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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
8 December 2005 (08.12.2005)

PCT

(10) International Publication Number
WO 2005/115375 A1

(51) International Patent Classification[7]: A61K 31/24

(21) International Application Number:
PCT/US2005/018350

(22) International Filing Date: 24 May 2005 (24.05.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/574,157 25 May 2004 (25.05.2004) US

(71) Applicant *(for all designated States except US)*: **OTHERA PHARMACEUTICALS, INC.** [US/US]; 730 Springdale Drive, Exton, PA 19341 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **MATIER, William, L.** [US/US]; 8 Larchmont Court, Hockessin, DE 19707 (US). **PATIL, Ghanshyam** [US/US]; 19 Linden Circle, Lincoln University, PA 19352 (US).

(74) Agents: **CALDWELL, John, W.** et al.; Woodcock Washburn LLP., One Liberty Place - 46th Floor, Philadelphia, PA 19103 (US).

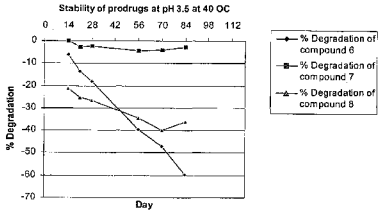
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, 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*

[Continued on next page]

(54) Title: OCULOSELECTIVE DRUGS AND PRODRUGS



(57) Abstract: Compounds of the following formula are disclosed: wherein R^1 and R^2 are each independently H, W, or a phenoxyl protecting group; and $R^4$is H or W, provided that at least one of R^1, R^2, and R^4 is W; R^3 is hydrogen, straight chain or branched C_1-C_{10} alkyl, cycloalkyl, amino, C_1-C_{10} alkoxy, -NHC(=O)Ra, or -C(=O)N(H)R^a; R^a is alkyl, aryl, or heterocyclyl; Z is -0-, -O(C=O)-, or NH(C=O)-, wherein when Z is -0-, R^5 is H, straight chain or branched C_1-C_{10} alkyl, cycloalkyl, cycloalkyl substituted with at least one straight or branched C_1-C_{10} alkyl, CI-Clo alkoxyalkyl, amino, benzyl, tetrahydrofuranyl, dihydrofuranyl, furanyl, morpholinyl, piperidinyl, tetrahydropyranyl, dioxolanyl, 2,2-dimethyl dioxolanyl, dioxanyl, pyrrolyl, pyrrolsdinyl, tetrahydrooxazolyl, dihydrooxazolyl, phenyl, or phenyl substituted with CI-Clo alkyl, C_1-C_{10} alkoxy, or halo; and W is:, wherein each R^6 is independently H, straight chain or branched C_1-C_{10} alkyl, or straight chain or branched C_1-C_{10} alkoxyalkyl; and R^7 is alkyl, cycloalkyl, aryl, or aralkyl; and wherein when Z is -O(C=O)-, R^5 is straight chain or branched C_1-C_{10} alkyl, cycloalkyl, cycloalkyl substituted with at least one straight or branched C_1-C_{10} alkyl, CI-CIO alkoxyalkyl, amino, benzyl, tetrahydrofuranyl, dihydrofuranyl, furanyl, morpholinyl, piperidinyl, tetrahydropyranyl, dioxolanyl, 2,2-dimethyl dioxolanyl, dioxanyl, pyrrolyl, pyrrolidinyl, tetrahydrooxazolyl, dihydrooxazolyl, phenyl, or phenyl substituted with C_1-C_{10} alkyl, C_1-C_{10} alkoxy, or halo; and W is: , wherein each R6 is independently H, straight chain or branched CI-C to alkyl, or straight chain or branched C,-C to alkoxyalkyl; and R7 is alkyl, cycloalkyl, aryl, or aralkyl; and wherein when Z is-NH(C=O)-, R5 is straight chain or branched C_1 -C_{10} alkyl, cycloalkyl, cycloalkyl substituted with at least one straight or branched C_1-C_{10} alkyl, CI-CIO alkoxyalkyl, amino, benzyl, tetrahydrofuranyl, dihydrofuranyl, furanyl, morpholinyl, piperidinyl, tetrahydropyranyl, &oxolanyl, 2,2-dimethyl dioxolanyl, dioxanyl, pyrrolyl, pyrrolidinyl, tetrahydrooxazolyl, dihydrooxazolyl, phenyl, or phenyl substituted with C_1-C_{10} alkyl, C_1-C_{10} alkoxy, or halo; and W is: ; wherein each R6 is independently H, straight chain or branched C1 -C to alkyl, or straight chain or branched C,-Clo alkoxyalkyl. Methods of preparing the compounds, pharmaceutical compositions comprising the compounds, and methods of treating patients by administration of the pharmaceutical compositions, are also disclosed.

WO 2005/115375 A1

— *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.