

CORRECTED VERSION

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
22 July 2010 (22.07.2010)

PCT

(10) International Publication Number
WO 2010/083414 A8

(51) International Patent Classification:
C07D 215/227 (2006.01) **A61P 35/00** (2006.01)
A61K 31/47 (2006.01)

(21) International Application Number:
PCT/US2010/021194

(22) International Filing Date:
15 January 2010 (15.01.2010)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/145,421 16 January 2009 (16.01.2009) US

(71) Applicants (for all designated States except US): **EX-ELIXIS, INC.** [US/US]; P.O. Box 511, 249 East Grand Avenue, South San Francisco, CA 94080 (US). **BRISTOL-MEYERS SQUIBB COMPANY** [US/US]; P.O. Box 4000, Princeton, NJ 08543 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BROWN, Adrian, St. Clair** [GB/GB]; 67 Stour Green, Ely, Cambridgeshire CB6 2XJ (GB). **LAMB, Peter** [US/US]; 814 Mandana Blvd., Oakland, CA 94610 (US). **GALLAGHER, William, P.** [US/US]; P.O. Box 4000, Princeton, NJ 08543 (US).

(74) Agent: **BERVEN, Heidi, M.**; Honigman Miller Schwartz and Cohn LLP, 350 East Michigan Avenue, Suite 300, Kalamazoo, MI 49007 (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, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (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, 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))

(48) Date of publication of this corrected version:

17 March 2011

(15) Information about Corrections:

see Notice of 17 March 2011

Previous Correction:

see Notice of 2 December 2010

(54) Title: MALATE SALT OF N-(4-{ [6, 7-BIS (METHYLOXY) QUINOLIN-4-YL] OXY}PHENYL)-N'-(4-FLUOROPHENYL) CYCLOPROPANE-1,1-DICARBOXAMIDE, AND CRYSTALLINE FORMS THEROF FOR THE TREATMENT OF CANCER

(57) Abstract: Disclosed are malate salts of N-(4-{ [6,7-bis(methyloxy)-quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide, including a (L)-malate salt, a (D)-malate salt, a (DL) malate salt, and mixtures thereof; and crystalline and amorphous forms of the malate salts. Also disclosed are pharmaceutical compositions comprising at least one malate salt of N-(4-{ [6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)-cyclopropane-1,1-dicarboxamide; and methods of treating cancer comprising administering at least one malate salt of N-(4-{ [6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide.



WO 2010/083414 A8