

Claims:

1. An isolated FcRn-antagonist which consists of a variant IgG1 Fc region, or FcRn-binding fragment thereof, wherein the Fc domains of the Fc region or FcRn-binding fragment thereof comprise the amino acids Y, T, E, K, F, and Y at EU positions 252, 254, 256, 433, 434, and 436 respectively, and wherein the Fc region binds to FcRn with increased affinity and reduced pH dependence relative to a wild-type IgG1 Fc region.
2. The isolated FcRn-antagonist of claim 1 wherein the Fc region has an increased affinity for an Fc gamma receptor relative to the affinity of a wild-type IgG1 Fc region for the Fc gamma receptor.
3. An isolated FcRn-antagonist which consists of a variant IgG1 Fc region, wherein the amino acid sequence of the Fc domains of the variant Fc region consists of the amino acid sequence set forth in SEQ ID NO:1, 2, or 3.
4. The isolated FcRn-antagonist of any one of claims 1-3, wherein the FcRn-antagonist does not comprise a free cysteine residue.
5. The isolated FcRn-antagonist of any one claims 1-4, wherein the variant Fc region has increased affinity for CD16a.
6. The isolated FcRn-antagonist of any one of claims 1-5, wherein the Fc domains of the variant Fc region do not comprise an N-linked glycan at EU position 297, or wherein the Fc domains of the variant Fc region comprise an Fc domain having an afucosylated N-linked glycan at EU position 297, or wherein the Fc domains of the variant Fc region comprise an N-linked glycan having a bisecting GlcNac at EU position 297 of the Fc domains.
7. The isolated FcRn-antagonist of any one of the preceding claims, wherein the variant Fc region is linked to a half-life extender, or linked to a binding molecule that specifically binds to a half-life extender present in a subject.
8. The isolated FcRn-antagonist of claim 7, wherein the half-life extender is polyethylene glycol or human serum albumin.

9. The isolated FcRn-antagonist of claim 7, wherein the half-life extender is a binding molecule that specifically binds to human serum albumin.
10. An FcRn-antagonist composition comprising a plurality of FcRn-antagonist molecules of claim 6, wherein at least 50% (optionally, at least 60, 70, 80, 90, 95, or 99%) of the molecules comprise a variant Fc region, or FcRn-binding fragment thereof, comprising an afucosylated N-linked glycan, or wherein at least 50% (optionally, at least 60, 70, 80, 90, 95, or 99%) of the molecules comprise a variant Fc region or FcRn-binding fragment thereof, comprising an N-linked glycan having a bisecting GlcNac.
11. A pharmaceutical composition comprising the FcRn-antagonist or FcRn-antagonist composition of any one of the preceding claims and a pharmaceutically acceptable carrier or excipient.
12. An FcRn-antagonist or FcRn-antagonist composition according to any one of claims 1-10 for use in reducing the serum levels of an Fc-containing agent in subject that has been administered the Fc-containing agent, wherein said FcRn-antagonist or FcRn-antagonist composition is to be simultaneously or sequentially administered to said subject.
13. An FcRn-antagonist or FcRn-antagonist composition for use according to claim 12, wherein the Fc-containing agent is an antibody or immunoadhesin, or wherein the Fc-containing agent is a therapeutic or diagnostic agent, or wherein the Fc-containing agent is an imaging agent, or wherein the Fc-containing agent is an antibody drug conjugate.
14. Use of an FcRn-antagonist or FcRn antagonist composition according to any one of claims 1-10 in the manufacture of a medicament for the treatment of an antibody-mediated disorder in a subject, wherein the antibody-mediated disorder is an autoimmune disease, optionally wherein the autoimmune disease is selected from the group consisting of allogenic islet graft rejection, alopecia areata, ankylosing spondylitis, antiphospholipid syndrome, autoimmune Addison's disease, Alzheimer's disease, antineutrophil cytoplasmic autoantibodies (ANCA), autoimmune diseases of the adrenal gland, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune myocarditis, autoimmune neutropenia, autoimmune oophoritis and orchitis, autoimmune thrombocytopenia, autoimmune urticaria, Behcet's disease, bullous pemphigoid, cardiomyopathy, Castleman's syndrome, celiac spruce-dermatitis, chronic

fatigue immune disfunction syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), Churg-Strauss syndrome, cicatricial pemphigoid, CREST syndrome, cold agglutinin disease, Crohn's disease, dermatomyositis, dilated cardiomyopathy, discoid lupus, epidermolysis bullosa acquisita, essential mixed cryoglobulinemia, factor VIII deficiency, fibromyalgia-fibromyositis, glomerulonephritis, Grave's disease, Guillain-Barre, Goodpasture's syndrome, graft-versus-host disease (GVHD), Hashimoto's thyroiditis, hemophilia A, idiopathic membranous neuropathy, idiopathic pulmonary fibrosis, idiopathic thrombocytopenia purpura (ITP), IgA neuropathy, IgM polyneuropathies, immune mediated thrombocytopenia, juvenile arthritis, Kawasaki's disease, lichen plantus, lichen sclerosus, lupus erthematosus, Meniere's disease, mixed connective tissue disease, mucous membrane pemphigoid, multiple sclerosis, type 1 diabetes mellitus, Multifocal motor neuropathy (MMN), myasthenia gravis, paraneoplastic bullous pemphigoid, pemphigoid gestationis, pemphigus vulgaris, pemphigus foliaceus, pernicious anemia, polyarteritis nodosa, polychondritis, polyglandular syndromes, polymyalgia rheumatica, polymyositis and dermatomyositis, primary agammaglobulinemia, primary biliary cirrhosis, psoriasis, psoriatic arthritis, relapsing polychondritis, Reynauld's phenomenon, Reiter's syndrome, rheumatoid arthritis, sarcoidosis, scleroderma, Sjorgen's syndrome, solid organ transplant rejection, stiff-man syndrome, systemic lupus erythematosus, takayasu arteritis, toxic epidermal necrolysis (TEN), Stevens Johnson syndrome (SJS), temporal arteritis/giant cell arteritis, thrombotic thrombocytopenia purpura, ulcerative colitis, uveitis, dermatitis herpetiformis vasculitis, anti-neutrophil cytoplasmic antibody-associated vasculitides, vitiligo, and Wegner's granulomatosis.

15. The use according to claim 14, wherein the antibody-mediated disorder is treatable using intravenous immunoglobulin (IVIG), plasmapheresis and/or immunoadsorption.

16. The use according to claim 14, wherein the autoimmune disease is an autoimmune channelopathy, optionally wherein the channelopathy is selected from the group consisting of autoimmune limbic encephalitis, epilepsy, neuromyelitis optica, Lambert-Eaton myasthenic syndrome, myasthenia gravis, anti-N-Methyl-D-aspartate (NMDA) receptor encephalitis, anti- α -Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor encephalitis, Morvan syndrome, neuromyotonia, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS), and Glycine receptor antibody-associated disorder.

17. The use according to claim 14, wherein the antibody-mediated disorder is hyperglobulinemia.
18. The use according to claim 14, wherein the FcRn antagonist is to be administered to the subject simultaneously or sequentially with an additional therapeutic agent, optionally an anti-inflammatory agent, or a leucocyte depleting agent.
19. The use according to claim 18, wherein the leucocyte depleting agent is a B-cell depleting agent, optionally an antibody, optionally wherein the antibody specifically binds to CD10, CD19, CD20, CD21, CD22, CD23, CD24, CD37, CD53, CD70, CD72, CD74, CD75, CD77, CD79a, CD79b, CD80, CD81, CD82, CD83, CD84, CD85, or CD86.
20. The use according to claim 18, wherein the additional therapeutic agent is rituximab, daclizumab, basiliximab, muronomab-CD3, infliximab, adalimumab, omalizumab, efalizumab, natalizumab, tocilizumab, eculizumab, golimumab, canakinumab, ustekinumab, belimumab, or a combination thereof.