

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

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
27 October 2011 (27.10.2011)

PCT

(10) International Publication Number
WO 2011/133751 A3

(51) International Patent Classification:

C07D 209/12 (2006.01) **C07D 405/12** (2006.01)
C07D 317/60 (2006.01)

(21) International Application Number:

PCT/US2011/033396

(22) International Filing Date:

21 April 2011 (21.04.2011)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/327,099	22 April 2010 (22.04.2010)	US
61/327,091	22 April 2010 (22.04.2010)	US
61/327,057	22 April 2010 (22.04.2010)	US
61/327,095	22 April 2010 (22.04.2010)	US
61/329,500	29 April 2010 (29.04.2010)	US
61/329,510	29 April 2010 (29.04.2010)	US
61/329,493	29 April 2010 (29.04.2010)	US
61/333,870	12 May 2010 (12.05.2010)	US

(71) Applicant (for all designated States except US): **VER-TEX PHARMACEUTICALS INCORPORATED** [US/US]; 130 Waverly Street, Cambridge, MA 02139 (US).

(72) Inventor; and

(71) Applicant (for all designated States except US): **LEE, Elaine, Chungmin** [US/US]; 303 Third Street, Apartment 316, Cambridge, MA 02142 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **TANOURY, Gerald, J.** [US/US]; 151 O'Malley Road, Marlborough, MA 01752 (US). **HARRISON, Cristian** [CA/US]; 13 Laurel Street, Beverly, MA 01915 (US). **LITTLER, Benjamin, Joseph** [GB/US]; 7016 Ivy Street, Carlsbad, CA 92011 (US). **ROSE, Peter, Jamison** [US/US]; 4 Pine Brook Lane, Littleton, MA 01460 (US). **HUGHES, Robert, Michael** [GB/US]; 10235 Arrow Rock Avenue, San Diego, CA 92126 (US). **JUNG, Young Chun** [KR/US];

22 Webb Street, Lexington, MA 02420 (US). **SIESEL, David, Andrew** [US/US]; 11145 Papoose Court, San Diego, CA 92127 (US). **BELMONT, Daniel, T.** [US/US]; 1 Gershom Drive, Grafton, MA 01536 (US).

(74) Agent: **DIVERDI, Michael, J.**; Vertex Pharmaceuticals Incorporated, 130 Waverly Street, Cambridge, MA 02139 (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, 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).

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))

(88) Date of publication of the international search report:

12 January 2012

(54) Title: PROCESS OF PRODUCING CYCLOALKYLCARBOXAMIDO-INDOLE COMPOUNDS

(57) Abstract: The present invention features processes for preparing compounds, such as (R)-1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-N-(1-(2,3-dihydroxypropyl)-6-fluoro-2- (1 -hydroxy-2-methylpropan-2-yl)- 1H-indol-5 -yl)cyclopropanecarboxamide (Compound 1), useful for treating CFTR mediated diseases such as cystic fibrosis.



WO 2011/133751 A3