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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
19 September 2013 (19.09.2013)

WIPO | PCT

(10) International Publication Number
WO 2013/138680 A4

(51) International Patent Classification:
A01K 67/027 (2006.01) *C12N 15/85* (2006.01)
C07K 16/00 (2006.01)

(21) International Application Number:
PCT/US2013/031823

(22) International Filing Date:
15 March 2013 (15.03.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/611,950 16 March 2012 (16.03.2012) US
61/736,930 13 December 2012 (13.12.2012) US

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

(72) Inventors: **MCWHIRTER, John**; 2035 Crescent Drive, Tarrytown, NY 10591 (US). **MACDONALD, Lynn**; 16 Gedney Way, White Plains, NY 10605 (US). **MURPHY, Andrew, J.**; 10 Newton Court, Croton-on-Hudson, NY 10520 (US).

(74) Agent: **KOWALCHYK, Katherine, M.**; Merchant & Gould P.C., P.O. Box 2903, Minneapolis, Minnesota 55402-0903 (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, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, 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, 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, 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, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*
— *with amended claims (Art. 19(1))*
— *with sequence listing part of description (Rule 5.2(a))*

Date of publication of the amended claims: 7 November 2013

(54) Title: HISTIDINE ENGINEERED LIGHT CHAIN ANTIBODIES AND GENETICALLY MODIFIED NON-HUMAN ANIMALS FOR GENERATING THE SAME

(57) Abstract: A genetically modified non-human animal is provided, wherein the non-human animal expresses an antibody repertoire capable of pH dependent binding to antigens upon immunization. A genetically modified non-human animal is provided that expresses a single light chain variable domain derived from a single rearranged light chain variable region gene in the germline of the non-human animal, wherein the single rearranged light chain variable region gene comprises a substitution of at least one non-histidine encoding codon with a histidine encoding codon. Methods of making non-human animals that express antibodies comprising a histidine-containing universal light chain are provided.

WO 2013/138680 A4