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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 July 2009 (02.07.2009)

PCT

(10) International Publication Number
WO 2009/080795 A1

(51) International Patent Classification:
C07D 493/04 (2006.01) *A61P 29/00* (2006.01)
A61K 31/34 (2006.01)

(21) International Application Number:
PCT/EP2008/068114

(22) International Filing Date:
19 December 2008 (19.12.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
2007/0934 21 December 2007 (21.12.2007) IE

(71) Applicant *(for all designated States except US)*: **THE PROVOST, FELLOWS AND SCHOLARS OF THE COLLEGE OF THE HOLY AND UNDIVIDED TRINITY OF QUEEN ELIZABETH, NEAR DUBLIN** [IE/IE]; College Green, Dublin, 2 (IE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **GILMER, John Francis** [IE/IE]; 3 Tynan Hall Park, Kingswood Heights, Dublin, 24 (IE). **CLUNE-MORIARTY, Louise** [IE/IE]; 11 The Park, Quinn, Co. Clare (IE). **LALLY, Maeve** [IE/IE]; 47 Anglesea Road, Ballsbridge, Dublin, 4 (IE).

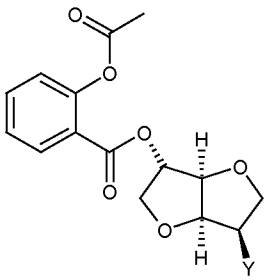
(74) Agents: **DUNNE, Sinead** et al.; Tomkins & Co., 5, Dartmouth Road, Dublin, 6 (IE).

(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, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, 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, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, 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*

(54) Title: EFFICIENT ASPIRIN PRODRUGS



(I)

(57) Abstract: Aspirin is one of the most widely used drugs in the treatment of inflammation, pain and fever. It has more recently found application in the prevention of heart attacks and stroke and is being studied as a cancer chemopreventative agent. Despite its value aspirin continues to be underutilized because it causes gastric bleeding. The technology under development potentially removes this problem. It is designed to reduce contact between the drug and the intestinal lining. An isosorbide aspirinate prodrug compound is thus provided. The compound has the general structure as shown in general formula (I) wherein Y is a C_1 - C_8 alkyl ester, a C_1 - C_8 alkoxy ester, a C_3 - C_{10} cycloalkyl ester, an arylester, a C_1 - C_8 alkylaryl ester or -C(O)OR_{ring}, wherein R_{ring} is a 5-membered aromatic or nonaromatic 5-member ring having at least one heteroatom substituted for a carbon of the ring system, which can be unsubstituted or substituted with at least one nitric oxide releasing group.

WO 2009/080795 A1