We claim:

1. A double stranded ribonucleic acid (dsRNA) agent for inhibiting expression of SNCA, wherein the dsRNA agent comprises a sense strand and an antisense strand forming a double stranded region, wherein the sense strand comprises a nucleotide sequence comprising at least 15 contiguous nucleotides, with 0 or 1 mismatches, of a portion of the nucleotide sequence of SEQ ID NO: 1, or a nucleotide sequence having at least 90% nucleotide sequence identity to a portion of the nucleotide sequence of SEQ ID NO: 1, and the antisense strand comprises a nucleotide sequence comprising at least 15 contiguous nucleotides, with 0 or 1 mismatches, of the corresponding portion of the nucleotide sequence of SEQ ID NO: 2, or a nucleotide sequence having at least 90% nucleotide sequence identity to a portion of the nucleotide sequence of SEQ ID NO: 2.

2. A double stranded ribonucleic acid (RNAi) agent for inhibiting expression of a SNCA gene, wherein the RNAi agent comprises a sense strand and an antisense strand, and wherein the antisense strand comprises a region of complementarity comprising at least 15 contiguous nucleotides differing by no more than 3 nucleotides from an antisense sequence selected from the group consisting of the antisense sequences of **Tables 2, 3, 12 and 13**.

3. The dsRNA agent of claim 1 or claim 2, wherein the sense strand comprises a nucleotide sequence comprising at least 17 contiguous nucleotides, with 0 or 1 mismatches, of a portion of the nucleotide sequence of SEQ ID NO: 1, and the antisense strand comprises a nucleotide sequence comprising at least 17 contiguous nucleotides, with 0 or 1 mismatches, of the corresponding portion of the nucleotide sequence of SEQ ID NO: 2, such that the sense strand is complementary to the at least 17 contiguous nucleotides in the antisense strand.

4. The dsRNA agent of any one of claims 1-3, wherein the sense strand comprises a nucleotide sequence comprising at least 19 contiguous nucleotides, with 0 or 1 mismatches, of a portion of the nucleotide sequence of SEQ ID NO: 1, and the antisense strand comprises a nucleotide sequence comprising at least 19 contiguous nucleotides, with 0 or 1 mismatches, of the corresponding portion of the nucleotide sequence of SEQ ID NO: 2, such that the sense strand is complementary to the at least 19 contiguous nucleotides in the antisense strand.

5. The dsRNA agent of any one of claims 1-4, wherein the sense strand comprises a nucleotide sequence comprising at least 21 contiguous nucleotides, with 0 or 1 mismatches, of a portion of the nucleotide sequence of SEQ ID NO: 1, and the antisense strand comprises a nucleotide sequence comprising at least 21 contiguous nucleotides, with 0 or 1 mismatches, of the corresponding portion of nucleotide sequence of SEQ ID NO: 2, such that the sense strand is complementary to the at least 21 contiguous nucleotides in the antisense strand.

6. The dsRNA agent of any one of claims 1-5, wherein the sense strand or the antisense strand is a sense strand or an antisense strand selected from the group consisting of any of the sense strands and antisense strands in any one of **Tables 2, 3, 12 and 13**.

7. The dsRNA agent of any one of claims 1-6, wherein the sense strand or the antisense strand is conjugated to one or more lipophilic moieties, or wherein both the sense strand and the antisense strand is conjugated to one or more lipophilic moieties, preferably wherein the lipophilic moiety is conjugated via a linker or a carrier.

8. The dsRNA agent of claim 2, wherein the lipophilic moiety is conjugated to one or more positions in the double stranded region of the dsRNA agent, preferably wherein the positions in the double stranded region exclude a cleavage site region of the sense strand.

9. The dsRNA agent of claim 7 or claim 8, wherein lipophilicity of the lipophilic moiety, measured by logKow, exceeds 0.

10. The dsRNA agent of any one of claims 1-9, wherein the hydrophobicity of the double-stranded RNAi agent, measured by the unbound fraction in a plasma protein binding assay of the double-stranded RNAi agent, exceeds 0.2, preferably wherein the plasma protein binding assay is an electrophoretic mobility shift assay using human serum albumin protein.

11. The dsRNA agent of any one of claims 1-10, wherein the dsRNA agent comprises at least one modified nucleotide, preferably wherein no more than five of the sense strand nucleotides and no more than five of the nucleotides of the antisense strand are unmodified nucleotides, or preferably wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a modification.

12. The dsRNA agent of claim 11, wherein at least one of the modified nucleotides is selected from the group a deoxy-nucleotide, a 3’-terminal deoxy-thymine (dT) nucleotide, a 2'-O-methyl modified nucleotide, a 2'-fluoro modified nucleotide, a 2'-deoxy-modified nucleotide, a locked nucleotide, an unlocked nucleotide, a conformationally restricted nucleotide, a constrained ethyl nucleotide, an abasic nucleotide, a 2’-amino-modified nucleotide, a 2’-O-allyl-modified nucleotide, 2’-C-alkyl-modified nucleotide, 2’-hydroxly-modified nucleotide, a 2’-methoxyethyl modified nucleotide, a 2’-O-alkyl-modified nucleotide, a morpholino nucleotide, a phosphoramidate, a non-natural base comprising nucleotide, a tetrahydropyran modified nucleotide, a 1,5-anhydrohexitol modified nucleotide, a cyclohexenyl modified nucleotide, a nucleotide comprising a 5'-phosphorothioate group, a nucleotide comprising a 5'-methylphosphonate group, a nucleotide comprising a 5’ phosphate or 5’ phosphate mimic, a nucleotide comprising vinyl phosphonate, a nucleotide comprising adenosine-glycol nucleic acid (GNA), a nucleotide comprising thymidine-glycol nucleic acid (GNA) S-Isomer, a nucleotide comprising 2-hydroxymethyl-tetrahydrofurane-5-phosphate, a nucleotide comprising 2’-deoxythymidine-3’phosphate, a nucleotide comprising 2’-deoxyguanosine-3’-phosphate, and a terminal nucleotide linked to a cholesteryl derivative and a dodecanoic acid bisdecylamide group; and combinations thereof.

13. The dsRNA agent of claim 12, wherein the modified nucleotide is selected from the group consisting of a 2'-deoxy-2'-fluoro modified nucleotide, a 2'-deoxy-modified nucleotide, 3’-terminal deoxy-thymine nucleotides (dT), a locked nucleotide, an abasic nucleotide, a 2’-amino-modified nucleotide, a 2’-alkyl-modified nucleotide, a morpholino nucleotide, a phosphoramidate, and a non-natural base comprising nucleotide; or wherein the modified nucleotide comprises a short sequence of 3’-terminal deoxy-thymine nucleotides (dT); or wherein the modifications on the nucleotides are 2’-O-methyl, GNA and 2’fluoro modifications; or wherein the dsRNA agent further comprises at least one phosphorothioate internucleotide linkage, preferably 6-8 phosphorothioate internucleotide linkages.

14. The dsRNA agent of any one of claims 1-13, wherein each strand is no more than 30 nucleotides in length.

15. The dsRNA agent of any one of claims 1-14, wherein at least one strand comprises a 3' overhang of at least 1 nucleotide or at least 2 nucleotides.

16. The dsRNA agent of any one of claims 1-15, wherein the double stranded region is 15-30 nucleotide pairs in length, preferably wherein the double stranded region is 17-23, or 17-25, or 23-27, or 19-21, or 21-23 nucleotide pairs in length.

17. The dsRNA agent of any one of claims 1-16, wherein each strand has 19-30, or 19-23, or 21-23 nucleotides.

18. The dsRNA agent of any one of claims 7-17, wherein one or more lipophilic moieties are conjugated to one or more internal positions on at least one strand, preferably wherein the one or more lipophilic moieties are conjugated to one or more internal positions on at least one strand via a linker or carrier, preferably wherein the internal positions include all positions except the terminal two or three positions from each end of the at least one strand.

19. The dsRNA agent of claim 18, wherein the internal positions exclude a cleavage site region of the sense strand; or wherein the internal positions include all positions except positions 11-13 on the sense strand, counting from the 3'-end, and positions 12-14 on the antisense strand, counting from the 5'-end.

20. The dsRNA agent of claim 19, wherein the internal positions include all positions except positions 9-12, counting from the 5'-end of the sense strand, or wherein the internal positions include all positions except positions 11-13, counting from the 3'-end of the sense strand.

21. The dsRNA agent of claim 18, wherein the internal positions exclude a cleavage site region of the antisense strand, preferably wherein the internal positions include all positions except positions 12-14, counting from the 5'-end of the antisense strand.

22. The dsRNA agent of any one of claims 1-21, wherein the one or more lipophilic moieties are conjugated to one or more of the internal positions selected from the group consisting of positions 4-8 and 13-18 on the sense strand, and positions 6-10 and 15-18 on the antisense strand, counting from the 5' end of each strand, preferably wherein the one or more lipophilic moieties are conjugated to one or more of the internal positions selected from the group consisting of

positions 5, 6, 7, 15, and 17 on the sense strand, and positions 15 and 17 on the antisense strand, counting from the 5'-end of each strand.

23. The dsRNA agent of any one of claims 1-22, wherein the sense strand is 21 nucleotides in length, the antisense strand is 23 nucleotides in length, and the lipophilic moiety is conjugated to position 21, position 20, position 15, position 1, position 7, position 6, or position 2 of the sense strand or position 16 of the antisense strand.

24. The dsRNA agent of claim 23, wherein the lipophilic moiety is conjugated to position 21, position 20, position 15, position 1, or position 7 of the sense strand; or wherein the lipophilic moiety is conjugated to position 21, position 20, or position 15 of the sense strand; or wherein the lipophilic moiety is conjugated to position 20 or position 15 of the sense strand; or wherein the lipophilic moiety is conjugated to position 16 of the antisense strand.

25. The dsRNA agent of any one of claims 1-24, wherein the lipophilic moiety is an aliphatic, alicyclic, or polyalicyclic compound, preferably wherein the lipophilic moiety is selected from the group consisting of lipid, cholesterol, retinoic acid, cholic acid, adamantane acetic acid, 1-pyrene butyric acid, dihydrotestosterone, 1,3-bis-O(hexadecyl)glycerol, geranyloxyhexyanol, hexadecylglycerol, borneol, menthol, 1,3-propanediol, heptadecyl group, palmitic acid, myristic acid, O3-(oleoyl)lithocholic acid, O3-(oleoyl)cholenic acid, dimethoxytrityl, or phenoxazine.

26. The dsRNA agent of claim 25, wherein the lipophilic moiety contains a saturated or unsaturated C_4-C_{30} hydrocarbon chain, and an optional functional group selected from the group consisting of hydroxyl, amine, carboxylic acid, sulfonate, phosphate, thiol, azide, and alkyne.

27. The dsRNA agent of claim 26, wherein the lipophilic moiety contains a saturated or unsaturated C_6-C_{18} hydrocarbon chain, or wherein the lipophilic moiety contains a saturated or unsaturated C_{16} hydrocarbon chain, preferably wherein the saturated or unsaturated C_{16} hydrocarbon chain is conjugated to position 6, counting from the 5'-end of the strand.

28. The dsRNA agent of any one of claims 1-27, wherein the lipophilic moiety is conjugated via a carrier that replaces one or more nucleotide(s) in the internal position(s) or the double stranded region, preferably wherein the carrier is a cyclic group selected from the group consisting of pyrrolidinyl, pyrazolinyl, pyrazolidinyl, imidazolinyl, imidazolidinyl, piperidinyl, piperazinyl,

[1,3]dioxolanyl, oxazolidinyl, isoxazolidinyl, morpholinyl, thiazolidinyl, isothiazolidinyl, quinoxalinyl, pyridazinonyl, tetrahydrofuranyl, and decalinyl; or is an acyclic moiety based on a serinol backbone or a diethanolamine backbone.

29. The dsRNA agent of any one of claims 1-27, wherein the lipophilic moiety is conjugated to the double-stranded iRNA agent via a linker containing an ether, thioether, urea, carbonate, amine, amide, maleimide-thioether, disulfide, phosphodiester, sulfonamide linkage, a product of a click reaction, or carbamate.

30. The double-stranded iRNA agent of any one of claims 1-29, wherein the lipophilic moiety is conjugated to a nucleobase, sugar moiety, or internucleosidic linkage.

31. The dsRNA agent of any one of claims 1-30, wherein the lipophilic moiety or targeting ligand is conjugated via a bio-cleavable linker selected from the group consisting of DNA, RNA, disulfide, amide, functionalized monosaccharides or oligosaccharides of galactosamine, glucosamine, glucose, galactose, mannose, and combinations thereof.

32. The dsRNA agent of any one of claims 1-31, wherein the 3’ end of the sense strand is protected via an end cap which is a cyclic group having an amine, said cyclic group being selected from the group consisting of pyrrolidinyl, pyrazolinyl, pyrazolidinyl, imidazolinyl, imidazolidinyl, piperidinyl, piperazinyl, [1,3]dioxolanyl, oxazolidinyl, isoxazolidinyl, morpholinyl, thiazolidinyl, isothiazolidinyl, quinoxalinyl, pyridazinonyl, tetrahydrofuranyl, and decalinyl.

33. The dsRNA agent of any one of claims 1-32, further comprising a targeting ligand that targets a liver tissue, preferably wherein the targeting ligand is a GalNAc conjugate.

34. The dsRNA agent of any one of claims 1-33 further comprising:

a terminal, chiral modification occurring at the first internucleotide linkage at the 3’ end of the antisense strand, having the linkage phosphorus atom in Sp configuration,

a terminal, chiral modification occurring at the first internucleotide linkage at the 5’ end of the antisense strand, having the linkage phosphorus atom in Rp configuration, or

a terminal, chiral modification occurring at the first internucleotide linkage at the 5’ end of the sense strand, having the linkage phosphorus atom in either Rp configuration or Sp configuration; or

a terminal, chiral modification occurring at the first and second internucleotide linkages at the 3’ end of the antisense strand, having the linkage phosphorus atom in Sp configuration,

a terminal, chiral modification occurring at the first internucleotide linkage at the 5’ end of the antisense strand, having the linkage phosphorus atom in Rp configuration, or

a terminal, chiral modification occurring at the first internucleotide linkage at the 5’ end of the sense strand, having the linkage phosphorus atom in either Rp or Sp configuration; or

a terminal, chiral modification occurring at the first, second and third internucleotide linkages at the 3’ end of the antisense strand, having the linkage phosphorus atom in Sp configuration,

a terminal, chiral modification occurring at the first internucleotide linkage at the 5’ end of the antisense strand, having the linkage phosphorus atom in Rp configuration, or

a terminal, chiral modification occurring at the first internucleotide linkage at the 5’ end of the sense strand, having the linkage phosphorus atom in either Rp or Sp configuration; or

a terminal, chiral modification occurring at the first, and second internucleotide linkages at the 3’ end of the antisense strand, having the linkage phosphorus atom in Sp configuration,

a terminal, chiral modification occurring at the third internucleotide linkages at the 3’ end of the antisense strand, having the linkage phosphorus atom in Rp configuration,

a terminal, chiral modification occurring at the first internucleotide linkage at the 5’ end of the antisense strand, having the linkage phosphorus atom in Rp configuration, or

a terminal, chiral modification occurring at the first internucleotide linkage at the 5’ end of the sense strand, having the linkage phosphorus atom in either Rp or Sp configuration; or

a terminal, chiral modification occurring at the first, and second internucleotide linkages at the 3’ end of the antisense strand, having the linkage phosphorus atom in Sp configuration,

a terminal, chiral modification occurring at the first, and second internucleotide linkages at the 5’ end of the antisense strand, having the linkage phosphorus atom in Rp configuration, or

a terminal, chiral modification occurring at the first internucleotide linkage at the 5’ end of the sense strand, having the linkage phosphorus atom in either Rp or Sp configuration.

35. The dsRNA agent of any one of claims 1-34, further comprising a phosphate or phosphate mimic at the 5'-end of the antisense strand, preferably wherein the phosphate mimic is a 5'-vinyl phosphonate (VP).

36. The dsRNA agent of any one of claims 1-34, wherein the base pair at the 1 position of the 5′-end of the antisense strand of the duplex is an A:U base pair., or wherein the sense strand has a total of 21 nucleotides and the antisense strand has a total of 23 nucleotides.

37. A cell containing the dsRNA agent of any one of claims 1-36.

38. A pharmaceutical composition comprising the dsRNA agent of any one of claims 1-36 and optionally a lipid formulation.

39. An *in vitro* or *ex vivo* method of inhibiting expression of a SNCA gene in a cell, the method comprising:

(a) contacting the cell with the dsRNA agent of any one of claims 1-36, or the pharmaceutical composition of claim 38; and

(b) maintaining the cell produced in step (a) for a time sufficient to obtain degradation of the mRNA transcript of the SNCA gene, thereby inhibiting expression of the SNCA gene in the cell, preferably wherein the expression of SNCA is inhibited by at least 50%.

40. Use of the dsRNA agent of any one of claims 1-36 or the pharmaceutical composition of claim 38 in the manufacture of a medicament for the treatment of a SNCA-associated neurodegenerative disease in a subject.

41. The use of claim 40, wherein the treatment comprises amelioration of at least one sign or symptom of the disease, or prevention of progression of the disease.

42. The use of claim 40, wherein the SNCA-associated disease is characterized by one or more symptoms selected from the group consisting of tremors, slowed movement (bradykinesia), rigid muscles, impaired posture and balance, loss of automatic movements, speech changes, writing changes, visual, auditory, olfactory, or tactile hallucinations, poor regulation of body functions (autonomic nervous systems) such as dizziness, falls and bowel issues, cognitive problems such as confusion, poor attention, visual-spatial problems and memory loss, sleep difficulties such as

rapid eye movement (REM) sleep behavior disorder (in which dreams are physically acted out while asleep), fluctuating attention including episodes of drowsiness, long periods of staring into space, long naps during the day or disorganized speech, depression, and apathy, orthostatic hypotension (a sudden drop in blood pressure that occurs when a person stands up, causing a person to feel dizzy and lightheaded, and the need to sit, squat, or lie down in order to prevent fainting), clumsiness or incoordination, bladder control problems, contractures (chronic shortening of muscles or tendons around joints, which prevents the joints from moving freely) in the hands or limbs, Pisa syndrome (an abnormal posture in which the body appears to be leaning to one side), antecollis (in which the neck bends forward and the head drops down), and involuntary and uncontrollable sighing or gasping, or

wherein the SNCA-associated neurodegenerative disease is selected from the group consisting of a synucleinopathy, such as PD, multiple system atrophy, Lewy body dementia (LBD), pure autonomic failure (PAF), Pick's disease, progressive supranuclear palsy, dementia pugilistica, parkinsonism linked to chromosome 17, Lytico-Bodig disease, tangle predominant dementia, Argyrophilic grain disease, ganglioglioma, gangliocytoma, meningioangiomatosis, subacute sclerosing panencephalitis, lead encephalopathy, tuberous sclerosis, Hallervorden-Spatz disease, lipofuscinosis, corticobasal degeneration, frontotemporal dementia, frontotemporal lobar degeneration, Alzheimer's disease, Huntington's disease, Down’s syndrome, psychosis, schizophrenia and Creutzfeldt-Jakob disease.

43. The use of any one of claims 40-42, wherein the dsRNA agent is to be administered to the subject at a dose of about 0.01 mg/kg to about 50 mg/kg, preferably intrathecally.

44. The use of any one of claims 40-42, wherein an additional agent or a therapy suitable for treatment or prevention of a SNCA-associated disease or disorder is to be further administered to the subject.

45. A modified double stranded ribonucleic acid (RNAi) agent for inhibiting expression of a SNCA gene as listed in **Tables 2, 9, or 12**, wherein the 3’-terminus of each sense strand is optionally modified by both (i) removing the 3’-terminal L96 ligand and (ii) replacing the two phosphodiester internucleotide linkages between the three 3’-terminal nucleotides with phosphorothioate internucleotide linkages.