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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
7 September 2007 (07.09.2007)

PCT

(10) International Publication Number
WO 2007/100990 A3

(51) International Patent Classification:
C07D 487/04 (2006.01) *A61K 31/407* (2006.01)

(21) International Application Number:
PCT/US2007/062329

(22) International Filing Date:
16 February 2007 (16.02.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/776,509 24 February 2006 (24.02.2006) US

(71) Applicant *(for all designated States except US)*: **ABBOTT LABORATORIES** [US/US]; Dept. 377 Bldg AP6A-1, 100 Abbott Park Road, Abbott Park, Illinois 60064-6008 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **COWART, Marlon, D.** [US/US]; 43 Dahlia Lane, Round Lake, Illinois 60073 (US). **ZHAO, Chen** [US/US]; 1417 Castleton Road, Libertyville, Illinois 60048 (US). **SUN, Minghua** [US/US]; 1733 Cedar Glenn Drive, Libertyville, Illinois 60048 (US). **BLACK, Lawrence, A.** [US/US]; 1173 Tamarack Lane, Libertyville, Illinois 60048 (US). **ZHENG, Guo Zhu** [CA/US]; 39607 N. Birch Avenue, Lake Bluff, Illinois 60044 (US). **GREGG, Robert, J.** [US/US]; 631 Meadow Lane, Libertyville, Illinois 60048 (US). **ZHANG, Geoff, G.Z.** [CN/US]; 1014 Dawes Street, Libertyville, Illinois 60048 (US). **SHEIKH, Ahmad, Y.** [PK/US]; 700 Pine Street; Deerfield, Deerfield, Illinois 60015 (US). **LOU, Xiaochun** [CN/US]; 8094 RFD Breckenridge Drive, Long Grove, Illinois 60047 (US). **HENRY, Rodger, F.** [US/US]; 33067 Tomahawk Court, Wildwood, Illinois 60030 (US). **BARNES, David, M.** [US/US]; 617 N. Lakewood Avenue, Lake Villa, Illinois 60046 (US). **KOLACZKOWSKI, Lawrence** [US/US]; 5822 Constitution Avenue, Gurnee, Illinois 60031 (US). **HAIGHT, Anthony, R.** [US/US]; 40381 Reed Court, Wadsworth, Illinois 60083 (US). **CHANG, Sou-Jen** [US/US]; 16139 Port Clinton Road, Prairie View, Illinois 60069 (US). **WITTENBERGER, Steven, J.** [US/US]; 45 S. Pershing Avenue, Mundelein, Illinois 60060 (US). **FICKES, Michael, G.** [US/US]; 2311 Ridgeway Avenue, Evanston, Illinois 60201 (US).

(74) Agents: **CHEN, Portia** et al.; Dept. 377 Bldg AP6A-1, 100 Abbott Park Road, Abbott Park, Illinois 60064-6008 (US).

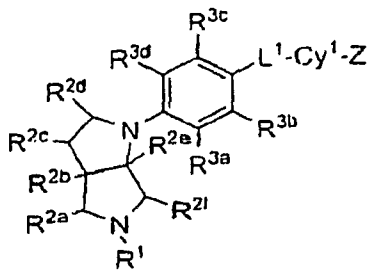
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, 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, 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, LV, 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*

[Continued on next page]

(54) **Title:** OCTAHYDRO-PYRROLO[3,4-B] PYRROLE DERIVATIVES AND THEIR USE AS HISTAMINE-3 RECEPTOR LIGANDS



(57) **Abstract:** Octahydro-pyrrolo[3,4-b]pyrrole derivatives or a pharmaceutically acceptable salt, ester, amide, prodrug, or radiolabeled form thereof, wherein R^1 is alkyl, C_3-C_5 cycloalkyl. or (C_3-C_5 cycloalkyl)methyl; R^{2a}, R^{2b}, R^{2c}, R^{2d}, R^{2e}, and R^{2f} each are independently hydrogen, methyl, or fluoromethyl; R^{3a}, R^{3b}, R^{3c}, and R^{3d} each are independently hydrogen, alkyl, fluoroalkyl, fluoroalkoxy, alkoxy, thioalkoxy, halogen, or nitrile, with the proviso that when one or more of R^{3a}, R^{3b}, R^{3c}, and R^{3d} are alkyl, then at least one of R^{3a}, R^{3b}, R^{3c}, and R^{3d} is fluoroalkyl, fluoroalkoxy, alkoxy, thioalkoxy, halogen, or nitrile; L^1 is a bond, oxygen, sulfur, carbonyl, alkylene,. alkylcarbonyl, alkylamino, -C(=N-Oalkyl)-, NR^4, -C(=O) NR^4-, or -NR4C(=O)-; R^4 is hydrogen or alkyl; Cy^1 is aryl, cycloalkyl, cycloalkenyl, heteroaryl, or heterocycle; Z is a substituent R^6 or a group represented by -L^3-Cy^3; R^6 is hydrogen, acyl, acyloxy, alkenyl, alkoxy, alkoxyalkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxyimino, alkoxysulfonyl, alkyl, alkylcarbonyl, alkylsulfonyl, alkynyl, amido, carboxy, cyano, cycloalkyl, fiuoroalkoxy, haloalkoxy, haloalkyl, halogen, hydroxy, hydroxyalkyl, mercapto, nitro, alkylthio, amino, NHR^7, NR^7R^8, -$N(R^7)C(=O)R^9$, -$C(=O)NR^7R^8$, or $N(R^7)SO_2(R^{10})$; L^3 is a bond, oxygen, sulfur, carbonyl, alkylene, alkylcarbonyl, alkylamino, -C(=N-Oalkyl)-, NR^{11}, -C(=O) NR^{11}-, or -$NR^{11}C(=O)$-;Cy^3 is aryl, cycloalkyl, cycloalkenyl, heteroaryl, or heterocycle; R^7, R^8, R^9, R^{10}, and R^{11} at each occurrence are independently hydrogen,C_{1-4} alkyl, C_3-C_4 cycloalkyl, or a (C_3-C_4 cycloalkyl)amine; are useful in treating conditions or disorders prevented by or ameliorated by histamine-3 receptor ligands. Octahydro-pyrrolo[3,4-b]pyrrole compounds, methods for using such compounds, compositions for making them, and processes for preparing such compounds are disclosed herein.

WO 2007/100990 A3

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

(88) Date of publication of the international search report:
18 October 2007

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.