



(51) International Patent Classification:

C07K 16/28 (2006.01) A61K 47/65 (2017.01)
C07K 16/30 (2006.01) A61K 39/395 (2006.01)

(21) International Application Number:

PCT/US2018/039157

(22) International Filing Date:

22 June 2018 (22.06.2018)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/524,558 25 June 2017 (25.06.2017) US

(71) Applicants: SYSTIMMUNE, INC. [US/US]; 15318 NE 95th St, Redmond, Washington 98052 (US). SICHUAN BAILI PHARMACEUTICAL CO. LTD. [CN/CN]; 161 Baili Road, Wenjiang District, Chengdu, Sichuan (CN).

(72) Inventors: ZHU, Yi; 8-24, Building 6, No. 6, Lidu Road, Wuhou District, Chengdu, Sichuan (CN). OLSEN, Ole; 5309 117th St SE, Everett, Washington 98208 (US). XIA, Dong; 17401 NE 97th Way, Redmond, Washington 98052 (US). JELLYMAN, David; 26918 NE Virginia St, Duvall,

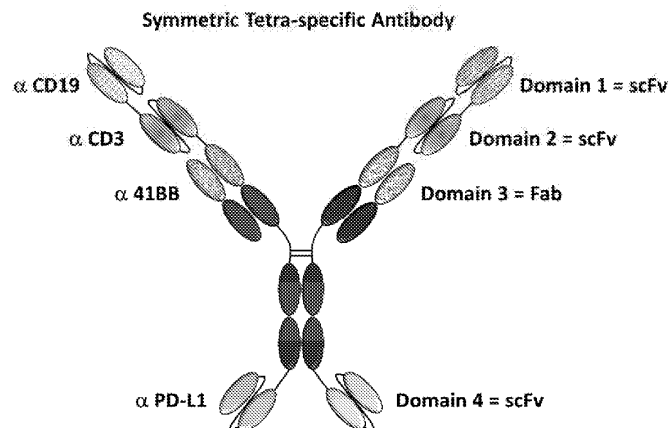
Washington 98019 (US). BYKOVA, Katrina; 12346 36th Ave NE, Seattle, Washington 98125 (US). ROUSSEAU, Anne-Marie; 11532 Dayton Ave. N., Seattle, Washington (US). BRADY, Bill; 618 219th Place SW, Bothell, Washington 98021 (US). RENSHAW, Blair; 16210 SE 166th Ct, Renton, Washington 98058 (US). KOVACEVICH, Brian; 13916 233rd St. SE, Snohomish, Washington 98296 (US). LIANG, Yu; 18411 NE 26 th Way, Redmond, Washington 98052 (US). GAO, Zeren; 9816 229th LN NE, Redmond, Washington 98053 (US).

(74) Agent: HAN, Zhihua; EpiMED LLC, 10398 NE 17th St. Unit 306, Bellevue, Washington 98004 (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, 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.

(54) Title: MULTI-SPECIFIC ANTIBODIES AND METHODS OF MAKING AND USING THEREOF

FIGURE 1. General format of example tetra-specific antibody



(57) Abstract: The disclosure provides a tetra-specific antibody monomer having a N-terminal and a C-terminal, comprising in tandem from the N-terminal to the C-terminal, a first scFv domain at the N-terminal, a second scFv domain, a Fab domain, a Fc domain, and a third scFv at the C-terminal, wherein the first scFv domain, the second scFv domain, the Fab domain, and the third scFv domain each has a binding specificity against a different antigen. In one embodiment, the antigen is a tumor antigen, an immune signaling antigen, or a combination thereof. In one embodiment, the antigen includes CD19, CD3, CD137, 4-1BB, and PD-L1. Multi-specific antibodies comprising the disclosed tetra-specific antibodies are also provided.

[Continued on next page]

(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))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(88) Date of publication of the international search report:

07 February 2019 (07.02.2019)