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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
14 February 2019 (14.02.2019)

WIPO | PCT

(10) International Publication Number
WO 2019/033023 A1

(51) International Patent Classification:
A01N 63/00 (2006.01) *C12N 15/00* (2006.01)
A61K 48/00 (2006.01) *C12N 15/11* (2006.01)
C12N 5/071 (2010.01) *C07H 21/04* (2006.01)

(21) International Application Number:
PCT/US2018/046306

(22) International Filing Date:
10 August 2018 (10.08.2018)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
17185992.9 11 August 2017 (11.08.2017) EP

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(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, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, 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:
— *with international search report (Art. 21(3))*
— *with sequence listing part of description (Rule 5.2(a))*

WO 2019/033023 A1

(54) Title: CD1D-RESTRICTED NKT CELLS AS A PLATFORM FOR OFF-THE-SHELF CANCER IMMUNOTHERAPY

(57) Abstract: Embodiments of the disclosure include methods and compositions for immunotherapy that comprise allogeneic cells that are able to be universally tolerated in host individuals. In specific embodiments the cells have reduced expression of endogenous beta2-microglobulin (B2M) and/or MHC class II-associated invariant chain (Ii), and in particular cases the cells are NKT cells that lack the ability to damage host tissues, have much reduced recognition by host immune cells, and surprisingly avoid destruction by host NK cells. In some embodiments, B2M- and/or Ii-targeting molecules are engineered to be expressed in combination (including within a single construct) with recombinantly engineered receptors, for example, for a one-hit generation of universally tolerated off-the-shelf immunotherapy.