

(51) International Patent Classification:

C07D 487/04 (2006.01) A61K 31/505 (2006.01)

C07D 487/02 (2006.01) A61P 35/00 (2006.01)

A61K 31/519 (2006.01)

(21) International Application Number:

PCT/US2012/052007

(22) International Filing Date:

23 August 2012 (23.08.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/526,830 24 August 2011 (24.08.2011) US

(71) Applicant (for all designated States except US): MIL-

LENNIUM PHARMACEUTICALS, INC. [US/US]; 40 Landsdowne Street, Cambridge, MA 02139 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): MCCARRON, Ash-

ley, Sue [US/US]; 21 Greenfield Parkway, Bedford, NH 03110 (US). SELLS, Todd, B. [US/US]; 1 Davis Road, Southborough, MA 01772 (US). STIRLING, Matthew [GB/US]; 1 Huckleberry Lane, Randolph, MA 02368 (US). STROUD, Stephen, G. [US/US]; 53 Tesla Avenue, Medford, MA 02155 (US).

(74) Agents: HERZFLED, Deborah, M. et al.; Finnegan,

Henderson, Farabow, Garrett & Dunner, L.L.P., 901 New York Ave., N.W., Washington, DC 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, 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

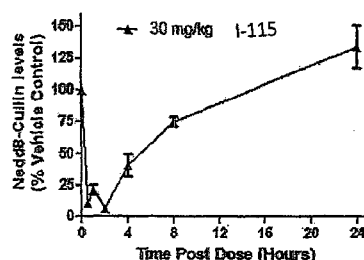
kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

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

(54) Title: INHIBITORS OF NEDD8-ACTIVATING ENZYME

HCT-116 PD study: I-115



PK Parameters of K-I-115 in Female Nude Mice
Bearing HCT 116 Tumor Xenografts
Following a Single Subcutaneous Administration at 30
mg/kg.

FIGURE 1

Sample	AUC _{last} (nM*hr)	C _{max} (nM)
Plasma	26271	27138

(57) **Abstract:** Disclosed are chemical entities which are inhibitors of Nedd8-activating enzyme (NAE), namely, the compound {(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 and pharmaceutically acceptable salts thereof; solid state forms thereof; and prodrugs thereof. Also disclosed are methods of using the chemical entities to treat disorders such as cancer.