

## CLAIMS

What is claimed is:

1. Use of an adenoviral vector in the manufacture of a medicament for use in selectively targeting a hematopoietic cell type, wherein the adenoviral vector is to be administered to a subject or system, and wherein the adenoviral vector comprises:
  - (a) a capsid comprising one or more viral polypeptides of an Ad3, Ad5, Ad7, Ad11, Ad14, Ad16, Ad21, Ad34, Ad35, Ad37, or Ad50 serotype, wherein the one or more viral polypeptides comprise one or more of a:
    - (i) fiber knob;
    - (ii) fiber shaft;
    - (iii) fiber tail;
    - (iv) penton; and
    - (v) hexon; and
  - (b) a double-stranded DNA genome comprising a heterologous nucleic acid payload.
2. The use of claim 1, wherein the genome further comprises:
  - (a) a 3' ITR and a 5' ITR, wherein each of the 3' ITR and the 5' ITR are of the viral polypeptide serotype; and
  - (b) a packaging sequence, wherein the packing sequence is of the viral polypeptide serotype.
3. The use of claim 1 or 2, wherein the hematopoietic cell type:
  - (i) is or comprises a terminally differentiated cell type;
  - (ii) is or comprises a progenitor cell type; or
  - (iii) is or comprises HSCs, common lymphoid progenitors (CLPs), T cells, NK cells, colony forming unit (CFU)-pre B cells, B cells, common myeloid progenitors (CMPs), granulocyte-macrophage progenitors (GMPs), CFU-M cells, monoblasts, monocytes, macrophages, CFU-G cells, myeloblasts, granulocytes, neutrophils, eosinophils, basophils, megakaryocyte-erythrocyte progenitors (MEPs), BFU-E cells, CFU-E cells, erythroblasts, erythrocytes, CFU-Mk cells, megakaryocytes,

and/or platelets, optionally wherein the HSCs are CD34<sup>+</sup> long-term hematopoietic stem cells (LT-HSCs) and/or CD34<sup>+</sup> short-term (ST)-HSCs.

4. The use of any one of claims 1-3, wherein the medicament is for use in *in vivo* gene therapy, optionally wherein:

- (i) the hematopoietic cell type is a mammalian hematopoietic cell type, further optionally wherein the mammalian hematopoietic cell type is a human hematopoietic cell type;
- (ii) the subject is a mammalian subject, further optionally wherein the mammalian subject is a human subject;
- (iii) hematopoietic cells of the subject are mobilized prior to the administration of the adenoviral vector;
- (iv) one or more immunosuppression agents is to be administered to the subject, further optionally wherein the administration of the one or more immunosuppression agents is prior to the administration of the adenoviral vector;  
or
- (v) a combination thereof.

5. The use of any one of claims 1-3, wherein the medicament is for use in *ex vivo* gene therapy, optionally wherein:

- (i) the hematopoietic cell type is a mammalian hematopoietic cell type, further optionally wherein the mammalian hematopoietic cell type is a human hematopoietic cell type; and/or
- (ii) the system is or comprises a biological sample derived from a mammalian donor, further optionally wherein the mammalian donor is a human donor.

6. The use of any one of claims 1-5, wherein the heterologous nucleic acid payload comprises a selectable marker, optionally wherein the selectable marker is MGMT<sup>P140K</sup>, optionally wherein a selecting agent is to be administered to the subject, optionally wherein the selecting agent comprises O<sup>6</sup>BG and/or BCNU.

7. The use of any one of claims 1-6, wherein the one or more viral polypeptides comprise the:

- (a) fiber knob and fiber shaft;
- (b) fiber knob and fiber tail;
- (c) fiber knob and penton;
- (d) fiber knob and hexon;
- (e) fiber knob, hexon, and penton;
- (f) fiber shaft and fiber tail;
- (g) fiber shaft and penton;
- (h) fiber shaft and hexon;
- (i) fiber shaft, hexon, and penton;
- (j) fiber tail and penton;
- (k) fiber tail and hexon;
- (l) fiber tail, hexon, and penton;
- (m) fiber knob, fiber shaft, and fiber tail;
- (n) fiber knob, fiber shaft, and penton;
- (o) fiber knob, fiber shaft, and hexon;
- (p) fiber knob, fiber shaft, hexon, and penton;
- (q) fiber knob, fiber shaft, fiber tail, and penton;
- (r) fiber knob, fiber shaft, fiber tail, penton, and hexon; or
- (s) penton and hexon.

8. The use of any one of claims 1-7, wherein:

- (i) the fiber knob has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 15, 33, 51, 69, 87, 105, 123, 141, 159, 177, and 195;
- (ii) the fiber shaft has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 14, 32, 50, 68, 86, 104, 122, 140, 158, 176, and 194;
- (iii) the fiber tail has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 18, 36, 54, 72, 90, 108, 126, 144, 162, 180, and 198;
- (iv) the penton has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 16, 34, 52, 70, 88, 106, 124, 142, 160, 178, and 196;

- (v) the hexon has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 17, 35, 53, 71, 89, 107, 125, 143, 161, 179, and 197; or
  - (vi) a combination thereof.
9. The use of any one of claims 1-8, wherein the adenoviral vector:
- (i) comprises a fiber of the serotype of the viral peptides, optionally wherein the fiber has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 13, 31, 49, 67, 85, 103, 121, 139, 157, 175, and 193;
  - (ii) is a chimeric vector characterized in that the capsid comprises at least one of a fiber knob, fiber shaft, fiber tail, hexon, or penton that is not of the serotype of the viral peptides;
  - (iii) is a helper dependent vector; or
  - (iv) a combination thereof.
10. The use of any one of claims 1-9, wherein the heterologous nucleic acid payload encodes:
- (i) a protein;
  - (ii) a chimeric antigen receptor (CAR), T cell receptor (TCR), antibody, or small RNA, optionally wherein the small RNA is an shRNA;
  - (iii) a chimeric antigen receptor (CAR) or T cell receptor (TCR) and the hematopoietic cell type is or comprises T cells;
  - (iv) an antibody and the hematopoietic cell type is or comprises B cells;
  - (v) a gene editing enzyme or system, wherein the gene editing is selected from CRISPR editing, base editing, prime editing, and zinc finger nuclease editing;
  - (vi) an agent for treatment of a condition selected from adenosine deaminase deficiency (ADA), adrenoleukodystrophy (ALD), agammaglobulinemia, alpha-1 antitrypsin deficiency, congenital amegakaryocytic thrombocytopenia, amyotrophic lateral sclerosis (Lou Gehrig's disease), ataxia telangiectasia, Batten disease, Bernard-Soulier Syndrome, CD40/CD40L deficiency, chronic granulomatous disease, common variable immune deficiency (CVID), congenital thrombotic thrombocytopenic purpura (cTTP), cystic fibrosis, Diamond Blackfan anemia (DBA), DOCK 8 deficiency, dyskeratosis congenital, Fabry disease,

Factor V Deficiency, Factor VII Deficiency, Factor X Deficiency, Factor XI Deficiency, Factor XII Deficiency, Factor XIII Deficiency, familial apolipoprotein E deficiency and atherosclerosis (ApoE), familial erythrophagocytic lymphohistiocytosis, Fanconi anemia (FA), Friedreich ataxia, Gaucher disease, Glanzmann thrombasthenia, glucosemia, glycogen storage disease, glycogen storage disease type I (GSDI), Gray Platelet Syndrome, hemophilia, hemophilia A, hemophilia B, hereditary hemochromatosis, Hurler's syndrome, hyper IgM, Hypogammaglobulinemia, Krabbe disease, major histocompatibility complex class II deficiency (MHC-II), maple syrup urine disease, metachromatic leukodystrophy (MLD), mucopolysaccharidoses, mucopolysaccharidosis type I (MPS I), MPS II (Hunter Syndrome), MPS III (Sanfilippo syndrome), MPS IV (Morquio syndrome), MPS V, MPS VI (Maroteaux-Lamy syndrome), MPS VII (sly syndrome), muscular dystrophy, Niemann-Pick disease, Parkinson's disease, paroxysmal nocturnal hemoglobinuria (PNH), pernicious anemia, phenylketonuria (PKU), Pompe disease, pulmonary alveolar proteinosis (PAP), pure red cell aplasia (PRCA), pyruvate kinase deficiency, refractory anemia, Shwachman-Diamond syndrome, selective IgA deficiency, severe aplastic anemia, severe combined immunodeficiency disease (SCID), Severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID), sickle cell anemia, sickle cell disease, sickle cell trait, Tay Sachs, thalassemia, thalassemia intermedia, von Gierke disease, von Willebrand Disease, Wiskott-Aldrich syndrome (WAS), X-linked agammaglobulinemia (XLA), X-linked severe combined immunodeficiency (SCID-X1), Zellweger syndrome,  $\alpha$ -mannosidosis,  $\beta$ -mannosidosis,  $\beta$ -thalassemia, and/or  $\beta$ -thalassemia major; or (vii) a combination thereof.

11. The use of any one of claims 1-10, wherein the capsid comprises:
  - (a) one or more viral polypeptides of (i) an Ad5, Ad7, Ad11, Ad16, Ad34, or Ad35 serotype, (ii) an Ad11, Ad16, Ad34, or Ad35 serotype, or (iii) an Ad11, Ad34, or Ad35 serotype, and wherein the hematopoietic cell type is or comprises monocytes, optionally wherein the monocytes are CD11+/CD14+ monocytes;

- (b) one or more viral polypeptides of (i) an Ad5, Ad7, Ad11, Ad16, Ad34, or Ad35 serotype, (ii) an Ad5, Ad16, Ad34, or Ad35 serotype, or (iii) an Ad34 or Ad35 serotype, and wherein the hematopoietic cell type is or comprises T cells, optionally wherein the T cells are CD3<sup>+</sup> T cells;
  - (c) one or more viral polypeptides of (i) an Ad5, Ad7, Ad11, Ad16, Ad34, or Ad35 serotype, (ii) an Ad11, Ad16, Ad34 or Ad35 serotype, or (iii) an Ad11, Ad34, or Ad35 serotype, and wherein the hematopoietic cell type is or comprises NK cells, optionally wherein the NK cells are CD3<sup>-</sup>/CD56<sup>+</sup> NK cells; or
  - (d) one or more viral polypeptides of (i) an Ad5, Ad7, Ad11, Ad16, Ad34, or Ad35 serotype, or (ii) an Ad16 serotype, and wherein the hematopoietic cell type is or comprises B cells, optionally wherein the B cells are CD20<sup>+</sup> B cells.
12. A hematopoietic cell comprising an adenoviral vector and an adenoviral vector genome, wherein the adenoviral vector comprises a capsid comprises one or more viral polypeptides of an Ad3, Ad5, Ad7, Ad11, Ad14, Ad16, Ad21, Ad34, Ad35, Ad37, or Ad50 serotype, the one or more viral polypeptides comprising one or more of a:
- (i) fiber knob;
  - (ii) fiber shaft;
  - (iii) fiber tail;
  - (iv) penton; and
  - (v) hexon,
- wherein the adenoviral vector genome comprises a double-stranded DNA genome comprising a heterologous nucleic acid payload, and
- wherein the hematopoietic cell is an HSC, common lymphoid progenitors (CLPs), T cell, NK cell, colony forming unit (CFU)-pre B cell, B cell, common myeloid progenitor (CMP) cell, granulocyte-macrophage progenitor (GMP) cell, CFU-M cell, monoblasts, monocyte, macrophage, CFU-G cell, myeloblast, granulocyte, neutrophil, eosinophil, basophil, megakaryocyte-erythrocyte progenitor (MEP) cell, BFU-E cell, CFU-E cell, erythroblast, erythrocyte, CFU-Mk cell, megakaryocyte, and/or platelet, optionally wherein the HSC cell is a CD34<sup>+</sup> long-term hematopoietic stem cell (LT-HSC) and/or CD34<sup>+</sup> short-term (ST)-HSC.

13. A hematopoietic cell comprising an adenoviral vector genome, wherein the adenoviral vector genome comprises (a) a 3' ITR and a 5' ITR, wherein the 3' ITR and the 5' ITR are each of the same serotype selected from Ad3, Ad5, Ad7, Ad11, Ad14, Ad16, Ad21, Ad34, Ad35, Ad37, and Ad50; (b) a packaging sequence, wherein the packing sequence is of the same serotype as the 3' ITR and a 5' ITR; and (c) a heterologous nucleic acid payload, and

wherein the hematopoietic cell is an HSC, common lymphoid progenitors (CLPs), T cell, NK cell, colony forming unit (CFU)-pre B cell, B cell, common myeloid progenitor (CMP) cell, granulocyte-macrophage progenitor (GMP) cell, CFU-M cell, monoblasts, monocyte, macrophage, CFU-G cell, myeloblast, granulocyte, neutrophil, eosinophil, basophil, megakaryocyte-erythrocyte progenitor (MEP) cell, BFU-E cell, CFU-E cell, erythroblast, erythrocyte, CFU-Mk cell, megakaryocyte, and/or platelet, optionally wherein the HSC cell is a CD34<sup>+</sup> long-term hematopoietic stem cell (LT-HSC) and/or CD34<sup>+</sup> short-term (ST)-HSC.

14. The hematopoietic cell of claim 12 or 13, wherein the cell is a cell of a subject suffering from a condition selected from adenosine deaminase deficiency (ADA), adrenoleukodystrophy (ALD), agammaglobulinemia, alpha-1 antitrypsin deficiency, congenital amegakaryocytic thrombocytopenia, amyotrophic lateral sclerosis (Lou Gehrig's disease), ataxia telangiectasia, Batten disease, Bernard-Soulier Syndrome, CD40/CD40L deficiency, chronic granulomatous disease, common variable immune deficiency (CVID), congenital thrombotic thrombocytopenic purpura (cTTP), cystic fibrosis, Diamond Blackfan anemia (DBA), DOCK 8 deficiency, dyskeratosis congenital, Fabry disease, Factor V Deficiency, Factor VII Deficiency, Factor X Deficiency, Factor XI Deficiency, Factor XII Deficiency, Factor XIII Deficiency, familial apolipoprotein E deficiency and atherosclerosis (ApoE), familial erythrophagocytic lymphohistiocytosis, Fanconi anemia (FA), Friedreich ataxia, Gaucher disease, Glanzmann thrombasthenia, glucosemia, glycogen storage disease, glycogen storage disease type I (GSDI), Gray Platelet Syndrome, hemophilia, hemophilia A, hemophilia B, hereditary hemochromatosis, Hurler's syndrome, hyper IgM, Hypogammaglobulinemia, Krabbe disease, major histocompatibility complex class II deficiency (MHC-II), maple syrup urine disease, metachromatic leukodystrophy (MLD), mucopolysaccharidoses, mucopolysaccharidosis type I (MPS I), MPS II (Hunter Syndrome), MPS III (Sanfilippo syndrome), MPS IV (Morquio

syndrome), MPS V, MPS VI (Maroteaux-Lamy syndrome), MPS VII (sly syndrome), muscular dystrophy, Niemann-Pick disease, Parkinson's disease, paroxysmal nocturnal hemoglobinuria (PNH), pernicious anemia, phenylketonuria (PKU), Pompe disease, pulmonary alveolar proteinosis (PAP), pure red cell aplasia (PRCA), pyruvate kinase deficiency, refractory anemia, Shwachman-Diamond syndrome, selective IgA deficiency, severe aplastic anemia, severe combined immunodeficiency disease (SCID), Severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID), sickle cell anemia, sickle cell disease, sickle cell trait, Tay Sachs, thalassemia, thalassemia intermedia, von Gierke disease, von Willebrand Disease, Wiskott-Aldrich syndrome (WAS), X-linked agammaglobulinemia (XLA), X-linked severe combined immunodeficiency (SCID-X1), Zellweger syndrome,  $\alpha$ -mannosidosis,  $\beta$ -mannosidosis,  $\beta$ -thalassemia, and/or  $\beta$ -thalassemia major.

15. Use of an adenoviral vector in the manufacture of a medicament for use in *in vivo* gene therapy in a mammalian subject, wherein the adenoviral vector is to be administered to the subject, and wherein the adenoviral vector comprises:

(a) a capsid comprising one or more viral polypeptides of an Ad3, Ad7, Ad11, Ad14, Ad16, Ad21, Ad34, Ad37, or Ad50 serotype, wherein the one or more viral polypeptides comprise one or more of a:

- (i) fiber knob;
- (ii) fiber shaft;
- (iii) fiber tail;
- (iv) penton; and
- (v) hexon; and

(b) a double-stranded DNA genome comprising a heterologous nucleic acid payload.

16. The use of claim 15, wherein the genome further comprises:

- (a) a 3' ITR and a 5' ITR, wherein each of the 3' ITR and the 5' ITR are of the viral polypeptide serotype; and
- (b) a packaging sequence, wherein the packaging sequence is of the viral polypeptide serotype.

17. The use of claim 15 or 16, wherein:
- (i) hematopoietic stem cells of the subject are mobilized prior to the administration of the adenoviral vector; and/or
  - (ii) one or more immunosuppression agents is to be administered to the subject, optionally wherein the administration of the one or more immunosuppression agents is prior to the administration of the adenoviral vector.
18. The use of any one of claims 15-17, wherein the heterologous nucleic acid payload comprises a selectable marker, optionally wherein the selectable marker is MGMT<sup>P140K</sup>, optionally wherein a selecting agent is to be administered to the subject, optionally wherein the selecting agent comprises O<sup>6</sup>BG and/or BCNU.
19. An adenoviral donor vector comprising:
- (a) a capsid comprising one or more viral polypeptides of an Ad3, Ad7, Ad11, Ad14, Ad16, Ad21, Ad34, Ad37, or Ad50 serotype, wherein the one or more viral polypeptides comprise one or more of a:
    - (i) fiber knob;
    - (ii) fiber shaft;
    - (iii) fiber tail;
    - (iv) penton; and
    - (v) hexon; and
  - (b) a double-stranded DNA genome comprising a heterologous nucleic acid payload.
20. The vector of claim 19, wherein the genome further comprises:
- (a) a 3' ITR and a 5' ITR, wherein each of the 3' ITR and the 5' ITR are of the viral polypeptide serotype; and
  - (b) a packaging sequence, wherein the packing sequence is of the viral polypeptide serotype.
21. The vector of claim 19 or 20, wherein the heterologous nucleic acid payload comprises a selectable marker, optionally wherein the selectable marker is MGMT<sup>P140K</sup>.

22. The use or vector of any one of claims 15-21, wherein the one or more viral polypeptides comprise the:

- (a) fiber knob and fiber shaft;
- (b) fiber knob and fiber tail;
- (c) fiber knob and penton;
- (d) fiber knob and hexon;
- (e) fiber knob, hexon, and penton;
- (f) fiber shaft and fiber tail;
- (g) fiber shaft and penton;
- (h) fiber shaft and hexon;
- (i) fiber shaft, hexon, and penton;
- (j) fiber tail and penton;
- (k) fiber tail and hexon;
- (l) fiber tail, hexon, and penton;
- (m) fiber knob, fiber shaft, and fiber tail;
- (n) fiber knob, fiber shaft, and penton;
- (o) fiber knob, fiber shaft, and hexon;
- (p) fiber knob, fiber shaft, hexon, and penton;
- (q) fiber knob, fiber shaft, fiber tail, and penton;
- (r) fiber knob, fiber shaft, fiber tail, penton, and hexon; or
- (s) penton and hexon.

23. The use or vector of any one of claims 15-22, wherein:

- (i) the fiber knob has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 15, 33, 51, 69, 87, 105, 123, 141, and 159;
- (ii) the fiber shaft has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 14, 32, 50, 68, 86, 104, 122, 140, and 158;
- (iii) the fiber tail has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 18, 36, 54, 72, 90, 108, 126, 144, and 162;

- (iv) the penton has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 16, 34, 52, 70, 88, 106, 124, 142, and 160;
  - (v) the hexon has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 17, 35, 53, 71, 89, 107, 125, 143, and 161; or
  - (vi) a combination thereof.
24. The use or vector of any one of claims 15-23, wherein the adenoviral vector:
- (i) comprises a fiber of the serotype of the viral peptides, optionally wherein the fiber has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: SEQ ID NOs: 13, 31, 49, 67, 85, 103, 121, 139, and 157;
  - (ii) is a chimeric vector characterized in that the capsid comprises at least one of a fiber knob, fiber shaft, fiber tail, hexon, or penton that is not of the serotype of the viral peptides;
  - (iii) is a helper dependent vector; or
  - (iv) a combination thereof.
25. An adenoviral donor vector genome comprising:
- (a) a 3' ITR and a 5' ITR, wherein the 3' ITR and the 5' ITR are each of the same serotype selected from Ad3, Ad7, Ad11, Ad14, Ad16, Ad21, Ad34, Ad37, and Ad50;
  - (b) a packaging sequence, wherein the packing sequence is of the ITR serotype; and
  - (c) a heterologous nucleic acid payload.
26. The genome of claim 25, wherein the heterologous nucleic acid payload comprises a selectable marker, optionally wherein the selectable marker is MGMT<sup>P140K</sup>.
27. The use, vector, or genome of any one of claims 15-26, wherein the heterologous nucleic acid payload encodes:
- (i) a protein;
  - (ii) a chimeric antigen receptor (CAR), T cell receptor (TCR), or small RNA, optionally wherein the small RNA is an shRNA;

- (iii) a gene editing enzyme or system, wherein the gene editing is selected from CRISPR editing, base editing, prime editing, or zinc finger nuclease editing;
- (iv) an agent for treatment of a condition selected from adenosine deaminase deficiency (ADA), adrenoleukodystrophy (ALD), agammaglobulinemia, alpha-1 antitrypsin deficiency, congenital amegakaryocytic thrombocytopenia, amyotrophic lateral sclerosis (Lou Gehrig's disease), ataxia telangiectasia, Batten disease, Bernard-Soulier Syndrome, CD40/CD40L deficiency, chronic granulomatous disease, common variable immune deficiency (CVID), congenital thrombotic thrombocytopenic purpura (cTTP), cystic fibrosis, Diamond Blackfan anemia (DBA), DOCK 8 deficiency, dyskeratosis congenital, Fabry disease, Factor V Deficiency, Factor VII Deficiency, Factor X Deficiency, Factor XI Deficiency, Factor XII Deficiency, Factor XIII Deficiency, familial apolipoprotein E deficiency and atherosclerosis (ApoE), familial erythrophagocytic lymphohistiocytosis, Fanconi anemia (FA), Friedreich ataxia, Gaucher disease, Glanzmann thrombasthenia, glucosemia, glycogen storage disease, glycogen storage disease type I (GSDI), Gray Platelet Syndrome, hemophilia, hemophilia A, hemophilia B, hereditary hemochromatosis, Hurler's syndrome, hyper IgM, Hypogammaglobulinemia, Krabbe disease, major histocompatibility complex class II deficiency (MHC-II), maple syrup urine disease, metachromatic leukodystrophy (MLD), mucopolysaccharidoses, mucopolysaccharidosis type I (MPS I), MPS II (Hunter Syndrome), MPS III (Sanfilippo syndrome), MPS IV (Morquio syndrome), MPS V, MPS VI (Maroteaux-Lamy syndrome), MPS VII (sly syndrome), muscular dystrophy, Niemann-Pick disease, Parkinson's disease, paroxysmal nocturnal hemoglobinuria (PNH), pernicious anemia, phenylketonuria (PKU), Pompe disease, pulmonary alveolar proteinosis (PAP), pure red cell aplasia (PRCA), pyruvate kinase deficiency, refractory anemia, Shwachman-Diamond syndrome, selective IgA deficiency, severe aplastic anemia, severe combined immunodeficiency disease (SCID), Severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID), sickle cell anemia, sickle cell disease, sickle cell trait, Tay Sachs, thalassemia, thalassemia intermedia, von Gierke disease, von Willebrand Disease, Wiskott-

- Aldrich syndrome (WAS), X-linked agammaglobulinemia (XLA), X-linked severe combined immunodeficiency (SCID-X1), Zellweger syndrome,  $\alpha$ -mannosidosis,  $\beta$ -mannosidosis,  $\beta$ -thalassemia, and/or  $\beta$ -thalassemia major; or
- (v) a combination thereof.

28. The use, vector, or genome of any one of claims 15-27, wherein the serotype of the viral polypeptides is Ad34.

29. A pharmaceutical composition comprising an adenoviral vector of any one of claims 19-28, wherein the pharmaceutical composition is formulated for injection to a subject in need thereof.