WHAT IS CLAIMED IS:

1. Use of a recombinant adeno-associated virus (rAAV) in the manufacture of a medicament for a method of treating CLN2 Batten disease in a subject in need thereof, the recombinant adeno-associated virus (rAAV) is to be administered to the subject via a first route and a second route, wherein said first route and said second route are into the central nervous system (CNS), wherein said first route is into the brain region and said second route is into the spinal cord region, and

wherein said recombinant adeno-associated virus (rAAV) comprises an AAV capsid and a vector genome packaged therein, and wherein said vector genome comprising:

(a) an AAV 5' inverted terminal repeat (ITR) sequence;

(b) a promoter;

(c) a CLN2 coding sequence encoding a human TPP1; and

(d) an AAV 3' ITR.

2. The use of claims 1, wherein said first route is intracerebroventricular (ICV) or intracisternal (IC).

3. The use according to any one of claims 1 to 2, wherein said second route is intrathecal-lumbar (IT-L).

4. The use according to any one of claims 1 to 3, wherein said rAAV is to be administered to said subject via a third route, wherein said third route is selected from the group consisting of intracerebroventricular (ICV), intracisternal (IC), intrathecal-lumbar, intracranial, intravenous, intravascular, intraarterial, intramuscular, intraocular, subcutaneous, and intradermal.

5. Use of a recombinant adeno-associated virus (rAAV) in the manufacture of medicament for a method of treating CLN2 Batten disease in a subject in need thereof, the recombinant adeno-associated virus (rAAV) is to be administered to the subject via a first route and a second route, wherein said first route is into the central nervous system (CNS), wherein said second route delivers the rAAV to the liver, and

wherein said recombinant adeno-associated virus (rAAV) comprises an AAV capsid and a vector genome packaged therein, and wherein said vector genome comprising:

(a) an AAV 5' inverted terminal repeat (ITR) sequence;

(b) a promoter;

(c) a CLN2 coding sequence encoding a human TPP1; and

(d) an AAV 3' ITR.

6. The use of claims 5, wherein said first route is intrathecal-lumbar (IT-L), intracerebroventricular (ICV) or intracisternal (IC).

7. The use according to any one of claims 5 to 6, wherein said second route is selected from the group consisting of intravenous, intravascular, intraarterial, intramuscular, intraocular, subcutaneous, and intradermal.

8. The use according to claim 7, wherein said second route is intravenous.

9. The use according to any one of claims 1 to 8, wherein said rAAV is to be administered to the subject via said first route simultaneously with the administration of said rAAV via said second route.

10. The use according to any one of claims 1 to 8, wherein said rAAV is to be administered via said first route prior to the administration of said rAAV via said second route.

11. The use according to any one of claims 1 to 8, wherein said rAAV is to be administered via said first route after administration of said rAAV via said second route.

12. The use according to any one of claims 10 to 11, wherein the interval between administration of said rAAV via said first route and administration of said rAAV via said second route is about 0.5 hour, about 1 hour, about 2 hours, about 3 hours, about 4 hours, about 5 hours, about 6 hours, about 7 hours, about 8 hours, about 9 hours, about 10 hours, about 11 hours, about 12 hours, about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 1 week, about 8 days, about 9 days, about 10 days, about 11 days, about 12 days, about 13 days, about 2 weeks, about 3 weeks, about 4 weeks, about 5 weeks, about 6 weeks, about 7 weeks, about 8 weeks, about 9 weeks, about 10 weeks, about 11 weeks, about 12 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, or more.

13. The use according to any one of claims 1 to 12, wherein said medicament results in a TPP1 activity in the spinal cord of said subject that is at least 2%, 3%, 5%, 6%, 7%, 8%, 9%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, or 50% higher than a reference TPP1 activity in the spinal cord of a second subject, and wherein the reference TPP1 activity in the spinal cord is measured when said second subject does not receive the treatment using said medicament, and wherein said second subject is the same or different from said subject.

14. The use according to any one of claims 1 to 13, wherein said medicament results in a hepatic TPP1 activity of said subject that is at least 2%, 3%, 5%, 6%, 7%, 8%, 9%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, or 50% higher than a reference hepatic TPP1 activity in a second subject, and wherein the reference hepatic TPP1 activity is measured when said second subject does not receive the treatment using said medicament, and wherein said second subject is the same or different from said subject.

15. The use according to any one of claims 1 to 14, wherein said medicament results in a serum TPP1 activity of said subject that is at least 2%, 3%, 5%, 6%, 7%, 8%, 9%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, or 50% higher than a reference serum TPP1 activity in a second subject, and wherein the reference serum TPP1 activity is measured when said second subject does not receive the treatment using said medicament, and wherein said second subject is the same or different from said subject.

16. The use according to any one of claims 1 to 15, wherein said medicament results in a microglial activity in the cortex of said subject that is at least 2%, 3%, 5%, 6%, 7%, 8%, 9%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, or 50% lower than a reference microglial activity in the cortex in a second subject, and wherein the reference microglial activity in the cortex is measured when said second subject does not receive the treatment using said medicament, and wherein said second subject is the same or different from said subject.

17. The use according to any one of claims 1 to 16, wherein said medicament results in a TPP1 activity in the brain of said subject that is at least 2%, 3%, 5%, 6%, 7%, 8%, 9%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, or 50% higher than a reference TPP1 activity in the brain of a second subject, wherein the reference TPP1 activity in the brain is

measured when said second subject does not receive the treatment using said medicament, and wherein said second subject is the same or different from said subject.

18. The use according to any one of claims 1 to 17, wherein said rAAV is to be administered in a therapeutically effective amount.

19. The use according to any one of claims 1 to 18, wherein said subject is human.

20. The use according to any one of claims 1 to 19, wherein the coding sequence of (c) is a codon optimized human CLN2, which is at least 70% identical to the native human coding sequence of SEQ ID NO: 2.

21. The use according to any one of claims 1 to 20, wherein the coding sequence of (c) is SEQ ID NO: 3.

22. The use according to any one of claims 1 to 21, wherein the rAAV capsid is an AAV9 or a variant thereof.

23. The use according to any one of claims 1 to 22, wherein the promoter is a chicken beta actin (CBA) promoter.

24. The use according to any one of claims 1 to 23, wherein the promoter is a hybrid promoter comprising a CBA promoter sequence and cytomegalovirus enhancer elements.

25. The use according to any of claims 1 to 24, wherein the AAV 5' ITR and/or AAV3' ITR is from AAV2.

26. The use according to any of claims 1 to 25, wherein the vector genome further comprises a polyA.

27. The use according to claim 26, wherein the polyA is a synthetic polyA or from bovine growth hormone (bGH), human growth hormone (hGH), SV40, rabbit β-globin (RGB), or modified RGB (mRGB).

28. The use according to any of claims 1 to 27, wherein the vector genome further comprises an intron.

29. The use according to claim 28, wherein the intron is from CBA, human beta globin, IVS2, SV40, bGH, alpha-globulin, beta-globulin, collagen, ovalbumin, or p53.

30. The use according to any of claims 1 to 29, wherein the vector genome further comprises an enhancer.

31. The use according to claim 30, wherein the enhancer is a CMV enhancer, an RSV enhancer, an APB enhancer, ABPS enhancer, an alpha mic/bik enhancer, TTR enhancer, en34, ApoE.

32. The use according to any of claims 1 to 31, wherein the vector genome is about 3 kilobases to about 5.5 kilobases in size.

33. The use according to any of claims 1 to 32, wherein the vector genome is about 4 kilobases in size.

34. The use according to any of claims 1 to 33, wherein the rAAV is manufactured using a method comprising growing in suspension culture a suspension cell line that is capable of producing the rAAV.

35. The use according to claim 34, wherein said suspension cell line is HEK293 suspension cell line.

36. A pharmaceutical composition comprising:
(a) a recombinant adeno-associated virus (rAAV),
(b) sodium chloride,
(c) magnesium chloride,
(d) potassium chloride,
(e) dextrose,
(f) poloxamer 188,
(g) sodium phosphate monobasic, and

(h) sodium phosphate dibasic,
wherein said recombinant adeno-associated virus (rAAV) comprises an AAV capsid and a vector genome packaged therein, and wherein said vector genome comprising: (i) an AAV 5' inverted terminal repeat (ITR) sequence; (ii) a promoter; (iii) a CLN2 coding sequence encoding a human TPP1; and (iv) an AAV 3' ITR.

37. The pharmaceutical composition according to claim 36 further comprising calcium chloride.

38. The pharmaceutical composition according to claim 37, wherein said sodium chloride, said magnesium chloride, said potassium chloride, said dextorse, said poloxamer 188, said sodium phosphate monobasic, said sodium phosphate dibasic, and said calcium chloride are each in anhydrous, monohydrate, dihydrate, 3-hydrate, 4-hydrate, 5-hydrate, 6-hydrate, 7-hydrate, 8-hydrate, 9-hydrate, or 10-hydrate form.

39. The pharmaceutical composition according to any one of claims 36 to 38 comprising:
(a) said rAAV,
(b) sodium chloride at a concentration of about 8.77 g/L,
(c) magnesium chloride 6-hydrate, at a concentration of about 0.244 g/L,
(d) potassium chloride at a concentration of about 0.224 g/L,
(e) calcium chloride dihydrate at a concentration of about 0.206 g/L,
(f) dextorse anhydrous at a concentration of about 0.793 g/L,
(g) poloxamer 188 at a concentration of about 0.001% (volume/volume),
(h) sodium phosphate monobasic monohydrate at a concentration of about 0.0278 g/L, and
(i) sodium phosphate dibasic anhydrous at a concentration of about 0.114 g/L.

40. The pharmaceutical composition according to any one of claims 36 to 39, wherein the vector genome concentration (VGC) of the pharmaceutical composition is about 1×10^{11} GC/mL, about 3×10^{11} GC/mL, about 6×10^{11} GC/mL, about 1×10^{12} GC/mL, about 3×10^{12} GC/mL, about 6×10^{12} GC/mL, about 1×10^{13} GC/mL, about 2×10^{13} GC/mL, about 3×10^{13} GC/mL, about 4×10^{13} GC/mL, about 5×10^{13} GC/mL, about 6×10^{13} GC/mL, about 7×10^{13} GC/mL, about 8×10^{13} GC/mL, about 9×10^{13} GC/mL, or about 1×10^{14} GC/mL, about 3×10^{14} GC/mL, about 6×10^{14} GC/mL, or about 1×10^{15} GC/mL.

41. The pharmaceutical composition according to any one of claims 36 to 40, wherein the pH of the pharmaceutical composition is in a range from about 6.0 to about 9.0.

42. The pharmaceutical composition according to claim 41, wherein the pH of the pharmaceutical composition is about 7.4.

43. The pharmaceutical composition according to any one of claims 36 to 42, wherein said rAAV is at least 2%, 5%, 7%, 10%, 12%, 15%, 17%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 100%, 2 times, 3 times, 5 times, 10 times, 100 times, or 1000 more stable to freeze/thaw cycles than the same recombinant rAAV in a reference pharmaceutical composition.

44. The pharmaceutical composition according to claim 43, wherein the stability of said rAAV is determined by
(a) the infectivity of rAAV,
(b) the levels of aggregation of rAAV, or
(c) the levels of free DNA released by the rAAV.

45. The pharmaceutical composition according to any one of claims 36 to 44, wherein the pharmaceutical composition is a liquid composition.

46. The pharmaceutical composition according to any one of claims 36 to 44, wherein the pharmaceutical composition is a frozen composition.

47. The pharmaceutical composition according to any one of claims 36 to 44, wherein the pharmaceutical composition is a lyophilized composition or a reconstituted lyophilized composition.

48. The pharmaceutical composition according to any one of claims 36 to 47, wherein the pharmaceutical composition has a property that is suitable for intracerebroventricular (ICV), intracisternal (IC), intrathecal-lumbar, intracranial, intravenous, intravascular, intraarterial, intramuscular, intraocular, intramuscular, subcutaneous, or intradermal administration.

49. The pharmaceutical composition according to any one of claims 36 to 48, wherein the coding sequence of (iii) is a codon optimized human CLN2, which is at least 70% identical to the native human coding sequence of SEQ ID NO: 2.

50. The pharmaceutical composition according to any one of claims 36 to 49, wherein the coding sequence of (iii) is SEQ ID NO: 3.

51. The pharmaceutical composition according to any one of claims 36 to 50, wherein the rAAV capsid is an AAV9 or a variant thereof.

52. The pharmaceutical composition according to any one of claims 36 to 51, wherein the promoter is a chicken beta actin (CBA) promoter.

53. The pharmaceutical composition according to any one of claims 36 to 52, wherein the promoter is a hybrid promoter comprising a CBA promoter sequence and cytomegalovirus enhancer elements.

54. The pharmaceutical composition according to any one of claims 36 to 53, wherein the AAV 5' ITR and/or AAV3' ITR is from AAV2.

55. The pharmaceutical composition according to any one of claims 36 to 54, wherein the vector genome further comprises a polyA.

56. The pharmaceutical composition according to any one of claims 36 to 55, wherein the polyA is a synthetic polyA or from bovine growth hormone (bGH), human growth hormone (hGH), SV40, rabbit β-globin (RGB), or modified RGB (mRGB).

57. The pharmaceutical composition according to any one of claims 36 to 56, wherein the vector genome further comprises an intron.

58. The pharmaceutical composition according to any one of claims 36 to 57, wherein the intron is from CBA, human beta globin, IVS2, SV40, bGH, alpha-globulin, beta-globulin, collagen, ovalbumin, or p53.

59. The pharmaceutical composition according to any one of claims 36 to 58, wherein the vector genome further comprises an enhancer.

60. The pharmaceutical composition according to any one of claims 36 to 59, wherein the enhancer is a CMV enhancer, an RSV enhancer, an APB enhancer, ABPS enhancer, an alpha mic/bik enhancer, TTR enhancer, en34, ApoE.

61. The pharmaceutical composition according to any one of claims 36 to 60, wherein the vector genome is about 3 kilobases to about 5.5 kilobases in size.

62. The pharmaceutical composition according to any one of claims 36 to 61, wherein the vector genome is about 4 kilobases in size.

63. The pharmaceutical composition according to any one of claims 36 to 62, wherein the rAAV is manufactured using a method comprising growing in suspension culture a suspension cell line that is capable of producing the rAAV.

64. Use of the pharmaceutical composition according to any one of claims 36 to 63 in the manufacture of a medicament for a method of treating CLN2 Batten disease in a subject.

65. The use according to claim 64, wherein said pharmaceutical composition is to be administered in a therapeutically effective amount.

66. The use according to any one of claims 64 to 65, wherein said subject is human.

67. A kit comprising one or more containers and instructions for use, wherein the one or more containers comprise the pharmaceutical composition according to any one of claims 36 to 63.