 33/18 (2006.01)

(21) International Application Number:

PCT/US2018/063451

(22) International Filing Date:

30 November 2018 (30.11.2018)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

17382829.4 01 December 2017 (01.12.2017) EP

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

(72) Inventors: LEMERCIER LEWANDOWSKI, Berenice; 50 Northern Avenue, Boston, MA 02210 (US). LEWIS, Robert; 99 Hayden Avenue, Lexington, MA 02421 (US). LOOKER, Adam; 50 Northern Avenue, Boston, MA 02210 (US). MORGAN, Adam; 14 Oak Ridge Lane, Ashland, MA 01721 (US). ROEPER, Stefanie; 50 Northern Avenue, Boston, MA 02210 (US). RYAN, Michael; 50 Northern Avenue, Boston, MA 02210 (US). SOLSONA ROCABERT, Juan, Gabriel; Caracas, 17-19, 08030 Barcelona (ES). WILDE, Nathan; 50 Northern Avenue, Boston, MA 02210 (US).

(74) Agent: MCDONELL, Leslie, A. 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,

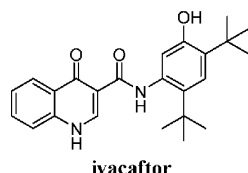
SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, 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).

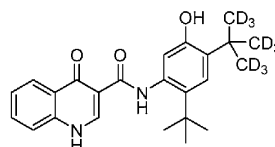
Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(54) Title: PROCESSES FOR MAKING MODULATORS OF CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR



ivacaftor



deuterated ivacaftor

(57) Abstract: The disclosure provides processes for synthesizing compounds for use as CFTR modulators.

WO 2019/109021 A1