

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 bone-liver tandem promoter and a nucleotide sequence encoding a transgene, wherein the transgene encodes hGALNS, wherein the bone-liver tandem promoter comprises a bone-specific promoter and a liver-specific promoter, and wherein the nucleotide sequence encoding the bone-liver tandem promoter is operably linked to the nucleotide sequence encoding the transgene.
2. 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 bone-liver tandem promoter and a nucleotide sequence encoding a transgene, wherein the transgene encodes a fusion protein that is hGALNS fused to an acidic oligopeptide, wherein the bone-liver tandem promoter comprises a bone-specific promoter and a liver-specific promoter, and wherein the nucleotide sequence encoding the bone-liver tandem promoter is operably linked to the nucleotide sequence encoding the transgene.
3. The rAAV of claim 2, wherein the acidic oligopeptide is D8.
4. The rAAV of any one of claims 1-3, wherein the bone-specific promoter is a Sp7/Osx promoter.
5. The rAAV of claim 4, wherein the Sp7/Osx promoter:
 - (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 23;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 23;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 23;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 23;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 23; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 23.

6. The rAAV of claim 4, wherein the Sp7/Osx promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 23.
7. The rAAV of any one of claims 1-3, wherein the bone-specific promoter is a minimal Sp7/Osx promoter.
8. The rAAV of claim 7, wherein the minimal Sp7/Osx promoter:
 - (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 24;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 24;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 24;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 24;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 24; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 24.
9. The rAAV of claim 7, wherein the minimal Sp7/Osx promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 24.
10. The rAAV of any one of claims 1-9, wherein the liver-specific promoter is an hAAT (Δ ATG) promoter.
11. The rAAV of claim 10, wherein the hAAT (Δ ATG) promoter:
 - (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 22;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 22;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 22;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 22;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 22; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 22.
12. The rAAV of claim 10, wherein the hAAT (Δ ATG) promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 22.
13. The rAAV of any one of claims 1-12, wherein the bone-liver tandem promoter further comprises a nucleotide sequence encoding an ApoE enhancer.
14. The rAAV of any one of claims 1-12, wherein the bone-liver tandem promoter further comprises a nucleotide sequence encoding a hepatic control region comprising an ApoE enhancer.
15. The rAAV of claim 13 or 14, wherein the ApoE enhancer:
 - (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 20;

- (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 20;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 20;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 20;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 20; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 20.
16. The rAAV of claim 13 or 14, wherein the ApoE enhancer comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 20.
17. The rAAV of claim 14, wherein the hepatic control region:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 19;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 19;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 19;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 19;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 19; or
 - (f) comprises a nucleotide sequence that is at least 100% identical to SEQ ID NO: 19.
18. The rAAV of claim 14, wherein the hepatic control region comprises a nucleotide sequence that is at least 100% identical to SEQ ID NO: 19.
19. The rAAV of any one of claims 1-3, wherein the bone-liver tandem promoter is an LBTP1 promoter.
20. The rAAV of claim 19, wherein the LBTP1 promoter:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 17;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 17;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 17;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 17;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 17; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 17.
21. The rAAV of claim 19, wherein the LBTP1 promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 17.
22. The rAAV of any one of claims 1-3, wherein the bone-liver tandem promoter is an LBTP2 promoter.
23. The rAAV of claim 22, wherein the LBTP2 promoter:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 18;

- (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 18;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 18;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 18;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 18; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 18.
24. The rAAV of claim 22, wherein the LBTP2 promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 18.
25. 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 Sp7/Osx promoter and a nucleotide sequence encoding a transgene, wherein the transgene encodes hGALNS, and wherein the nucleotide sequence encoding the Sp7/Osx promoter is operably linked to the nucleotide sequence encoding the transgene.
26. 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 Sp7/Osx promoter and a nucleotide sequence encoding a transgene, wherein the transgene encodes a fusion protein that is hGALNS fused to an acidic oligopeptide, and wherein the nucleotide sequence encoding the Sp7/Osx promoter is operably linked to the nucleotide sequence encoding the transgene.
27. The rAAV of claim 26, wherein the acidic oligopeptide is D8.
28. The rAAV of any one of claims 25-27, wherein the Sp7/Osx promoter:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 23;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 23;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 23;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 23;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 23; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 23.

29. The rAAV of any one of claims 25-27, wherein the Sp7/Osx promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 23.
30. 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 minimal Sp7/Osx promoter and a nucleotide sequence encoding a transgene, wherein the transgene encodes hGALNS, and wherein the nucleotide sequence encoding the minimal Sp7/Osx promoter is operably linked to the nucleotide sequence encoding the transgene.
31. 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 minimal Sp7/Osx promoter and a nucleotide sequence encoding a transgene, wherein the transgene encodes a fusion protein that is hGALNS fused to an acidic oligopeptide, and wherein the nucleotide sequence encoding the minimal Sp7/Osx promoter is operably linked to the nucleotide sequence encoding the transgene.
32. The rAAV of claim 31, wherein the acidic oligopeptide is D8.
33. The rAAV of any one of claims 30-32, wherein the minimal Sp7/Osx promoter:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 24;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 24;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 24;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 24;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 24; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 24.
34. The rAAV of any one of claims 30-32, wherein the minimal Sp7/Osx promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 24.
35. The rAAV of any one of claims 1-34, wherein the hGALNS expression cassette further comprises a nucleotide sequence encoding an intron.
36. The rAAV of claim 35, wherein the intron is a chimeric intron.

37. The rAAV of claim 36, wherein the chimeric intron is a β -globin/Ig intron.
38. The rAAV of claim 37, wherein the β -globin/Ig intron:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 10;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 10;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 10;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 10;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 10; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 10.
39. The rAAV of claim 37, wherein the β -globin/Ig intron comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 10.
40. The rAAV of any one of claims 1-39, wherein the nucleotide sequence encoding the transgene is codon-optimized.
41. The rAAV of any one of claims 1-40, wherein the nucleotide sequence encoding the transgene has CpG sites depleted.
42. The rAAV of any one of claims 1-41, wherein the nucleotide sequence encoding the transgene comprises a nucleotide sequence encoding hGALNS that:
- (a) is at least 80% identical to SEQ ID NO: 12;
 - (b) is at least 85% identical to SEQ ID NO: 12;
 - (c) is at least 90% identical to SEQ ID NO: 12;
 - (d) is at least 95% identical to SEQ ID NO: 12;
 - (e) is at least 98% identical to SEQ ID NO: 12; or
 - (f) is 100% identical to SEQ ID NO: 12.
43. The rAAV of any one of claims 1-41, wherein the nucleotide sequence encoding the transgene comprises a nucleotide sequence encoding hGALNS that is 100% identical to SEQ ID NO: 12.
44. The rAAV of any one of claims 1-43, wherein the nucleotide sequence encoding the transgene comprises a polyadenylation signal.
45. The rAAV of claim 44, wherein the polyadenylation signal is a β -globin polyadenylation signal.
46. The rAAV of claim 45, wherein the β -globin polyadenylation signal:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 25;

- (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 25;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 25;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 25;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 25; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 25.
47. The rAAV of claim 45, wherein the β -globin polyadenylation signal comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 25.
48. The rAAV of claim 44, wherein the polyadenylation signal is a rabbit globin poly A site.
49. The rAAV of claim 48, wherein the rabbit globin poly A site:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 9;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 9;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 9;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 9;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 9; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 9.
50. The rAAV of claim 48, wherein the rabbit globin poly A site comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 9.
51. The rAAV of any one of claims 1-50, wherein the AAV is AAV8.
52. The rAAV of any one of claims 1-50, wherein the AAV is AAV9.
53. A pharmaceutical composition comprising the rAAV of any one of claims 1-52 and a pharmaceutically acceptable carrier.
54. A polynucleotide comprising an hGALNS expression cassette flanked by AAV-ITRs, the hGALNS expression cassette comprising a nucleotide sequence encoding a bone-liver tandem promoter and a nucleotide sequence encoding a transgene, wherein the transgene encodes hGALNS, wherein the bone-liver tandem promoter comprises a bone-specific promoter and a liver-specific promoter, and wherein the nucleotide sequence encoding the bone-liver tandem promoter is operably linked to the nucleotide sequence encoding the transgene.
55. A polynucleotide comprising an hGALNS expression cassette flanked by AAV-ITRs, the hGALNS expression cassette comprising a nucleotide sequence encoding a bone-liver tandem promoter and a nucleotide sequence encoding a transgene, wherein the transgene

- encodes a fusion protein that is hGALNS fused to an acidic oligopeptide, wherein the bone-liver tandem promoter comprises a bone-specific promoter and a liver-specific promoter, and wherein the nucleotide sequence encoding the bone-liver tandem promoter is operably linked to the nucleotide sequence encoding the transgene.
56. The polynucleotide of claim 55, wherein the acidic oligopeptide is D8.
57. The polynucleotide of any one of claims 54-56, wherein the bone-specific promoter is a Sp7/Osx promoter.
58. The polynucleotide of claim 57, wherein the Sp7/Osx promoter:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 23;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 23;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 23;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 23;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 23; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 23.
59. The polynucleotide of claim 57, wherein the Sp7/Osx promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 23.
60. The polynucleotide of any one of claims 54-56, wherein the bone-specific promoter is a minimal Sp7/Osx promoter.
61. The polynucleotide of claim 60, wherein the minimal Sp7/Osx promoter:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 24;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 24;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 24;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 24;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 24; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 24.
62. The polynucleotide of claim 60, wherein the minimal Sp7/Osx promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 24.
63. The polynucleotide of any one of claims 54-62, wherein the liver-specific promoter is an hAAT (Δ ATG) promoter.
64. The polynucleotide of claim 63, wherein the hAAT (Δ ATG) promoter:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 22;

- (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 22;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 22;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 22;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 22; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 22.
65. The polynucleotide of claim 63, wherein the hAAT (Δ ATG) promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 22.
66. The polynucleotide of any one of claims 54-65, wherein the bone-liver tandem promoter further comprises a nucleotide sequence encoding an ApoE enhancer.
67. The polynucleotide of any one of claims 54-65, wherein the bone-liver tandem promoter further comprises a nucleotide sequence encoding a hepatic control region comprising an ApoE enhancer.
68. The polynucleotide of claim 66 or 67, wherein the ApoE enhancer:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 20;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 20;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 20;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 20;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 20; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 20.
69. The polynucleotide of claim 66 or 67, wherein the ApoE enhancer comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 20.
70. The polynucleotide of claim 67, wherein the hepatic control region:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 19;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 19;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 19;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 19;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 19; or
 - (f) comprises a nucleotide sequence that is at least 100% identical to SEQ ID NO: 19.
71. The polynucleotide of claim 67, wherein the hepatic control region comprises a nucleotide sequence that is at least 100% identical to SEQ ID NO: 19.

72. The polynucleotide of any one of claims 54-56, wherein the bone-liver tandem promoter is an LBTP1 promoter.
73. The polynucleotide of claim 72, wherein the LBTP1 promoter:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 17;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 17;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 17;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 17;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 17; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 17.
74. The polynucleotide of claim 72, wherein the LBTP1 promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 17.
75. The polynucleotide of any one of claims 54-56, wherein the bone-liver tandem promoter is an LBTP2 promoter.
76. The polynucleotide of claim 75, wherein the LBTP2 promoter:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 18;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 18;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 18;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 18;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 18; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 18.
77. The polynucleotide of claim 75, wherein the LBTP2 promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 18.
78. A polynucleotide comprising an hGALNS expression cassette flanked by AAV-ITRs, the hGALNS expression cassette comprising a nucleotide sequence encoding a Sp7/Osx promoter and a nucleotide sequence encoding a transgene, wherein the transgene encodes hGALNS, and wherein the nucleotide sequence encoding the Sp7/Osx promoter is operably linked to the nucleotide sequence encoding the transgene.
79. A polynucleotide comprising an hGALNS expression cassette flanked by AAV-ITRs, the hGALNS expression cassette comprising a nucleotide sequence encoding a Sp7/Osx promoter and a nucleotide sequence encoding a transgene, wherein the transgene encodes a fusion protein that is hGALNS fused to an acidic oligopeptide, and wherein the

nucleotide sequence encoding the Sp7/Osx promoter is operably linked to the nucleotide sequence encoding the transgene.

80. The polynucleotide of claim 79, wherein the acidic oligopeptide is D8.
81. The polynucleotide of any one of claims 78-80, wherein the Sp7/Osx promoter:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 23;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 23;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 23;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 23;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 23; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 23.
82. The polynucleotide of any one of claims 78-80, wherein the Sp7/Osx promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 23.
83. A polynucleotide comprising an hGALNS expression cassette flanked by AAV-ITRs, the hGALNS expression cassette comprising a nucleotide sequence encoding a minimal Sp7/Osx promoter and a nucleotide sequence encoding a transgene, wherein the transgene encodes hGALNS, and wherein the nucleotide sequence encoding the minimal Sp7/Osx promoter is operably linked to the nucleotide sequence encoding the transgene.
84. A polynucleotide comprising an hGALNS expression cassette flanked by AAV-ITRs, the hGALNS expression cassette comprising a nucleotide sequence encoding a minimal Sp7/Osx promoter and a nucleotide sequence encoding a transgene, wherein the transgene encodes a fusion protein that is hGALNS fused to an acidic oligopeptide, and wherein the nucleotide sequence encoding the minimal Sp7/Osx promoter is operably linked to the nucleotide sequence encoding the transgene.
85. The polynucleotide of claim 84, wherein the acidic oligopeptide is D8.
86. The polynucleotide of any one of claims 83-85, wherein the minimal Sp7/Osx promoter:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 24;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 24;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 24;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 24;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 24; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 24.

87. The polynucleotide of any one of claims 83-85, wherein the minimal Sp7/Osx promoter comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 24.
88. The polynucleotide of any one of claims 54-87, wherein the hGALNS expression cassette further comprises a nucleotide sequence encoding an intron.
89. The polynucleotide of claim 88, wherein the intron is a chimeric intron.
90. The polynucleotide of claim 89, wherein the chimeric intron is a β -globin/Ig intron.
91. The polynucleotide of claim 90, wherein the β -globin/Ig intron:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 10;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 10;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 10;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 10;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 10; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 10.
92. The polynucleotide of claim 90, wherein the β -globin/Ig intron comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 10.
93. The polynucleotide of any one of claims 54-92, wherein the nucleotide sequence encoding the transgene is codon-optimized.
94. The polynucleotide of any one of claims 54-93, wherein the nucleotide sequence encoding the transgene has CpG sites depleted.
95. The polynucleotide of any one of claims 54-94, wherein the nucleotide sequence encoding the transgene comprises a nucleotide sequence encoding hGALNS that:
- (a) is at least 80% identical to SEQ ID NO: 12;
 - (b) is at least 85% identical to SEQ ID NO: 12;
 - (c) is at least 90% identical to SEQ ID NO: 12;
 - (d) is at least 95% identical to SEQ ID NO: 12;
 - (e) is at least 98% identical to SEQ ID NO: 12; or
 - (f) is 100% identical to SEQ ID NO: 12.
96. The polynucleotide of any one of claims 54-94, wherein the nucleotide sequence encoding the transgene comprises a nucleotide sequence encoding hGALNS that is 100% identical to SEQ ID NO: 12.

97. The polynucleotide of any one of claims 54-96, wherein the nucleotide sequence encoding the transgene comprises a polyadenylation signal.
98. The polynucleotide of claim 97, wherein the polyadenylation signal is a β -globin polyadenylation signal.
99. The polynucleotide of claim 98, wherein the β -globin polyadenylation signal:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 25;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 25;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 25;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 25;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 25; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 25.
100. The polynucleotide of claim 98, wherein the β -globin polyadenylation signal comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 25.
101. The polynucleotide of claim 97, wherein the polyadenylation signal is a rabbit globin poly A site.
102. The polynucleotide of claim 101, wherein the rabbit globin poly A site:
- (a) comprises a nucleotide sequence that is at least 80% identical to SEQ ID NO: 9;
 - (b) comprises a nucleotide sequence that is at least 85% identical to SEQ ID NO: 9;
 - (c) comprises a nucleotide sequence that is at least 90% identical to SEQ ID NO: 9;
 - (d) comprises a nucleotide sequence that is at least 95% identical to SEQ ID NO: 9;
 - (e) comprises a nucleotide sequence that is at least 98% identical to SEQ ID NO: 9; or
 - (f) comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 9.
103. The polynucleotide of claim 101, wherein the rabbit globin poly A site comprises a nucleotide sequence that is 100% identical to SEQ ID NO: 9.
104. The polynucleotide of any one of claims 54-103, wherein the AAV is AAV8.
105. The polynucleotide of any one of claims 54-103, wherein the AAV is AAV9.
106. An rAAV plasmid comprising the polynucleotide of any one of claims 54-105.
107. An *ex vivo* cell comprising the polynucleotide of any one of claims 54-105 or the rAAV plasmid of claim 106.

108. A method of making an rAAV comprising transfecting an *ex vivo* cell with the rAAV plasmid of claim 106 and one or more helper plasmids collectively comprising the nucleotide sequences of AAV genes Rep, Cap, VA, E2a and E4.
109. A method for treating a human subject diagnosed with mucopolysaccharidosis type IVA (MPS IVA), comprising administering to the human subject the rAAV of any one of claims 1-52 or the pharmaceutical composition of claim 53.
110. A method for treating a human subject diagnosed with MPS IVA, comprising delivering to the bone and liver of the human subject a therapeutically effective amount of hGALNS or a fusion protein that is hGALNS fused to an acidic oligopeptide, by administering to the human subject an rAAV of any one of claims 1-24, or of any one of claims 35-52 when dependent directly or indirectly on any one of claims 1-24.
111. The method of claim 110, wherein the hGALNS or the fusion protein is glycosylated with mannose-6-phosphate by having been produced in and secreted from a liver cell.
112. A method for treating a human subject diagnosed with MPS IVA, comprising delivering to the bone of the human subject a therapeutically effective amount of hGALNS or a fusion protein that is hGALNS fused to an acidic oligopeptide, by administering to the human subject an rAAV of any one of claims 25-34, or of any one of claims 35-52 when dependent directly or indirectly on any one of claims 25-34.
113. 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 a transgene, wherein the transgene encodes hGALNS, wherein the nucleotide sequence encoding the promoter is operably linked to the nucleotide sequence encoding the transgene, and wherein the nucleotide sequence encoding the transgene comprises:
 - (a) a nucleotide sequence that is at least 80% identical to SEQ ID NO: 27;
 - (b) a nucleotide sequence that is at least 85% identical to SEQ ID NO: 27;
 - (c) a nucleotide sequence that is at least 90% identical to SEQ ID NO: 27;
 - (d) a nucleotide sequence that is at least 95% identical to SEQ ID NO: 27;

- (e) a nucleotide sequence that is at least 98% identical to SEQ ID NO: 27; or
 - (f) a nucleotide sequence that is 100% identical to SEQ ID NO: 27.
114. The rAAV of claim 13, wherein the AAV capsid is an AAV8 capsid or a variant thereof.
115. The rAAV of claim 13, wherein the AAV capsid is an AAV9 capsid or a variant thereof.
116. 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 a transgene, and wherein the nucleotide sequence encoding the promoter is operably linked to the nucleotide sequence encoding the transgene.
117. The rAAV of any one of claims 113-115 or the polynucleotide of claim 116, wherein the promoter is TBG.
118. The rAAV of any one of claims 113-115 or 117 or the polynucleotide of any one of claims 116-117, wherein the nucleotide sequence encoding the promoter comprises:
- (a) a nucleotide sequence that is at least 80% identical to SEQ ID NO: 6;
 - (b) a nucleotide sequence that is at least 85% identical to SEQ ID NO: 6;
 - (c) a nucleotide sequence that is at least 90% identical to SEQ ID NO: 6;
 - (d) a nucleotide sequence that is at least 95% identical to SEQ ID NO: 6;
 - (e) a nucleotide sequence that is at least 98% identical to SEQ ID NO: 6; or
 - (f) a nucleotide sequence that is 100% identical to SEQ ID NO: 6.
119. The rAAV of any one of claims 113-115 or the polynucleotide of claim 116, wherein the promoter is CAG.
120. The rAAV of any one of claims 113-115 or 119 or the polynucleotide of any one of claims 116 or 119, wherein the nucleotide sequence encoding the promoter comprises:
- (a) a nucleotide sequence that is at least 80% identical to SEQ ID NO: 28;
 - (b) a nucleotide sequence that is at least 85% identical to SEQ ID NO: 28;
 - (c) a nucleotide sequence that is at least 90% identical to SEQ ID NO: 28;
 - (d) a nucleotide sequence that is at least 95% identical to SEQ ID NO: 28;
 - (e) a nucleotide sequence that is at least 98% identical to SEQ ID NO: 28; or
 - (f) a nucleotide sequence that is 100% identical to SEQ ID NO: 28.

121. The rAAV of any one of claims 113-115 or the polynucleotide of claim 116, wherein the promoter is LSPX1.
122. The rAAV of any one of claims 113-115 or 121 or the polynucleotide of any one of claims 116 or 121, wherein the nucleotide sequence encoding the promoter comprises:
- (a) a nucleotide sequence that is at least 80% identical to SEQ ID NO: 13;
 - (b) a nucleotide sequence that is at least 85% identical to SEQ ID NO: 13;
 - (c) a nucleotide sequence that is at least 90% identical to SEQ ID NO: 13;
 - (d) a nucleotide sequence that is at least 95% identical to SEQ ID NO: 13;
 - (e) a nucleotide sequence that is at least 98% identical to SEQ ID NO: 13; or
 - (f) a nucleotide sequence that is 100% identical to SEQ ID NO: 13.
123. The rAAV of any one of claims 113-115 or the polynucleotide of claim 116, wherein the promoter is LMTP6.
124. The rAAV of any one of claims 113-115 or 123 or the polynucleotide of any one of claims 116 or 124, wherein the nucleotide sequence encoding the promoter comprises:
- (a) a nucleotide sequence that is at least 80% identical to SEQ ID NO: 16;
 - (b) a nucleotide sequence that is at least 85% identical to SEQ ID NO: 16;
 - (c) a nucleotide sequence that is at least 90% identical to SEQ ID NO: 16;
 - (d) a nucleotide sequence that is at least 95% identical to SEQ ID NO: 16;
 - (e) a nucleotide sequence that is at least 98% identical to SEQ ID NO: 16; or
 - (f) a nucleotide sequence that is 100% identical to SEQ ID NO: 16.
125. The rAAV of any one of claims 113-115 or the polynucleotide of claim 116, wherein the promoter is LBTP2.
126. The rAAV of any one of claims 113-115 or 125 or the polynucleotide of any one of claims 116 or 125, wherein the nucleotide sequence encoding the promoter comprises:
- (a) a nucleotide sequence that is at least 80% identical to SEQ ID NO: 18;
 - (b) a nucleotide sequence that is at least 85% identical to SEQ ID NO: 18;
 - (c) a nucleotide sequence that is at least 90% identical to SEQ ID NO: 18;
 - (d) a nucleotide sequence that is at least 95% identical to SEQ ID NO: 18;
 - (e) a nucleotide sequence that is at least 98% identical to SEQ ID NO: 18; or
 - (f) a nucleotide sequence that is 100% identical to SEQ ID NO: 18.

127. The rAAV of any one of claims 113-115 or 117-126 or the polynucleotide of any one of claims 116-126, wherein the AAV-ITRs is AAV2-ITRs.
128. A pharmaceutical composition comprising the rAAV of any one of claims 113-115 or 117-127 and a pharmaceutically acceptable carrier.
129. A method for treating a human subject diagnosed with mucopolysaccharidosis type IVA (MPS IVA), comprising administering to the human subject the rAAV of any one of claims 113-115 or 117-127 or the pharmaceutical composition of claim 128.