



(51) International Patent Classification:

C12N 15/85 (2006.01) *C12N 9/64* (2006.01)
A01K 67/027 (2006.01) *C07K 16/46* (2006.01)

(21) International Application Number:

PCT/US2012/026416

(22) International Filing Date:

24 February 2012 (24.02.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/446,895	25 February 2011 (25.02.2011)	US
61/497,650	16 June 2011 (16.06.2011)	US
61/595,200	6 February 2012 (06.02.2012)	US

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

(72) Inventors; and

(75) Inventors/Applicants (for US only): **MACDONALD, Lynn** [US/US]; 16 Gedney Way, White Plains, NY 10605 (US). **STEVENS, Sean** [US/US]; 355 Berry Street, #413, San Francisco, CA 94158 (US). **MURPHY, Andrew, J.** [US/US]; 10 Newton Court, Croton-on-Hudson, NY 10520 (US).

(74) Agent: **POBURSKY, Kevin, J.**; Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, NY 10591 (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, 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, 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, MD, 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 sequence listing part of description (Rule 5.2(a))

(54) Title: ADAM6 MICE

(57) Abstract: Mice are provided that comprise a reduction or deletion of ADAM6 activity from an endogenous ADAM6 locus, or that lack an endogenous locus encoding a mouse ADAM6 protein, wherein the mice comprise a sequence encoding an ADAM6 or ortholog or homolog or fragment thereof that is functional in a male mouse. In one embodiment, the sequence is an ectopic ADAM6 sequence or a sequence that confers upon a male mouse the ability to generate offspring by mating. Mice and cells with genetically modified immunoglobulin heavy chain loci that comprise an ectopic nucleotide sequence encoding a mouse ADAM6 or functional fragment or homolog or ortholog thereof are also provided.

