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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 January 2006 (05.01.2006)

PCT

(10) International Publication Number
WO 2006/002236 A1

(51) International Patent Classification[7]: C07D 233/54, 401/12, 405/12, 413/12, 417/12, A61K 31/4174, 31/4178, A61P 35/00

(21) International Application Number: PCT/US2005/022062

(22) International Filing Date: 20 June 2005 (20.06.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/580,927 18 June 2004 (18.06.2004) US

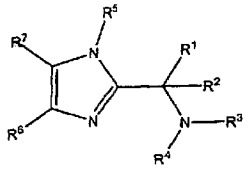
(71) Applicant *(for all designated States except US)*: **CHIRON CORPORATION** [US/US]; 4560 Horton Street, Emeryville, CA 94608-2916 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **WANG, Weibo** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **BARSANTI, Paul, A.** [GB/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **XI, Yi** [CN/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **BOYCE, Rustum, S.** [IN/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **PECCHI, Sabina** [IT/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **BRAMMEIER, Nathan** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **PHILLIPS, Megan** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **MENDENHALL, Kris** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **WAYMAN, Kelly** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **LAGNITON, Liana, Marie** [AU/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **CONSTANTINE, Ryan** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **YANG, Hong** [CN/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **MIEULI, Elizabeth** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **RAMURTHY, Savithri** [IN/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **JAZAN, Elisa** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **SHARMA, Anu** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **RAMA, Jain** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **SABRAMANIAN, Sharadha** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **RENHOWE, Paul** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **BAIR, Kenneth, Walter** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **DUHL, David** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **WALTER, Annette** [DE/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **ABRAMS, Tinya** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **HUH, Kay** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **MARTIN, Eric** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville,

[Continued on next page]

(54) **Title:** N- (1- (1-BENZYL -4-PHENYL-1H-IMIDAZOL-2-YL) -2,2-DYMETHYLPROPYL) BENZAMIDE DERIVATIVES AND RELATED COMPOUNDS AS KINESIN SPINDLE PROTEIN (KSP) INHIBITORS FOR THE TREATMENT OF CANCER



(I)

(57) **Abstract:** This invention is directed to substituted imidazole compounds which modulate the activity of KSP and are useful for the treatment of cancer and are represented by the formula (I) wherein: R^1 is selected from the group consisting of aminoacyl, acylamino, carboxyl, carboxyl ester, aryl, and alkyl optionally substituted with hydroxy or halo; R^2 is selected from the group consisting of hydrogen, alkyl, and aryl; R^3 is selected from the group consisting of hydrogen and -X-A, wherein X is selected from the group consisting of-C(O)-, -C(S)-, -S(O)-, $-S(O)_2-$, and -S(O)2-N(R)-, where R is hydrogen or alkyl; and A is selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted aryl, carboxyl, carboxyl ester, aminoacyl, optionally substituted heteroaryl, optionally substituted heterocyclic, and optionally substituted cycloalkyl, wherein the optionally substituted groups are substituted with 1 to 4 substituents; R^5 is selected from the group consisting of L-A^1, wherein L is selected from the group consisting of-$S(O)_q$- where q is one or two, and C_1 to C_5 alkylene optionally substituted with hydroxy, halo, or acylamino; and A^1 is selected from the group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkyl, and substituted cycloalkyl; and one of either R^6 or R^7 is selected from the group consisting of heterocyclic, aryl and heteroaryl, all of which may be optionally substituted with $-(R^8)_m$ where R^8 is as defined herein and m is an integer from 1 to 3, and the other Of R^6 or R^7 is selected from the group consisting of hydrogen, halo, and alkyl; or R^6 and R^7 are both hydrogen; the other substituents are defined in the claims.

WO 2006/002236 A1

CA 94662-8097 (US). **KNAPP, Mark** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US). **LE, Vincent** [US/US]; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US).

(74) **Agent: SUH, Young, J.**; Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US).

(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, 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, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.