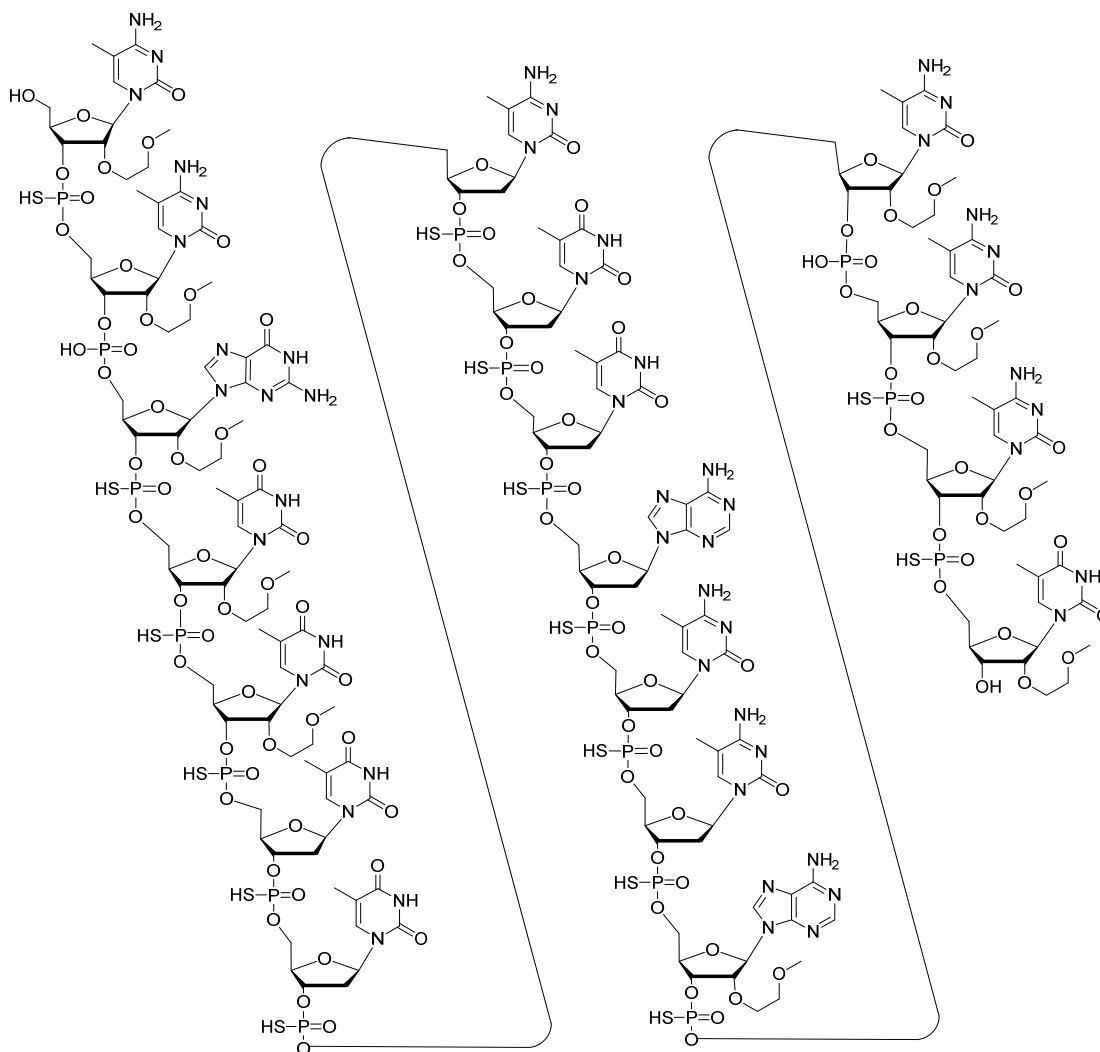


CLAIMS:

1. Use of a therapeutically effective amount of a modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 4), or a sodium or potassium salt thereof, in the manufacture of a medicament for treating a disease or disorder associated with Tau protein, reducing Tau RNA, or reducing Tau protein, in a human subject in need thereof, wherein the medicament is to be administered to the human subject.

2. Use of a therapeutically effective amount of a modified oligonucleotide in the manufacture of a medicament for treating a disease or disorder associated with Tau protein, reducing Tau RNA, or reducing Tau protein, in a human subject in need thereof, wherein the medicament is to be administered to the human subject, wherein the modified oligonucleotide has the following chemical notation (5' to 3'): mCes mCeo Ges Tes Tes Tds Tds mCds Tds Tds Ads mCds mCds Aes mCeo mCes mCes Te (SEQ ID NO: 4); wherein:

A = an adenine nucleobase,
mC = a 5-methyl cytosine nucleobase,
G = a guanine nucleobase,
T = a thymine nucleobase,
e = a 2'-O-methoxyethyl (MOE) sugar moiety,
d = a 2'-β-D-deoxyribosyl sugar moiety,
s = a phosphorothioate internucleoside linkage, and
o = a phosphodiester internucleoside linkage.

3. The use of claim 1 or claim 2, wherein the disease or disorder associated with Tau protein is a neurodegenerative disease or disorder, or a taupathy.

4. The use of any one of claims 1-3, wherein the disease or disorder associated with Tau protein is Alzheimer's disease (AD), mild AD, MCI due to AD, mild AD dementia, Frontotemporal Dementia (FTD), Frontotemporal Dementia with Parkinsonism-17 (FTDP-17), Progressive Supranuclear Palsy (PSP), Chronic Traumatic Encephalopathy (CTE), Corticobasal Ganglionic Degeneration (CBD), Pick Disease, Argyrophilic Grain Disease (AGD), Globular Glial Tauopathies, Epilepsy, Dravet's Syndrome, Down syndrome, Prion diseases (sCJD, vCJD, gCJD, GSS, FFI), Diffuse neurofibrillary tangles with calcification, Familial British and Danish dementia, Postencephalitic parkinsonism, Subacute sclerosing panencephalitis, Myotonic dystrophy (DM1), PROMM (DM2), Aging-related tau astroglipathy, Traumatic brain injury, Chronic traumatic encephalopathy, IgLON5-related tauopathy, Guadeloupean parkinsonism, Parkinson-dementia complex of Guam, Non-Guamanian motor neuron disease with NFTs, Amyotrophic lateral sclerosis of Guam, X-linked parkinsonism with spasticity, Cerebrotendinous xanthomatosis, Niemann-Pick disease type C, PANK2-associated Neurodegeneration with Brain Iron Accumulation (NBIA), PLA2G6-associated NBIA, SLC9A6 mental retardation, or diseases or disorders associated with mutations in LRRK2, PRKN, SNCA, TARDBP, and/or C9orf72 genes.

5. The use of any one of claims 1-4, wherein at least one symptom or hallmark of the disease or disorder associated with Tau protein is ameliorated.

6. The use of claim 5, wherein the at least one symptom or hallmark comprises loss of memory, cognitive decline, loss of ability to understand or express speech, abnormal behavior, impaired motor function, loss of cognitive function, neuropsychiatric behavior dysfunction,

impaired global function, loss of motor function, impaired cognitive function, impaired neuropsychiatric function, impaired daily function, impaired attention, impaired visuoperceptual processing, impaired memory, impaired degree of independence, increased apathy, impaired learning ability, impaired mental concentration, impaired understanding and expression of speech, impaired behavior, depression, irritability, anger, impaired mobility, impaired self-care, pain, discomfort, anxiety, seizures, suicidal ideation, suicidal behavior, increase in the number and/or volume of neurofibrillary inclusions.

7. The use of any one of claims 1-5, wherein the therapeutically effective amount is 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 55 mg, 60 mg, 65 mg, 70 mg, 75 mg, 80 mg, 85 mg, 90 mg, 95 mg, 100 mg, 105 mg, 110 mg, 115 mg, 120 mg, 125 mg, 130 mg, 135 mg, 140 mg, 145 mg, 150 mg, 155 mg, 160 mg, 165 mg, 170 mg, 175 mg, 180 mg, 185 mg, 190 mg, 195 mg, 200 mg, 205 mg, 210 mg, 215 mg, 220 mg, 225 mg, 230 mg, 235 mg, 240 mg, 245 mg, 250 mg, 255 mg, 260 mg, 265 mg, 270 mg, 275 mg, 280 mg, 285 mg, 290 mg, 295 mg, 300 mg, 305 mg, 310 mg, 315 mg, 320 mg, 325 mg, 330 mg, 335 mg, 340 mg, 345 mg, or 350 mg.

8. The use of any one of claims 1-5, wherein the therapeutically effective amount is 50 mg, 50.1 mg, 50.2 mg, 50.3 mg, 50.4 mg, 50.5 mg, 50.6 mg, 50.7 mg, 50.8 mg, 50.9 mg, 51 mg, 51.1 mg, 51.2 mg, 51.3 mg, 51.4 mg, 51.5 mg, 51.6 mg, 51.7 mg, 51.8 mg, 51.9 mg, 52 mg, 52.1 mg, 52.2 mg, 52.3 mg, 52.4 mg, 52.5 mg, 52.6 mg, 52.7 mg, 52.8 mg, 52.9 mg, 53 mg, 53.1 mg, 53.2 mg, 53.3 mg, 53.4 mg, 53.5 mg, 53.6 mg, 53.7 mg, 53.8 mg, 53.9 mg, 54 mg, 54.1 mg, 54.2 mg, 54.3 mg, 54.4 mg, 54.5 mg, 54.6 mg, 54.7 mg, 54.8 mg, 54.9 mg, 55 mg, 55.1 mg, 55.2 mg, 55.3 mg, 55.4 mg, 55.5 mg, 55.6 mg, 55.7 mg, 55.8 mg, 55.9 mg, 56 mg, 56.1 mg, 56.2 mg, 56.3 mg, 56.4 mg, 56.5 mg, 56.6 mg, 56.7 mg, 56.8 mg, 56.9 mg, 57 mg, 57.1 mg, 57.2 mg, 57.3 mg, 57.4 mg, 57.5 mg, 57.6 mg, 57.7 mg, 57.8 mg, 57.9 mg, 58 mg, 58.1 mg, 58.2 mg, 58.3 mg, 58.4 mg, 58.5 mg, 58.6 mg, 58.7 mg, 58.8 mg, 58.9 mg, 59 mg, 59.1 mg, 59.2 mg, 59.3 mg, 59.4 mg, 59.5 mg, 59.6 mg, 59.7 mg, 59.8 mg, 59.9 mg, 60 mg, 60.1 mg, 60.2 mg, 60.3 mg, 60.4 mg, 60.5 mg, 60.6 mg, 60.7 mg, 60.8 mg, 60.9 mg, 61 mg, 61.1 mg, 61.2 mg, 61.3 mg, 61.4 mg, 61.5 mg, 61.6 mg, 61.7 mg, 61.8 mg, 61.9 mg, 62 mg, 62.1 mg, 62.2 mg, 62.3 mg, 62.4 mg, 62.5 mg, 62.6 mg, 62.7 mg, 62.8 mg, 62.9 mg, 63 mg, 63.1 mg, 63.2 mg, 63.3 mg, 63.4 mg, 63.5 mg, 63.6 mg, 63.7 mg, 63.8 mg, 63.9 mg, 64 mg, 64.1 mg, 64.2 mg, 64.3 mg, 64.4 mg, 64.5 mg, 64.6 mg, 64.7 mg, 64.8 mg, 64.9 mg, 65 mg, 65.1 mg, 65.2 mg, 65.3 mg, 65.4 mg, 65.5 mg, 65.6 mg, 65.7 mg, 65.8 mg, 65.9 mg, 66 mg, 66.1 mg, 66.2 mg, 66.3 mg, 66.4 mg, 66.5 mg, 66.6 mg, 66.7 mg, 66.8 mg, 66.9 mg, 67 mg, 67.1 mg, 67.2 mg, 67.3 mg, 67.4 mg, 67.5 mg, 67.6 mg, 67.7 mg, 67.8 mg, 67.9

mg, 68 mg, 68.1 mg, 68.2 mg, 68.3 mg, 68.4 mg, 68.5 mg, 68.6 mg, 68.7 mg, 68.8 mg, 68.9 mg, 69 mg, 69.1 mg, 69.2 mg, 69.3 mg, 69.4 mg, 69.5 mg, 69.6 mg, 69.7 mg, 69.8 mg, 69.9 mg, or 70 mg.

9. The use of any one of claims 1-5, wherein the therapeutically effective amount is 80 mg, 80.1 mg, 80.2 mg, 80.3 mg, 80.4 mg, 80.5 mg, 80.6 mg, 80.7 mg, 80.8 mg, 80.9 mg, 81 mg, 81.1 mg, 81.2 mg, 81.3 mg, 81.4 mg, 81.5 mg, 81.6 mg, 81.7 mg, 81.8 mg, 81.9 mg, 82 mg, 82.1 mg, 82.2 mg, 82.3 mg, 82.4 mg, 82.5 mg, 82.6 mg, 82.7 mg, 82.8 mg, 82.9 mg, 83 mg, 83.1 mg, 83.2 mg, 83.3 mg, 83.4 mg, 83.5 mg, 83.6 mg, 83.7 mg, 83.8 mg, 83.9 mg, 84 mg, 84.1 mg, 84.2 mg, 84.3 mg, 84.4 mg, 84.5 mg, 84.6 mg, 84.7 mg, 84.8 mg, 84.9 mg, 85 mg, 85.1 mg, 85.2 mg, 85.3 mg, 85.4 mg, 85.5 mg, 85.6 mg, 85.7 mg, 85.8 mg, 85.9 mg, 86 mg, 86.1 mg, 86.2 mg, 86.3 mg, 86.4 mg, 86.5 mg, 86.6 mg, 86.7 mg, 86.8 mg, 86.9 mg, 87 mg, 87.1 mg, 87.2 mg, 87.3 mg, 87.4 mg, 87.5 mg, 87.6 mg, 87.7 mg, 87.8 mg, 87.9 mg, 88 mg, 88.1 mg, 88.2 mg, 88.3 mg, 88.4 mg, 88.5 mg, 88.6 mg, 88.7 mg, 88.8 mg, 88.9 mg, 89 mg, 89.1 mg, 89.2 mg, 89.3 mg, 89.4 mg, 89.5 mg, 89.6 mg, 89.7 mg, 89.8 mg, 89.9 mg, 90 mg, 90.1 mg, 90.2 mg, 90.3 mg, 90.4 mg, 90.5 mg, 90.6 mg, 90.7 mg, 90.8 mg, 90.9 mg, 91 mg, 91.1 mg, 91.2 mg, 91.3 mg, 91.4 mg, 91.5 mg, 91.6 mg, 91.7 mg, 91.8 mg, 91.9 mg, 92 mg, 92.1 mg, 92.2 mg, 92.3 mg, 92.4 mg, 92.5 mg, 92.6 mg, 92.7 mg, 92.8 mg, 92.9 mg, 93 mg, 93.1 mg, 93.2 mg, 93.3 mg, 93.4 mg, 93.5 mg, 93.6 mg, 93.7 mg, 93.8 mg, 93.9 mg, 94 mg, 94.1 mg, 94.2 mg, 94.3 mg, 94.4 mg, 94.5 mg, 94.6 mg, 94.7 mg, 94.8 mg, 94.9 mg, 95 mg, 95.1 mg, 95.2 mg, 95.3 mg, 95.4 mg, 95.5 mg, 95.6 mg, 95.7 mg, 95.8 mg, 95.9 mg, 96 mg, 96.1 mg, 96.2 mg, 96.3 mg, 96.4 mg, 96.5 mg, 96.6 mg, 96.7 mg, 96.8 mg, 96.9 mg, 97 mg, 97.1 mg, 97.2 mg, 97.3 mg, 97.4 mg, 97.5 mg, 97.6 mg, 97.7 mg, 97.8 mg, 97.9 mg, 98 mg, 98.1 mg, 98.2 mg, 98.3 mg, 98.4 mg, 98.5 mg, 98.6 mg, 98.7 mg, 98.8 mg, 98.9 mg, 99 mg, 99.1 mg, 99.2 mg, 99.3 mg, 99.4 mg, 99.5 mg, 99.6 mg, 99.7 mg, 99.8 mg, 99.9 mg, or 100 mg.

10. The use of any one of claims 1-5, wherein the therapeutically effective amount is 105 mg, 105.1 mg, 105.2 mg, 105.3 mg, 105.4 mg, 105.5 mg, 105.6 mg, 105.7 mg, 105.8 mg, 105.9 mg, 106 mg, 106.1 mg, 106.2 mg, 106.3 mg, 106.4 mg, 106.5 mg, 106.6 mg, 106.7 mg, 106.8 mg, 106.9 mg, 107 mg, 107.1 mg, 107.2 mg, 107.3 mg, 107.4 mg, 107.5 mg, 107.6 mg, 107.7 mg, 107.8 mg, 107.9 mg, 108 mg, 108.1 mg, 108.2 mg, 108.3 mg, 108.4 mg, 108.5 mg, 108.6 mg, 108.7 mg, 108.8 mg, 108.9 mg, 109 mg, 109.1 mg, 109.2 mg, 109.3 mg, 109.4 mg, 109.5 mg, 109.6 mg, 109.7 mg, 109.8 mg, 109.9 mg, 110 mg, 110.1 mg, 110.2 mg, 110.3 mg, 110.4 mg, 110.5 mg, 110.6 mg, 110.7 mg, 110.8 mg, 110.9 mg, 111 mg, 111.1 mg, 111.2 mg, 111.3 mg, 111.4 mg, 111.5 mg, 111.6 mg, 111.7 mg, 111.8 mg, 111.9 mg, 112 mg, 112.1 mg, 112.2 mg,

112.3 mg, 112.4 mg, 112.5 mg, 112.6 mg, 112.7 mg, 112.8 mg, 112.9 mg, 113 mg, 113.1 mg, 113.2 mg, 113.3 mg, 113.4 mg, 113.5 mg, 113.6 mg, 113.7 mg, 113.8 mg, 113.9 mg, 114 mg, 114.1 mg, 114.2 mg, 114.3 mg, 114.4 mg, 114.5 mg, 114.6 mg, 114.7 mg, 114.8 mg, 114.9 mg, 115 mg, 115.1 mg, 115.2 mg, 115.3 mg, 115.4 mg, 115.5 mg, 115.6 mg, 115.7 mg, 115.8 mg, 115.9 mg, 116 mg, 116.1 mg, 116.2 mg, 116.3 mg, 116.4 mg, 116.5 mg, 116.6 mg, 116.7 mg, 116.8 mg, 116.9 mg, 117 mg, 117.1 mg, 117.2 mg, 117.3 mg, 117.4 mg, 117.5 mg, 117.6 mg, 117.7 mg, 117.8 mg, 117.9 mg, 118 mg, 118.1 mg, 118.2 mg, 118.3 mg, 118.4 mg, 118.5 mg, 118.6 mg, 118.7 mg, 118.8 mg, 118.9 mg, 119 mg, 119.1 mg, 119.2 mg, 119.3 mg, 119.4 mg, 119.5 mg, 119.6 mg, 119.7 mg, 119.8 mg, 119.9 mg, 120 mg, 120.1 mg, 120.2 mg, 120.3 mg, 120.4 mg, 120.5 mg, 120.6 mg, 120.7 mg, 120.8 mg, 120.9 mg, 121 mg, 121.1 mg, 121.2 mg, 121.3 mg, 121.4 mg, 121.5 mg, 121.6 mg, 121.7 mg, 121.8 mg, 121.9 mg, 122 mg, 122.1 mg, 122.2 mg, 122.3 mg, 122.4 mg, 122.5 mg, 122.6 mg, 122.7 mg, 122.8 mg, 122.9 mg, 123 mg, 123.1 mg, 123.2 mg, 123.3 mg, 123.4 mg, 123.5 mg, 123.6 mg, 123.7 mg, 123.8 mg, 123.9 mg, 124 mg, 124.1 mg, 124.2 mg, 124.3 mg, 124.4 mg, 124.5 mg, 124.6 mg, 124.7 mg, 124.8 mg, 124.9 mg, or 125 mg.

11. The use of any one of claims 1-5, wherein the therapeutically effective amount is within the range of 40 mg to 200 mg, 40 mg to 190 mg, 40 mg to 180 mg, 40 mg to 170 mg, from 40 mg to 160 mg, 40 mg to 150 mg, 40 mg to 140 mg, 40 mg to 120 mg, 40 mg to 110 mg, 40 mg to 100 mg, 40 mg to 80 mg, 40 mg to 70 mg, 40 mg to 60 mg, 40 mg to 50 mg, 50 mg to 200 mg, 50 mg to 190 mg, 50 mg to 180 mg, 50 mg to 170 mg, 50 mg to 160 mg, 50 mg to 150 mg, 50 mg to 140 mg, 50 mg to 120 mg, 50 mg to 110 mg, 50 mg to 100 mg, 50 mg to 80 mg, 50 mg to 70 mg, 50 mg to 60 mg, 60 mg to 200 mg, 60 mg to 190 mg, 60 mg to 180 mg, 60 mg to 170 mg, 60 mg to 160 mg, 60 mg to 150 mg, 60 mg to 140 mg, 60 mg to 120 mg, 60 mg to 110 mg, 60 mg to 100 mg, 60 mg to 80 mg, 60 mg to 70 mg, 70 mg to 200 mg, 70 mg to 190 mg, 70 mg to 180 mg, 70 mg to 170 mg, 70 mg to 160 mg, 70 mg to 150 mg, 70 mg to 140 mg, 70 mg to 120 mg, 70 mg to 110 mg, 70 mg to 100 mg, 70 mg to 80 mg, 80 mg to 200 mg, 80 mg to 190 mg, 80 mg to 180 mg, 80 mg to 170 mg, 80 mg to 160 mg, 80 mg to 150 mg, 80 mg to 140 mg, 80 mg to 120 mg, 80 mg to 110 mg, 80 mg to 100 mg, 80 mg to 90 mg, 90 mg to 200 mg, 90 mg to 190 mg, 90 mg to 180 mg, 90 mg to 170 mg, 90 mg to 160 mg, 90 mg to 150 mg, 90 mg to 140 mg, 90 mg to 120 mg, 90 mg to 110 mg, 90 mg to 100 mg, 100 mg to 200 mg, 100 mg to 190 mg, 100 mg to 180 mg, 100 mg to 170 mg, 100 mg to 160 mg, 100 mg to 150 mg, 100 mg to 140 mg, 100 mg to 120 mg, 100 mg to 110 mg, 110 mg to 200 mg, 110 mg to 190 mg, 110 mg to 180 mg, 110 mg to 170 mg, 110 mg to 160 mg, 110 mg to 150 mg, 110 mg to 140 mg, 110 mg to 130 mg, 110 mg to 120 mg, 120 mg to 200 mg, 120 mg to 190 mg, 120 mg to 180 mg, 120 mg to 170 mg,

120 mg to 160 mg, 120 mg to 150 mg, 120 mg to 140 mg, 120 mg to 130 mg, 130 mg to 200 mg, 130 mg to 190 mg, 130 mg to 180 mg, 130 mg to 170 mg, 130 mg to 160 mg, 130 mg to 150 mg, 130 mg to 140 mg, 140 mg to 200 mg, 140 mg to 190 mg, 140 mg to 180 mg, 140 mg to 170 mg, 140 mg to 160 mg, 140 mg to 150 mg, 150 mg to 200 mg, 150 mg to 190 mg, 150 mg to 180 mg, 150 mg to 170 mg, 150 mg to 160 mg, 160 mg to 200 mg, 160 mg to 190 mg, 160 mg to 180 mg, 160 mg to 170 mg, 180 mg to 200 mg, 180 mg to 190 mg, 190 mg to 200 mg, 105 mg to 135 mg, 105 mg to 130 mg, 105 mg to 125 mg, 105 mg to 120 mg, 110 mg to 135 mg, 110 mg to 130 mg, 110 mg to 125 mg, 110 mg to 120 mg, 115 mg to 135 mg, 115 mg to 130 mg, 115 mg to 125 mg, 115 mg to 120 mg, 115 mg to 125 mg, 115 mg to 120 mg, 120 mg to 135 mg, 120 mg to 125 mg, 125 mg to 140 mg, 125 mg to 130 mg, 130 mg to 135 mg, 135 mg to 140 mg, 120 mg to 129 mg, 120 mg to 128 mg, 120 mg to 127 mg, 120 mg to 86 mg, 120 mg to 124 mg, 120 mg to 123 mg, 120 mg to 122 mg, 120 mg to 121 mg, 121 mg to 130 mg, 122 mg to 129 mg, 122 mg to 128 mg, 122 mg to 127 mg, 122 mg to 126 mg, 122 mg to 125 mg, 122 mg to 124 mg, 122 mg to 123 mg, 123 mg to 130 mg, 123 mg to 129 mg, 123 mg to 128 mg, 123 mg to 127 mg, 123 mg to 126 mg, 123 mg to 125 mg, 123 mg to 124 mg, 124 mg to 130 mg, 124 mg to 129 mg, 124 mg to 128 mg, 124 mg to 127 mg, 124 mg to 126 mg, 124 mg to 125 mg, 125 mg to 129 mg, 125 mg to 128 mg, 125 mg to 127 mg, 125 mg to 126 mg, 126 mg to 130 mg, 126 mg to 129 mg, 126 mg to 128 mg, 126 mg to 127 mg, 127 mg to 130 mg, 127 mg to 129 mg, 127 mg to 128 mg, 128 mg to 130 mg, 128 mg to 129 mg, or 129 mg to 130 mg.

12. The use of any one of claims 1-5, wherein the therapeutically effective amount is less than 350 mg, less than 345 mg, less than 340 mg, less than 335 mg, less than 330 mg, less than 325 mg, less than 320 mg, less than 315 mg, less than 310 mg, less than 305 mg, less than 300 mg, less than 295 mg, less than 290 mg, less than 285 mg, less than 280 mg, less than 275 mg, less than 270 mg, less than 265 mg, less than 260 mg, less than 255 mg, less than 250 mg, less than 245 mg, less than 240 mg, less than 235 mg, less than 230 mg, less than 225 mg, less than 220 mg, less than 215 mg, less than 210 mg, less than 205 mg, less than 200 mg, less than 195 mg, less than 190 mg, less than 185 mg, less than 180 mg, less than 175 mg, less than 170 mg, less than 165 mg, less than 160 mg, less than 150 mg, less than 145 mg, less than 140 mg, less than 135 mg, less than 130 mg, less than 125 mg, less than 120 mg, less than 115 mg, less than 110 mg, less than 105 mg, less than 100 mg, less than 95 mg, less than 90 mg, less than 85 mg, less than 80 mg, less than 75 mg, less than 70 mg, less than 65 mg, less than 60 mg, less than 55 mg, less than 50 mg, less than 45 mg, less than 40 mg, less than 35 mg, less than 30 mg, less than 25 mg, less than 20 mg, less than 15 mg, less than 10 mg, or less than 5 mg.

13. The use of any one of claims 1-5, wherein the therapeutically effective amount is at least 5 mg, at least 10 mg, at least 15 mg, at least 20 mg, at least 25 mg, at least 30 mg, at least 35 mg, at least 40 mg, at least 45 mg, at least 50 mg, at least 55 mg, at least 60 mg, at least 65 mg, at least 70 mg, at least 75 mg, at least 80 mg, at least 85 mg, at least 90 mg, at least 95 mg, at least 100 mg, at least 105 mg, at least 115 mg, at least 120 mg, at least 125 mg, at least 130 mg, at least 135 mg, at least 140 mg, at least 145 mg, at least 150 mg, at least 155 mg, at least 160 mg, at least 165 mg, at least 170 mg, at least 175 mg, at least 180 mg, at least 185, at least 190 mg, at least 195 mg, or at least 200 mg.

14. The use of any one of claims 1-5, wherein the medicament is to be administered once every 1 week, once every 2 weeks, once every 3 weeks, once every 4 weeks, once every 5 weeks, once every 6 weeks, once every 7 weeks, once every 8 weeks, once every 9 weeks, once every 10 weeks, once every 11 weeks, once every 12 weeks, once every 13 weeks, once every 14 weeks, once every 15 weeks, once every 16 weeks, once every 17 weeks, once every 18 weeks, once every 19 weeks, once every 20 weeks, once every 21 weeks, once every 22 weeks, once every 23 weeks, once every 24 weeks, once every month, once every 2 months, once every 3 months, once every 4 months, once every 5 months, once every 6 months, once every 7 months, once every 8 months, once every 9 months, once every 10 months, once every 11 months, once every year, or once every two years.

15. The use of any one of claims 1-5, wherein the human subject is to be administered a dose of 10 mg, 30 mg, 60 mg and/or 115 mg of the modified oligonucleotide once every four weeks.

16. The use of any one of claims 1-5, wherein the human subject is to be administered a dose of 10 mg, 30 mg, or 60 mg of the modified oligonucleotide once every four weeks for total of four doses, and subsequently the human subject is to be administered a dose of 60 mg of the modified oligonucleotide once every 12 weeks.

17. The use of any one of claims 1-5, wherein the human subject is to be administered a dose of 115 mg of the modified oligonucleotide once every 12 weeks, once every three months, once every quarter, four times yearly, once every 6 months, or twice a year.

18. The use of any one of claims 1-5, wherein the human subject is to be administered a dose of 60 mg of the modified oligonucleotide once every three months, once every quarter, or four times yearly.

19. The use of any one of claims 1-5, wherein the human subject has Progressive Supranuclear Palsy (PSP), and the subject is to be administered a first dosing regimen comprising a dose of 115 mg of the modified oligonucleotide once every 12 weeks, once every 3 months, once every quarter, or four times yearly.
20. The use of claim 19, further comprising monitoring safety of the dosing regimen, ceasing the administration of the first dosing regimen, and subsequently the subject is to be administered a second dosing regimen comprising:
- a dose of 60 mg of the modified oligonucleotide once every 8 weeks or once every two months,
 - a dose of 90 mg of the modified oligonucleotide once every 12 weeks, once every three months, or once quarterly, or
 - a dose of 60 mg of the modified oligonucleotide once every 4 weeks or once every month.
21. The use of any one of claims 15-20, wherein 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40 doses are to be administered.
22. The use of any one of claims 1-5, wherein the human subject is to be administered an initial loading dose of 10 mg, 30 mg, 60 mg, 90 mg, or 115 mg of the modified oligonucleotide.
23. The use of claim 22, wherein the human subject is to be administered a maintenance dose of 10 mg, 30 mg, 60 mg, 90 mg, or 115 mg of the modified oligonucleotide 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, or 12 months after the second loading dose.
24. The use of claim 22 or claim 23, wherein the human subject is to be administered a maintenance dose of 10 mg, 30 mg, 60 mg, 90 mg, or 115 mg of the modified oligonucleotide 4 weeks, 8 weeks, 12 weeks, 16 weeks, 20 weeks, 24 weeks, or 6 months after the second loading dose and every 4 weeks thereafter.
25. The use of claim 24, wherein at least 2, at least 3, at least 4, at least 5, or at least 6 maintenance doses are to be administered to the human subject.

26. The use of claim 1 or claim 2, wherein two doses or four doses of the modified oligonucleotide are to be administered.
27. The use of claim 1, wherein the human subject is to be administered:
- a) an initial loading dose of 10 mg, 30 mg, 60 mg, 90 mg, or 115 mg of the modified oligonucleotide,
 - b) a second loading dose of 10 mg, 30 mg, 60 mg, 90 mg, or 115 mg of the modified oligonucleotide 4 weeks, 8 weeks, or 12 weeks after the initial loading dose;
 - c) a first maintenance dose of 10 mg, 30 mg, 60 mg, 90 mg, or 115 mg of the modified oligonucleotide 8 or 12 weeks after the second loading dose;
 - d) a second maintenance dose of 10 mg, 30 mg, 60 mg, 90 mg, or 115 mg of the modified oligonucleotide 8 weeks or 12 weeks after the first maintenance dose.
28. The use of any one of claims 1-27, wherein the human subject has a mutation in at least one gene selected from MAPT, APOE, APP, PSEN1, PSEN2, LRRK2, STX6, EIF2AK3, and MOBP.
29. The use of any one of claims 1-28, wherein the medicament is to be administered to the CNS of the human subject.
30. The use of any one of claims 1-29, wherein the medicament is to be administered by intrathecal administration.
31. The use of any one of claims 1-30, wherein the medicament is to be administered by bolus intrathecal administration.
32. The use of any one of claims 1-31, wherein Tau RNA is reduced.
33. The use of any one of claims 1-32, wherein Tau protein is reduced.
34. The use of any one of claims 1-33, comprising detecting an amount of Tau RNA in a biological sample from the human subject.
35. The use of any one of claims 1-34, comprising detecting an amount of Tau protein in a biological sample from the human subject.

36. The use of claim 34 or claim 35, wherein the biological sample comprises cerebrospinal fluid.
37. The use of claims 34 or claim 35, wherein the detecting occurs before and/or after the administration of the medicament.
38. The use of any one of claims 35-37, comprising adjusting the initial loading dose, the loading dose, maintenance dose, or therapeutically effective amount to be administered after detecting the amount of Tau RNA, Tau protein, or combination thereof.
39. The use of any one of claims 1-38, comprising analyzing brain activity, brain size, size of neurofibrillary inclusions, volume of neurofibrillary inclusions, amount or concentration of total tau protein, phosphorylated tau protein, or amyloid beta protein in the cerebral spinal fluid, or a combination thereof by performing magnetic resonance imaging (MRI), Positron Emission Tomography (PET), Electroencephalogram (EEG), or CSF analysis of the subject.
40. The use of claim 39, wherein performing the MRI, PET, EEG, or CSF analysis occurs before the administration of the medicament, after the administration of the medicament, or a combination thereof.
41. The use of claim 40, comprising determining or adjusting the therapeutically effective amount after performing the MRI, PET, EEG, or CSF analysis.
42. The use of claim 41, comprising performing the MRI, PET, EEG, or CSF analysis after the administration of the medicament, and adjusting the frequency of the administration after performing the MRI, PET, EEG, or CSF analysis.
43. The use of any one of claims 40-42, wherein the MRI, PET, EEG, or CSF analysis is performed within 1, 2, 4, 6, 8, 12 or 24 hours of the administration of the medicament.
44. The use of claim 43, wherein a loading dose is to be administered once every 4 weeks and a maintenance dose is to be administered once every 8 or 16 weeks before performing the first MRI, PET, EEG, or CSF analysis, and subsequently the maintenance dose is to be administered less than every 8 weeks or less than every 16 weeks.