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62/689,628 25 June 2018 (25.06.2018) US(71) Applicant: **REGENERON PHARMACEUTICALS, INC.** [US/US]; 777 Old Saw Mill River Road, Tarrytown, NY 10591-6706 (US).(72) Inventors: **VORONINA, Vera**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, NY 10591 (US). **MOMONT, Corey**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, NY 10591 (US). **MCWHIRTER, John**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, NY 10591 (US). **TU, Naxin**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, NY 10591 (US). **MACDONALD, Lynn**; 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).(74) Agent: **JONES, Brendan T.** et al.; Foley Hoag LLP, 155 Seaport Boulevard, Boston, MA 02210-2600 (US).(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM,

(54) Title: HUMANIZED RODENTS FOR TESTING THERAPEUTIC AGENTS

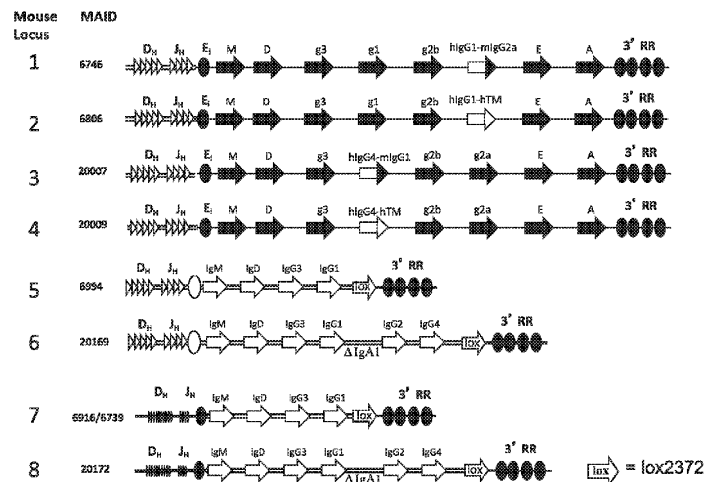


Figure 1A

(57) **Abstract:** Provided herein are methods and compositions related to the *in vivo* testing of therapeutic agents comprising a human Fc in genetically modified rodents (*e.g.*, the testing of the pharmacokinetic and/or pharmacodynamic properties of such a therapeutic agent in genetically modified rodents). In some embodiments the genetically modified rodents express antibodies comprising a human Fc (*e.g.*, a human IgG1 Fc, a human IgG4 Fc). In some embodiments, the rodents express fully human antibodies (*i.e.*, antibodies having human heavy chains and human light (γ or κ) chains). In certain embodiments the genetically modified rodents comprise one or more Fc receptors with a human extracellular domain (*e.g.*, a Neonatal Fc Receptor (FcRn), a β -2-microglobulin polypeptide (β 2M), a Fc ϵ receptor 1 α (Fc ϵ R1 α), a Fc γ receptor 1 alpha (Fc γ R1 α), a Fc gamma receptor 2a (Fc γ R2a), a Fc gamma receptor 2b (Fc γ R2b), a Fc gamma receptor 3a (Fc γ R3a), a Fc gamma receptor 3b (Fc γ R3b), a Fc gamma receptor 2c (Fc γ R2c)). The transmembrane and

[Continued on next page]

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