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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
23 June 2011 (23.06.2011)

PCT

(10) International Publication Number
WO 2011/075684 A1

(51) International Patent Classification:
A61K 31/34 (2006.01)

(21) International Application Number:
PCT/US2010/061122

(22) International Filing Date:
17 December 2010 (17.12.2010)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/284,478 18 December 2009 (18.12.2009) US
61/345,045 14 May 2010 (14.05.2010) US

(71) Applicant *(for all designated States except US)*: **ACTIVESITE PHARMACEUTICALS, INC.** [US/US]; 187 Magellan Avenue, San Francisco, California 94116 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **SINHA, Sukanto** [US/US]; 187 Magellan Avenue, San Francisco, California 94116 (US). **CHILCOTE, Tamie Jo** [US/US]; 187 Magellan Avenue, San Francisco, California 94116 (US).

(74) Agents: **KEZER, William B.** et al.; TOWNSEND and TOWNSEND and CREW LLP, Two Embarcadero Center, Eighth Floor, San Francisco, California 94111-3834 (US).

[Continued on next page]

(54) Title: PRODRUGS OF INHIBITORS OF PLASMA KALLIKREIN

(57) Abstract: The present invention provides prodrugs of compounds that inhibit the activity of plasma kallikrein (PK) and methods of preventing and treating plasma kallikrein dependent diseases or conditions, for example, diabetic macular edema, with the prodrugs having the formula (I).

FIG. 1 (Sheet 1 of 2)

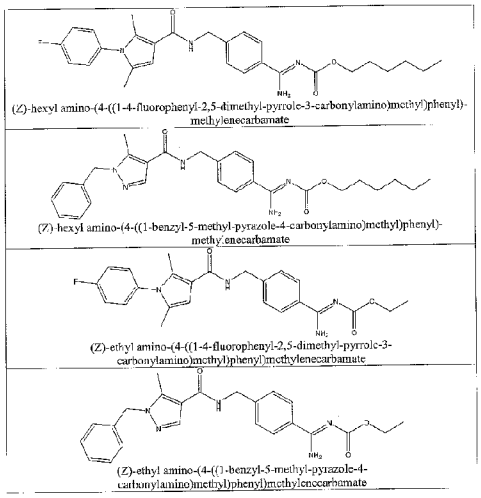
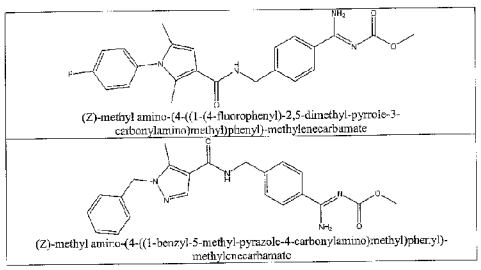
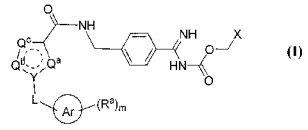


FIG. 1 (Sheet 2 of 2)





(I)

WO 2011/075684 A1

(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, 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, RO, RS, RU, 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, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, 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:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*