

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
01 October 2020 (01.10.2020)

WIPO | PCT

(10) International Publication Number
WO 2020/198009 A8

(51) International Patent Classification:

C07K 16/28 (2006.01) A61P 35/00 (2006.01)
C07K 16/30 (2006.01) C07K 16/40 (2006.01)

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.

(21) International Application Number:

PCT/US2020/023857

(22) International Filing Date:

20 March 2020 (20.03.2020)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/822,124 22 March 2019 (22.03.2019) US

(71) Applicant: **REGENERON PHARMACEUTICALS, INC.** [US/US]; 777 Old Saw Mill River Road, Tarrytown, NY 10591 (US).

(72) Inventors: **SKOKOS, Dimitris**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, NY 10591 (US). **MURPHY, Andrew, J.**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, NY 10591 (US). **YANCOPOULOS, George, D.**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, NY 10591 (US). **HABER, Laurie**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, NY 10591 (US). **LIN, Chia-Yang**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, NY 10591 (US).

(74) Agent: **CLARKE, Marcie, B.** et al.; McCarter & English, LLP, 265 Franklin Street, Boston, MA 02110 (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,

(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).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

Published:

- with international search report (Art. 21(3))
- with sequence listing part of description (Rule 5.2(a))

(48) Date of publication of this corrected version:

19 November 2020 (19.11.2020)

(15) Information about Correction:

see Notice of 19 November 2020 (19.11.2020)

(54) Title: EGFR x CD28 MULTISPECIFIC ANTIBODIES

(57) Abstract: The present invention provides multispecific antibodies that bind to EGFR and CD28 (EGFRxCD28) as well as anti-EGFR antibodies. Such antibodies may be combined with a further therapeutic agent such as an anti-PD1 antibody. Methods for treating cancers (e.g., EGFR-expressing cancer) by administering the antibodies (e.g., and combinations thereof with anti-PD1) are also provided. The EGFRxCD28 antibodies of the present invention embody a tumor-targeted immunotherapeutic modality combined with PD-1 inhibition. These bispecific antibodies bind a tumor-specific antigen (TSA) (EGFR) with one arm and the co-stimulatory receptor, CD28, on T-cells with the other arm. Combination therapy with PD-1 inhibitors specifically potentiated intra-tumoral T cell activation, promoting an effector memory-like T cell phenotype without systemic cytokine secretion in a variety of syngeneic and human tumor xenograft models. Combining this class of CD28-co-stimulatory bispecific antibodies with the clinically validated anti-PD-1 treatment provides a well-tolerated antibody therapy with markedly enhanced anti-tumor efficacy.