

Claims

1. A nucleic acid molecule comprising a first AAV inverted terminal repeat sequence, a P546 promoter comprising the sequence of SEQ ID NO: 3, a nucleic acid sequence encoding the CLN3 polypeptide of SEQ ID NO: 1 and a second inverted terminal repeat sequence.
2. The nucleic acid molecule of claim 1 comprising, a first AAV inverted terminal repeat sequence, a P546 promoter comprising the nucleotide sequence of SEQ ID NO: 3, an SV40 intron, a nucleic acid sequence encoding the CLN3 polypeptide of SEQ ID NO: 1 and a second AAV inverted terminal repeat sequence.
3. The nucleic acid molecule of claim 1 comprising a first AAV inverted terminal repeat sequence, P546 promoter comprising the nucleotide sequence of SEQ ID NO: 3, a nucleic acid encoding the CLN3 polypeptide of SEQ ID NO: 1, a bovine growth hormone polyadenylation poly A sequence and a second AAV inverted terminal repeat sequence.
4. The nucleic acid molecule of any one of claims 1 to 3, wherein the nucleic acid encoding the CLN3 polypeptide comprises a sequence at least 90% identical to SEQ ID NO: 2.
5. The nucleic acid molecule of any one of claims 1 to 3, wherein the nucleic acid encoding the CLN3 polypeptide comprises the nucleic acid sequence of SEQ ID NO: 2.
6. The nucleic acid molecule of any one of claims 1 to 5, comprising a nucleic acid sequence at least 90% identical to the nucleic acid sequence of SEQ ID NO: 4.
7. The nucleic acid molecule of any one of claims 1 to 5, comprising a nucleic acid sequence at least 95% identical to the nucleic acid sequence of SEQ ID NO: 4.
8. The nucleic acid molecule of any one of claims 1 to 6 comprising a nucleic acid sequence of SEQ ID NO: 4.
9. The nucleic acid molecule of any one of claims 4 to 8, wherein the AAV inverted terminal repeats are AAV2 inverted terminal repeats.
10. A self-complementary recombinant adeno-associated virus 9 (scAAV9) comprising a nucleic acid molecule of any one of claims 1 to 9.
11. The scAAV9 of claim 10, wherein the scAAV9 comprising a single-stranded genome.

12. A rAAV particle comprising a nucleic acid molecule of any one of claims 1 to 9.
13. The rAAV particle of claim 12 wherein the rAAV particle comprising a single-stranded genome.
14. A composition comprising the scAAV of claim 10 or 11, the nucleic acid molecule of any one of claims 1 to 9, rAAV9 viral particle of claims 12 or 13 and a pharmaceutically acceptable excipient, carrier, or diluent.
15. The composition of claim 14, wherein the excipient comprises a non-ionic low osmolar compound, a buffer, a polymer, a salt, or a combination thereof.
16. Use of a therapeutically effective amount of the scAAV of claim 10 or 11, the nucleic acid molecule of any one of claims 1 to 9, rAAV9 viral particle of claim 12 or 13, or the composition of claim 14 or claim 15 for the preparation of a medicament for the treatment of CLN3 Batten Disease.
17. The use of claim 16, wherein the medicament is formulated for administration via a route selected from the group consisting of intrathecal, intracerebroventricular, intraparenchymal, intravenous, and a combination thereof.
18. The use of claim 16, wherein the medicament is formulated for intrathecal administration.
19. The use of claim 16, wherein the medicament is formulated for intracerebroventricular administration.
20. The use of claim 16, wherein the medicament is formulated for intravenous administration.
21. The use of any one of claims 16 to 20, wherein the medicament comprises about 1×10^{12} to about 1×10^{15} vg of the rAAV9 viral particle.
22. The use of any one of claims 16 to 21, wherein the medicament comprises about 6×10^{13} to about 1.2×10^{14} of the rAAV9 viral particle.
23. The use of any one of claims 16 to 22, wherein administration of the medicament reduces one or more symptoms of CLN3-Batten Disease selected from:
 - (a) reduced or slowed lysosomal accumulation of autofluorescent storage material,
 - (b) reduced or slowed lysosomal accumulation of ATP Synthase Subunit C,
 - (c) reduced or slowed glial activation (astrocytes and/or microglia) activation,
 - (d) reduced or slowed astrogliosis,
 - (e) reduced or slowed brain volume loss measured by MRI,

- (f) reduced or slowed onset of seizures,
- (g) stabilization, reduced or delayed progression, or improvement in one or more of the UBDRS assessment scales, wherein the reduction, stabilization, or improvement is as compared to the subject prior to administration of the composition or to an untreated CLN3-Batten Disease patient.
24. The use of any one of claims 16 to 23, wherein the subject is placed in the Trendelenberg position after administration of the rAAV9 viral particle.
25. A composition suitable for treating of CLN3 Batten Disease, wherein the composition comprises a therapeutically effective amount of the scAAV of claim 10 or 11, the nucleic acid molecule of any one of claims 1 to 9, rAAV9 viral particle of claim 12 or 13, or the composition of claim 14 or claim 15 for the preparation of a medicament for the treatment of CLN3 Batten Disease.
26. The composition of claim 25, wherein the composition is formulated for administration via a route selected from the group consisting of intrathecal, intracerebroventricular, intraparenchymal, intravenous, and a combination thereof.
27. The composition of claim 26, wherein the composition is formulated for intrathecal administration.
28. The composition of claim 26, wherein the composition is formulated for intracerebroventricular administration.
29. The composition of claim 26, wherein the composition is formulated for intravenous administration.
30. The composition of any one of claims 25 to 29, wherein the composition comprises about 1×10^{12} to about 1×10^{15} vg of the rAAV9 viral particles.
31. The composition of any one of claims 25 to 29, wherein the medicament comprises about 6×10^{13} to about 1.2×10^{14} of the rAAV9 viral particles.
32. The composition of any one of claims 25 to 31, wherein administration of the composition reduces one or more symptoms of CLN3-Batten Disease selected from:
- (a) reduced or slowed lysosomal accumulation of autofluorescent storage material,
 - (b) reduced or slowed lysosomal accumulation of ATP Synthase Subunit C,
 - (c) reduced or slowed glial activation (astrocytes and/or microglia) activation,

- (d) reduced or slowed astrocytosis,
- (e) reduced or slowed brain volume loss measured by MRI,
- (f) reduced or slowed onset of seizures,
- (g) stabilization, reduced or delayed progression, or improvement in one or more of the UBDRS assessment scales, wherein the reduction, stabilization, or improvement is as compared to the subject prior to administration of the composition or to an untreated CLN3-Batten Disease patient.