WHAT IS CLAIMED IS:

1. A method of enhancing the efficacy of gene therapy treatment in a subject, comprising:
(a) administering to a subject an agent that reduces the interaction of immunoglobulin G (IgG) with the neonatal Fc receptor (FcRn); and
(b) administering to said subject a recombinant viral vector comprising a therapeutic heterologous polynucleotide.
2. The method of claim 1, wherein
(a) said subject is in need of treatment for a disease caused by a loss of function or activity of a protein, and said heterologous polynucleotide encodes a polypeptide or peptide that provides or supplements a function or activity of said protein, or
(b) said subject is in need of treatment for a disease caused by a gain of function, activity or expression of a protein, and said heterologous polynucleotide is transcribed into a nucleic acid that inhibits, decreases or reduces expression of said gain of function, activity or expression of said protein.
3. The method of claim 1 or 2, wherein FcRn-mediated IgG recycling is reduced in said subject.
4. The method of any of claims 1 – 3, wherein IgG clearance is enhanced in said subject.
5. The method of any of claims 1 – 4, wherein said agent that reduces interaction of IgG with FcRn is selected from the group consisting of an anti-FcRn antibody, an FcRn binding affibody, an antibody that enhances IgG degradation (ABDEG), an FcRn binding peptide (FcBP), and an FcRn binding small molecule.
6. The method of any of claims 1 – 5, wherein step (a) is performed before step (b).
7. The method of any of claims 1 – 5, wherein step (b) is performed before step (a).
8. The method of any of claims 1 – 5, wherein step (a) and step (b) are performed at about the same time.
9. The method of any of claims 1 – 5, wherein step (a) is performed two or more times before or after step (b).
10. The method of any of claims 1 – 9, wherein step (b) is performed within about 90 days before or after step (a).
11. The method of any of claims 1 – 9, wherein step (b) is performed within about 60 days before or after step (a).

12. The method of any of claims 1 – 9, wherein step (b) is performed within about 45 days before or after step (a).
13. The method of any of claims 1 – 9, wherein step (b) is performed within about 30 days before or after step (a).
14. The method of any of claims 1 – 9, wherein step (b) is performed within about 21 days before or after step (a).
15. The method of any of claims 1 – 9, wherein step (b) is performed within about 14 days before or after step (a).
16. The method of any of claims 1 – 9, wherein step (b) is performed within about 7 days before or after step (a).
17. The method of any of claims 1 – 9, wherein step (b) is performed within about 72 hours before or after step (a).
18. The method of any of claims 1 – 9, wherein step (b) is performed within about 48 hours before or after step (a).
19. The method of any of claims 1 – 9, wherein step (b) is performed within about 24 hours before or after step (a).
20. The method of any of claims 1 – 9, wherein step (b) is performed within about 12 hours before or after step (a).
21. The method of any of claims 1 – 9, wherein step (b) is performed within about 6 hours before or after step (a).
22. The method of any of claims 1 - 21, further comprising administering to said subject an amount of a protease or glycosidase effective to degrade or digest and/or inhibit or reduce effector function of antibodies that bind to said recombinant viral vector and/or said polypeptide or peptide encoded by said heterologous polynucleotide and/or said heterologous polynucleotide.
23. The method of claim 22, wherein said protease or glycosidase is administered before, after or at about the same time as step (a).
24. The method of claim 22, wherein said protease or glycosidase is administered before, after or at about the same time as step (b).
25. The method of claim 22, wherein said protease or glycosidase is administered two or more times before, after or at about the same time as step (a).
26. The method of claim 22, wherein said protease or glycosidase is administered two or more times before, after or at about the same time as step (b).

27. The method of any of claims 22 – 26, wherein said protease or glycosidase is administered within about 90 days before or after step (a) or step (b).
28. The method of any of claims 22 – 26, wherein said protease or glycosidase is administered within about 60 days before or after step (a) or step (b).
29. The method of any of claims 22 – 26, wherein said protease or glycosidase is administered within about 45 days before or after step (a) or step (b).
30. The method of any of claims 22 – 26, wherein said protease or glycosidase is administered within about 30 days before or after step (a) or step (b).
31. The method of any of claims 22 – 26, wherein said protease or glycosidase is administered within about 21 days before or after step (a) or step (b).
32. The method of any of claims 22 – 26 wherein said protease or glycosidase is administered within about 14 days before or after step (a) or step (b).
33. The method of any of claims 22 – 26, wherein said protease or glycosidase is administered within about 7 days before or after step (a) or step (b).
34. The method of any of claims 22 – 26, wherein said protease or glycosidase is administered within about 72 hours before or after step (a) or step (b).
35. The method of any of claims 22 – 26, wherein said protease or glycosidase is administered within about 48 hours before or after step (a) or step (b).
36. The method of any of claims 22 – 26, wherein said protease or glycosidase is administered within about 24 hours before or after step (a) or step (b).
37. The method of any of claims 22 – 26, wherein said protease or glycosidase is administered within about 12 hours before or after step (a) or step (b).
38. The method of any of claims 22 – 26, wherein said protease or glycosidase is administered within about 6 hours before or after step (a) or step (b).
39. The method of any of claims 22 – 38, wherein said protease comprises a cysteine protease or a thiol protease.
40. The method of any of claims 22 – 38, wherein said protease comprises a protease from *Streptococcus pyogenes*, *Streptococcus equi* or *Mycoplasma canis*.
41. The method of any of claims 22 – 38, wherein said protease comprises IdeS or a modified variant thereof set forth in any of SEQ ID NOs:3 – 18, 23 or 48.
42. The method of any of claims 22 – 38, wherein said glycosidase comprises an endoglycosidase.

43. The method of claim 42, wherein said endoglycosidase comprises a sequence set forth in any of SEQ ID NOs: 44 – 47.
44. The method of any of claims 22 – 43, wherein said protease or glycosidase degrades or digests and/or inhibits or reduces effector function of human antibodies.
45. The method of any of claims 1 – 44, wherein said viral vector comprises a lentiviral vector, an adenoviral vector or an adeno-associated virus (AAV) vector.
46. The method of claim 45, wherein said lentiviral vector comprises envelope proteins to which said antibodies or IgG bind.
47. The method of claim 45, wherein said AAV vector comprises capsid proteins to which the antibodies or IgG bind.
48. The method of claim 45, wherein said AAV vector comprises VP1, VP2 and/or VP3 capsid proteins to which the antibodies or IgG bind.
49. The method of any of claims 45 – 48, wherein said AAV vector comprises VP1, VP2 and/or VP3 capsid protein having 60% or more sequence identity to VP1, VP2 and/or VP3 capsid protein selected from the group consisting of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV3B, AAV-2i8, Rh10, Rh74, SEQ ID NO:1 and SEQ ID NO:2 VP1, VP2 and/or VP3 capsid proteins.
50. The method of any of claims 45 – 48, wherein said AAV vector comprises VP1, VP2 and/or VP3 capsid protein having 100% sequence identity to VP1, VP2 and/or VP3 capsid protein selected from the group consisting of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV3B, AAV-2i8, Rh10, Rh74, SEQ ID NO:1 and SEQ ID NO:2 VP1, VP2 and/or VP3 capsid proteins.
51. The method of any of claims 1 – 50, wherein said subject has antibodies or IgG that bind to said viral vector.
52. The method of any of claims 1 – 50, wherein antibodies or IgG that bind to said viral vector are absent from said subject.
53. The method of any of claims 1 – 52, wherein said subject has antibodies or IgG that bind to said polypeptide or peptide encoded by said heterologous polynucleotide.
54. The method of any of claims 22 – 53, wherein said antibodies comprise IgG, IgM, IgA, IgD and/or IgE.
55. The method of any of claims 1 – 54, further comprising determining the presence of, quantifying the amount of or an effector function of viral vector binding antibodies or

IgG present in said subject before performing step (a), after performing step (a) but before performing step (b) and/or after performing steps (a) and (b).

56. The method of any of claims 1 – 54, further comprising analyzing a biological sample from said subject for the presence, amount or an effector function of viral vector binding antibodies or IgG present in said sample before performing step (a), after performing step (a) but before performing step (b) and/or after performing steps (a) and (b).

57. The method of claim 55 or 56, wherein said determining and/or analyzing step is carried out before and/or after administration of said protease or glycosidase.

58. The method of claim 56 or 57, wherein said biological sample from said subject is a blood product.

59. The method of any of claims 1 – 58, wherein said method leads to a reduction of 20-50%, 50-75%, 75-90%, 90-95% or 95% or more of said viral vector binding antibodies or IgG.

60. The method of any of claims 56 – 58, wherein said viral vector binding antibodies or IgG present in said biological sample or blood product from said subject is less than about 1:100,000 where 1 part of said biological sample or blood product diluted in 100,000 parts of buffer results in 50% viral vector neutralization.

61. The method of any of claims 56 – 58, wherein said viral vector binding antibodies or IgG present in said biological sample or blood product from said subject is less than about 1:50,000, where 1 part of said biological sample or blood product diluted in 50,000 parts of buffer results in 50% viral vector neutralization.

62. The method of any of claims 56 – 58, wherein said viral vector binding antibodies or IgG present in said biological sample or blood product from said subject is less than about 1:10,000, where 1 part of said biological sample or blood product diluted in 10,000 parts of buffer results in 50% viral vector neutralization.

63. The method of any of claims 56 – 58, wherein said viral vector binding antibodies or IgG present in said biological sample or blood product from said subject is less than about 1:1,000, where 1 part of said biological sample or blood product diluted in 1,000 parts of buffer results in 50% viral vector neutralization.

64. The method of any of claims 56 – 58, wherein said viral vector binding antibodies or IgG present in said biological sample or blood product from said subject is less than

about 1:100, where 1 part of said biological sample or blood product diluted in 100 parts of buffer results in 50% viral vector neutralization.

65. The method of any of claims 56 – 58, wherein said viral vector binding antibodies or IgG present in said biological sample or blood product from said subject is less than about 1:10, where 1 part of said biological sample or blood product diluted in 10 parts of buffer results in 50% viral vector neutralization.

66. The method of any of claims 56 – 58, wherein said viral vector binding antibodies or IgG present in said biological sample or blood product is less than about 1:5, where 1 part of said biological sample or blood product diluted in 5 parts of buffer results in 50% viral vector neutralization.

67. The method of any of claims 56 – 58, wherein the ratio of viral vector binding antibodies or IgG present in said biological sample or blood product is less than about 1:4, where 1 part of said biological sample or blood product diluted in 4 parts of buffer results in 50% viral vector neutralization.

68. The method of any of claims 56 – 58, wherein the ratio of viral vector binding antibodies or IgG present in said biological sample or blood product is less than about 1:3, where 1 part of said biological sample or blood product diluted in 3 parts of buffer results in 50% viral vector neutralization.

69. The method of any of claims 1 – 58, wherein the ratio of viral vector binding antibodies or IgG present in said subject, biological sample or blood product is less than about 1:2, where 1 part of said biological sample or blood product diluted in 2 parts of buffer results in 50% viral vector neutralization.

70. The method of any of claims 1 – 58, wherein the ratio of viral vector binding antibodies or IgG present in said subject, biological sample or blood product is less than about 1:1, where 1 part of said biological sample or blood product diluted in 1 part of buffer results in 50% viral vector neutralization.

71. The method of any of claims 1 – 70, further comprising determining the presence of or quantifying the amount of antibodies or IgG that bind to a polypeptide or peptide encoded by said heterologous polynucleotide, after performing step (a) but before performing step (b) and/or after performing steps (a) and (b).

72. The method of any of claims 1 – 70, further comprising determining the presence of or quantifying the amount of antibodies or IgG that bind to said heterologous

polynucleotide or nucleic acid after performing step (a) but before performing step (b) and/or after performing steps (a) and (b).

73. The method of any of claims 1 – 72, wherein said subject has a lung disease (*e.g.*, cystic fibrosis), a bleeding disorder (*e.g.*, hemophilia A or hemophilia B with or without inhibitors), thalassemia, a blood disorder (*e.g.*, anemia), Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis (ALS), epilepsy, a lysosomal storage disease, (*e.g.*, aspartylglucosaminuria, Batten disease, late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), cystinosis, Fabry disease, Gaucher disease types I, II, and III, glycogen storage disease II (Pompe disease), GM2-gangliosidosis type I (Tay Sachs disease), GM2-gangliosidosis type II (Sandhoff disease), mucolipidosis types I (sialidosis type I and II), II (I-cell disease), III (pseudo-Hurler disease) and IV, mucopolysaccharide storage diseases (Hurler disease and variants, Hunter, Sanfilippo Types A,B,C,D, Morquio Types A and B, Maroteaux-Lamy and Sly diseases), Niemann-Pick disease types A/B, C1 and C2, and Schindler disease types I and II), hereditary angioedema (HAE), a copper or iron accumulation disorder (*e.g.*, Wilson's or Menkes disease), lysosomal acid lipase deficiency, a neurological or neurodegenerative disorder, cancer, type 1 or type 2 diabetes, adenosine deaminase deficiency, a metabolic defect (*e.g.*, glycogen storage diseases), a disease of solid organs (*e.g.*, brain, liver, kidney, heart), or an infectious viral (*e.g.*, hepatitis B and C, HIV, etc.), bacterial or fungal disease.

74. The method of any of claims 1 – 72, wherein said subject has a blood clotting disorder.

75. The method of any of claims 1 – 72, wherein said subject has hemophilia A, hemophilia A with inhibitory antibodies, hemophilia B, hemophilia B with inhibitory antibodies, a deficiency in any coagulation Factor: VII, VIII, IX, X, XI, V, XII, II, von Willebrand factor, or a combined FV/FVIII deficiency, thalassemia, vitamin K epoxide reductase C1 deficiency or gamma-carboxylase deficiency.

76. The method of any of claims 1 – 72, wherein said subject has anemia, bleeding associated with trauma, injury, thrombosis, thrombocytopenia, stroke, coagulopathy, disseminated intravascular coagulation (DIC); over-anticoagulation associated with heparin, low molecular weight heparin, pentasaccharide, warfarin, small molecule antithrombotics (*i.e.*, FXa inhibitors), or a platelet disorder such as, Bernard Soulier syndrome, Glanzmann thrombasthenia, or storage pool deficiency.

77. The method of any of claims 1 – 72, wherein said heterologous polynucleotide encodes a protein selected from the group consisting of insulin, glucagon, growth hormone (GH), parathyroid hormone (PTH), growth hormone releasing factor (GRF), follicle stimulating hormone (FSH), luteinizing hormone (LH), human chorionic gonadotropin (hCG), vascular endothelial growth factor (VEGF), angiopoietins, angiostatin, granulocyte colony stimulating factor (GCSF), erythropoietin (EPO), connective tissue growth factor (CTGF), basic fibroblast growth factor (bFGF), acidic fibroblast growth factor (aFGF), epidermal growth factor (EGF), transforming growth factor α (TGFα), platelet-derived growth factor (PDGF), insulin growth factors I and II (IGF-I and IGF-II), TGFβ, activins, inhibins, bone morphogenic protein (BMP), nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophins NT-3 and NT4/5, ciliary neurotrophic factor (CNTF), glial cell line derived neurotrophic factor (GDNF), neurturin, agrin, netrin-1 and netrin-2, hepatocyte growth factor (HGF), ephrins, noggin, sonic hedgehog and tyrosine hydroxylase.

78. The method of any of claims 1 – 72, wherein said heterologous polynucleotide encodes a protein selected from the group consisting of thrombopoietin (TPO), interleukins (IL1 through IL-36), monocyte chemoattractant protein, leukemia inhibitory factor, granulocyte-macrophage colony stimulating factor, Fas ligand, tumor necrosis factors α and β, interferons α, β, and γ, stem cell factor, flk-2/flt3 ligand, IgG, IgM, IgA, IgD and IgE, chimeric immunoglobulins, humanized antibodies, single chain antibodies, T cell receptors, chimeric T cell receptors, single chain T cell receptors, class I and class II MHC molecules.

79. The method of any of claims 1 – 72, wherein said heterologous polynucleotide encodes CFTR (cystic fibrosis transmembrane regulator protein), a blood coagulation (clotting) factor (Factor XIII, Factor IX, Factor VIII, Factor X, Factor VII, Factor VIIa, protein C, etc.) a gain of function blood coagulation factor, an antibody, retinal pigment epithelium-specific 65 kDa protein (RPE65), erythropoietin, LDL receptor, lipoprotein lipase, ornithine transcarbamylase, β-globin, α-globin, spectrin, α-antitrypsin, adenosine deaminase (ADA), a metal transporter (ATP7A or ATP7), sulfamidase, an enzyme involved in lysosomal storage disease (ARSA), hypoxanthine guanine phosphoribosyl transferase, β-25 glucocerebrosidase, sphingomyelinase, lysosomal hexosaminidase, branched-chain keto acid dehydrogenase, a hormone, a growth factor, insulin-like growth factor 1 or 2, platelet derived growth factor,

epidermal growth factor, nerve growth factor, neurotrophic factor -3 and -4, brain-derived neurotrophic factor, glial derived growth factor, transforming growth factor α and β, a cytokine, α-interferon, β-interferon, interferon-γ, interleukin-2, interleukin-4, interleukin 12, granulocyte-macrophage colony stimulating factor, lymphotoxin, a suicide gene product, herpes simplex virus thymidine kinase, cytosine deaminase, diphtheria toxin, cytochrome P450, deoxycytidine kinase, tumor necrosis factor, a drug resistance protein, a tumor suppressor protein (*e.g.*, p53, Rb, Wt-1, NF1, Von Hippel–Lindau (VHL), adenomatous polyposis coli (APC)), a peptide with immunomodulatory properties, a tolerogenic or immunogenic peptide or protein Tregitope or hCDR1, insulin, glucokinase, guanylate cyclase 2D (LCA-GUCY2D), Rab escort protein 1 (Choroideremia), LCA 5 (LCA-Lebercilin), ornithine ketoacid aminotransferase (Gyrate Atrophy), Retinoschisin 1 (X-linked Retinoschisis), USH1C (Usher's Syndrome 1C), X-linked retinitis pigmentosa GTPase (XLRP), MERTK (AR forms of RP: retinitis pigmentosa), DFNB1 (Connexin 26 deafness), ACHM 2, 3 and 4 (Achromatopsia), PKD-1 or PKD-2 (Polycystic kidney disease), TPP1, CLN2, a sulfatase, N-acetylglucosamine-1-phosphate transferase, cathepsin A, GM2-AP, NPC1, VPC2, a sphingolipid activator protein, one or more zinc finger nuclease for genome editing, and one or more donor sequence used as repair templates for genome editing.

80. The method of any of claims 1 – 72, wherein said heterologous polynucleotide encodes an inhibitory nucleic acid.

81. The method of claim 80, wherein said inhibitory nucleic acid is selected from the group consisting of a siRNA, an antisense molecule, miRNA, RNAi, a ribozyme and a shRNA.

82. The method of claim 80, wherein said inhibitory nucleic acid binds to a gene, a transcript of a gene, or a transcript of a gene associated with a polynucleotide repeat disease selected from the group consisting of a huntingtin (HTT) gene, a gene associated with dentatorubropallidoluysian atrophy (atrophin 1, ATN1), androgen receptor on the X chromosome in spinobulbar muscular atrophy, human Ataxin-1, -2, -3, and -7, $Ca_v2.1$ P/Q voltage-dependent calcium channel (CACNA1A), TATA-binding protein, Ataxin 8 opposite strand (ATXN8OS), Serine/threonine-protein phosphatase 2A 55 kDa regulatory subunit B beta isoform in spinocerebellar ataxia (type 1, 2, 3, 6, 7, 8, 12 17), *FMR1* (fragile X mental retardation 1) in fragile X syndrome, *FMR1* (fragile X mental retardation 1) in fragile X-associated

tremor/ataxia syndrome, *FMR1* (fragile X mental retardation 2) or AF4/FMR2 family member 2 in fragile XE mental retardation; Myotonin-protein kinase (MT-PK) in myotonic dystrophy; Frataxin in Friedreich's ataxia; a mutant of superoxide dismutase 1 (SOD1) gene in amyotrophic lateral sclerosis; a gene involved in pathogenesis of Parkinson's disease and/or Alzheimer's disease; apolipoprotein B (APOB) and proprotein convertase subtilisin/kexin type 9 (PCSK9), hypercholesterolemia; HIV Tat, human immunodeficiency virus transactivator of transcription gene, in HIV infection; HIV TAR, HIV TAR, human immunodeficiency virus transactivator response element gene, in HIV infection; C-C chemokine receptor (CCR5) in HIV infection; Rous sarcoma virus (RSV) nucleocapsid protein in RSV infection, liver-specific microRNA (miR-122) in hepatitis C virus infection; p53, acute kidney injury or delayed graft function kidney transplant or kidney injury acute renal failure; protein kinase N3 (PKN3) in advance recurrent or metastatic solid malignancies; LMP2, LMP2 also known as proteasome subunit beta-type 9 (PSMB 9), metastatic melanoma; LMP7,also known as proteasome subunit beta-type 8 (PSMB 8), metastatic melanoma; MECL1 also known as proteasome subunit beta-type 10 (PSMB 10), metastatic melanoma; vascular endothelial growth factor (VEGF) in solid tumors; kinesin spindle protein in solid tumors, apoptosis suppressor B-cell CLL/lymphoma (BCL-2) in chronic myeloid leukemia; ribonucleotide reductase M2 (RRM2) in solid tumors; Furin in solid tumors; polo-like kinase 1 (PLK1) in liver tumors, diacylglycerol acyltransferase 1 (DGAT1) in hepatitis C infection, beta-catenin in familial adenomatous polyposis; beta2 adrenergic receptor, glaucoma; RTP801/Redd1 also known as DNA damage-inducible transcript 4 protein, in diabetic macular edema (DME) or age-related macular degeneration; vascular endothelial growth factor receptor I (VEGFR1) in age-related macular degeneration or choroidal neovascularization, caspase 2 in non-arteritic ischaemic optic neuropathy; Keratin 6A N17K mutant protein in pachyonychia congenital; influenza A virus genome/gene sequences in influenza infection; severe acute respiratory syndrome (SARS) coronavirus genome/gene sequences in SARS infection; respiratory syncytial virus genome/gene sequences in respiratory syncytial virus infection; Ebola filovirus genome/gene sequence in Ebola infection; hepatitis B and C virus genome/gene sequences in hepatitis B and C infection; herpes simplex virus (HSV) genome/gene sequences in HSV infection, coxsackievirus B3 genome/gene sequences in

coxsackievirus B3 infection; silencing of a pathogenic allele of a gene (allele-specific silencing) like torsin A (TOR1A) in primary dystonia, pan-class I and HLA-allele specific in transplant; and mutant rhodopsin gene (RHO) in autosomal dominantly inherited retinitis pigmentosa (adRP).

83. The method of any of claims 1 – 82, wherein said polypeptide encoded by said heterologous polynucleotide comprises a gene editing nuclease.

84. The method of claim 83, wherein said gene editing nuclease comprises a zinc finger nuclease (ZFN) or a transcription activator-like effector nuclease (TALEN).

85. The method of claim 83, wherein said gene editing nuclease comprises a functional Type II CRISPR-Cas9.

86. The method of any of claims 1 – 85, wherein step (a) and/or step (b) are performed two or more times.

87. The method of any of claims 1 – 86, wherein said subject is a human.

88. A package having disposed therein:

(a) a recombinant viral vector comprising a heterologous polynucleotide that encodes a polypeptide or peptide;

(b) an agent that reduces interaction of IgG with FcRn;

(c) optionally, a protease or glycosidase that degrades or digests antibodies; and

(d) a label with instructions for performing a method according to any of claims 1 – 87, wherein (a), (b) and (c) are in separate or the same container.

89. A package having disposed therein:

(a) a recombinant viral vector comprising a heterologous polynucleotide that is transcribed into a nucleic acid that inhibits, decreases or reduces expression of a protein;

(b) an agent that reduces interaction of IgG with FcRn;

(c) optionally, a protease or glycosidase that degrades or digests antibodies; and

(d) a label with instructions for performing a method according to any of claims 1 – 87, wherein (a), (b) and (c) are in separate or the same container.

WHAT IS CLAIMED IS:

1. Use of (a) an agent that reduces the interaction of immunoglobulin G (IgG) with the neonatal Fc receptor (FcRn); and (b) a recombinant viral vector comprising a therapeutic heterologous polynucleotide in the manufacture of a medicament for a combinatorial therapy to enhance the efficacy of gene therapy treatment in a subject, wherein (a) the agent; and (b) the recombinant viral vector are to be administered to said subject.
2. The use of claim 1, wherein
(a) said subject is in need of treatment for a disease caused by a loss of function or activity of a protein, and said heterologous polynucleotide encodes a polypeptide or peptide that provides or supplements a function or activity of said protein, or
(b) said subject is in need of treatment for a disease caused by a gain of function, activity or expression of a protein, and said heterologous polynucleotide is transcribed into a nucleic acid that inhibits, decreases or reduces expression of said gain of function, activity or expression of said protein.
3. The use of claim 1 or 2, wherein FcRn-mediated IgG recycling is to be reduced in said subject.
4. The use of any of claims 1 – 3, wherein IgG clearance is to be enhanced in said subject.
5. The use of any of claims 1 – 4, wherein said agent that reduces interaction of IgG with FcRn is selected from the group consisting of an anti-FcRn antibody, an FcRn binding affibody, an antibody that enhances IgG degradation (ABDEG), an FcRn binding peptide (FcBP), and an FcRn binding small molecule.
6. The use of any of claims 1 – 5, wherein (a) the agent is to be administered before (b) the recombinant viral vector.
7. The use of any of claims 1 – 5, wherein (b) the recombinant viral vector is to be administered before (a) the agent.
8. The use of any of claims 1 – 5, wherein (a) the agent and (b) the recombinant viral vector are to be administered at about the same time.
9. The use of any of claims 1 – 5, wherein (a) the agent is to be administered two or more times before or after (b) the recombinant viral vector.
10. The use of any of claims 1 - 9, wherein an amount of a protease or glycosidase is to be further administered to said subject.

11. The use of claim claim 10, wherein said protease or glycosidase is effective to degrade or digest and/or inhibit or reduce effector function of antibodies that bind to said recombinant viral vector and/or said polypeptide or peptide encoded by said heterologous polynucleotide and/or said heterologous polynucleotide.
12. The use of claim 10, wherein said protease or glycosidase is to be further administered before, after or at about the same time as (a) the agent.
13. The use of claim 10, wherein said protease or glycosidase is to be further administered before, after or at about the same time as (b) the recombinant viral vector.
14. The use of claim 10, wherein said protease or glycosidase is to be further administered two or more times before, after or at about the same time as (a) the agent.
15. The use of claim 10, wherein said protease or glycosidase is to be further administered two or more times before, after or at about the same time as (b) the recombinant viral vector.
16. The use of any of claims 10 – 15, wherein said protease comprises a cysteine protease or a thiol protease.
17. The use of any of claims 10 – 15, wherein said protease comprises a protease from *Streptococcus pyogenes*, *Streptococcus equi* or *Mycoplasma canis*.
18. The use of any of claims 10 – 15, wherein said protease comprises IdeS or a modified variant thereof set forth in any of SEQ ID NOs:3 – 18, 23 or 48.
19. The use of any of claims 10 – 15, wherein said glycosidase comprises an endoglycosidase.
20. The use of claim 19, wherein said endoglycosidase comprises a sequence set forth in any of SEQ ID NOs: 44 – 47.
21. The use of any of claims 1 – 20, wherein said viral vector comprises a lentiviral vector, an adenoviral vector or an adeno-associated virus (AAV) vector.
22. The use of claim 21, wherein said AAV vector comprises capsid proteins to which the antibodies or IgG bind.
23. The use of claim 21, wherein said AAV vector comprises VP1, VP2 and/or VP3 capsid proteins to which the antibodies or IgG bind.
24. The use of any of claims 21 – 23, wherein said AAV vector comprises VP1, VP2 and/or VP3 capsid protein having 60% or more sequence identity to VP1, VP2 and/or

VP3 capsid protein selected from the group consisting of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV3B, AAV-2i8, Rh10, Rh74, SEQ ID NO:1 and SEQ ID NO:2 VP1, VP2 and/or VP3 capsid proteins.

25. The use of any of claims 1 – 24, wherein said subject has antibodies or IgG that bind to said viral vector.

26. The use of any of claims 1 – 24, wherein antibodies or IgG that bind to said viral vector are absent from said subject.

27. The use of any of claims 1 – 26, wherein said subject has antibodies or IgG that bind to said polypeptide or peptide encoded by said heterologous polynucleotide.

28. The use of any of claims 10 – 27, wherein said antibodies comprise IgG, IgM, IgA, IgD and/or IgE.

29. The use of any of claims 1 – 28, wherein a biological sample from said subject is to be analyzed for the presence, amount or an effector function of viral vector binding antibodies or IgG present in said sample before (a) the agent has been administered, after (a) the agent but before (b) the recombinant viral vector has been administered and/or after (a) the agent and (b) the recombinant viral vector have been administered.

30. The use of any of claims 1 – 29, wherein said use leads to a reduction of 20-50%, 50-75%, 75-90%, 90-95% or 95% or more of said viral vector binding antibodies or IgG.

31. The use of claim 29, wherein said viral vector binding antibodies or IgG present in said biological sample or blood product from said subject is less than about 1:100,000 where 1 part of said biological sample or blood product diluted in 100,000 parts of buffer results in 50% viral vector neutralization.

32. The use of any of claims 1 – 31, wherein the presence or quantity of the amount of antibodies or IgG that bind to a polypeptide or peptide encoded by said heterologous polynucleotide is to be determined, after (a) the agent but before (b) the recombinant viral vector has been administered and/or after (a) the agent and (b) the recombinant viral vector have been administered.

33. The use of any of claims 1 – 31, wherein the presence or quantity of the amount of antibodies or IgG that bind to said heterologous polynucleotide or nucleic acid is to be determined after (a) the agent has been administered but before (b) the recombinant viral vector and/or after (a) the agent and (b) the recombinant viral vector have been administered.

34. The use of any of claims 1 – 33, wherein said subject has a lung disease (*e.g.*, cystic fibrosis), a bleeding disorder (*e.g.*, hemophilia A or hemophilia B with or without inhibitors), thalassemia, a blood disorder (*e.g.*, anemia), Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis (ALS), epilepsy, a lysosomal storage disease, (*e.g.*, aspartylglucosaminuria, Batten disease, late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), cystinosis, Fabry disease, Gaucher disease types I, II, and III, glycogen storage disease II (Pompe disease), GM2-gangliosidosis type I (Tay Sachs disease), GM2-gangliosidosis type II (Sandhoff disease), mucolipidosis types I (sialidosis type I and II), II (I-cell disease), III (pseudo-Hurler disease) and IV, mucopolysaccharide storage diseases (Hurler disease and variants, Hunter, Sanfilippo Types A,B,C,D, Morquio Types A and B, Maroteaux-Lamy and Sly diseases), Niemann-Pick disease types A/B, C1 and C2, and Schindler disease types I and II), hereditary angioedema (HAE), a copper or iron accumulation disorder (*e.g.*, Wilson's or Menkes disease), lysosomal acid lipase deficiency, a neurological or neurodegenerative disorder, cancer, type 1 or type 2 diabetes, adenosine deaminase deficiency, a metabolic defect (*e.g.*, glycogen storage diseases), a disease of solid organs (*e.g.*, brain, liver, kidney, heart), or an infectious viral (*e.g.*, hepatitis B and C, HIV, etc.), bacterial or fungal disease.

35. The use of any of claims 1 – 33, wherein said subject has hemophilia A, hemophilia A with inhibitory antibodies, hemophilia B, hemophilia B with inhibitory antibodies, a deficiency in any coagulation Factor: VII, VIII, IX, X, XI, V, XII, II, von Willebrand factor, or a combined FV/FVIII deficiency, thalassemia, vitamin K epoxide reductase C1 deficiency or gamma-carboxylase deficiency.

36. The use of any of claims 1 – 33, wherein said subject has anemia, bleeding associated with trauma, injury, thrombosis, thrombocytopenia, stroke, coagulopathy, disseminated intravascular coagulation (DIC); over-anticoagulation associated with heparin, low molecular weight heparin, pentasaccharide, warfarin, small molecule antithrombotics (*i.e.*, FXa inhibitors), or a platelet disorder such as, Bernard Soulier syndrome, Glanzmann thrombasthenia, or storage pool deficiency.

37. The use of any of claims 1 – 33, wherein said heterologous polynucleotide encodes a protein selected from the group consisting of insulin, glucagon, growth hormone (GH), parathyroid hormone (PTH), growth hormone releasing factor (GRF), follicle stimulating hormone (FSH), luteinizing hormone (LH), human chorionic

gonadotropin (hCG), vascular endothelial growth factor (VEGF), angiopoietins, angiostatin, granulocyte colony stimulating factor (GCSF), erythropoietin (EPO), connective tissue growth factor (CTGF), basic fibroblast growth factor (bFGF), acidic fibroblast growth factor (aFGF), epidermal growth factor (EGF), transforming growth factor α (TGFα), platelet-derived growth factor (PDGF), insulin growth factors I and II (IGF-I and IGF-II), TGFβ, activins, inhibins, bone morphogenic protein (BMP), nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophins NT-3 and NT4/5, ciliary neurotrophic factor (CNTF), glial cell line derived neurotrophic factor (GDNF), neurturin, agrin, netrin-1 and netrin-2, hepatocyte growth factor (HGF), ephrins, noggin, sonic hedgehog and tyrosine hydroxylase.

38. The use of any of claims 1 – 33, wherein said heterologous polynucleotide encodes a protein selected from the group consisting of thrombopoietin (TPO), interleukins (IL1 through IL-36), monocyte chemoattractant protein, leukemia inhibitory factor, granulocyte-macrophage colony stimulating factor, Fas ligand, tumor necrosis factors α and β, interferons α, β, and γ, stem cell factor, flk-2/flt3 ligand, IgG, IgM, IgA, IgD and IgE, chimeric immunoglobulins, humanized antibodies, single chain antibodies, T cell receptors, chimeric T cell receptors, single chain T cell receptors, class I and class II MHC molecules.

39. The use of any of claims 1 – 33, wherein said heterologous polynucleotide encodes CFTR (cystic fibrosis transmembrane regulator protein), a blood coagulation (clotting) factor (Factor XIII, Factor IX, Factor VIII, Factor X, Factor VII, Factor VIIa, protein C, etc.) a gain of function blood coagulation factor, an antibody, retinal pigment epithelium-specific 65 kDa protein (RPE65), erythropoietin, LDL receptor, lipoprotein lipase, ornithine transcarbamylase, β-globin, α-globin, spectrin, α-antitrypsin, adenosine deaminase (ADA), a metal transporter (ATP7A or ATP7), sulfamidase, an enzyme involved in lysosomal storage disease (ARSA), hypoxanthine guanine phosphoribosyl transferase, β-25 glucocerebrosidase, sphingomyelinase, lysosomal hexosaminidase, branched-chain keto acid dehydrogenase, a hormone, a growth factor, insulin-like growth factor 1 or 2, platelet derived growth factor, epidermal growth factor, nerve growth factor, neurotrophic factor -3 and -4, brain-derived neurotrophic factor, glial derived growth factor, transforming growth factor α and β, a cytokine, α-interferon, β-interferon, interferon-γ, interleukin-2, interleukin-4, interleukin 12, granulocyte-macrophage colony stimulating factor, lymphotoxin, a

suicide gene product, herpes simplex virus thymidine kinase, cytosine deaminase, diphtheria toxin, cytochrome P450, deoxycytidine kinase, tumor necrosis factor, a drug resistance protein, a tumor suppressor protein (*e.g.*, p53, Rb, Wt-1, NF1, Von Hippel–Lindau (VHL), adenomatous polyposis coli (APC)), a peptide with immunomodulatory properties, a tolerogenic or immunogenic peptide or protein Tregitope or hCDR1, insulin, glucokinase, guanylate cyclase 2D (LCA-GUCY2D), Rab escort protein 1 (Choroideremia), LCA 5 (LCA-Lebercilin), ornithine ketoacid aminotransferase (Gyrate Atrophy), Retinoschisin 1 (X-linked Retinoschisis), USH1C (Usher's Syndrome 1C), X-linked retinitis pigmentosa GTPase (XLRP), MERTK (AR forms of RP: retinitis pigmentosa), DFNB1 (Connexin 26 deafness), ACHM 2, 3 and 4 (Achromatopsia), PKD-1 or PKD-2 (Polycystic kidney disease), TPP1, CLN2, a sulfatase, N-acetylglucosamine-1-phosphate transferase, cathepsin A, GM2-AP, NPC1, VPC2, a sphingolipid activator protein, one or more zinc finger nuclease for genome editing, and one or more donor sequence used as repair templates for genome editing.

40. The use of any of claims 1 – 33, wherein said heterologous polynucleotide encodes an inhibitory nucleic acid.

41. The use of claim 40, wherein said inhibitory nucleic acid is selected from the group consisting of a siRNA, an antisense molecule, miRNA, RNAi, a ribozyme and a shRNA.

42. The use of claim 40, wherein said inhibitory nucleic acid binds to a gene, a transcript of a gene, or a transcript of a gene associated with a polynucleotide repeat disease selected from the group consisting of a huntingtin (HTT) gene, a gene associated with dentatorubropallidoluysian atrophy (atrophin 1, ATN1), androgen receptor on the X chromosome in spinobulbar muscular atrophy, human Ataxin-1, -2, -3, and -7, $Ca_v2.1$ P/Q voltage-dependent calcium channel (CACNA1A), TATA-binding protein, Ataxin 8 opposite strand (ATXN8OS), Serine/threonine-protein phosphatase 2A 55 kDa regulatory subunit B beta isoform in spinocerebellar ataxia (type 1, 2, 3, 6, 7, 8, 12 17), *FMR1* (fragile X mental retardation 1) in fragile X syndrome, *FMR1* (fragile X mental retardation 1) in fragile X-associated tremor/ataxia syndrome, *FMR1* (fragile X mental retardation 2) or AF4/FMR2 family member 2 in fragile XE mental retardation; Myotonin-protein kinase (MT-PK) in myotonic dystrophy; Frataxin in Friedreich's ataxia; a mutant of superoxide dismutase 1 (SOD1) gene in amyotrophic lateral sclerosis; a gene involved in pathogenesis of Parkinson's disease and/or

Alzheimer's disease; apolipoprotein B (APOB) and proprotein convertase subtilisin/kexin type 9 (PCSK9), hypercholesterolemia; HIV Tat, human immunodeficiency virus transactivator of transcription gene, in HIV infection; HIV TAR, HIV TAR, human immunodeficiency virus transactivator response element gene, in HIV infection; C-C chemokine receptor (CCR5) in HIV infection; Rous sarcoma virus (RSV) nucleocapsid protein in RSV infection, liver-specific microRNA (miR-122) in hepatitis C virus infection; p53, acute kidney injury or delayed graft function kidney transplant or kidney injury acute renal failure; protein kinase N3 (PKN3) in advance recurrent or metastatic solid malignancies; LMP2, LMP2 also known as proteasome subunit beta-type 9 (PSMB 9), metastatic melanoma; LMP7,also known as proteasome subunit beta-type 8 (PSMB 8), metastatic melanoma; MECL1 also known as proteasome subunit beta-type 10 (PSMB 10), metastatic melanoma; vascular endothelial growth factor (VEGF) in solid tumors; kinesin spindle protein in solid tumors, apoptosis suppressor B-cell CLL/lymphoma (BCL-2) in chronic myeloid leukemia; ribonucleotide reductase M2 (RRM2) in solid tumors; Furin in solid tumors; polo-like kinase 1 (PLK1) in liver tumors, diacylglycerol acyltransferase 1 (DGAT1) in hepatitis C infection, beta-catenin in familial adenomatous polyposis; beta2 adrenergic receptor, glaucoma; RTP801/Redd1 also known as DNA damage-inducible transcript 4 protein, in diabetic macular edema (DME) or age-related macular degeneration; vascular endothelial growth factor receptor I (VEGFR1) in age-related macular degeneration or choroidal neovascularization, caspase 2 in non-arteritic ischaemic optic neuropathy; Keratin 6A N17K mutant protein in pachyonychia congenital; influenza A virus genome/gene sequences in influenza infection; severe acute respiratory syndrome (SARS) coronavirus genome/gene sequences in SARS infection; respiratory syncytial virus genome/gene sequences in respiratory syncytial virus infection; Ebola filovirus genome/gene sequence in Ebola infection; hepatitis B and C virus genome/gene sequences in hepatitis B and C infection; herpes simplex virus (HSV) genome/gene sequences in HSV infection, coxsackievirus B3 genome/gene sequences in coxsackievirus B3 infection; silencing of a pathogenic allele of a gene (allele-specific silencing) like torsin A (TOR1A) in primary dystonia, pan-class I and HLA-allele specific in transplant; and mutant rhodopsin gene (RHO) in autosomal dominantly inherited retinitis pigmentosa (adRP).

43. The use of any of claims 1 – 42, wherein said polypeptide encoded by said heterologous polynucleotide comprises a gene editing nuclease.

44. The use of any of claims 1 – 43, wherein (a) the agent and/or (b) the recombinant viral vector are to be administered two or more times.

45. The use of any of claims 1 – 44, wherein said subject is a human.

46. A package having disposed therein:

(a) a recombinant viral vector comprising a heterologous polynucleotide that encodes a polypeptide or peptide;

(b) an agent that reduces interaction of IgG with FcRn;

(c) optionally, a protease or glycosidase that degrades or digests antibodies; and

(d) a label with instructions for the use according to any of claims 1 – 45, wherein (a), (b) and (c) are in separate or the same container.

47. A package having disposed therein:

(a) a recombinant viral vector comprising a heterologous polynucleotide that is transcribed into a nucleic acid that inhibits, decreases or reduces expression of a protein;

(b) an agent that reduces interaction of IgG with FcRn;

(c) optionally, a protease or glycosidase that degrades or digests antibodies; and

(d) a label with instructions for the use according to any of claims 1 – 45, wherein (a), (b) and (c) are in separate or the same container.

48. The use of any of claims 5 – 45 or the package of any of claims 46 – 47, wherein the anti-FcRn antibody comprises any one of SEQ ID NOs:51-56.

49. The use of any of claims 5 – 45 or the package of any of claims 46 – 47, wherein the anti-FcRN antibody comprises any one or both of SEQ ID NO:49 and SEQ ID NO:50.

50. The use of any of claims 5 – 45 or the package of any of claims 46 – 47, wherein the anti-FcRn antibody comprises efgartigimod.