



- (51) **International Patent Classification:**
C07K 14/495 (2006.01) *A61K 38/00* (2006.01)
- (21) **International Application Number:**
PCT/US2022/077879
- (22) **International Filing Date:**
11 October 2022 (11.10.2022)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
63/254,249 11 October 2021 (11.10.2021) US
- (71) **Applicant: UNIVERSITY OF PITTSBURGH - OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION** [US/US]; 1st Floor Gardner Steel Conference Center, 130 Thackeray Avenue, Pittsburgh, Pennsylvania 15260 (US).
- (72) **Inventors: HINCK, Andrew P.**; 123 Yorkshire Drive, Pittsburgh, Pennsylvania 15208 (US). **DEPEAUX, Kristin**; 375 Lehigh Ave., Apt. 2, Pittsburgh, Pennsylvania 15232 (US). **DELGOFFE, Greg M.**; 2747 Beechwood Blvd., Unit 14, Pittsburgh, Pennsylvania 15217 (US).
- (74) **Agent: CONNOLLY, Jodi L.** et al.; Klarquist, One World Trade Center, Suite 1600, 121 SW Salmon Street, Portland, Oregon 97204 (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, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, 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, ME, 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).

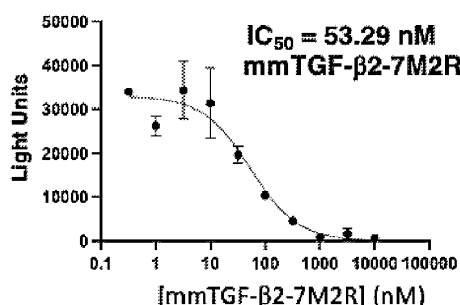
Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

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))
- with sequence listing part of description (Rule 5.2(a))

- (54) **Title:** ENGINEERED TGF- β 2 MONOMERS AND METHODS OF USE

FIG. 6B

(57) **Abstract:** Recombinant TGF- β 2 monomers engineered to prevent dimerization and block TGF- β signaling are described. The engineered monomers lack the ability to bind and recruit TGF- β type I receptor (TbRI), but retain the capacity to bind the high affinity TGF- β type II receptor (TbRII). The TGF- β 2 monomers also include additional modifications that increase their affinity for TbRII, reduce their aggregation and/or improve their folding. Nucleic acid molecules and vectors encoding the recombinant TGF- β 2 monomers are also described. Isolated cells, such as T cells, can be re-programmed with a TGF- β 2 monomer-encoding nucleic acid or vector to secrete the monomer. Use of the recombinant TGF- β 2 monomers and/or cells producing the recombinant TGF- β 2 monomers, to inhibit TGF- β signaling, such as to treat disorders associated with aberrant TGF- β signaling, are also described.