**What is claimed is:**

1. A method of treating a mammal having a lysosomal storage disease (LSD), said method comprising the steps:

(a) administering to the brain or spine of a mammal a plurality of AAV particles,

said AAV particles (i) comprising an AAV capsid protein and a nucleic acid inserted between a pair of AAV inverted terminal repeats (ITRs), said nucleic acid encoding a polypeptide having lysosomal hydrolase activity, and (ii) being capable of transducing cells of said mammal and providing expression of said polypeptide; and

(b) administering to said mammal a first immunosuppressive agent and a second immunosuppressive agent,

wherein at least one of said first immunosuppressive agent and said second immunosuppressive agent are administered to said mammal prior to administration of said AAV particles.

2. A method of treating a mammal according to Claim 1, wherein said polypeptide has tripeptidyl-peptidase 1 (TPP1) activity.

3. A method of treating a mammal according to Claim 2, wherein said polypeptide comprises TPP1, a pro-enzyme thereof, or an enzymatically active variant thereof.

4. A method of treating a mammal according to any one of Claims 1-3, wherein said first immunosuppressive agent is administered prior to administration of said AAV particles and said second immunosuppressive agent is administered prior to, concurrently with, or after administration of said AAV particles.

5. A method of treating a mammal according to any one of Claims 1-4, wherein said first immunosuppressive agent comprises cyclosporine.

6. A method of treating a mammal according to any one of Claims 1-5, wherein said second immunosuppressive agent comprises mycophenolate or a derivative thereof.

7. A method of treating a mammal according to Claim 6, wherein said mycophenolate derivative is mycophenolate mofitil (MMF).

8. A method of treating a mammal according to any one of Claims 1-7, wherein, tripeptidyl-peptidase 1 (TPP1) activity in the cerebrospinal fluid of said mammal is detectable at a level of at least 5 pmol TPP1/mg protein for greater than 350 days.

9. A method of treating a mammal according to any one of Claims 1-8, wherein cells comprising the cerebrospinal fluid (CSF) of said mammal are transduced by said AAV particles.

10. A method of treating a mammal according to any one of Claims 1-9, wherein (i) said first immunosuppressive agent is administered at least about two weeks prior to administration of said AAV particles and (ii) said second immunosuppressive agent is administered about two weeks before or within 40 days after administration of said AAV particles.

11. A method of treating a mammal according to any one of Claims 1-10, wherein administration of said AAV particles comprises administration to the cisterna magna, intraventricular space, brain ventricle, subarachnoid space, intrathecal space or ependyma of said mammal.

12. A method of treating a mammal according to any one of Claims 1-10, wherein administration of said AAV particles comprises administration to the cerebral spinal fluid (CSF) of said mammal.

13. A method of treating a mammal according to any one of Claims 1-10, wherein administration of said AAV particles comprises contacting ependymal cells of said mammal with said AAV particles.

14. A method of treating a mammal according to any one of Claims 1-13, wherein cells transduced with said AAV particles express and secrete said polypeptide into the CSF of said mammal.

15. A method of treating a mammal according to any one of Claims 1-10, wherein administration of said AAV particles comprises contacting a pial cell, endothelial cell, or meningeal cell of said mammal with said AAV particles.

16. A method of treating a mammal according to any one of Claims 1-15, wherein said mammal is a non-rodent mammal.

17. A method of treating a mammal according to Claim 16, wherein said non-rodent mammal is a primate, horse, sheep, goat, pig, or dog.

18. A method of treating a mammal according to Claim 16, wherein said non-rodent mammal is a human.

19. A method of treating a mammal according to Claim 18, wherein said human is a child.

20. A method of treating a mammal according to Claim 19, wherein said child is from about 1 to about 4 years of age.

21. A method of treating a mammal according to any one of Claims 1-20, wherein said LSD is infantile or late infantile ceroid lipofuscinoses (LINCL), neuronopathic Gaucher, Juvenile Batten, Fabry, MLD, Sanfilippo A, Hunter, Krabbe, Morquio, Pompe, Niemann-Pick C, Tay-Sachs, Hurler (MPS-I H), Sanfilippo B, Maroteaux-Lamy, Niemann-Pick A, Cystinosis, Hurler-Scheie (MPS-I H/S), Sly Syndrome (MPS VII), Scheie (MPS-I S), Infantile Batten, GM1 Gangliosidosis, Mucolipidosis type II/III, or Sandhoff disease.

22. A method of treating a mammal according to any one of Claims 1-21, wherein administration of said AAV particles comprises injection of said AAV particles into a tissue or fluid of the brain or spinal cord of said mammal.

23. A method of treating a mammal according to any one of Claims 1-21, wherein administration of said AAV particles comprises injection of said AAV particles into cerebral spinal fluid of said mammal.

24. A method of treating a mammal according to any one of Claims 1-23, wherein said AAV particles transduce ependymal cells of said mammal.

25. A method of treating a mammal according to any one of Claims 1-24, wherein onset of a symptom associated with said LSD is delayed by 5-10, 10-25, 25-50 or 50-100 days when said first immunosuppressive agent and second immunosuppressive agent are administered, compared to administration of said second immunosuppressive agent without prior administration of said first immunosuppressive agent.

26. A method of treating a mammal according to Claim 25, wherein said symptom is selected from the group consisting of proionceptive response, nystagmus, menace, pupillary light reflex, cerebellar ataxia and intention tremor.

27. A method of treating a mammal according to any one of Claims 1-21, wherein onset of a loss of cognitive function associated with said LSD is delayed by 5–10, 10–25, 25–50 or 50–100 days when said first immunosuppressive agent and second immunosuppressive agent are administered, compared to administration of said second immunosuppressive agent without prior administration of said first immunosuppressive agent.

28. A method of treating a mammal according to any one of Claims 1-27, wherein lifespan of a mammal having said LSD is extended by 5–10, 10–25, 25–50 or 50–100 days when said first immunosuppressive agent and second immunosuppressive agent are administered, compared to administration of said second immunosuppressive agent without prior administration of said first immunosuppressive agent.

29. A method of treating a mammal according to any one of Claims 5-28, wherein said cyclosporine is administered at a dosage of about 5–20 mg/kg twice a day for a period of at least 3 months.

30. A method of treating a mammal according to any one of Claims 5-28, wherein the dose of said cyclosporine administered is reduced after a 1–2 months after administration of said AAV particles.

31. A method of treating a mammal according to any one of Claims 6-30, wherein said mycophenolate or a derivative thereof is administered at a dosage of about 5–20 mg/kg a day.

32. A method of treating a mammal according to any one of Claims 1-31, wherein said AAV particles are administered at a dose of about $1\times10^{8}$ to about $1\times10^{15}$ vg/kg.

33. A method of treating a mammal according to any one of Claims 1-32, wherein neutralizing antibodies are not detected in CSF of said mammal for at least 30, 60, 90, 120 or more days after administration of said AAV particles.

34. A method of treating a mammal according to any one of Claims 1-32, wherein neutralizing antibodies are not detected in CSF of said mammal for at least 250 days after said administration of said AAV particles.

35. A method of treating a mammal according to any one of Claims 1-34, wherein said polypeptide is expressed in the spleen or heart of said mammal.

36. A method of treating a mammal according to any one of Claims 1-34, wherein said polypeptide is expressed in the cerebellum of said mammal.

37. A method of treating a mammal according to any one of Claims 1-36, wherein said AAV particles are selected from the group consisting of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, AAV-rh74, AAV-rh10 and AAV-2i8 particles.

38. A method of treating a mammal according to any one of Claims 1-36, wherein one or more of said ITRs is selected from the group consisting of an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, AAV-rh74, AAV-rh10 and AAV-2i8 ITR.

39. An AAV vector, comprising an AAV ITR sequence, a nucleic acid encoding TPP1, and an expression control element driving expression of the nucleic acid encoding TPP1.

40. An AAV particle comprising the AAV vector according to Claim 39 and an AAV capsid sequence.

41. The AAV vector or AAV particle according to Claim 39 or 40, wherein the AAV ITR sequence comprisesg one or more AAV2 ITRs.

42. The AAV vector or AAV particle according to any one of Claims 39-41, wherein the nucleic acid encodes mammalian TPP1.

43. The AAV vector or AAV particle according to any one of Claims 39-41, wherein the nucleic acid encodes human TPP1.

44. The AAV vector or AAV particle according to any one of Claims 39-41, wherein the nucleic acid encodes a protein with TPP1 activity and having 80% or more identity to human TPP1 set forth as SEQ ID NO:5.

45. The AAV vector or AAV particle according to any one of Claims 39-41, wherein the nucleic acid encodes human TPP1 set forth as SEQ ID NO:5.

46. The AAV vector or AAV particle according to any one of Claims 39-45, wherein the expression control element comprises a CMV enhancer.

47. The AAV vector or AAV particle according to any one of Claims 39-45, wherein the expression control element comprises a beta actin promoter.

48. The AAV vector or AAV particle according to any one of Claims 39-45, wherein the expression control element comprises a chicken beta actin promoter.

49. The AAV vector or AAV particle according to any one of Claims 39-45, wherein the expression control element comprises a CMV enhancer and a chicken beta actin promoter.

50. The AAV vector or AAV particle according to any one of Claims 39-45, wherein the expression control element comprises a sequence having 80% or more identity to SEQ ID NO:9.

51. The AAV vector or AAV particle according to any one of Claims 39-45, wherein the expression control element comprises SEQ ID NO:9.

52. The AAV particle according to Claim 40, wherein the capsid sequence comprises a VP1, VP2 and/or VP3 capsid sequence having 90% or more identity to AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, Rh10, Rh74 or AAV-2i8 VP1, VP2 and/or VP3 sequences.

53. The AAV particle according to any one of Claims 40-51, wherein the capsid sequence comprises a VP1 capsid sequence having 80% or more identity to AAV2, wherein the capsid sequence has a tyrosine at positions 444, 500 and/or 730 substituted with an amino acid that is not tyrosine.

54. The AAV particle according to any one of Claims 40-51, wherein the capsid sequence comprises a VP1 capsid sequence having 80% or more identity to.

55. The AAV particle according to any one of Claims 40-51, wherein the capsid sequence comprises a VP1 capsid sequence having 90% or more identity to AAV2, wherein the capsid sequence has a tyrosine at positions 444, 500 and/or 730 substituted with phenylalanine.

56. The AAV particle according to any one of Claims 40-51, wherein the capsid sequence comprises an AAV2 VP1 capsid sequence having a tyrosine at positions 444, 500 and/or 730 substituted with phenylalanine.

57. The AAV particle according to any one of Claims 40-51, wherein the capsid sequence of the vector comprises a VP1, VP2 or VP3 capsid sequence selected from any of: AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, Rh10, Rh74 or AAV-2i8 AAV serotypes.