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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
12 December 2002 (12.12.2002)

PCT

(10) International Publication Number
WO 02/098427 A3

(51) International Patent Classification[7]: A61K 31/485, 31/16, 31/216, 31/60, C07D 489/00, 489/02, 489/04, C07C 65/10, A61P 25/04, 29/00

(21) International Application Number: PCT/US02/17613

(22) International Filing Date: 5 June 2002 (05.06.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/295,556 5 June 2001 (05.06.2001) US

(71) Applicant: CONTROL DELIVERY SYSTEMS [US/US]; 313 Pleasant Street, Watertown, MA 02472 (US).

(72) Inventors: ASHTON, Paul; 19 Brimmer Street, Boston, MA 02114 (US). SMITH, Thomas, J.; 167 Kings Grant Avenue, Weston, MA 02193 (US). CYNKOWSKI, Tadeusz; 99 Pont Avenue #220, Brookline, MA 02445 (US). CYNKOWSKA, Grazyna; 99 Pond Avenue #220, Brookline, MA 02445 (US). MICKUNAS, Edmund; 65 Woods Crossing, Holliston, MA 01746 (US).

(74) Agents: KRAUS, Eric, J. et al.; McDermott, Will & Emery, 600 13th Street, N.W., Washington, DC 20005-3096 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
20 February 2003

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.

WO 02/098427 A3

(54) Title: SUSTAINED-RELEASE ANALGESIC COMPOUNDS

(57) Abstract: A pharmaceutically active inventive compound comprises two independently active analgesic moieties covalently conjoined through a physiologically labile linker. A preferred embodiment comprises an opioid, such as morphine, covalently linked to at least one analgesic compound selected from the group consisting of an opioid or a no-opioid compound through a physiologically labile linker. Suitable covalent linkers are covalently bonded to the two independently active analgesic compounds through one or more lactone, lactam, or sulfonamido linkages. Suitable linkers include endogenous carboxylate, amido, and sulfonamido moieties, and exogenous moieties that form the aforementioned lactone, lactam or sulfonamido linkages.