WHAT IS CLAIMED IS:

1. A recombinant adeno-associated virus (rAAV) comprising:
   (a) an AAV capsid; and
   (b) a recombinant AAV genome comprising a human N-acetylgalactosamine-6-sulfate sulfatase (hGALNS) expression cassette flanked by AAV-inverted terminal repeats (ITRs), the hGALNS expression cassette comprising a nucleotide sequence encoding a transgene, wherein the transgene encodes a fusion protein that is hGALNS fused to an acidic oligopeptide.
2. The rAAV of claim 1, wherein the acidic oligopeptide is D8.
3. The rAAV of claim 1 or 2, wherein the hGALNS expression cassette further comprises a nucleotide sequence encoding a liver-specific promoter, wherein the nucleotide sequence encoding the liver-specific promoter is operably linked to the nucleotide sequence encoding the fusion protein.
4. The rAAV of claim 3,wherein the liver-specific promoter:
   (a) is a TBG promoter; or
   (b) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:13; or
   (c) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:13; or
   (d) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:13; or
   (e) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:13; or
   (f) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:13; or
   (g) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:13, or
   (h) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:14; or
   (i) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:14; or

(j) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:14; or

(k) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:14; or

(l) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:14; or

(m) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:14, or

(n) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:15; or

(o) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:15; or

(p) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:15; or

(q) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:15; or

(r) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:15; or

(s) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:15.

5. The rAAVof claim 1 or 2, wherein the hGALNS expression cassette further comprises a nucleotide sequence encoding a promoter, which nucleotide sequence encoding the promoter is operably linked to the nucleotide sequence encoding the fusion protein.
6. The rAAV of claims 5, wherein the promoter is a CAG promoter.
7. The rAAV of claim 5, wherein the promoter is a liver- and muscle-specific promoter.
8. The rAAV of claim 7, wherein the liver- and muscle-specific promoter:

(a) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:16; or

(b) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:16; or

(c) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:16; or

(d) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:16; or

(e) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:16; or

(f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:16.

9. The rAAV of any one of claims 1-10, wherein the AAV is AAV8.

10. The rAAV of any one of claims 1-10, wherein the AAV is AAV9.

11. The rAAV of any one of claims 1-10, wherein the nucleotide sequence encoding hGALNS or the nucleotide sequence encoding the fusion protein is codon-optimized.

12. The rAAV of any one of claims 1-13, wherein the nucleotide sequence encoding hGALNS or the nucleotide sequence encoding the fusion protein has CpG sites depleted.

13. An rAAV comprising:

(a) an AAV capsid; and

(b) a recombinant AAV genome comprising an hGALNS expression cassette flanked by AAV-ITRs, the hGALNS expression cassette comprising a nucleotide sequence encoding a liver-specific promoter and a nucleotide sequence encoding hGALNS, wherein the nucleotide sequence encoding the liver-specific promoter is operably linked to the nucleotide sequence encoding hGALNS.

14. The rAAV of claim 13, wherein the liver-specific promoter:

(a) is a TBG promoter; or

(b) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:13; or

(c) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:13; or

(d) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:13; or

(e) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:13; or

(f) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:13; or

(g) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:13, or

(h) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:14; or

(i) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:14; or

(j) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:14; or

(k) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:14; or

(l) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:14; or

(m) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:14, or

(n) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:15; or

(o) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:15; or

(p) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:15; or

(q) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:15; or

(r) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:15; or

(s) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:15.

15. An rAAV comprising:

(a) an AAV capsid; and

(b) a recombinant AAV genome comprising an hGALNS expression cassette flanked by AAV-ITRs, the hGALNS expression cassette comprising a nucleotide sequence encoding a promoter and a nucleotide sequence encoding hGALNS, wherein the nucleotide sequence encoding the promoter is operably linked to the nucleotide sequence encoding hGALNS, and wherein the promoter is a CAG promoter.

16. An rAAV comprising:

(a) an AAV capsid; and

(b) a recombinant AAV genome comprising an hGALNS expression cassette flanked by AAV-ITRs, the hGALNS expression cassette comprising a nucleotide sequence encoding a liver- and muscle-specific promoter and a nucleotide sequence encoding hGALNS, wherein the nucleotide sequence encoding the promoter is operably linked to the nucleotide sequence encoding hGALNS, and wherein the liver- and muscle-specific promoter:

(a) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:16; or

(b) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:16; or

(c) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:16; or

(d) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:16; or

(e) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:16; or

(f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:16.

17. The rAAV of any one of claims 13-18, wherein the AAV is AAV8.
18. The rAAV of any one of claims 13-18, wherein the AAV is AAV9.
19. The rAAV of any one of claims 13-18, wherein the nucleotide sequence encoding hGALNS or the nucleotide sequence encoding the fusion protein is codon-optimized.
20. The rAAV of any one of claims 13-19, wherein the nucleotide sequence encoding hGALNS or the nucleotide sequence encoding the fusion protein has CpG sites depleted.
21. A pharmaceutical composition comprising the rAAV of any one of claims 1-20 and a pharmaceutically acceptable carrier.
22. A polynucleotide comprising an hGALNS expression cassette flanked by AAV-ITRs, the hGALNS expression cassette comprising a nucleotide sequence encoding a transgene, wherein the transgene encodes a fusion protein that is hGALNS fused to an acidic oligopeptide.
23. The polynucleotide of claim 22, wherein the acidic oligopeptide is D8.

24. The polynucleotide of claim 22 or 23, wherein the hGALNS expression cassette further comprises a nucleotide sequence encoding a liver-specific promoter, wherein the nucleotide sequence encoding the liver-specific promoter is operably linked to the nucleotide sequence encoding the fusion protein.

25. The polynucleotide of claim 24, wherein the liver-specific promoter:

(a) is a TBG promoter; or

(b) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:13; or

(c) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:13; or

(d) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:13; or

(e) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:13; or

(f) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:13; or

(g) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:13, or

(h) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:14; or

(i) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:14; or

(j) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:14; or

(k) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:14; or

(l) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:14; or

(m) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:14, or

(n) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:15; or

(o) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:15; or

(p) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:15; or

(q) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:15; or

(r) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:15; or

(s) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:15.

26. The polynucleotide of claim 22 or 23, wherein the hGALNS expression cassette further comprises a nucleotide sequence encoding a liver- and muscle-specific promoter, wherein the nucleotide sequence encoding the liver- and muscle-specific is operably linked to the nucleotide sequence encoding the fusion protein.

27. The polynucleotide of claim 26, wherein the liver- and muscle-specific promoter:

(a) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:16; or

(b) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:16; or

(c) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:16; or

(d) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:16; or

(e) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:16; or

(f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:16.

28. The polynucleotide of claim 22 or 23, wherein the hGALNS expression cassette further comprises a nucleotide sequence encoding a promoter, wherein the nucleotide sequence encoding the promoter is operably linked to the nucleotide sequence encoding the fusion protein.

29. The polynucleotide of claim 28, wherein the promoter is a CAG promoter.

30. A polynucleotide comprising an hGALNS expression cassette flanked by AAV-ITRs, the hGALNS expression cassette comprising a nucleotide sequence encoding a liver-specific promoter and a nucleotide sequence encoding hGALNS, wherein the nucleotide sequence encoding the liver-specific promoter is operably linked to the nucleotide sequence encoding hGALNS, wherein the liver-specific promoter:
    (a) is a TBG promoter; or
    (b) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:13; or
    (c) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:13; or
    (d) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:13; or
    (e) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:13; or
    (f) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:13; or
    (g) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:13, or
    (h) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:14; or
    (i) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:14; or
    (j) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:14; or
    (k) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:14; or
    (l) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:14; or
    (m) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:14, or
    (n) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:15; or

(o) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:15; or

(p) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:15; or

(q) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:15; or

(r) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:15; or

(s) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:15.

31. A polynucleotide comprising an hGALNS expression cassette flanked by AAV-ITRs, the hGALNS expression cassette comprising a nucleotide sequence encoding a promoter and a nucleotide sequence encoding hGALNS, wherein the nucleotide sequence encoding the promoter is operably linked to the nucleotide sequence encoding hGALNS, wherein the promoter is a CAG promoter.

32. A polynucleotide comprising an hGALNS expression cassette flanked by AAV-ITRs, the hGALNS expression cassette comprising a nucleotide sequence encoding a liver- and muscle-specific promoter and a nucleotide sequence encoding hGALNS, wherein the nucleotide sequence encoding the liver- and muscle-specific promoter is operably linked to the nucleotide sequence encoding hGALNS, wherein the liver- and muscle-specific promoter:

(a) comprises a nucleotide sequence that is at least about 80% identical to SEQ ID NO:16; or

(b) comprises a nucleotide sequence that is at least about 85% identical to SEQ ID NO:16; or

(c) comprises a nucleotide sequence that is at least about 90% identical to SEQ ID NO:16; or

(d) comprises a nucleotide sequence that is at least about 95% identical to SEQ ID NO:16; or

(e) comprises a nucleotide sequence that is at least about 98% identical to SEQ ID NO:16; or

(f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO:16.

33. The polynucleotide of any one of claims 22-32, wherein the AAV is AAV8.
34. The polynucleotide of any one of claims 22-32, wherein the AAV is AAV9.
35. An rAAV plasmid comprising the polynucleotide of any one of claims 22-34.
36. An *ex vivo* cell comprising the polynucleotide of any one of claims 22-34 or the rAAV plasmid of claim 35.
37. A method of making an rAAV comprising transfecting an *ex vivo* cell with the rAAV plasmid of claim 35 and one or more helper plasmids collectively comprising the nucleotide sequences of AAV genes Rep, Cap, VA, E2a and E4.
38. Use of the rAAV of any one of claims 1-20 or the pharmaceutical composition of claim 21 in the manufacture of a medicament for treating a human subject diagnosed with mucopolysaccharidosis type IVA (MPS IVA).
39. Use of the rAAV of any one of claims 1-5 and 7-12 in the manufacture of a medicament for treating a human subject diagnosed with mucopolysaccharidosis type IVA (MPS IVA), wherein the medicament is to be administered to the bone, cartilage, ligament, meniscus, growth plate, liver, spleen, lung, kidney, trachea, heart muscle, and/or heart valve of the human subject, and wherein the medicament comprises a therapeutically effective amount of a fusion protein that is hGALNS fused to an acidic oligopeptide.
40. The use of claim 39, wherein the hGALNS is glycosylated with mannose-6-phosphate by having been produced in and secreted from a liver cell.
41. Use of the rAAV of any one of claims 13-14 and 16-20 in the manufacture of a medicament for treating a human subject diagnosed with mucopolysaccharidosis type IVA (MPS IVA), wherein the medicament comprises a therapeutically effective amount of hGALNS that is glycosylated with mannose-6-phosphate by having been produced in and secreted from a liver cell, wherein the medicament is to be administered to the bone, cartilage, ligament, meniscus, growth plate, liver, spleen, lung, kidney, trachea, heart muscle, and/or heart valve of the human subject.
42. Use of a fusion protein that is hGALNS fused to an acidic oligopeptide in the manufacture of a medicament for treating a human subject diagnosed with mucopolysaccharidosis type IVA (MPS IVA), wherein the medicament is to be administered to the bone, cartilage, ligament, meniscus, growth plate, liver, spleen, lung,

kidney, trachea, heart muscle, and/or heart valve of the human subject, and wherein the fusion protein is produced from an rAAV genome.

43. Use of a fusion protein that is hGALNS fused to an acidic oligopeptide in the manufacture of a medicament for treating a human subject diagnosed with mucopolysaccharidosis type IVA (MPS IVA), wherein the medicament is to be administered to the bone, cartilage, ligament, meniscus, growth plate, liver, spleen, lung, kidney, trachea, heart muscle, and/or heart valve of the human subject, and wherein the fusion protein is produced from an rAAV genome and is glycosylated with mannose-6-phosphate by having been produced in and secreted from a liver cell.
44. Use of hGALNS that is produced from an rAAV genome and is glycosylated with mannose-6-phosphate by having been produced in and secreted from a liver cell in the manufacture of a medicament for treating a human subject diagnosed with mucopolysaccharidosis type IVA (MPS IVA), wherein the medicament is to be administered to the bone, cartilage, ligament, meniscus, growth plate, liver, spleen, lung, kidney, trachea, heart muscle, and/or heart valve of the human subject.
45. The use of any one of claims 42-44, wherein the AAV is AAV8.
46. The use of any one of claims 42-44, wherein the AAV is AAV9.
47. The use of any one of claims 39-46, wherein the step of delivering to the bone, cartilage, ligament, meniscus, growth plate, liver, spleen, lung, kidney, trachea, heart muscle, and/or heart valve is a step of delivering to the bone and/or cartilage.
48. The use of any one of claims 39-46, wherein the step of delivering to the bone, cartilage, ligament, meniscus, growth plate, liver, spleen, lung, kidney, trachea, heart muscle, and/or heart valve is a step of delivering to (a) the bone and/or cartilage, and (b) ligament, meniscus, growth plate, liver, spleen, lung, kidney, trachea, heart muscle, and/or heart valve.
49. A recombinant adeno-associated virus (rAAV) comprising:

    (a) an AAV capsid; and

    (b) a recombinant AAV genome comprising a human N-acetylgalactosamine-6-sulfate sulfatase (hGALNS) expression cassette flanked by AAV-inverted terminal repeats (ITRs), the hGALNS expression cassette comprising a nucleotide sequence encoding a transgene, wherein the transgene encodes hGALNS.

50. The rAAV of claims 49, wherein the AAV is AAV8.
51. The rAAV of claim 49, wherein the AAV is AAV9.
52. The rAAV of claim 49, wherein the nucleotide sequence encoding hGALNS is codon-optimized.
53. The rAAV of claim 49, wherein the nucleotide sequence encoding hGALNS has CpG sites depleted.