

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
27 July 2006 (27.07.2006)

PCT

(10) International Publication Number
WO 2006/077397 A3

(51) International Patent Classification:
A61K 39/385 (2006.01) **C07H 5/04** (2006.01)

(21) International Application Number:
PCT/GB2006/000160

(22) International Filing Date: 18 January 2006 (18.01.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0501008.7 18 January 2005 (18.01.2005) GB

(71) Applicant (for all designated States except US): **AMURA THERAPEUTICS LIMITED** [GB/GB]; Horizon Park, Barton Road, Comberton, Cambridge CB3 7AJ (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **FLINN, Nicholas** [GB/GB]; c/o Amura Therapeutics Limited, Horizon Park, Barton Road, Comberton, Cambridge CB3 7AJ (GB). **QUIBELL, Martin** [GB/GB]; c/o Amura Therapeutics Limited, Horizon Park, Barton Road, Comberton, Cambridge CB3 7AJ (GB). **RAMJEE, Manoj** [GB/GB]; c/o Amura Therapeutics Limited, Horizon Park, Barton Road, Comberton, Cambridge CB3 7AJ (GB). **TURNELL, William** [GB/US]; c/o MediVas LLC, 6275 Nancy Ridge Drive, San Diego, CA 92121 (US).

(74) Agents: **CLYDE-WATSON, Zoe** et al.; D Young & Co, 21 Holborn, London EC1N 2DY (GB).

(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, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, 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, 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
- 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:
30 November 2006

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.

(54) Title: METHOD OF PRODUCING CONJUGATE VACCINES

(57) Abstract: The present invention relates to a method of production of a hydrazide modified sugar comprising a step of reacting a sugar with a hydrazide in a reaction solvent at a pH of between 3 and 5.5, wherein the solvent comprises an aqueous based solvent and an optional polar organic co-solvent. A further aspect of the invention relates to a method of production of a polysaccharide epitope carrier protein conjugate comprising the steps of: (a) reacting a polysaccharide epitope with a hydrazide to form a hydrazide modified polysaccharide epitope; (b) reacting the hydrazide modified polysaccharide epitope with a linker that has been pre-coupled to a carrier protein. Another aspect of the invention relates to a method of production of a sugar-dihydrazide-aldehyde adduct comprising the steps of: (a) producing a hydrazide modified sugar using a method according to the invention, wherein the hydrazide modified sugar includes a further unreacted hydrazide moiety; and (b) reacting the further hydrazide moiety with the aldehyde functionality of a linker group.



WO 2006/077397 A3