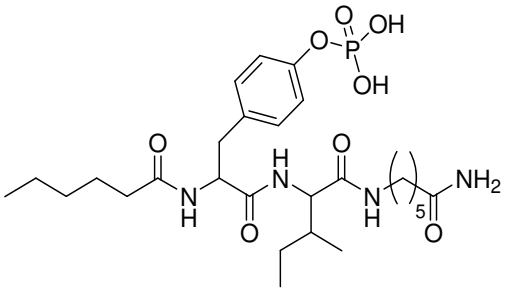
of a critical neurotrophic factor system (HGF/MET) may stop neurodegeneration and promote neuro-regeneration. Neurotrophic factors represent a promising therapeutic target for the treatment of dementia caused by neurodegeneration, including PDD, by protecting existing neurons, promoting synaptogenesis, stimulating neuronal growth, and inducing regenerative mechanisms. Pharmacological stimulation of neurotrophic systems has the potential to treat all stages of PDD by directly targeting neurodegeneration, improving cognition, and addressing multiple aspects of the disease, by decreasing inflammation and improving cerebral blood flow (Funakoshi, 2011). The therapeutic promise of neurotrophic factors in neurodegenerative disorders is hampered by the lack of efficient and non-invasive delivery to the brain. Gene therapy strategies, primarily using adeno-associated viral vectors, have been developed and clinically evaluated for therapeutic potential in PDD patients. These strategies are largely hindered by challenges related to gene delivery and transduction with limited brain exposure, uncontrollable dose over long-term treatment, and potential immune complications (Piguet, 2017).

[0006] Therefore, a small molecule approach capable of passing the blood brain barrier and entering all regions of the brain, presents a superior therapeutic strategy for targeting neurotrophic factors to treat neurodegenerative disorders.

SUMMARY

[0007] The present disclosure provides, in some examples, methods of treating Parkinson's disease dementia.

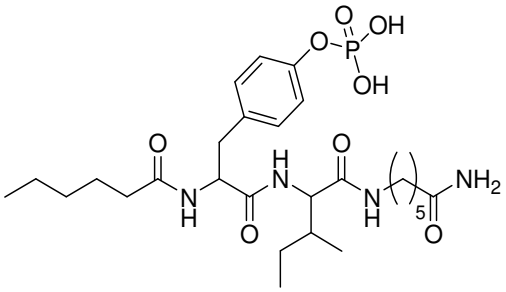
Example 1. A method of treating Parkinson's disease (PD) and/or Lewy body disease or disorder(s) (LBD), comprising administering to a patient in need thereof 2-90 mg per day of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof.

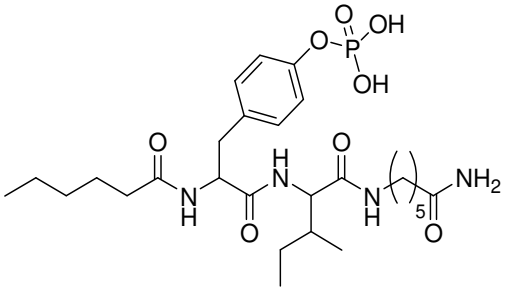
Example 2. A method of treating Parkinson's Disease Dementia (PDD), comprising administering to a patient in need thereof 2-90 mg per day of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof.

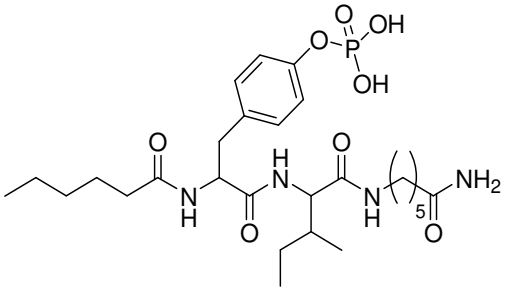
Example 3. A method of treating dementia with Lewy bodies (DLB), comprising administering to a patient in need thereof 2-90 mg per day of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof.

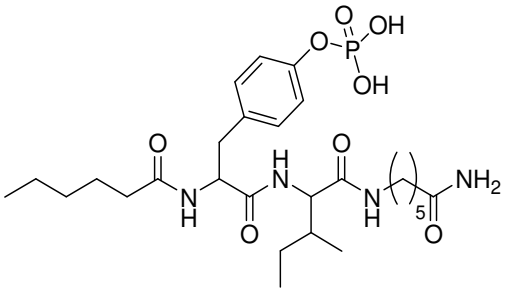
Example 4. A method of treating mild to moderate dementia associated with Parkinson's disease (PD), comprising administering to a patient in need thereof 2-90 mg per day of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof.

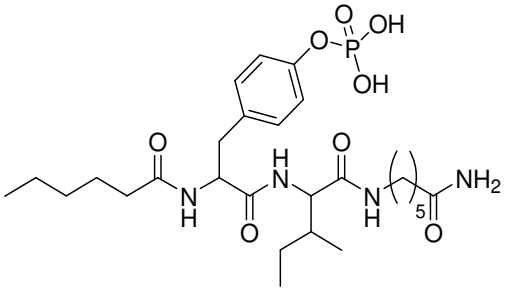
Example 5. A method of improving event related potential (ERP) P300 latency in a patient diagnosed with PDD and/or DLB, comprising administering to the patient thereof 2-90 mg per day of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof.

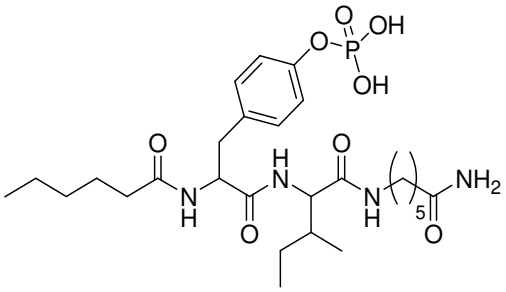
Example 6. A method of slowing the decline in cognition or improving cognition in a patient diagnosed with PDD and/or DLB, comprising administering to the patient 2-90 mg per day of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof.

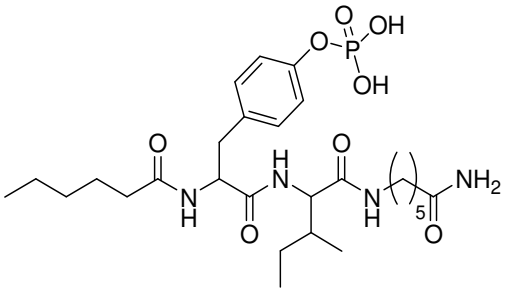
Example 7. A method of slowing the decline in the ability to perform activities of daily living and verbal fluency or improving the ability to perform activities of daily living and verbal fluency in a patient diagnosed with PDD and/or DLB, comprising administering to the patient 2-90 mg per day of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof.

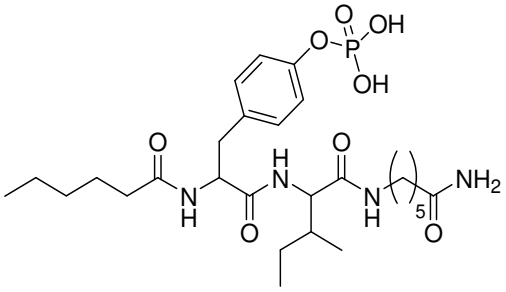
Example 8. A method of slowing the decline in functional or cognitive capacity in a patient diagnosed with PDD and/or DLB, comprising administering to the patient 2-90 mg per day of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof.

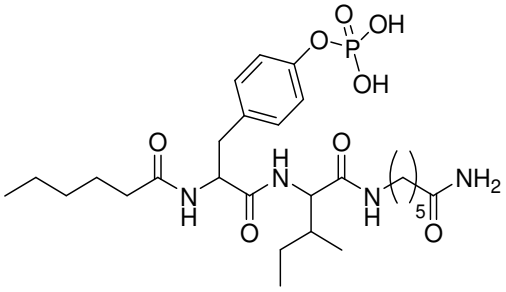
Example 9. A method of slowing clinical decline in a patient diagnosed with PDD and/or DLB, comprising administering to the patient 2-90 mg per day of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof.

Example 10. A method of improving executive memory function in a patient diagnosed with PDD and/or DLB, comprising administering to the patient 2-90 mg per day of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof.

Example 11. The method of any one of the preceding examples, comprising treating dementia.

Example 12. The method of any one of the preceding examples, wherein the treating comprises improving one or more symptoms of dementia.

Example 13. The method of any one of the preceding examples, wherein the treating comprises improving one or more symptoms of a motor disorder.

Example 14. The method of any one of the preceding examples, wherein the patient has been diagnosed with PDD.

Example 15. The method of any one of the preceding examples, wherein the patient has been diagnosed with Lewy body disease or disorder(s) (LBD).

Example 16. The method of any one of the preceding examples, wherein the patient has been diagnosed with probable idiopathic Parkinson's disease or probable Lewy body disease or disorder(s) (LBD).

Example 17. The method of any one of the preceding examples, wherein the patient has been diagnosed with probable idiopathic Parkinson's disease or probable LBD for at least one year.

Example 18. The method of any one of the preceding examples, wherein the patient has been diagnosed with Parkinson's disease.

Example 19. The method of any one of the preceding examples, wherein the patient has been diagnosed with PD for at least one year.

Example 20. The method of any one of the preceding examples, wherein the patient has been diagnosed with PDD inclusive of probable LBD.

Example 21. The method of any one of the preceding examples, wherein the patient has a MOCA score between 11 and 23, between 12 and 23, between 13 and 23, between 14 and 23, between 15 and 23, between 16 and 23, between 17 and 23, between 18 and 23, between 19 and 23, between 20 and 23, between 21 and 23, between 22 and 23, between 11 and 22, between 11 and 21, between 11 and 20, between 11 and 19, between 11 and 18, between 11 and 17, between 11 and 16, between 11 and 15, between 11 and 14, between 11 and 13, between 11 and 12, prior to the start of treatment with the compound of formula A19.

Example 22. The method of any one of the preceding examples, wherein the patient is concurrently treated with an acetylcholinesterase inhibitor (AChEI) other than high dose donepezil.

Example 23. The method of any one of the preceding examples, wherein the patient is between age 40 and 85.

Example 24. The method of any one of the preceding examples, wherein the patient is at Hoehn-Yahr stage 1 to 4.

Example 25. The method of any one of the preceding examples, wherein the patient is at Hoehn-Yahr stage 2 or Hoehn-Yahr stage 3.

Example 26. The method of any one of the preceding examples, wherein the compound of formula A19 or the pharmaceutically acceptable salt thereof is administered by subcutaneous injection.

Example 27. The method of any one of the preceding examples, comprising administering the compound of formula A19 or the pharmaceutically acceptable salt thereof at a dose of 2 mg, 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg, 80 mg, or 90 mg.

Example 28. The method of any one of the preceding examples, comprising administering the compound of formula A19 or the pharmaceutically acceptable salt thereof at a dose of 40 mg or 70 mg.

Example 29. The method of any one of the preceding examples, comprising administering the compound of formula A19 or the pharmaceutically acceptable salt thereof at a dose of 40 mg.

Example 30. The method of any one of the preceding examples, comprising administering the compound of formula A19 or the pharmaceutically acceptable salt thereof at a dose of 70 mg.

Example 31. The method of any one of the preceding examples, comprising administering the compound of formula A19 or the pharmaceutically acceptable salt thereof for 26 weeks or more.

Example 32. The method of any one of the preceding examples, which slows the decline in functional or cognitive capacity in the patient.

Example 33. The method of any one of the preceding examples, which slows the decline in cognition in the patient.

Example 34. The method of any one of the preceding examples, which improves cognition in the patient.

Example 35. The method of any one of the preceding examples, which slows the decline in the ability to perform activities of daily living and verbal fluency in the patient.

Example 36. The method of any one of the preceding examples, which improves the ability to perform activities of daily living and verbal fluency in the patient.

Example 37. The method of any one of examples 32 to 36, wherein the slowing of the decline or the improvement is determined after administering the treatment for at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12

weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks.

Example 38. The method of any one of the preceding examples, wherein cognitive capacity is assessed by determining the patient's score before and after administration of the compound of formula A19 or the pharmaceutically acceptable salt thereof using a 13-item Alzheimer's Disease Assessment Scale – cognitive subscale (ADAS-Cog13).

Example 39. The method of example 38, wherein cognitive capacity is assessed prior to the start of treatment and at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 40. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves ADAS-Cog13.

Example 41. The method of example 40, wherein reducing the rate of decline, stabilizing, or improving is assessed by determining the patient's score prior to the start of treatment and at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 42. The method of any one of examples 38 to 41, wherein the onset of the effect on ADAS-Cog13 begins by 2 weeks, or by 4 weeks, or by 6 weeks, or by 8 weeks, or by 10 weeks, or by 12 weeks, or by 14 weeks, or by 16 weeks, or by 18 weeks, or by 20 weeks, or by 22 weeks, or by 24 weeks, or by 26 weeks after the start of treatment.

Example 43. The method of any one of examples 38 to 42, wherein the effect on ADAS-Cog13 is maintained for at least 2 weeks or at least 4 weeks after the end of treatment.

Example 44. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves a Clinician Global Impression of Change (CGI-C) score.

Example 45. The method of example 44, wherein the reduction in the rate of decline, stabilization, or improvement occurs by at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 46. The method of example 44 or example 45, wherein reducing the rate of decline, stabilizing, or improving is assessed by determining the patient's score prior

to the start of treatment and at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 47. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves a Clinician Global Impression of Severity (CGI-S) score.

Example 48. The method of example 47, wherein the reduction in the rate of decline, stabilization, or improvement occurs by at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 49. The method of example 47 or example 48, wherein reducing the rate of decline, stabilizing, or improving is assessed by determining the patient's score prior to the start of treatment and at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 50. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves an Alzheimer's disease cooperative study-activities of daily living, 23-item version (ADCS-ADL23) score.

Example 51. The method of example 50, wherein the reduction in the rate of decline, stabilization, or improvement occurs by at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 52. The method of example 50 or example 51, wherein reducing the rate of decline, stabilizing, or improving is assessed by determining the patient's score prior to the start of treatment and at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 53. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves a Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) score.

Example 54. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves a MDS-UPDRS, Part I score.

Example 55. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves a MDS-UPDRS, Part I, domains 1.2, 1.5, and/or 1.8 score.

Example 56. The method of any one of examples 53 to 55, wherein the reduction in the rate of decline, stabilization, or improvement occurs by at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 57. The method of any one of examples 53 to 56, wherein reducing the rate of decline, stabilizing, or improving is assessed by determining the patient's score prior to the start of treatment and at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 58. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves a Caregiver Global Impression of Change (CaGI-C) score.

Example 59. The method of example 58, wherein the reduction in the rate of decline, stabilization, or improvement occurs by at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 60. The method of example 58 or example 59, wherein reducing the rate of decline, stabilizing, or improving is assessed by determining the patient's score prior to the start of treatment and at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 61. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves a Non-Motor Symptom Scale (NMSS) score.

Example 62. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves a NMSS domain 2 and/or domain 4 score.

Example 63. The method of example 61 or example 62, wherein the reduction in the rate of decline, stabilization, or improvement occurs by at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16

weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 64. The method of any one of examples 61 to 63, wherein reducing the rate of decline, stabilizing, or improving is assessed by determining the patient's score prior to the start of treatment and at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 65. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves a Mini-Mental State Examination (MMSE) score.

Example 66. The method of example 65, wherein the reduction in the rate of decline, stabilization, or improvement occurs by at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 67. The method of example 65 or example 66, wherein reducing the rate of decline, stabilizing, or improving is assessed by determining the patient's score prior to the start of treatment and at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 68. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves a Controlled Oral Word Association Test (COWAT) score.

Example 69. The method of example 68, wherein the reduction in the rate of decline, stabilization, or improvement occurs by at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 70. The method of example 68 or example 69, wherein reducing the rate of decline, stabilizing, or improving is assessed by determining the patient's score prior to the start of treatment and at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 71. The method of any one of the preceding examples, which provides persistence in improvement in ERP 300 latency.

Example 72. The method of example 71, which provides persistence in improvement in ERP 300 latency at least 30 weeks after the start of treatment.

Example 73. The method of any one of the preceding examples, which provides fast improvement or normalization of ERP P300 values.

Example 74. The method of any one of the preceding examples, which provides fast improvement or normalization of EPR P300 latency values.

Example 75. The method of any one of the preceding examples, which provides fast improvement or normalization of ERP P300 latency values with some maintenance of effect at at least 26 weeks of treatment.

Example 76. The method of any one of the preceding examples, which provides fast improvement or normalization of ERP P300 latency values, which is maintained at at least 26 weeks of treatment.

Example 77. The method of any one of the preceding examples, which improves event-related potential (ERP) P300 latency.

Example 78. The method of any one of examples 71 to 77, wherein the improvement or normalization occurs by at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 79. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves a non-motor symptom in the patient.

Example 80. The method of example 79, wherein the non-motor symptom includes delusions, apathy, hallucinations, daytime sleepiness, and/or depression.

Example 81. The method of example 79 or example 80, wherein the reduction in the rate of decline, stabilization, or improvement occurs by at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 82. The method of any one of examples 79 to 81, wherein reducing the rate of decline, stabilizing, or improving is assessed by determining the patient's symptom(s) prior to the start of treatment and at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 83. The method of any one of the preceding examples, which reduces the rate of decline, stabilizes, or improves a motor symptom in the patient.

Example 84. The method of example 83, wherein the reduction in the rate of decline, stabilization, or improvement occurs by at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 85. The method of example 83 or example 84, wherein reducing the rate of decline, stabilizing, or improving is assessed by determining the patient's symptom(s) prior to the start of treatment and at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, at least 10 weeks, at least 12 weeks, at least 16 weeks, at least 18 weeks, at least 20 weeks, at least 22 weeks, at least 24 weeks, or at least 26 weeks after the start of treatment.

Example 86. The method of any one of the preceding examples, which has an acceptable safety and tolerability profile.

Example 87. The method of any one of the preceding examples, which is generally safe and well tolerated.

Example 88. The method of any one of the preceding examples, which is not associated with an increase in nausea, vomiting or tremor.

Example 89. The method of any one of the preceding examples, which does not produce drug-drug interactions with a drug administered for Parkinson's disease.

Example 90. The method of any one of the preceding examples, which does not prolong the QT interval.

Example 91. The method of any one of the preceding examples, comprising administering a sodium salt of the compound of formula A19.

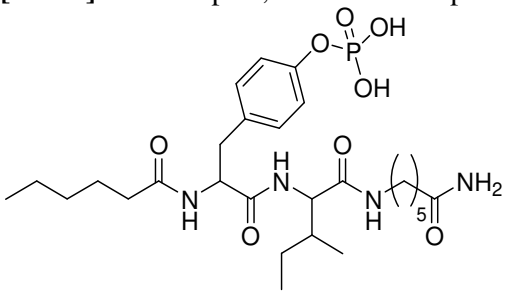
Example 92. The method of any one of the preceding examples, comprising administering a monosodium salt of the compound of formula A19.

Example 93. The method of any one of the preceding examples, comprising administering ATH-1017.

Example 94. The method of any one of the preceding examples, wherein the patient is acetylcholinesterase inhibitor (AChEI) naïve or received an AChEI in the past, or received AChEI in the past and discontinued at least 4 weeks prior to administration of the compound.

Example 95. The method of any one of examples 1 to 22 and 23 to 94, wherein the patient is not concurrently treated with an AChEI.

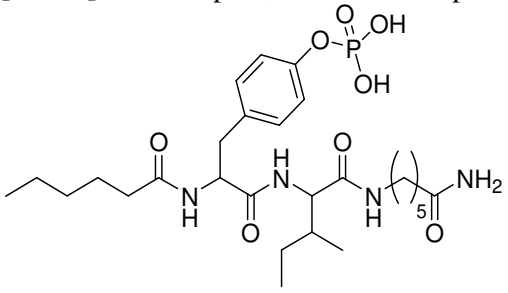
[0007a] In one aspect, the disclosure provides use of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating Parkinson's disease (PD) and/or Lewy body disease or disorder(s) (LBD), wherein the medicament is to be administered at 2-90 mg per day to a patient in need thereof.

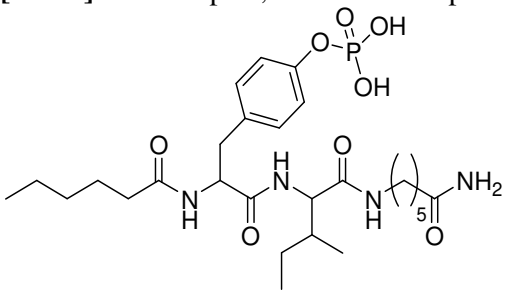
[0007b] In one aspect, the disclosure provides use of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating Parkinson's Disease Dementia (PDD), wherein the medicament is to be administered at 2-90 mg per day to a patient in need thereof.

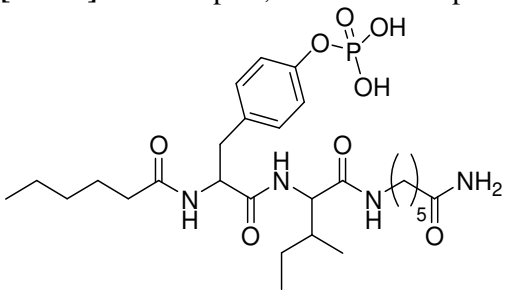
[0007c] In one aspect, the disclosure provides use of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating dementia with Lewy bodies (DLB), wherein the medicament is to be administered at 2-90 mg per day to a patient in need thereof.

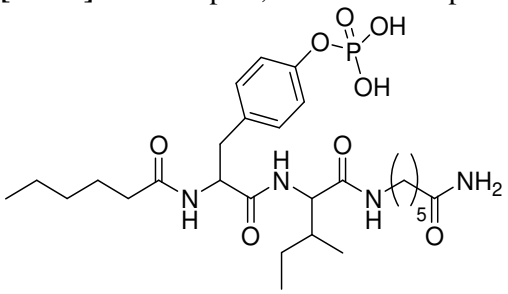
[0007d] In one aspect, the disclosure provides use of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for slowing the decline in cognition or improving cognition in a patient diagnosed with PDD and/or DLB, wherein the medicament is to be administered at 2-90 mg per day to the patient.

[0007e] In one aspect, the disclosure provides use of a compound of formula A19

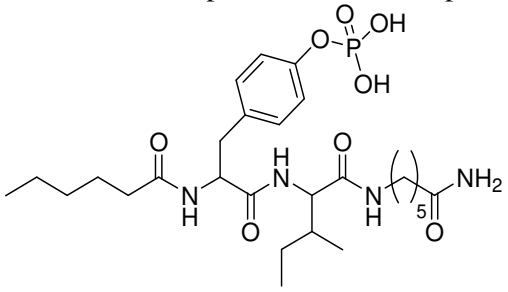


A19

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for slowing

the decline in the ability to perform activities of daily living and verbal fluency or improving the ability to perform activities of daily living and verbal fluency in a patient diagnosed with PDD and/or DLB, wherein the medicament is to be administered at 2-90 mg per day to the patient.

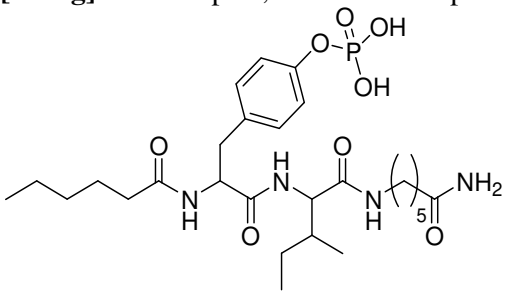
[0007f] In one aspect, the disclosure provides use of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for slowing the decline in functional or cognitive capacity in a patient diagnosed with PDD and/or DLB, wherein the medicament is to be administered at 2-90 mg per day to the patient.

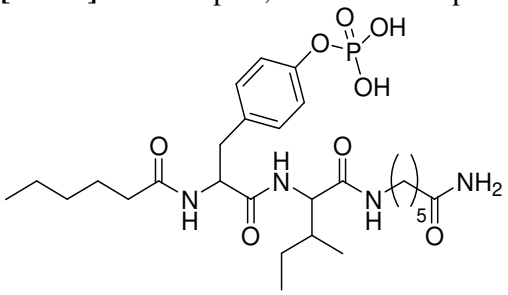
[0007g] In one aspect, the disclosure provides use of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for slowing clinical decline in a patient diagnosed with PDD and/or DLB, wherein the medicament is to be administered at 2-90 mg per day to the patient.

[0007h] In one aspect, the disclosure provides use of a compound of formula A19



A19

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for improving executive memory function in a patient diagnosed with PDD and/or DLB, wherein the medicament is to be administered at 2-90 mg per day to the patient.