

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
9 February 2006 (09.02.2006)

PCT

(10) International Publication Number
WO 2006/014287 A1

(51) International Patent Classification⁷: **C07K 14/605**

(21) International Application Number:
PCT/US2005/023076

(22) International Filing Date: 30 June 2005 (30.06.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/585,358 2 July 2004 (02.07.2004) US
60/684,805 26 May 2005 (26.05.2005) US

(71) Applicant (for all designated States except US): **BRISTOL-MYERS SQUIBB COMPANY** [US/US]; Route 206 and Province Line Road, Princeton, New Jersey 08543-4000 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **EWING, William R.** [US/US]; 1193 Waterwheel Drive, Yardley, Pennsylvania 19067 (US). **MAPELLI, Claudio** [IT/US]; 8 Silvers Lane, Plainsboro, New Jersey 08536 (US). **SULSKY, Richard B.** [US/US]; 2 Coventry Square, West Trenton, New Jersey 08628 (US). **HAQUE, Tasir S.** [US/US]; 1015 Summit Drive, Yardley, Pennsylvania 19067 (US). **LEE, Ving G.** [US/US]; 11 Colts Neck Terrace, Hamilton Township, New Jersey 08620 (US). **RIEXINGER, Douglas James** [US/US]; 87 Biser Road, Flemington, New Jersey 08822 (US). **MARTINEZ, Rogelio L.** [GB/US]; 16 Black Gum Drive, Monmouth, New Jersey 08852 (US). **ZHU, Yeheng** [US/US]; 20 Meszaros Road, Stockton, New Jersey 08559 (US).

(74) Agents: **LANGE, Keith** et al.; Bristol-Myers Squibb Company, P.O. Box 4000, Princeton, New Jersey 08543-4000 (US).

(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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, 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, 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).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations: 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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, 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, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, 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, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

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

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: HUMAN GLUCAGON-LIKE-PEPTIDE-1 MODULATORS AND THEIR USE IN THE TREATMENT OF DIABETES AND RELATED CONDITIONS

(57) Abstract: The present invention provides novel human glucagon-like peptide-1 (GLP-1)-receptor modulators that have biological activity similar or superior to native GLP-1 peptide and thus are useful for the treatment or prevention of diseases or disorders associated with GLP activity. Further, the present invention provides novel, chemically modified peptides that not only stimulate insulin secretion in type II diabetics, but also produce other beneficial insulinotropic responses. These synthetic peptide GLP-1 receptor modulators exhibit increased stability to proteolytic cleavage making them ideal therapeutic candidates for oral or parenteral administration. The peptides of this invention show desirable pharmacokinetic properties and desirable potency in efficacy models of diabetes.

WO 2006/014287 A1