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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
10 May 2013 (10.05.2013)

WIPO | PCT

(10) International Publication Number
WO 2013/067396 A2

(51) **International Patent Classification**:
A61K 31/706 (2006.01) *A61P 35/02* (2006.01)
A61P 35/00 (2006.01)

(21) **International Application Number**:
PCT/US2012/063382

(22) **International Filing Date**:
2 November 2012 (02.11.2012)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:
61/555,049 3 November 2011 (03.11.2011) US

(71) **Applicant**: **MILLENNIUM PHARMACEUTICALS, INC.** [US/US]; 40 Landsdowne Street, Cambridge, Massachusetts 02139 (US).

(72) **Inventor**: **SMITH, Peter G.**; 173A Franklin Street, Arlington, Massachusetts 02474 (US).

(74) **Agent**: **HERZFELD, Deborah M.**; Finnegan, Henderson, Farabow, Garrett & Dunner LLP, 901 New York Avenue, NW, Washington, D.C., District of Columbia 20001-4413 (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, 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, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, 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, 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, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

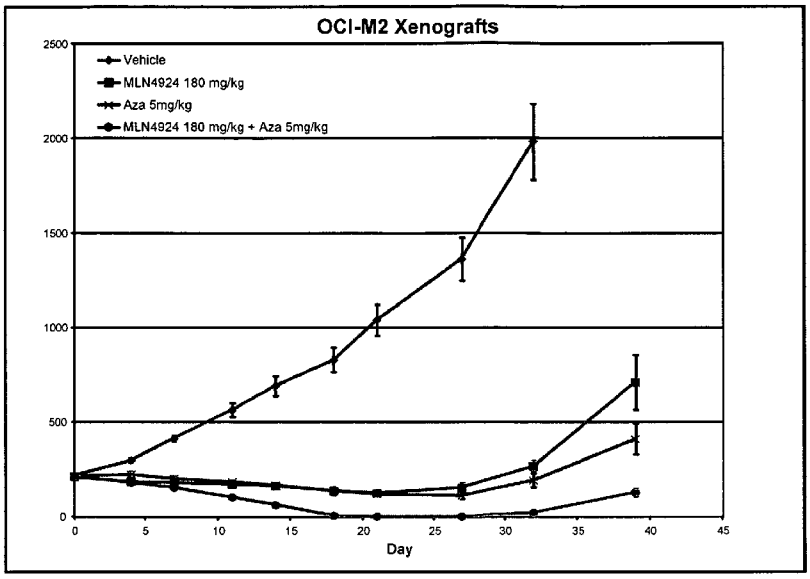
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

(54) **Title**: ADMINISTRATION OF NEDD8-ACTIVATING ENZYME INHIBITOR AND HYPOMETHYLATING AGENT

FIG. 4



(57) **Abstract**: The present disclosure relates to methods for the treatment of cancer in patients in recognized need of such treatment. The methods comprise administering to such a patient an NAE inhibitor or a pharmaceutically acceptable salt thereof, such as ((1S,2S,4R)-4-(4-((1S)-2,3-dihydro-1H-inden-1-ylamino)-7H-pyrrolo[2,3 d]pyrimidin 7-yl)-2-hydroxycyclopentyl)methyl sulfamate (MLN4924) or {(1S,2S,4R)-4-[(6-{[(1R,2S)-5-chloro-2 methoxy-2,3-dihydro-1H-inden-1-yl]amino}pyrimidin-4-yl)oxy]-2-hydroxycyclopentyl}-methyl sulfamate (I-216), and a hypomethylating agent or a pharmaceutically acceptable salt thereof, such as azacitidine or decitabine. Also disclosed are medicaments for use in the treatment of cancer.

WO 2013/067396 A2