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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
20 September 2007 (20.09.2007)

PCT

(10) International Publication Number
WO 2007/106707 A2

(51) International Patent Classification:
G06F 19/00 (2006.01)

(21) International Application Number:
PCT/US2007/063548

(22) International Filing Date: 8 March 2007 (08.03.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/781,564 10 March 2006 (10.03.2006) US

(71) Applicant *(for all designated States except US)*: **MACROGENICS, INC.** [US/US]; 1500 East Gude Drive, Rockville, MD 20850 (US).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **STAVENHAGEN, Jeffrey** [US/US]; 19417 Treadway Road, Brookeville, MD 20833 (US).

(74) Agent: **AUERBACH, Jeffrey, I.**; Edell, Shapiro & Finnan, Llc, 1901 Research Blvd., Suite 400, Rockville, MD 20850 (US).

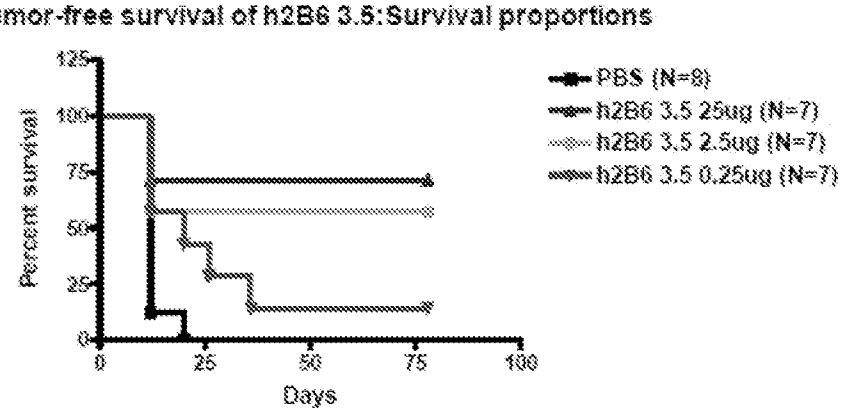
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, 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, 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, HU, IE, IS, IT, LT, LU, LV, MC, MT, 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:
— *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:** IDENTIFICATION AND ENGINEERING OF ANTIBODIES WITH VARIANT HEAVY CHAINS AND METHODS OF USING SAME



(57) **Abstract:** The present invention relates to molecules, particularly polypeptides, more particularly immunoglobulins (e.g., antibodies), comprising a variant heavy chain, which variant heavy chain comprises constant domains from more than one IgG isotype. The variant heavy chain of the invention may further comprise at least one amino acid modification relative to the parental heavy chain, such that the Fc region of said variant heavy chain binds an FcγR with an altered affinity relative to a comparable molecule comprising the wild-type heavy cahin. The molecules of the invention are particularly useful in preventing, treating, or ameliorating one or more symptoms associated with a disease, disorder, or infection. The molecules of the invention are particularly useful for the treatment or prevention of a disease or disorder where an enhanced efficacy of effector cell function (e.g., ADCC) mediated by FcγR is desired, e.g., cancer, infectious disease, and in enhancing the therapeutic efficacy of therapeutic antibodies the effect of which is mediated by ADCC.

WO 2007/106707 A2