



(43) International Publication Date
23 December 2015 (23.12.2015)

WIPO | PCT

(10) International Publication Number
WO 2015/196051 A1

- (51) **International Patent Classification:**
C07K 16/28 (2006.01) *C07K 14/705* (2006.01)
A01K 67/027 (2006.01) *C12N 15/85* (2006.01)
- (21) **International Application Number:**
PCT/US2015/036649
- (22) **International Filing Date:**
19 June 2015 (19.06.2015)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
62/014,181 19 June 2014 (19.06.2014) US
62/086,518 2 December 2014 (02.12.2014) US
62/138,221 25 March 2015 (25.03.2015) US
- (71) **Applicant:** REGENERON PHARMACEUTICALS, INC. [US/US]; 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US).
- (72) **Inventors:** BUROVA, Elena; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). MUJICA, Alexander O.; c/o Regeneron Pharmaceuticals, Inc, 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). LAI, Ka-Man Venus; c/o Regeneron Pharmaceuticals, Inc, 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). MURPHY, Andrew J.; c/o Regeneron Pharmaceuticals, Inc, 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US).
- (74) **Agent:** GROLZ, Edward W.; Scully, Scott, Murphy & Presser, 400 Garden City Plaza, Suite 300, Garden City, New York 11530 (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, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, 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))

(54) **Title:** NON-HUMAN ANIMALS HAVING A HUMANIZED PROGRAMMED CELL DEATH 1 GENE

(57) **Abstract:** Non-human animals, and methods and compositions for making and using the same, are provided, wherein said non-human animals comprise a humanization of a Programmed cell death 1 (Pcd1) gene. Said non-human animals may be described, in some embodiments, as having a genetic modification to an endogenous Pcd1 gene so that said non-human animals express a PD-1 polypeptide that includes a human portion and an endogenous portion (e.g., a non-human portion).



WO 2015/196051 A1