

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
4 December 2003 (04.12.2003)

PCT

(10) International Publication Number
WO 03/100024 A2

- (51) International Patent Classification⁷: **C12N** **CRUZ, Antonio** [CA/CA]; 89 Dunloe Road, Toronto, Ontario M5P 2T7 (CA).
- (21) International Application Number: PCT/US03/16660
- (22) International Filing Date: 27 May 2003 (27.05.2003) (74) Agent: **RAE-VENTER, Barbara**; P.O. Box 1898, Monterey, CA 93942 (US).
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/382,921 24 May 2002 (24.05.2002) US
60/384,357 30 May 2002 (30.05.2002) US
- (71) Applicants (for all designated States except US): **WARATAH PHARMACEUTICALS, INC.** [CA/CA]; 415 Yonge Street, Suite 1103, Toronto, Ontario M5B 2E7 (CA). **UNIVERSITY OF ALBERTA** [CA/CA]; Department of Medicine, 430 Heritage Medical Research Centre, Edmonton, Alberta T6G 2S2 (CA).
- (71) Applicant and
- (72) Inventor: **BRAND, Stephen J** [AU/US]; 161 Bedford Road, Lincoln, MA 01733 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **RABINOVITCH, Alex** [CA/CA]; 148-35 64th Ave, Edmonton, Alberta T6H 4Y1 (CA). **SUAREZ-PINZON, Wilma Lucia** [CO/CA]; 111-35 83rd Ave, Edmonton, Alberta T6G 2C6 (CA).
- (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, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, 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, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— without international search report and to be republished upon receipt of that report
- 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: TREATMENT FOR DIABETES

(57) Abstract: Proliferating pancreatic islet cells obtained by the method of isolating a population of cells that preferably includes predominantly islet precursor cells that express one or more marker associated with an islet precursor cell and providing the precursor cells with one or more a pancreatic differentiation agent so that a population of cells is obtained that has a high proportion of cells with phenotypic characteristics of functional pancreatic islet β -cells. Optionally, the precursor cells are pretreated by providing them with one or more cell expansion agent to increase the number of cells in the population prior to differentiation. The pancreatic differentiation agent composition comprises a gastrin/CCK receptor ligand, e.g., a gastrin, in an amount sufficient to effect differentiation of pancreatic islet precursor cells to mature insulin-secreting cells. The cell expansion agent composition comprises one or more epidermal growth factor (EGF) receptor ligand in an amount sufficient to stimulate proliferation of the precursor cells. The methods of treatment include transplanting either undifferentiated precursor cells and providing the pancreatic differentiation agent either alone or in combination with the cell expansion agent in situ, or transplanting the functional pancreatic islet β -cells into the patient. The pancreatic islet β -cells can be used for drug screening, and replenishing pancreatic function in the context of clinical treatment.



WO 03/100024 A2