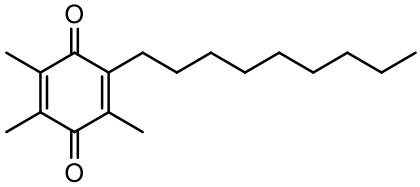
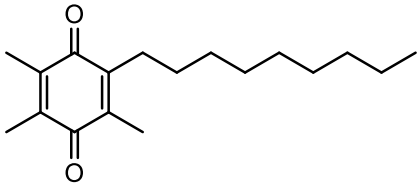
examples, the method is for treating or suppressing Parkinson's Disease. In some examples, including any of the foregoing examples, the method is for treating or suppressing traumatic brain injury. In some examples, including any of the foregoing examples, the method is for treating or suppressing ischemic-reperfusion related injury. In some examples, including any of the foregoing examples, the method is for treating or suppressing stroke. In some examples, including any of the foregoing examples, the method is for treating or suppressing Amyotrophic lateral sclerosis (ALS). In some examples, including any of the foregoing examples, the method is for treating the disorder. In some examples, including any of the foregoing examples, the method is for suppressing the disorder. In some examples, including any of the foregoing examples, the compound is administered orally. In some examples, including any of the foregoing examples, the compound is administered intravenously.

[0005a] In one aspect, the present disclosure refers to a pharmaceutical composition comprising a therapeutically effective amount of 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione:



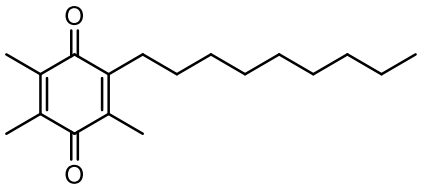
for use in the treatment or suppression of a disorder selected from the group consisting of an α-synucleinpathy, a tauopathy, amyotrophic lateral sclerosis (ALS), traumatic brain injury, and ischemic-reperfusion related injury in a subject in need thereof wherein the pharmaceutical composition is prepared with 1) a polymorph of an anhydrate of 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.10, 12.12, and 16.14, and wherein the data are obtained with a Cu Kα1 source and a wavelength of 1.540598 Å; and 2) a pharmaceutically acceptable solvent, carrier, or excipient.

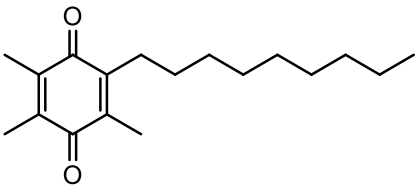
[0005b] In another aspect, the present disclosure refers to a use of ~~a pharmaceutical composition comprising~~ a therapeutically effective amount of 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione:



in the manufacture of a medicament for the treatment or suppression of a disorder selected from the group consisting of an α-synucleinpathy, a tauopathy, amyotrophic lateral sclerosis (ALS), traumatic brain injury, and ischemic-reperfusion related injury in a subject in need thereof wherein the 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione ~~pharmaceutical composition~~ is prepared with ~~1)~~ a polymorph of an anhydrate of 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione, and wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.10, 12.12, and 16.14, wherein the data are obtained with a Cu Kα1 source and a wavelength of 1.540598 Å~~; and 2) a pharmaceutically acceptable solvent, carrier, or excipient~~.

[0006] In another example is a method of treating or suppressing a disorder selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, traumatic brain injury, and ischemic-reperfusion related injuries, comprising administering to a subject in need thereof a therapeutically effective amount of a compound of the formula:



or the hydroquinone form thereof; or a solvate or hydrate thereof. In some examples, the compound is:  ; or the hydroquinone form thereof. In some examples, including any of the foregoing examples, the compound is in the quinone form. In some examples, including any of the foregoing examples, the compound is in the hydroquinone form. In some examples, the method is for suppressing or treating Alzheimer's Disease. In some examples, the method is for suppressing or treating Parkinson's Disease. In some examples, the method for suppressing or treating Parkinson's Disease includes treating or suppressing idiopathic Parkinson's Disease. In some examples, the method for suppressing or treating Parkinson's Disease includes treating or suppressing familial (i.e. genetic) Parkinson's Disease. In some examples, the method for suppressing or treating Parkinson's Disease is that wherein the patient has a mutation in one or more of the following genes: *MAPT* (Microtubule-associated protein tau), *PRKN* (parkin), *PINK1* (PINK1), LRRK2

[0007h] In another aspect, the present disclosure refers to a composition comprising the polymorph or the composition as described herein, wherein the polymorph is present as a plurality of particles, wherein the particles have a ratio of D90:D10 less than about 11:1.

[0007i] In another aspect, the present disclosure refers to a composition comprising the polymorph or the composition as described herein, wherein the polymorph is present as a plurality of particles, wherein the particles have a ratio of D90:D10 less than about 7:1.

[0007j] In another aspect, the present disclosure refers to a composition comprising the polymorph or the composition as described herein, wherein the polymorph was recrystallized by a solvent comprising about 75-85% IPA/water.

[0007k] In another aspect, the present disclosure refers to a composition comprising the polymorph or the composition as described herein, wherein the polymorph was recrystallized by a solvent comprising about 80-85% IPA/water.

[0007l] In another aspect, the present disclosure refers to a composition comprising the polymorph or the composition as described herein, wherein the polymorph was recrystallized by a solvent comprising about 85% IPA/water.

[0008] In another aspect, the present disclosure refers to a pharmaceutical composition comprising the polymorph as described herein, or a composition as described herein, and a pharmaceutically acceptable solvent, carrier, or excipient, or a pharmaceutical composition prepared with the polymorph as described herein, or a composition as described herein, and a pharmaceutically acceptable solvent, carrier, or excipient.

[0009] In another aspect, this present disclosure refers to the polymorph, ~~or~~ the composition or the pharmaceutical composition as described herein for use in treating or suppressing an α-synucleinpathy, a tauopathy, Amyotrophic lateral sclerosis (ALS), traumatic brain injury, or ischemic-reperfusion related injury.

[0009a] In another aspect, the present disclosure refers to a use of ~~a~~ the polymorph, ~~or~~ the composition or the pharmaceutical composition as described herein, in the manufacture of a medicament for treating or suppressing an α-synucleinpathy, a tauopathy, Amyotrophic lateral sclerosis (ALS), traumatic brain injury, or ischemic-reperfusion related injury.

[0010] In another aspect, the present disclosure refers to a method of recrystallizing 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione from a composition, comprising: a) contacting the composition with IPA and water such that the resulting ratio of IPA to water is about 75-87% isopropanol (IPA)/25-13% water (v:v), at a temperature of about 40-45 °C; b) cooling the mixture to about 32 °C; and c) filtering the 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione from the mixture. In some examples, step (a) comprises: a1) contacting the

composition with IPA; a2) warming the mixture to about 40-45°C; and a3) adding water to the mixture such that the ratio of IPA to water is about 75-85% IPA:25-15% water (v:v). In some examples, including any of the foregoing examples, step (a) comprises stirring to dissolve the composition. In some examples, including any of the foregoing examples, the ratio of IPA:water is about 80-85% IPA:20-15% water (v:v). In some examples, including any of the foregoing examples, the ratio of IPA:water is about 85% IPA:15% water (v:v). In some examples, including any of the foregoing examples, step (a3) comprises returning the temperature of the mixture to about 40-45°C. In some examples, including any of the foregoing examples, the method comprising polish filtering the mixture after step (a). In some examples, including any of the foregoing examples, step (b) comprises cooling to about 32°C over about 2-10 hours. In some examples, including any of the foregoing examples, step (b) comprises cooling to about 32°C over about 6 hours. In some

examples, including any of the foregoing examples, the method comprises a step (b1) after step (b), comprising holding the mixture at about 32°C for about 2-24 hours. In some examples, including any of the foregoing examples, the method comprises a step (b1) after step (b), comprising holding the mixture at about 32°C for about 6 hours. In some examples, including any of the foregoing examples, the method comprises a step (b2) after step (b) or (b1), when present, comprising cooling the mixture to about 0°C. In some examples, including any of the foregoing examples, step (b2) comprises cooling the mixture to about 0°C over about 3-24 hours. In some examples, including any of the foregoing examples, step (b2) further comprises holding the mixture at about 0°C for about one hour.

[0011] In another aspect, the present disclosure refers to a composition comprising 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione as made according to a method of the immediately preceding paragraph.

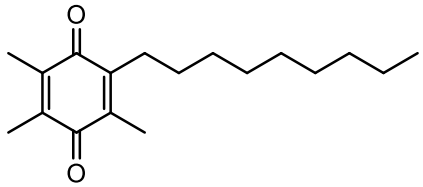
[0012] In another aspect, the present disclosure refers to a method of making a pharmaceutical composition, comprising converting the polymorph as described in any one of the preceding paragraphs, ~~or~~ the composition of any one of the preceding paragraphs, or the pharmaceutical composition of any one of the preceding paragraphs to a liquid or emulsion form. In some examples, the pharmaceutical composition is provided as an oral solution, a liquid-filled capsule, or an injectable solution. In another aspect the present disclosure refers to a pharmaceutical composition produced according to these methods.

[0013] In another aspect, the present disclosure refers to a metastable melted amorphous form of 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione, having an XRPD plot substantially as shown in Figure 31.

[0014] The present disclosure relates to a method of treating or suppressing a disorder selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, traumatic brain injury, and ischemic-reperfusion related injuries, comprising administering to a subject in need thereof a therapeutically effective amount of a compound of the formula:

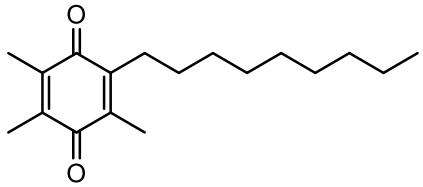
CLAIMS

1. A pharmaceutical composition comprising a therapeutically effective amount of 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione:



for use in the treatment or suppression of a disorder selected from the group consisting of an α-synucleinpathy, a tauopathy, amyotrophic lateral sclerosis (ALS), traumatic brain injury, and ischemic-reperfusion related injury in a subject in need thereof wherein the pharmaceutical composition is prepared with 1) a polymorph of an anhydrate of 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.10, 12.12, and 16.14, and wherein the data are obtained with a Cu Kα1 source and a wavelength of 1.540598 Å; and 2) a pharmaceutically acceptable solvent, carrier, or excipient.

2. A use of ~~a pharmaceutical composition comprising~~ a therapeutically effective amount of 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione:



in the manufacture of a medicament for the treatment or suppression of a disorder selected from the group consisting of an α-synucleinpathy, a tauopathy, amyotrophic lateral sclerosis (ALS), traumatic brain injury, and ischemic-reperfusion related injury in a subject in need thereof wherein the 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione ~~pharmaceutical composition~~ is prepared with ~~1)~~ a polymorph of an anhydrate of 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione, and wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.10, 12.12, and 16.14, wherein the data are obtained with a Cu Kα1 source and a wavelength of 1.540598 Å~~; and 2) a pharmaceutically acceptable solvent, carrier, or excipient~~.

3. The pharmaceutical composition for use of claim 1, or the use of claim 2, wherein the disorder is Amyotrophic lateral sclerosis (ALS).

4. The pharmaceutical composition for use of claim 1, or the use of claim 2, wherein the disorder is α-synucleinpathy.

5. The pharmaceutical composition for use or the use of claim 4, wherein the α-synucleinpathy is selected from the group consisting of: Parkinson's Disease, Parkinson's Disease with dementia (PDD), multisystem atrophy (MSA), Frontotemporal Dementia, Dementia with Lewy Bodies (DLB), Gaucher's disease (GD), Neurodegeneration with Brain Iron Accumulation (NBIA), and neuroaxonal dystrophies (PLA2G6-associated neurodegeneration).

6. The pharmaceutical composition for use or the use of claim 5, wherein the Parkinson's Disease is genetic.

7. The pharmaceutical composition for use or the use of claim 5, wherein the Parkinson's Disease is idiopathic.

8. The pharmaceutical composition for use of claim 1, or the use of claim 2, wherein the disorder is tauopathy.

9. The pharmaceutical composition for use, or the use of claim 8, wherein the tauopathy is selected from the group consisting of: Alzheimer's disease, dementia pugilistica, Guam Amyotrophic lateral sclerosis-Parkinsonism-Dementia (Guam ALS/PD), Pick Disease, Argyrophilic grain dementia, Nieman-Pick type C, Subacute sclerosing panencephalitis (SSPE), Progressive supranuclear palsy (PSP), multisystem atrophy (MSA), Corticobasoganlionic degeneration, Frontotemporal dementia with parkinsonism-17 (FTDP-17), Postencephalitic Parkinsonism (PEP), and Autosomal recessive Parkinsonism.

10. The pharmaceutical composition for use of claim 1, or the use of claim 2, wherein the disorder is Alzheimer's Disease.

11. The pharmaceutical composition for use of claim 1, or the use of claim 2, wherein the disorder is Parkinson's Disease.

12. The pharmaceutical composition for use of claim 1, or the use of claim 2, wherein the disorder is traumatic brain injury.

13. The pharmaceutical composition for use of claim 1, or the use of claim 2, wherein the disorder is ischemic-reperfusion related injury.

14. The pharmaceutical composition for use of claim 1, or the use of claim 2, wherein the disorder is stroke.

15. The pharmaceutical composition for use of any one of claims 1, 3-14, or the use of any one of claims 2-14, wherein the pharmaceutical composition or the medicament is for treating the disorder.

16. The pharmaceutical composition for use of any one of claims 1, 3-14, or the use of any one of claims 2-14, wherein the pharmaceutical composition or the medicament is for suppressing the disorder.

17. The pharmaceutical composition for use of any one of claims 1, 3-16, or the use of any one of claims 2-16, wherein the pharmaceutical composition or medicament is to be administered orally.

18. The pharmaceutical composition for use of any one of claims 1, 3-16, or the use of any one of claims 2-16, wherein the pharmaceutical composition or the medicament is to be administered intravenously.

19. The pharmaceutical composition of any one of claims 1, 3-18 ~~or~~, or the ~~medicament~~ use of any one of claims 2-18, wherein the data are obtained at a temperature selected from 23-25 °C.

20. A polymorph of an anhydrate of 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.10, 12.12, and 16.14, wherein the data are obtained with a Cu Kα1 source and a wavelength of 1.540598 Å.

21. The polymorph of claim 20, comprising characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.10, 11.77, 12.12, and 16.14.

22. The polymorph of claim 20, comprising characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.10, 11.77, 12.12, 16.14, and 22.41.

23. The polymorph of any one of claims 20-22, wherein the angular positions may vary by ± 0.1.

24. The polymorph of any one of claims 20-22, wherein the angular positions may vary by ± 0.05.

25. The polymorph of any one of claims 20-24, wherein the polymorph has a powder x-ray diffraction pattern substantially as shown in any one of Figures 5, 11, 14, and 16.

26. The polymorph of any one of claims 20-25, having a differential scanning calorimetry (DSC) thermogram substantially as shown in Figure 7.

27. The polymorph of any one of claims 20-26, wherein a DSC thermogram has a single endothermic peak at about 47 to about 53°C.

28. The polymorph of any one of claims 20-27, having a thermogravimetric analysis (TGA) thermogram substantially as shown in Figure 8.

29. The polymorph of any one of claims 20-28, having a ^{1}H NMR spectrum substantially as shown in Figure 6.

30. The polymorph of any of claims 20-28, wherein the data are obtained at a temperature of 23-25 °C.

31. A composition comprising the polymorph of any one of claims 20-30, wherein at least about 95% by mole of the 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione is the polymorph, exclusive of any solvents, carriers or excipients.

32. A composition comprising the polymorph of any one of claims 20-30, wherein at least about 99% by mole of the 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione is the polymorph, exclusive of any solvents, carriers or excipients.

33. A composition comprising the polymorph of any one of claims 20-30, or the composition of claim 31 or 32, wherein at least about 95% a/a as measured by HPLC of the composition is the 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione, exclusive of any solvents, carriers or excipients.

34. A composition comprising the polymorph of any one of claims 20-30, or the composition of claim 31 or 32, wherein at least about 99% a/a as measured by HPLC of the composition is the 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione, exclusive of any solvents, carriers or excipients.

35. A composition comprising the polymorph of any one of claims 20-30, or the composition of any one of claims 31-34, wherein the potency of the 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione is at least about 95%.

36. A composition comprising the polymorph of any one of claims 20-30, or the composition of any one of claims 31-34, wherein the potency of the 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione is at least about 99%.

37. A composition comprising the polymorph of any one of claims 20-30, or the composition of any one of claims 31-36, wherein the polymorph is present as a plurality of particles, wherein the particles have a ratio of D90:D10 less than about 11:1.

38. A composition comprising the polymorph of any one of claims 20-30, or the composition of any one of claims 31-36, wherein the polymorph is present as a plurality of particles, wherein the particles have a ratio of D90:D10 less than about 7:1.

39. A composition comprising the polymorph of any one of claims 20-30, or the composition of any one of claims 31-38, wherein the polymorph was recrystallized by a solvent comprising about 75-85% IPA/water.

40. A composition comprising the polymorph of any one of claims 20-30, or the composition of any one of claims 31-38, wherein the polymorph was recrystallized by a solvent comprising about 80-85% IPA/water.

41. A composition comprising the polymorph of any one of claims 20-30, or the composition of any one of claims 31-38, wherein the polymorph was recrystallized by a solvent comprising about 85% IPA/water.

42. A pharmaceutical composition comprising the polymorph of any one of claims 20-30, or the composition of any one of claims 31-41, and a pharmaceutically acceptable solvent, carrier, or excipient, or a pharmaceutical composition prepared with the polymorph of any one of claims 20-30, or the composition of any one of claims 31-41, and a pharmaceutically acceptable solvent, carrier, or excipient.

43. The polymorph of any one of claims 20-30, ~~or~~ the composition of any one of claims 31-~~42~~ 41, or the pharmaceutical composition of claim 42 for use in treating or suppressing an α-synucleinpathy, a tauopathy, Amyotrophic lateral sclerosis (ALS), traumatic brain injury, or ischemic-reperfusion related injury.

44. A use of the polymorph of any one of claims 20-30, ~~or~~ the composition of any one of claims 31-41, or the pharmaceutical composition of claim 42, in the manufacture of a medicament for treating or suppressing an α-synucleinpathy, a tauopathy, Amyotrophic lateral sclerosis (ALS), traumatic brain injury, or ischemic-reperfusion related injury.

45. A method of recrystallizing 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione from a composition, comprising:

a) contacting the composition with IPA and water such that the resulting ratio of IPA to water is about 75-87% isopropanol (IPA)/25-13% water (v:v), at a temperature of about 40-45 °C;

b) cooling the mixture to about 32 °C; and

c) filtering the 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione from the mixture.

46. A composition comprising 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione as made according to claim 45.

47. A method of making a pharmaceutical composition, comprising converting the polymorph of any one of claims 20-30, or the composition of any one of claims 31-41, or the pharmaceutical composition of claim 42, to a liquid or emulsion form.

48. The method of claim 47, wherein the liquid or emulsion form is provided as an oral solution, a liquid-filled capsule, or an injectable solution.

49. A pharmaceutical composition produced according to claim 47 or 48.

50. A metastable melted amorphous form of 2,3,5-trimethyl-6-nonylcyclohexa-2,5-diene-1,4-dione, having an XRPD plot substantially as shown in Figure 31.