

CORRECTED VERSION

(19) World Intellectual Property
Organization
International Bureau



(10) International Publication Number
WO 2016/112251 A8

(43) International Publication Date
14 July 2016 (14.07.2016)

(51) International Patent Classification:

C07D 403/12 (2006.01) *C07D 417/12* (2006.01)
C07D 233/44 (2006.01) *C07D 487/08* (2006.01)
C07D 401/04 (2006.01) *A61K 31/454* (2006.01)
C07D 235/02 (2006.01) *A61K 31/496* (2006.01)
C07D 401/12 (2006.01) *A61K 31/4995* (2006.01)
C07D 409/12 (2006.01) *A61P 35/00* (2006.01)
C07D 413/12 (2006.01)

(21) International Application Number:

PCT/US2016/012588

(22) International Filing Date:

8 January 2016 (08.01.2016)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/101,933 9 January 2015 (09.01.2015) US

(71) Applicants: **GENENTECH, INC.** [US/US]; 1 DNA Way, South San Francisco, California 94080-4990 (US). **CON-STELLATION PHARMACEUTICALS, INC.** [US/US]; 215 First Street, Suite 200, Cambridge, Massachusetts 02142 (US).

(72) Inventors: **ALBRECHT, Brian, K.**; 215 First Street, Suite 200, Cambridge, Massachusetts 02142 (US). **COTE, Alexandre**; 215 First Street, Suite 200, Cambridge, Massachusetts 02142 (US). **GEHLING, Victor**; 215 First Street, Suite 200, Cambridge, Massachusetts 02142 (US). **HSIAO-WEI TSUI, Vickie**; 1 DNA Way, South San Francisco, California 94080-4990 (US). **KIEFER, James, Richard, Jr.**; 1 DNA Way, South San Francisco, California 94080-4990 (US). **LIANG, Jun**; 1 DNA Way, South San Francisco, California 94080-4990 (US). **MAG-NUSON, Steven**; 1 DNA Way, South San Francisco, California 94080-4990 (US). **NASVESCHUK, Christopher, G.**; 215 First Street, Suite 200, Cambridge, Massachusetts

02142 (US). **ROMERO, F. Anthony**; 1 DNA Way, South San Francisco, California 94080-4990 (US). **TAYLOR, Alexander, M.**; 215 First Street, Suite 200, Cambridge, Massachusetts 02142 (US).

(74) Agents: **HARRIS, Robert, J.** et al.; Viksnins Harris & Padys PLLP, 7851 Metro Parkway, Suite 325, Bloomington, Minnesota 55425 (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.

(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:

2 February 2017

(15) Information about Correction:

see Notice of 2 February 2017

(54) Title: 4,5-DIHYDROIMIDAZOLE DERIVATIVES AND THEIR USE AS HISTONE DEMETHYLASE (KDM2B) INHIBITORS

(57) Abstract: The present invention relates to compounds of formula (I), wherein: X is C(=O) or S(O)₂; R¹ is selected from the group consisting of N-linked piperazinyl, relinked piperidine, and N-linked diazabicyclo[3.2.1]octane, wherein R¹ is optionally substituted with one or more groups; R² and R³ are each independently selected from H, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, and C₃₋₈cycloalkyl, wherein any C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, and C₃₋₈cycloalkyl is optionally substituted with one or more groups; or R² and R³ taken together with the carbon to which they are attached form a 3-, 4-, 5-, or 6-membered carbocyclic ring that is optionally substituted with one or more groups; R⁴ and R⁵ are each independently selected from H, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, and C₃₋₈cycloalkyl, wherein any C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, and C₃₋₈cycloalkyl is optionally substituted with one or more groups; or R⁴ and R⁵ taken together with the carbon to which they are attached form a 3-, 4-, 5-, or 6-membered carbocyclic ring that is optionally substituted with one or more groups; and R⁶ is a 5-10 membered heteroaryl, 5-10 membered heterocycle, or a 6-10 membered aryl, which 5-10 membered heteroaryl, 5-10 membered heterocycle, and 6-10 membered aryl is optionally substituted with one or more groups; useful as inhibitors of one or more histone demethylases, such as KDM2b. The invention also provides pharmaceutically acceptable compositions comprising compounds of the present invention and methods of using said compositions in the treatment of various disorders.

WO 2016/112251 A8