

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
26 August 2021 (26.08.2021)



(10) International Publication Number
WO 2021/168194 A1

(51) International Patent Classification:

A61K 39/00 (2006.01) A61K 45/06 (2006.01)
A61K 39/395 (2006.01) A61K 47/48 (2006.01)

(21) International Application Number:

PCT/US2021/018705

(22) International Filing Date:

19 February 2021 (19.02.2021)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/978,758 19 February 2020 (19.02.2020) US

(71) Applicant: **DENALI THERAPEUTICS INC.** [US/US];
161 Oyster Point Blvd., South San Francisco, California
94080 (US).

(72) Inventors: **KANNAN, Gunasekaran**; c/o Denali Therapeutics Inc., 161 Oyster Point Blvd., South San Francisco, California 94080 (US). **KIM, Do Jin**; c/o Denali Therapeutics Inc., 161 Oyster Point Blvd., South San Francisco, California 94080 (US). **KWAN, Wanda**; c/o Denali Therapeutics Inc., 161 Oyster Point Blvd., South San Francisco, California 94080 (US). **TONG, Raymond Ka Hang**; c/o De-

nali Therapeutics Inc., 161 Oyster Point Blvd., South San Francisco, California 94080 (US).

(74) Agent: **YAO, Zhengzheng** et al.; Kilpatrick Townsend & Stockton LLP, Mailstop: IP Docketing - 22, 1100 Peachtree Street, Suite 2800, Atlanta, Georgia 30309 (US).

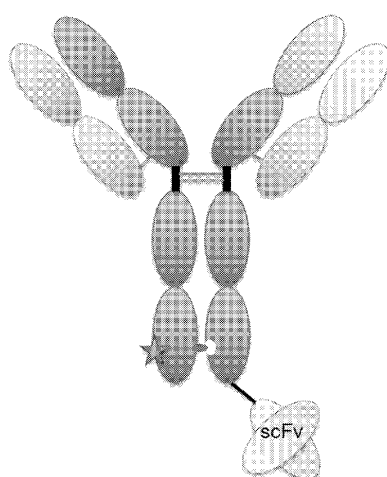
(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, 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, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, 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,

(54) Title: ENGINEERED ANTI-HER2 BISPECIFIC PROTEINS

FIG. 2A

Monovalent scFv on C-terminus of HC



(57) Abstract: In one aspect, bispecific proteins having the ability to specifically bind to both subdomain II of human HER2 and subdomain IV of human HER2 are provided. In another aspect, methods of treating a cancer or treating brain metastasis of a cancer using a bispecific protein that specifically binds to subdomain II and subdomain IV of human HER2 are provided.

WO 2021/168194 A1

[Continued on next page]

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))*