WHAT IS CLAIMED IS:

1. A method for improving neural function in a mammal with a proteinopathy comprising administering a therapeutically effective amount of an agent that increases glucocerebrosidase activity in the mammal.

2. The method of claim 1, wherein the mammal has reduced neural function due to the proteinopathy.

3. A method for preventing loss of neural function in a mammal in need thereof comprising administering a therapeutically effective amount of an agent that increases glucocerebrosidase activity.

4. The method of claim 3, wherein the mammal has a proteinopathy.

5. A method for reducing toxic lipids, reducing α-synuclein, reducing tau or inhibiting the accumulation of protein aggregates in a mammal with a proteinopathy comprising administering a therapeutically effective amount of an agent that increases glucocerebrosidase activity.

6. The method of any one of claims 1-5, wherein the mammal has reduced glucocerebrosidase activity prior to administration of the agent.

7. The method of any one of claims 1-6, wherein the mammal has one or more mutations in the glucocerebrosidase 1 (GBA1) gene.

8. The method of claim 7, wherein the mutation is a D409V mutation.

9. The method of claim 5, wherein the method comprises reducing tau.

10. The method of claim 5, wherein the method comprises reducing α-synuclein.

11. The method of claim 5, wherein the method comprises reducing toxic lipids.

12. The method of claim 11, wherein the toxic lipid is glucosylsphingosine.

13. The method of claim 12, wherein the toxic glucosylsphingosine is reduced by at least about 30%.

14. The method of claim 12, wherein the toxic glucosylsphingosine is reduced by at least about 50%.

15. The method of claim 12, wherein the toxic glucosylsphingosine is reduced to a level not significantly different than a mammal without a proteinopathy.

16. The method of claim 5, wherein the method comprises inhibiting the accumulation of protein aggregates.

17. The method of claim 16, wherein the protein aggregates comprise a protein selected from the group consisting of ubiquitin, tau, and α-synuclein.

18. The method of any one of claims 1-17, wherein the mammal has been diagnosed with a disease selected from the group consisting of Alzheimer's disease, Gaucher disease, frontotemporal dementia, progressive supranuclear palsy, Parkinsonism, Parkinson's disease, Lytico-Bodig disease, dementia with Lewy bodies, tangle-predominant dementia, dementia pugilistica, Pick's disease, corticobasal degeneration, Argyrophilic grain disease, ganglioglioma and gangliocytoma, meningioangiomatosis, subacute sclerosing panencephalitis, lead encephalopathy, tuberous sclerosis, Hallervorden-Spatz disease, and lipofuscinosis.

19. The method of any one of claims 1, 2, and 4-18, wherein the proteinopathy comprises protein aggregates.

20. The method of claim 19, wherein the protein aggregates comprise a protein selected from the group consisting of ubiquitin, tau, and α-synuclein.

21. The method of claim 20, wherein the proteinopathy is a tauopathy.

22. The method of claim 21, wherein the tauopathy is a disease selected from the group consisting of Alzheimer's disease, frontotemporal dementia, progressive supranuclear palsy, Parkinsonism, Parkinson's disease, Lytico-Bodig disease, dementia with Lewy bodies, tangle- predominant dementia, dementia pugilistica, Pick's disease, corticobasal degeneration, Argyrophilic grain disease, ganglioglioma and gangliocytoma, meningioangiomatosis, subacute sclerosing panencephalitis, lead encephalopathy, tuberous sclerosis, Hallervorden-Spatz

disease, and lipofuscinosis.

23. The method of claim 20, wherein the proteinopathy is a synucleinopathy.

24. The method of any one of claims 1-23, wherein the agent comprises a small molecule, an antibody, a nucleic acid molecule, or a polypeptide.

25. The method of claim 24, wherein the agent is a nucleic acid encoding a GBA1 gene or equivalent thereof.

26. The method of claim 24, wherein the agent is a GBA1 polypeptide or equivalent thereof.

27. The method of claim 24, wherein the agent is an antibody that specifically binds GBA1.

28. The method of claim 24, wherein the agent is a small molecule.

29. The method of claim 28, wherein the small molecule is a small molecule activator of glucocerebrosidase activity.

30. The method of claim 24, wherein the agent is a virus.

31. The method of claim 30, wherein the virus comprises a nucleic acid encoding a GBA1 gene or an equivalent thereof.

32. The method of claim 25 or 31, wherein the GBA1 gene or equivalent thereof is operably linked to a promoter that regulates expression of the GBA1 protein.

33. The method of any one of claims 30-32, wherein the virus infects neuronal cells.

34. The method of any one of claims 30-33, wherein the virus is an adeno-associated virus (AAV).

35. The method of claim 34, wherein the AAV comprises an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAVrh8, AAV9, AAV10, AAVrh10, AAV11, or AAV12 serotype capsid.

36. The method of claim 34 or 35, wherein the AAV comprises an AAV serotype

capsid from Clades A-F.

37. The method of claim 34, wherein the AAV comprises an AAV serotype 1 capsid.

38. The method of any one of claims 34-37, wherein the AAV comprises an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAVrh8, AAV9, AAV10, AAVrh10, AAV11, or AAV12 inverted terminal repeat (ITR).

39. The method of any one of claims 34-38, wherein the AAV comprises an AAV ITR from Clades A-F.

40. The method of claim 38, wherein the AAV comprises an AAV serotype 2 ITR.

41. The method of any one of claims 34-40, wherein the ITR and the capsid are derived from the same AAV serotype.

42. The method of any one of claims 34-40, wherein the ITR and the capsid are derived from different AAV serotypes.

43. The method of claim 42, wherein the AAV comprises an AAV1 capsid and an AAV2 ITR.

44. The method of any one of claims 34-43, wherein the AAV is a self-complementary AAV.

45. The method of claim 44, wherein the nucleic acid comprises a first heterologous polynucleotide sequence encoding a GBA1 transgene and a second heterologous polynucleotide sequence encoding a complement of the GBA1 transgene, wherein the first heterologous polynucleotide sequence can form intrastrand base pairs with the second polynucleotide sequence.

46. The method of claim 45, wherein the first heterologous polynucleotide sequence and the second heterologous polynucleotide sequence are linked by a mutated AAV ITR.

47. The method of claim 46, wherein the mutated AAV ITR comprises a deletion of the D region and comprises a mutation of the terminal resolution sequence.

48. The method of any one of claims 32-47, wherein the promoter is capable of expressing the GBA1 gene or equivalent thereof in neurons of the central nervous system (CNS).

49. The method of any one of claims 32-48, wherein the promoter comprises a human β-glucuronidase promoter or a cytomegalovirus enhancer linked to a chicken β-actin promoter.

50. The method of any one of claims 1-49, wherein the agent is in a pharmaceutical composition.

51. The method of claim 50, wherein the pharmaceutical composition further comprises a pharmaceutically acceptable carrier.

52. The method of any one of claims 1-51, wherein the agent or pharmaceutical composition is administered by injection.

53. The method of claim 52, wherein the agent or pharmaceutical composition is administered into the CNS.

54. The method of claim 53, wherein the agent or pharmaceutical composition is administered via direct injection into the spinal cord, via intrathecal injection, via intracerebroventricular injection, or via intrahippocampal injection.

55. The method of any one of claims 1-54, wherein the method comprises increasing the glucocerebrosidase activity over baseline levels in a neuron of the mammal.

56. The method of claim 55, wherein the method comprises increasing the glucocerebrosidase activity by at least about 2 fold over baseline levels in the neuron of the mammal.

57. The method of claim 55, wherein the method comprises increasing the glucocerebrosidase activity by at least about 3 fold over baseline levels in the neuron of the mammal.

WHAT IS CLAIMED IS:

1. Use of a therapeutically effective amount of an agent for the manufacture of a medicament for improving neural function in a mammal with a proteinopathy wherein the agent increases glucocerebrosidase activity in the mammal.

2. The use of claim 1, wherein the mammal has reduced neural function due to the proteinopathy.

3. Use of a therapeutically effective amount of an agent for the manufacture of a medicament for preventing loss of neural function in a mammal in need thereof wherein the agent increases glucocerebrosidase activity.

4. The use of claim 3, wherein the mammal has a proteinopathy.

5. Use of a therapeutically effective amount of an agent for the manufacture of a medicament for reducing toxic lipids, reducing α-synuclein, reducing tau or inhibiting the accumulation of protein aggregates in a mammal with a proteinopathy wherein the agent increases glucocerebrosidase activity.

6. The use of any one of claims 1-5, wherein the mammal has reduced glucocerebrosidase activity prior to administration of the agent.

7. The use of any one of claims 1-6, wherein the mammal has one or more mutations in the glucocerebrosidase 1 (GBA1) gene.

8. The use of claim 7, wherein the mutation is a D409V mutation.

9. The use of claim 5, wherein the use comprises reducing tau.

10. The use of claim 5, wherein the use comprises reducing α-synuclein.

11. The use of claim 5, wherein the use comprises reducing toxic lipids.

12. The use of claim 11, wherein the toxic lipid is glucosylsphingosine.

13. The use of claim 12, wherein the toxic glucosylsphingosine is reduced by at least about 30%.

14. The use of claim 12, wherein the toxic glucosylsphingosine is reduced by at least about 50%.

15. The use of claim 12, wherein the toxic glucosylsphingosine is reduced to a level not significantly different than a mammal without a proteinopathy.

16. The use of claim 5, wherein the use comprises inhibiting the accumulation of protein aggregates.

17. The use of claim 16, wherein the protein aggregates comprise a protein selected from the group consisting of ubiquitin, tau, and α-synuclein.

18. The use of any one of claims 1-17, wherein the mammal has been diagnosed with a disease selected from the group consisting of Alzheimer's disease, Gaucher disease, frontotemporal dementia, progressive supranuclear palsy, Parkinsonism, Parkinson's disease, Lytico-Bodig disease, dementia with Lewy bodies, tangle-predominant dementia, dementia pugilistica, Pick's disease, corticobasal degeneration, Argyrophilic grain disease, ganglioglioma and gangliocytoma, meningioangiomatosis, subacute sclerosing panencephalitis, lead encephalopathy, tuberous sclerosis, Hallervorden-Spatz disease, and lipofuscinosis.

19. The use of any one of claims 1, 2, and 4-18, wherein the proteinopathy comprises protein aggregates.

20. The use of claim 19, wherein the protein aggregates comprise a protein selected from the group consisting of ubiquitin, tau, and α-synuclein.

21. The use of claim 20, wherein the proteinopathy is a tauopathy.

22. The use of claim 21, wherein the tauopathy is a disease selected from the group consisting of Alzheimer's disease, frontotemporal dementia, progressive supranuclear palsy, Parkinsonism, Parkinson's disease, Lytico-Bodig disease, dementia with Lewy bodies, tangle- predominant dementia, dementia pugilistica, Pick's disease, corticobasal degeneration, Argyrophilic grain disease, ganglioglioma and gangliocytoma, meningioangiomatosis, subacute sclerosing panencephalitis, lead encephalopathy, tuberous sclerosis, Hallervorden-Spatz

disease, and lipofuscinosis.

23. The use of claim 20, wherein the proteinopathy is a synucleinopathy.

24. The use of any one of claims 1-23, wherein the agent comprises a small molecule, an antibody, a nucleic acid molecule, or a polypeptide.

25. The use of claim 24, wherein the agent is a nucleic acid encoding a GBA1 gene or equivalent thereof.

26. The useof claim 24, wherein the agent is a GBA1 polypeptide or equivalent thereof.

27. The use of claim 24, wherein the agent is an antibody that specifically binds GBA1.

28. The use of claim 24, wherein the agent is a small molecule.

29. The use of claim 28, wherein the small molecule is a small molecule activator of glucocerebrosidase activity.

30. The use of claim 24, wherein the agent is a virus.

31. The use of claim 30, wherein the virus comprises a nucleic acid encoding a GBA1 gene or an equivalent thereof.

32. The use of claim 25 or 31, wherein the GBA1 gene or equivalent thereof is operably linked to a promoter that regulates expression of the GBA1 protein.

33. The use of any one of claims 30-32, wherein the virus infects neuronal cells.

34. The use of any one of claims 30-33, wherein the virus is an adeno-associated virus (AAV).

35. The use of claim 34, wherein the AAV comprises an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAVrh8, AAV9, AAV10, AAVrh10, AAV11, or AAV12 serotype capsid.

36. The use of claim 34 or 35, wherein the AAV comprises an AAV serotype capsid

from Clades A-F.

37. The use of claim 34, wherein the AAV comprises an AAV serotype 1 capsid.

38. The use of any one of claims 34-37, wherein the AAV comprises an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAVrh8, AAV9, AAV10, AAVrh10, AAV11, or AAV12 inverted terminal repeat (ITR).

39. The use of any one of claims 34-38, wherein the AAV comprises an AAV ITR from Clades A-F.

40. The use of claim 38, wherein the AAV comprises an AAV serotype 2 ITR.

41. The use of any one of claims 34-40, wherein the ITR and the capsid are derived from the same AAV serotype.

42. The use of any one of claims 34-40, wherein the ITR and the capsid are derived from different AAV serotypes.

43. The use of claim 42, wherein the AAV comprises an AAV1 capsid and an AAV2 ITR.

44. The use of any one of claims 34-43, wherein the AAV is a self-complementary AAV.

45. The use of claim 44, wherein the nucleic acid comprises a first heterologous polynucleotide sequence encoding a GBA1 transgene and a second heterologous polynucleotide sequence encoding a complement of the GBA1 transgene, wherein the first heterologous polynucleotide sequence can form intrastrand base pairs with the second polynucleotide sequence.

46. The use of claim 45, wherein the first heterologous polynucleotide sequence and the second heterologous polynucleotide sequence are linked by a mutated AAV ITR.

47. The use of claim 46, wherein the mutated AAV ITR comprises a deletion of the D region and comprises a mutation of the terminal resolution sequence.

48. The use of any one of claims 32-47, wherein the promoter is capable of expressing the GBA1 gene or equivalent thereof in neurons of the central nervous system (CNS).

49. The use of any one of claims 32-48, wherein the promoter comprises a human β-glucuronidase promoter or a cytomegalovirus enhancer linked to a chicken β-actin promoter.

50. The use of any one of claims 1-49, wherein the agent is in a pharmaceutical composition.

51. The use of claim 50, wherein the pharmaceutical composition further comprises a pharmaceutically acceptable carrier.

52. The use of any one of claims 1-51, wherein the agent or pharmaceutical composition is administered by injection.

53. The use of claim 52, wherein the agent or pharmaceutical composition is administered into the CNS.

54. The use of claim 53, wherein the agent or pharmaceutical composition is administered via direct injection into the spinal cord, via intrathecal injection, via intracerebroventricular injection, or via intrahippocampal injection.

55. The use of any one of claims 1-54, wherein the use comprises increasing the glucocerebrosidase activity over baseline levels in a neuron of the mammal.

56. The use of claim 55, wherein the use comprises increasing the glucocerebrosidase activity by at least about 2 fold over baseline levels in the neuron of the mammal.

57. The use of claim 55, wherein the use comprises increasing the glucocerebrosidase activity by at least about 3 fold over baseline levels in the neuron of the mammal.