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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
7 May 2015 (07.05.2015)

WIPO | PCT

(10) International Publication Number
WO 2015/066379 A2

(51) International Patent Classification:
C07K 16/28 (2006.01)

(21) International Application Number:
PCT/US2014/063254

(22) International Filing Date:
30 October 2014 (30.10.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/897,809 30 October 2013 (30.10.2013) US

(71) Applicants: **GENZYME CORPORATION** [US/US]; 500 Kendall Street, Cambridge, MA 02142 (US). **CHILDREN'S UNIVERSITY HOSPITAL TÜBINGEN** [DE/DE]; Hoppe-Seyler-Strasse 1, 72076 Tübingen (DE).

(72) Inventors: **BLANK, Gregor**; c/o Children's University Hospital Tübingen, Hoppe-Seyler-Strasse 3, 72076 Tübingen (DE). **HANDGRETINGER, Rupert**; c/o Children's University Hospital Tübingen, Hoppe-Seyler-Strasse 1, 72076 Tübingen (DE). **SCHILBACH, Karin**; c/o Children's University Hospital Tübingen, Hoppe-Seyler-Strasse 1, 72076 Tübingen (DE). **LACORCIA, Gina**; c/o Sanofi, 55 Corporate Drive, Mail Code: 55A-505A, Bridgewater, NJ 08807 (US). **SNELL, Daniel**; Im Sunnebuel 8, Thalwil 8800 (CH). **MENRAD, Andreas**; Allerstrasse 7, 16515 Oranienburg (DE).

(74) Agents: **VELEMA, James, H.** et al.; Lathrop & Gage LLP, 28 State Street, Boston, MA 02109 (US).

(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, BN, BR, BW, BY, BZ, CA, CH, CL, 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, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, 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, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

— *with sequence listing part of description (Rule 5.2(a))*

WO 2015/066379 A2

(54) Title: METHODS FOR ENHANCING IMMUNOSUPPRESSIVE THERAPY BY MULTIPLE ADMINISTRATION OF ALPHA BETA TCR-BINDING POLYPEPTIDE

(57) Abstract: The present disclosure is related to improved methods for use of a humanized binding polypeptide specific for the alpha beta T cell receptor (αβ-TCR). In particular, this disclosure relates to improved methods of use of a humanized anti-αβ-TCR antibody, which is derived from the murine monoclonal antibody BMA031, in immunosuppressive therapy. Novel methods using humanized monoclonal antibodies and/or humanized monoclonal antibody fragments (e.g., anti-αβTCR antibodies and/or fragments thereof) are also provided. Novel methods using repetitive administration of humanized monoclonal antibodies and/or humanized monoclonal antibody fragments (e.g., anti-αβTCR antibodies and/or fragments thereof) to reduce αβ T cells in the subject relative to γδ T cells in the subject are provided.