What is claimed is:

~~1. A method for treating hepatosplenomegaly in a human subject diagnosed with mucopolysaccharidosis type II (MPS II), the method comprising administering to the cerebrospinal fluid (CSF) of the human subject in need of treatment a recombinant adeno-associated virus vector (rAAV) encoding human iduronate-2-sulfatase (hIDS).~~

~~2. A method for treating hepatosplenomegaly and central nervous system (CNS) symptoms in a human subject diagnosed with MPS II, the method comprising administering to the CSF of the human subject in need of treatment a single dose of an rAAV encoding hIDS, wherein no additional therapy for MPS II is administered outside the CNS.~~

1. Use of a human iduronate-2-sulfatase (hIDS) in the preparation of a composition for treating mucopolysaccharidosis II (MPS II) in a human subject, wherein:

a. the level of D2S6 present in a biological sample obtained from the human subject is measured;

b. the human subject is diagnosed with MPS II when the level of D2S6 in the biological sample is higher than a reference; and

c. the composition is suitable to be delivered to the central nervous system (CNS) of the human subject diagnosed with MPS II.

2. Use of a human iduronate-2-sulfatase (hIDS) in the preparation of a composition for treating mucopolysaccharidosis II (MPS II) in a human subject, wherein the composition is suitable to be delivered to the central nervous system (CNS) of the human subject diagnosed with MPS II, and wherein the level of D2S6 present in a biological sample obtained from the human subject is measured after the composition is delivered to the CNS.

~~3.~~ 3. The ~~method~~use of claim ~~0, wherein the CNS symptom is cognitive ability as measured by the Bayley Scale of Infant and Toddler Development, 3rd Edition (BSID-III).~~1 or 2, wherein a ratio of D2S6 to total heparan sulfate disaccharides (HS) in the biological sample is calculated, wherein the total HS comprises disaccharides D2S6, D0A0, D0S0, and D0A6.

~~4. The method of claim 0, wherein the CNS symptom is language as measured by the language domain of the BSID III.~~

~~5. The method of claim 0, wherein the CNS symptom is motor function as determined by the motor domain of the BSID-III.~~

~~6. A method of delivering to the liver and/or spleen of a human subject diagnosed with MPS II an rAAV encoding hIDS, the method comprising administering a single dose of the rAAV to the CSF of the human subject.~~

~~7. The method of any one of claims 0-0, wherein the methods results in the size of the liver decreasing by about 10%, about 20%, or about 30% compared to the size of the liver prior to administration of the rAAV.~~

~~8. The method of any one of claims 0-0, wherein the method results in the size of the spleen decreasing by about 10%, about 20%, or about 30% compared to the size of the spleen prior to administration of the rAAV.~~

~~9. A method for treating a human subject diagnosed with MPS II, the method comprising (i) administering to the CSF of the human subject a therapeutically effective amount of an rAAV encoding hIDS and (ii) measuring the levels of heparin sulfate (HS) D2S6 in the CSF of the subject.~~

~~10.~~ 4. The ~~method~~use of claim ~~0~~3, wherein ~~the reduction in HS D2S6 correlates with improved neurocognitive parameters in~~ the human subject is determined to be responsive to the hIDS if the D2S6 level is at least 20% of the total HS.

~~11. The method of claim 0 or 0, further comprising a step of determining whether an additional treatment is required.~~

~~12. The method of claim 0, further comprising a step of administering an additional treatment.~~

~~13. The method of claim 0, wherein the additional treatment is a second administration of the same rAAV as in step (i).~~

~~14. The method of claim 0, wherein the additional treatment is a second administration of the same rAAV as in step (i) at a higher dose.~~

~~15. The method of claim 0, wherein the additional treatment is enzyme replacement therapy with recombinant idursulfase.~~

~~16. The method of anyone of claims 0-0, wherein the method results in a decrease in the levels of HS D2S6 in the CSF of the subject of about 10%, about 20%, about 30, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, or more than 95% compared to the levels of HS D2S6 in the CSF of the subject prior to administration of the rAAV.~~

~~17. The method of claim 0, wherein the levels of HS D2S6 are determined about 2 months, about 4 months, about 6 months, about 8 months, about 10 months, about 12 months, about 18 months, about 24 months, about 3 years, about 4 years, or about 5 years after administration of the rAAV.~~

~~18. The method of claim 0 or 0, wherein the decrease in levels of HS D2S6 is sustained for at least 6 months, at least 9 months, at last 12 months, at least 15 months, at least 18 months, at least 21 months, or at least 24 months after administration of the rAAV.~~

~~19.~~ 5. The ~~method~~use of any one of claims ~~0-0~~1-4, wherein the ~~rAAV is administered at a dose of about 1.3×10^{10} GC/g brain mass, about 6.5×10^{10} GC/g brain mass, or about 2×10^{11} GC/g brain mass, as determined by MRI.~~composition is suitable to be delivered to the CNS via a medicament comprising an adeno-associated virus (AAV) vector comprising a nucleotide sequence encoding hIDS.

~~20. The method of any one of claims 0-0, wherein the human subject is 5 years old or older and less than 18 years old.~~

~~21. The method of any one of claims 0-0, wherein the human subject is 4 months old or older and less than 5 years old.~~

~~22.~~ 6. The ~~method~~use of any one of claims ~~0-0~~1-4, wherein the ~~human subject is receiving~~composition is suitable to be delivered to the CNS via an enzyme replacement therapy ~~(ERT) at the time of the administration of the rAAV~~with recombinant hIDS.

~~23. The method of claim 0, wherein the human subject is not responsive to ERT.~~

~~24. The method of claim 0 or 0, wherein the ERT is recombinant idursulfase.~~

~~25.~~ 7. The ~~method~~use of any one of ~~claim 0-0~~claims 1-4, wherein the ~~ERT is discontinued about 6 months, about 90 months, about 12 months, about 15 months, about 18 months, about 21 months, or about 24 months after the administration of the rAAV.~~composition is suitable to be delivered via a viral vector, liposome, a lipid-containing complex, a macromolecular complex, a synthetic modified mRNA, an unmodified mRNA, a small molecule, a non-biologically active molecule, a polymerized molecule, a naked DNA, a plasmid, a phage, a transposon, a cosmid, or an episome.

8. The use of any one of claims 1-7, wherein the composition is suitable to be delivered to the CNS via intrathecal, intracisternal (IC), intravenous, or intracerebroventricular (ICV) administration.

~~26.~~ 9. The ~~method~~use of any one of claims ~~0-0~~1-7, wherein the ~~rAAV is administered~~composition is suitable to be delivered to the CNS via intracisternal (IC) ~~administration~~or intracerebroventricular (ICV) injection.

~~27. The method of any one of claims 0-0, wherein the rAAV is administered via intracerebroventricular (ICV) administration.~~

~~28.~~ 10. The ~~method~~use of any one of claims ~~0-0~~1-9, wherein the ~~rAAV is administered at a volume that does not exceed 10% of the total~~biological sample is obtained from the cerebrospinal fluid ~~volume~~(CSF) of the human subject.

~~29. The method of any one of claims 0-0, wherein the rAAV is a recombinant adeno-associated virus serotype 9~~

~~30. The method of claim 0, wherein the rAAV contains a human IDS expression cassette, wherein expression is driven by a hybrid of the cytomegalovirus (CMV) enhancer and the chicken beta actin promoter (CB7),~~

31. The method of claim 0, wherein the human IDS expression cassette comprises (i) an IDS transgene flanked by inverted terminal repeats (ITRs), (ii) the chicken beta-actin intron, and (iii) a rabbit beta-globin polyadenylation (polyA) signal.

32. The method of claim 0, wherein the ITRs are AAV2 ITRs.

33. The method of any one of claims 0-0, wherein the human IDS expression cassette comprises a nucleic acid comprising the nucleotide sequence of SEQ ID NO:45.

34. The method of any one of claims 0-0, further comprising administering an immune suppression therapy to the human subject before or concurrently with the rAAV and optionally continuing immune suppression therapy thereafter.

35. The method of claim 0, wherein the immune suppression therapy comprises administering one or more corticosteroids, sirolimus, and/or tacrolimus.

36. The method of claim 0, wherein the one or more corticosteroids are methylprednisolone and/or prednisone.

37. The method of any one of claims 0-0, further comprising administering one or more antibiotics to the human subject before or concurrently with the rAAV.

38. The method of claim 0, wherein the one or more antibiotics are trimethoprim, sulfamethoxazole, pentamidine, dapsone, and/or atovaquone.

39. The method of any one of claims 0-0, further comprising administering one or more antifungal therapies to the human subject before or concurrently with rAAV.

40. A method of treating a human subject diagnosed with MPS II, comprising:

(a) administering a therapeutically effective amount of an rAAV encoding hIDS to the human subject, wherein the human subject was treated with ERT or is being treated with ERT; and

(b) discontinuing ERT treatment in the human subject if the level of at least one biomarker in a biological sample from the human subject is lower than a reference, wherein the biological sample was obtained from the human subject after the administering, and wherein the at least one biomarker comprises D2S6, HS, and/or total GAG.

~~41. A method of treating a human subject diagnosed with MPS II comprising:~~

~~(a) administering a therapeutically effective amount of an rAAV encoding hIDS to the human subject, wherein the human subject was treated with ERT or is being treated with ERT; and~~

~~(b) discontinuing ERT treatment in the human subject if the level of at least one biomarker in a biological sample from the human subject is higher than a reference, wherein the biological sample was obtained from the human subject before the administering, and wherein the at least one biomarker is an anti-IDS antibody.~~

~~42. The method of claim 0, wherein the at least one biomarker is D2S6.~~

~~43. The method of any one of claims 0 or 0, wherein the at least one biomarker is about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% lower than the reference before ERT is discontinued.~~

~~44. The method of claim 0, wherein the at least one biomarker is about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% higher than the reference before ERT is discontinued.~~

~~45. The method of any one of claims 0-0, wherein the reference is a predetermined value.~~

~~46.~~ 11. The ~~method~~use of any one of claims ~~0-0~~1 and 3-10, wherein the reference is the level of ~~the at least one biomarker in a biological~~D2S6 in a CSF sample obtained from ~~the~~a human subject ~~prior to administration of the rAAV to the human subject~~with attenuated MPS II.

~~47.~~ 12. The ~~method~~use of any one of claims ~~0-0~~1 and 3-10, wherein the reference is the level of ~~the at least one biomarker in a biological~~D2S6 in a CSF sample obtained from a human subject not diagnosed with MPS II ~~but not receiving ERT~~.

~~48.~~ 13. The ~~method~~use of any one of claims ~~0-0~~1-12, wherein the ~~ERT treatment is discontinued on the same day that the rAAV is administered to the human subject~~MPS II is neuronopathic MPS II.

~~49.~~ 14. The ~~method~~use of any one of claims ~~0 or 0-0~~1-13, wherein ~~the ERT treatment is discontinued 52 weeks after the rAAV is administered to~~ the human subject~~.~~ is:

a) an adult human subject;

~~50. The method of any one of claims 0-0, wherein the biological sample is CSF, urine, plasma, or serum.~~

b) younger than 18 years old;

c) 5 years old or older and younger than 18 years old; or

d) 4 months old or older and younger than 5 years old.

~~51. A method of treating a human subject diagnosed with MPS II comprising:~~

~~(a) discontinuing ERT treatment in the human subject, wherein the human subject was treated with ERT or is being treated with ERT; and~~

~~(b) administering a therapeutically effective amount of an rAAV encoding hIDS to the human subject, wherein the administering is after ERT treatment is discontinued in the human subject.~~

~~52. The method of claim 51, wherein the ERT treatment is discontinued about or at least about 1 year, 6 months, 5 months, 4 months, 3 months, 2 months, 1 month, 3 weeks, 2 weeks, 1 week, 10 days, 5 days, or one day before the administering.~~

~~53~~15. The ~~method~~use of any one of claims ~~51-52~~1 and 3-14, wherein the level of ~~at least one biomarker is not detected~~D2S6 present in a biological sample obtained from the human subject ~~prior to the discontinuing.~~

is monitored after step c, wherein

~~54. The method of claim 53, wherein the at least one biomarker is an anti-AAV antibody.~~

~~55. The method of claim 54, wherein the anti-AAV antibody is an anti-AAV9 antibody.~~

~~56. The method of any one of claims 51-55, wherein the biological sample is serum.~~

~~57. A method of determining efficacy or monitoring efficacy of MPS II treatment in a human subject, comprising administering a therapeutically effective amount of an rAAV encoding hIDS to the human subject, wherein~~ a decrease in the level of D2S6 ~~in a biological sample from the human subject as~~ compared to ~~a reference~~the level of D2S6 measured in step a is indicative of ~~efficacy of the MPS II~~ treatment ~~in the human subject, wherein the biological sample was obtained from the human subject after the administering~~.

16. The use of claim 15, wherein the biological sample obtained after step c is obtained from the human subject after about 1, 2, 3, 4, 5, 6, 7, 8, 10, 16, 20, 24, 30, 35, 40, 45, 48, 50, 52, or 56 weeks, or 1, 2, 3, 4, 5, or 6 months after step c.

~~58. The method of any one of claims 0-57, wherein the human subject has hepatosplenomegaly.~~

17. The use of claim 15, wherein the decrease in the level of D2S6 after step c is about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, or 90%, as compared to the level of D2S6 measured in step a.

~~59. The method of claim 58, wherein the human subject was treated with ERT prior to the administering and/or received ERT treatment after the administering.~~

~~60. The method of any one of claims 0-59, wherein the ERT is enzyme replacement therapy with recombinant idursulfase.~~

~~61. The method of any one of claims 57-60, wherein the biological sample is CSF.~~

~~62~~18. The ~~method~~use of any one of claims ~~57-61~~1 and 3-14, wherein the ~~decrease in the~~ level of D2S6 is ~~a decrease of~~higher by about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% ~~as compared to~~than the reference.

~~63. The method of any one of claims 57-62, wherein the efficacy of MPS II treatment is an improvement in at least one subtest of the Bayley Scales of Infant and Toddler Development, 3rd Edition (BSID-III) as compared to a reference.~~

~~64. The method of claim 63, wherein the at least one subtest is age equivalence score, cognitive developmental quotient (DQ), expressive language DQ, receptive language DQ, gross motor DQ, and/or fine motor DQ.~~

~~65. The method of claim 63 or 64, wherein the improvement is an improvement in DQ of about or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, 17, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, or more than 100.~~

~~66. The method of claim 64, wherein the age equivalence score is increased by about or at least about 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 monts, 8 months, 9 months, 10 months, 11 months, 12 months, 18 months, 24 months, or more than 24 months.~~

~~67. The method of any one of claims 63-66, wherein the reference is the score of the at least one subtest of the BSID-III obtained from the human subject prior to the administering.~~

~~68. The method of any one of claims 63-66, wherein the reference is an average score of the at least one subtest of the BSID-III obtained from human subjects with MPS II of the same age as the human subject.~~

~~69~~19. The ~~method~~use of any one of claims ~~57-68~~2, 3-10, 13, and 14, wherein the ~~reference is the~~ level of D2S6 is measured in a first biological sample obtained from the human

subject ~~prior to the administering.~~before the composition is delivered to the human subject and the level of D2S6 present in a second biological sample obtained from the human subject is measured after the composition is delivered to the human subject, and wherein the first and second biological samples are obtained from the cerebrospinal fluid (CSF) of the human subject.

~~70. The method of any one of claims 57-69, wherein the biological sample was obtained from the human subject at about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320, 330, 340, 350, 360, 370, 380, 390, 400, 410, 420, 430, 440, 450, 460, 470, 480, 490 days, or 1, 2, 3, 4, 5, 6, 7, 8, 10, 16, 20, 24, 30, 35, 40, 45, 48, 50, 52, 56, 104 weeks, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 months, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 years after the administering.~~

~~71. The method of any one of claims 51-70, wherein the human subject is a pediatric subject.~~

~~72. The method of any one of claims 57-71, wherein the efficacy of MPS II treatment is demonstrated by a decrease in the level of D2S6 of about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% as compared to the level of D2S6 in the human subject prior to the administering.~~

~~73. The method of any one of claims 1-72, wherein the rAAV is administered intrathecally to the human subject.~~

~~74. The method of any one of claims 1-73, wherein the rAAV is administered to the human subject in a solution comprising:~~

~~(a) sodium chloride at a concentration of about 8.77 g/L,~~

~~(b) magnesium chloride, at a concentration of about 0.244 g/L,~~

~~(c) potassium chloride at a concentration of about 0.224 g/L,~~

~~(d) calcium chloride at a concentration of about 0.206 g/L,~~

~~(e) dextrose at a concentration of about 0.793 g/L,~~

~~(f) poloxamer 188 at a concentration of about 0.001% (volume/volume),~~

~~(g) sodium phosphate monobasic monohydrate at a concentration of about 0.0278 g/L, and~~

(h) sodium phosphate dibasic anhydrous at a concentration of about 0.114 g/L.

75. A method of identifying or diagnosing a subject as having neuronopathic MPS II, wherein the method comprises:

(a) determining the level of one or more heparan sulfate disaccharide(s) in a biological sample from the subject;

(b) identifying or diagnosing the subject as having neuronopathic MPS II if the level of the one or more heparan sulfate disaccharide(s) is elevated as compared to a reference level; and

(c) administering a therapeutically effective amount of an rAAV encoding hIDS to the subject identified or diagnosed as having neuronopathic MPS II.

76. The method of claim 75, wherein the one or more heparan sulfate disaccharide(s) comprises one or more of D0A0, D0S0, D0A6, D2S6, or a combination thereof.

77. The method of claim 76, wherein the one or more heparan sulfate disaccharide(s) is D2S6.

78. A method of identifying or diagnosing a subject as having neuronopathic MPS II, wherein the subject is identified or diagnosed as having neuronopathic MPS II if the level of D2S6 in a biological sample from the subject is elevated as compared to a reference level, and wherein a therapeutically effective amount of an rAAV encoding hIDS is administerd to the subject identified or diagnosed as having neuronopathic MPS II.

79. The method of any one of claims 75-78, wherein the biological sample is cerebrospinal fluid.

80. The method of any one of claims 75-79, wherein the subject is presymptomatic or has no visible or detectable MPS II symptom.

81. The method of any one of claims 75-80, wherein the subject has MPS II.

~~82. The method of any one of claims 75-77 and 79-81, wherein the reference level is the level of the at least one or more heparan sulfate disaccharide(s) in a biological sample from one or more healthy subjects and/or from one or more non-neuronopathic subjects.~~

~~83. The method of any one of claims 77-81, wherein the reference level is the level of D2S6 in a biological sample from one or more healthy subjects. and/or from one or more non-neuronopathic subjects.~~

~~84. The method of claim 82 or 83, wherein the biological sample from one or more healthy subjects and/or from one or more non-neuronopathic subjects is a CSF sample.~~

~~85. The method of any one of claims 75-84, wherein the reference level is a pre-determined level.~~

~~86. The method of any one of claims 77-85, wherein the level of D2S6 is about or at least about 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19%, 20%, 25%, 30%, 35%, 40%, or higher than 40% of the total heparan sulfate disaccharides (HS) in the biological sample from the subject.~~

~~87. The method of claim 86, wherein the level of D2S6 is about or at least about 20% of the total heparan sulfate disaccharides (HS) in the biological sample from the subject.~~

~~88. The method of any one of claims 75-87, wherein the level of the one or more heparan sulfate disaccharide(s) or the level of D2S6 in the biological sample from the subject is about or at least about 50 ng/mL, 75 ng/mL, 80 ng/mL, 85 ng/mL, 90 ng/mL, 95 ng/mL, 100 ng/mL, 105 ng/mL, 110 ng/mL, 115 ng/mL, 120 ng/mL, 125 ng/mL, 130 ng/mL, 135 ng/mL, 140 ng/mL, 145 ng/mL, 150 ng/mL, 155 ng/mL, 160 ng/mL, 165 ng/mL, 170 ng/mL, 175 ng/mL, 180 ng/mL, 185 ng/mL, 190 ng/mL, 195 ng/mL, 200 ng/mL, 210 ng/mL, 220 ng/mL, 230 ng/mL, 240 ng/mL, 250 ng/mL, 260 ng/mL, 270 ng/mL, 280 ng/mL, 290 ng/mL, 300 ng/mL, 310 ng/mL, 320 ng/mL, 330 ng/mL, 340 ng/mL, 350 ng/mL, 360 ng/mL, 370 ng/mL, 380 ng/mL, 390 ng/mL, 400 ng/mL, or more than 400 ng/mL.~~

89. The method of any one of claims 75-88, wherein the level of the one or more heparan sulfate disaccharide(s) or the level of D2S6 in the biological sample from the subject is about or at least about 100 ng/mL, 110 ng//mL, 120 ng/mL, 130 ng/mL, 140 ng/mL, 150 ng/mL, 160 ng/mL, 170 ng/mL, 180 ng/mL, 190 ng/ mL, 200 ng/mL, or more than 200 ng/mL.

90. The method of any one of claims 75-89, wherein the level of the one or more heparan sulfate disaccharide(s) or the level of D2S6 in the biological sample from the subject is elevated by about or at least about 10 ng/mL, 20 ng/mL, 30 ng/mL, 40 ng/mL, 50 ng/mL, 60 ng/mL, 70 ng/mL, 80 ng/mL, 90 ng/mL, 100 ng/mL, 150 ng/mL, 160 ng/mL, 170 ng/mL, 180 ng/mL, 190 ng/mL, 200 ng/mL, 210 ng/mL, 220 ng/mL, 230 ng/mL, 240 ng/mL, 250 ng/mL, 260 ng/mL, 270 ng/mL, 280 ng/mL, 290 ng/mL, 300 ng/mL, 310 ng/mL, 320 ng/mL, 330 ng/mL, 340 ng/mL, 350 ng/mL, 360 ng/mL, 370 ng/mL, 380 ng/mL, 390 ng/mL, 400 ng/mL, 410 ng/mL, 420 ng/mL, 430 ng/mL, 440 ng/mL, 450 ng/mL, 460 ng/mL, 470 ng/mL, 480 ng/mL, 490 ng/mL, 500 ng/mL, or more than 500 ng/mL as compared to the reference level.

91. A method of determining efficacy or monitoring efficacy of MPS I treatment in a human subject, comprising administering a therapeutically effective amount of an rAAV encoding human IDUA to the human subject, wherein a decrease in the level of I0S6 in a biological sample from the human subject as compared to a reference is indicative of efficacy of the MPS I treatment in the human subject, wherein the biological sample was obtained from the human subject after the administering.

92. The method of claim 91, wherein the biological sample is plasma.

93. The method of claim 90 or 91, wherein the human subject was treated with ERT prior to the administering and/or received ERT treatment after the administering.

94. The method of any one of claims 91-93, wherein the ERT is enzyme replacement therapy with recombinant idursulfase.

~~95. The method of any one of claims 91-94, wherein the decrease in the level of I0S6 is a decrease of about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% as compared to the reference.~~

~~96. The method of any one of claims 91-95, wherein the reference is the level of I0S6 in a biological sample obtained from the human subject prior to the administering.~~

~~97~~20. The ~~method~~use of any one of claims ~~91-95~~1 and 3-18, wherein the reference is a predetermined value.

~~98. The method of any one of claims 91-95, wherein the reference is the level of I0S6 in a biological sample obtained from another human subject diagnosed with MPS I or a population of human subjects diagnosed with MPS I.~~

~~99. The method of any one of claims 91-98, wherein the efficacy of MPS I treatment is an improvement in at least one subtest of the Bayley Scales of Infant and Toddler Development, 3rd Edition (BSID-III) as compared to a reference.~~

~~100. The method of claim 99, wherein the at least one subtest is age equivalence score, cognitive developmental quotient (DQ), expressive language DQ, receptive language DQ, gross motor DQ, and/or fine motor DQ.~~

~~101. The method of claim 99 or 100, wherein the reference is the score of the at least one subtest of the BSID-III obtained from the human subject prior to the administering.~~

~~102. The method of any one of claims 99-101, wherein the reference is an average score of the at least one subtest of the BSID-III obtained from human subjects with MPS I of the same age as the human subject.~~

~~103. The method of any one of claims 91-102, wherein the rAAV is administered to the human subject in a solution comprising:~~

~~(a) sodium chloride at a concentration of about 8.77 g/L,~~

~~(b) magnesium chloride, at a concentration of about 0.244 g/L,~~

~~(c) potassium chloride at a concentration of about 0.224 g/L,~~

~~(d) calcium chloride at a concentration of about 0.206 g/L,~~

~~(e) dextrose at a concentration of about 0.793 g/L,~~

~~(f) poloxamer 188 at a concentration of about 0.001% (volume/volume),~~

~~(g) sodium phosphate monobasic monohydrate at a concentration of about 0.0278 g/L, and~~

~~(h) sodium phosphate dibasic anhydrous at a concentration of about 0.114 g/L.~~