

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
30 June 2016 (30.06.2016)



(10) International Publication Number
WO 2016/106331 A8

(51) International Patent Classification:

C07D 215/22 (2006.01) *A61K 31/4436* (2006.01)
C07D 401/04 (2006.01) *A61K 31/4704* (2006.01)
C07D 417/04 (2006.01) *A61K 31/4725* (2006.01)
C07D 417/14 (2006.01) *A61K 31/5377* (2006.01)
C07D 471/04 (2006.01) *A61K 31/55* (2006.01)
A61K 31/4545 (2006.01) *A61P 35/00* (2006.01)

(21) International Application Number:

PCT/US2015/067406

(22) International Filing Date:

22 December 2015 (22.12.2015)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/095,322 22 December 2014 (22.12.2014) US

(71) Applicants: **THE UNITED STATES OF AMERICA AS REPRESENTED BY THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES** [US/US]; Office of Technology Transfer National Institutes of Health, 6011 Executive Boulevard, Suite 325, MSC 7660, Bethesda, Maryland 20892-7660 (US). **UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL** [US/US]; Office of Commercialization and Economic Development, 100 Europa Drive, Suite 430, Chapel Hill, NC 27517 (US).

(72) Inventors: **BOXER, Matthew Brian**; 6813 Rehnquist Court, New Market, Maryland 21774 (US). **ROHDE, Jason Matthew**; 17117 Chiswell Rd., Poolesville, Maryland 20837 (US). **PRAGANI, Rajan**; 183 Crossbow Lane,

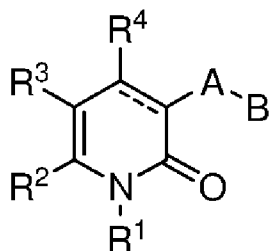
Gaithersburg, Maryland 20878 (US). **LIU, Li**; 12914 Summit Ridge Terrace, Germantown, Maryland 20874 (US). **DAVIS, Mindy Irene Emily**; 9905 Gable Ridge Terrace, Apt. A, Rockville, Maryland 20850 (US). **BRIMACOMBE, Kyle Ryan**; 4890 Battery Lane, Apt. 105, Bethesda, Maryland 20814 (US). **SHEN, Min**; 14301 Gate Dancer Ln, Boyds, Maryland 20841 (US). **SIMEONOV, Anton**; 7805 Green Twig Rd., Bethesda, Maryland 20817 (US). **KARAVADHI, Surendra**; 313 West Side Drive, Apt#103, Gaithersburg, Maryland 20878 (US). **URBAN, Daniel Jason**; 9800 Medical Center Drive, Building B, Room 1034A, Rockville, Maryland 20850 (US). **JADHAV, Ajit**; 27358 Bridle Place, Chantilly, Virginia 20152 (US). **WANG, Xiaodong**; 116 Woodshire Lane, Chapel Hill, North Carolina 27514 (US). **MCIVER, Andrew Louis**; 7103 Montibillo Pkwy, Durham, North Carolina 27713 (US).

(74) Agent: **MAXWELL, Leslie-Anne**; Cantor Colburn LLP, 20 Church Street, 22nd Floor, Hartford, Connecticut 06103-3207 (US).

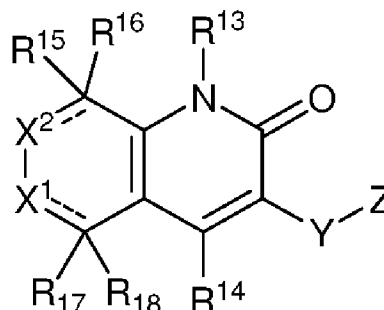
(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, 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.

[Continued on next page]

(54) Title: MUTANT IDH1 INHIBITORS USEFUL FOR TREATING CANCER



Formula I



Formula II

(57) Abstract: Compounds of Formula I and Formula II and the pharmaceutically acceptable salts thereof are disclosed. The variables A, B, Y, Z, X¹, X², R¹⁻⁴ and R¹³⁻¹⁸ are disclosed herein. The compounds are useful for treating cancer disorders, especially those involving mutant IDH1 enzymes. Pharmaceutical compositions containing compounds of Formula I or Formula II and methods of treatment comprising administering compounds of Formula I and Formula II are also disclosed.



(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))*

(48) Date of publication of this corrected version:

29 September 2016

(15) Information about Correction:

see Notice of 29 September 2016