

CLAIMS:

1. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides, wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to an equal length portion of an HTT RNA, and wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.
2. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides and having a nucleobase sequence comprising at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of any of SEQ ID NOs: 26-3707.
3. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides and having a nucleobase sequence comprising:
 - a) at least 12, at least 13, at least 14, at least 15, at least 16, or 17 contiguous nucleobases of any of SEQ ID NOs: 26-857 or 3552-3590;
 - b) at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of any of SEQ ID NOs: 858-3551 or 3591-3682; or
 - c) at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, or 18 contiguous nucleobases of any of SEQ ID NOs: 3683-3707.
4. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases complementary to:
 - an equal length portion of nucleobases 56443-56500 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 62833-62860 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 69788-69824 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 9984-10008 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 106863-106924 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 115297-115337 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 117868-117902 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 119644-119670 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 126780-126829 of SEQ ID NO: 2; or
 - an equal length portion of nucleobases 130388-130418 of SEQ ID NO: 2;wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.
5. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of a sequence selected from:

SEQ ID NOs: 1184, 1274, 1331, 1455, 1481, 1562, and 1684;

SEQ ID NOs: 3029, 3104, 3557, 3562, 3569, 3586, 3610, 3620, 3622, 3623, 3627, 3634, 3664, 3687, 3692, and 3697;

SEQ ID NOs: 2750, 2814, 2887, 2991, and 3090;

SEQ ID NOs: 2581, 2640, 2736, 2857, and 2917;

SEQ ID NOs: 1105, 1232, 1249, 3330, 3342, 3344, 3362, 3382, 3411, 3419, 3439, 3456, 3475, 3488, 3491, 3511, 3531, 3550, and 3551;

SEQ ID NOs: 2208, 2310, 2335, 2471, 3553, 3559, 3563, 3565, 3570, 3580, 3581, 3583, 3585, 3589, 3593, 3594, 3597, 3600, 3601, 3604, 3614, 3616, 3630, 3631, 3637, 3648, 3650, 3652, 3653, 3660, 3661, 3662, 3684, and 3689;

SEQ ID NOs: 2644, 2770, 2786, 2916, 3574, 3576, 3578, 3587, 3665, 3666, 3667, 3668, 3669, 3670, 3671, 3672, 3673, 3674, 3675, 3676, 3686, 3694, and 3698;

SEQ ID NOs: 919, 940, 3677, 3678, 3679, 3680, 3681, 3682, 3705, 3706, and 3707;

SEQ ID NOs: 1576, 1652, 1771, 1813, 1933, 1987, 2078, 3552, 3555, 3558, 3560, 3572, 3573, 3575, 3579, 3584, 3598, 3608, 3611, 3613, 3619, 3628, 3635, 3644, 3646, 3649, 3663, 3683, 3688, 3690, 3700, 3701, 3702, 3703, and 3704; and

SEQ ID NOs: 1343, 1406, 1539, 3335, 3401, 3472, 3477, 3519, and 3591;

wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.

6. The oligomeric compound of any of claims 1-5, wherein the modified oligonucleotide has a nucleobase sequence that is at least 85%, at least 90%, at least 95%, or 100% complementary to the nucleobase sequence of any one of SEQ ID NOS: 1-5 when measured across the entire nucleobase sequence of the modified oligonucleotide.
7. The oligomeric compound of any of claims 1-6, wherein the modified oligonucleotide consists of 10 to 25, 10 to 30, 12 to 20, 12 to 25, 12 to 30, 13 to 20, 13 to 25, 13 to 30, 14 to 20, 14 to 25, 14 to 30, 15 to 20, 15 to 25, 15 to 30, 16 to 18, 16 to 20, 16 to 25, 16 to 30, 17 to 20, 17 to 25, 17 to 30, 18 to 20, 18 to 25, 18 to 30, 19 to 20, 19 to 25, 19 to 30, 20 to 25, 20 to 30, 21 to 25, 21 to 30, 22 to 25, 22 to 30, 23 to 25, or 23 to 30 linked nucleosides.
8. The oligomeric compound of any of claims 1-7, wherein the modified oligonucleotide comprises at least one modified nucleoside.
9. The oligomeric compound of claim 8, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a modified sugar moiety.
10. The oligomeric compound of claim 9, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a bicyclic sugar moiety.
11. The oligomeric compound of claim 10, wherein the bicyclic sugar moiety has a 2'-4' bridge selected from -O-CH₂-; and -O-CH(CH₃)-.
12. The oligomeric compound of any of claims 8-11, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a non-bicyclic modified sugar moiety.

13. The oligomeric compound of claim 12, wherein the non-bicyclic modified sugar moiety is a 2'-MOE modified sugar moiety or a 2'-cEt modified sugar moiety.
14. The oligomeric compound of any of claims 8-13, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a sugar surrogate.
15. The oligomeric compound of claim 14, wherein the sugar surrogate is any of morpholino, modified morpholino, PNA, THP, and F-HNA.
16. The oligomeric compound of any of claims 1-15, wherein the modified oligonucleotide is a gapmer.
17. The oligomeric compound of any of claims 1-16, wherein the modified oligonucleotide has a sugar motif comprising:
 - a 5'-region consisting of 1-6 linked 5'-region nucleosides;
 - a central region consisting of 6-10 linked central region nucleosides; and
 - a 3'-region consisting of 1-6 linked 3'-region nucleosides,wherein each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety and each of the central region nucleosides comprises a 2'-β-D-deoxyribosyl sugar moiety.
18. The oligomeric compound of claim 17, wherein
 - the 5'-region consists of 5 linked 5'-region nucleosides;
 - the central region consists of 10 linked central region nucleosides; and
 - the 3'-region consists of 5 linked 3'-region nucleosides, andwherein each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a 2'-MOE sugar moiety and each of the central region nucleosides comprises a 2'-β-D-deoxyribosyl sugar moiety.
19. The oligomeric compound of claim 17, wherein
 - the 5'-region consists of 6 linked 5'-region nucleosides;
 - the central region consists of 10 linked central region nucleosides; and
 - the 3'-region consists of 4 linked 3'-region nucleosides, andwherein each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a 2'-MOE sugar moiety and each of the central region nucleosides comprises a 2'-β-D-deoxyribosyl sugar moiety.
20. The oligomeric compound of claim 17, wherein
 - the 5'-region consists of 5 linked 5'-region nucleosides;
 - the central region consists of 8 linked central region nucleosides; and
 - the 3'-region consists of 5 linked 3'-region nucleosides, andwherein each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a 2'-MOE sugar moiety and each of the central region nucleosides comprises a 2'-β-D-deoxyribosyl sugar moiety.
21. The oligomeric compound of claim 17, wherein

the central region consists of 8 linked central region nucleosides; and

wherein each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety selected from a 2'-MOE sugar moiety and a 2'-cEt sugar moiety and each of the central region nucleosides comprises a 2'-β-D-deoxyribosyl sugar moiety.

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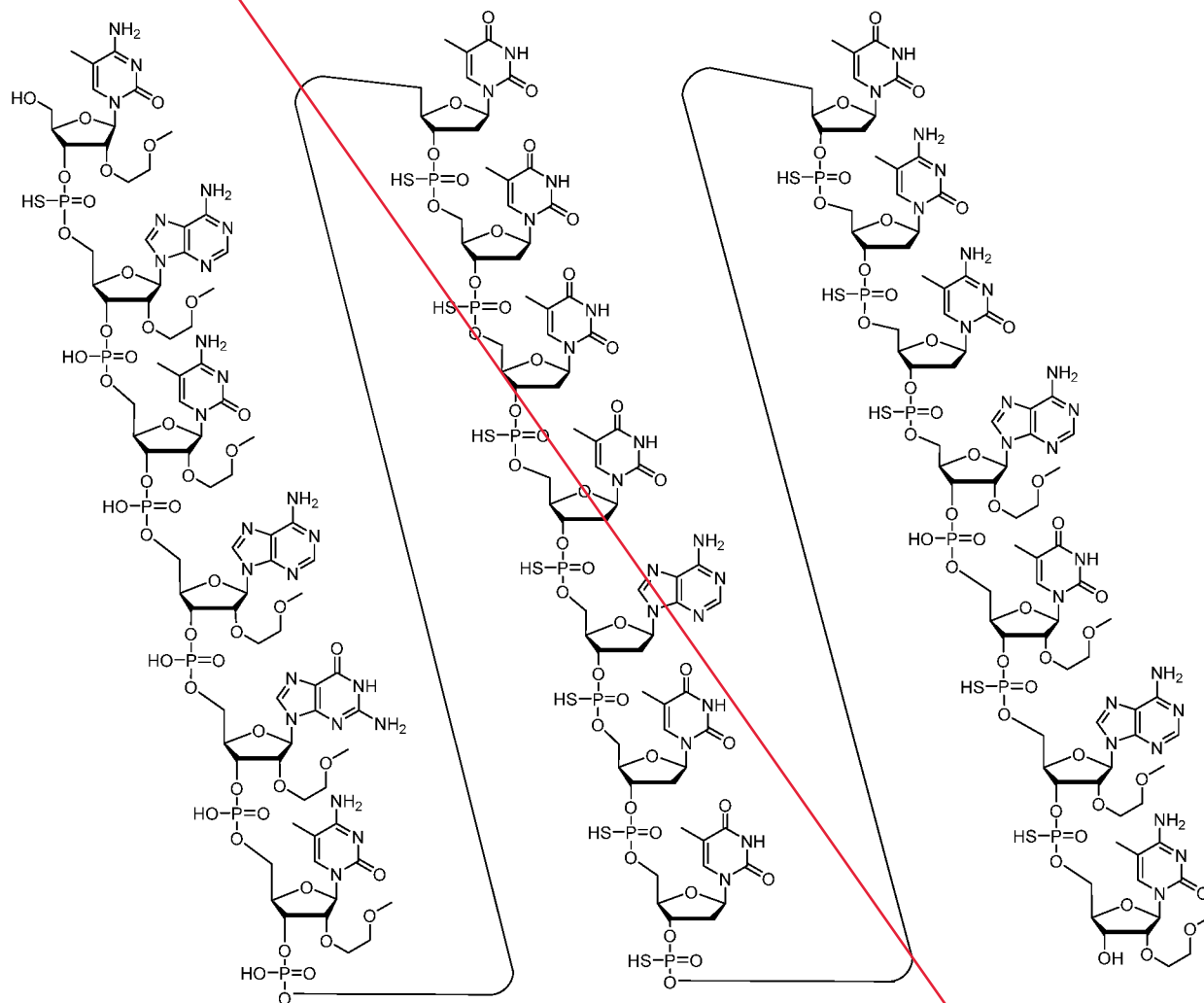
35. The oligomeric compound of any of claims 31-34, wherein the deoxy region is flanked on the 5'-side by a 5'-region consisting of 1-6 linked 5'-region nucleosides and on the 3'-side by a 3'-region consisting of 1-6 linked 3'-region nucleosides; wherein at least one nucleoside of the 5'-region comprises a modified sugar moiety; and at least one nucleoside of the 3'-region comprises a modified sugar moiety.
36. The oligomeric compound of claim 35, wherein each nucleoside of the 5'-region comprises a modified sugar moiety.
37. The oligomeric compound of claim 35 or claim 36, wherein each nucleoside of the 3'-region comprises a modified sugar moiety.
38. The oligomeric compound of any of claims 1-37, wherein the modified oligonucleotide consists of 12-30, 12-22, 12-20, 14-18, 14-20, 15-17, 15-25, 16-20, 18-22, or 18-20 linked nucleosides.
39. The oligomeric compound of any of claims 1-38, wherein the modified oligonucleotide consists of 17 linked nucleosides.
40. The oligomeric compound of any of claims 1-38, wherein the modified oligonucleotide consists of 18 linked nucleosides.
41. The oligomeric compound of any of claims 1-38, wherein the modified oligonucleotide consists of 20 linked nucleosides.
42. The oligomeric compound of any of claims 1-41, wherein the modified oligonucleotide is a pharmaceutically acceptable salt.
43. The oligomeric compound of claim 42, which is a pharmaceutically acceptable salt comprising one or more cations selected from sodium, potassium, calcium, and magnesium.
44. The oligomeric compound of any of claims 1-43, consisting of the modified oligonucleotide.
45. The oligomeric compound of any of claims 1-44, wherein the oligomeric compound comprises a conjugate group.
46. The oligomeric compound of claim 45, wherein the conjugate group comprises a conjugate moiety and a conjugate linker.
47. The oligomeric compound of claim 46, wherein the conjugate linker consists of a single bond.
48. The oligomeric compound of claim 46, wherein the conjugate linker is cleavable.
49. The oligomeric compound of claim 46, wherein the conjugate linker comprises 1-3 linker-nucleosides.
50. The oligomeric compound of claim 46, wherein the oligomeric compound does not comprise a linker-nucleoside.
51. The oligomeric compound of any of claims 45-50, wherein the conjugate group is attached to the modified oligonucleotide at the 5'-end of the modified oligonucleotide.
52. The oligomeric compound of any of claims 45-50, wherein the conjugate group is attached to the modified oligonucleotide at the 3'-end of the modified oligonucleotide.
53. The oligomeric compound of any of claims 1-52, comprising a terminal group.
54. The oligomeric compound of claim 53, wherein the terminal group is an abasic sugar moiety.

55. The oligomeric compound of any of claims 1-54, wherein the modified oligonucleotide is a single-stranded modified oligonucleotide.
56. The oligomeric compound of any of claims 1-55, wherein the oligomeric compound is an RNase H agent comprising the oligomeric compound.
57. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation:
 ${}^m\text{C}_{\text{es}} \text{A}_{\text{eo}} {}^m\text{C}_{\text{eo}} \text{A}_{\text{eo}} \text{G}_{\text{eo}} {}^m\text{C}_{\text{eo}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{A}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} {}^m\text{C}_{\text{ds}} {}^m\text{C}_{\text{ds}} \text{A}_{\text{eo}} \text{T}_{\text{es}} \text{A}_{\text{es}} {}^m\text{C}_{\text{e}}$ (SEQ ID NO: 3619), wherein
 A = an adenine,
 ${}^m\text{C}$ = a 5-methylcytosine,
 G = a guanine,
 T = a thymine,
 e = a 2'-O-methoxyethylribose modified sugar,
 d = a 2'-deoxyribose sugar moiety,
 s = a phosphorothioate internucleoside linkage, and
 o = a phosphodiester internucleoside linkage.
58. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation:
 $\text{G}_{\text{es}} {}^m\text{C}_{\text{eo}} \text{T}_{\text{eo}} \text{T}_{\text{eo}} \text{T}_{\text{es}} \text{G}_{\text{ds}} \text{A}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{A}_{\text{ds}} {}^m\text{C}_{\text{ds}} {}^m\text{C}_{\text{ds}} \text{A}_{\text{eo}} \text{G}_{\text{eo}} \text{T}_{\text{es}} \text{T}_{\text{es}} \text{A}_{\text{e}}$ (SEQ ID NO: 1502),
 wherein
 A = an adenine,
 ${}^m\text{C}$ = a 5-methylcytosine,
 G = a guanine,
 T = a thymine,
 e = a 2'-O-methoxyethylribose modified sugar,
 d = a 2'-deoxyribose sugar moiety,
 s = a phosphorothioate internucleoside linkage, and
 o = a phosphodiester internucleoside linkage.
59. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation:
 $\text{A}_{\text{es}} {}^m\text{C}_{\text{eo}} \text{A}_{\text{eo}} \text{G}_{\text{eo}} {}^m\text{C}_{\text{eo}} \text{T}_{\text{eo}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{A}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} {}^m\text{C}_{\text{ds}} {}^m\text{C}_{\text{ds}} \text{A}_{\text{ds}} \text{T}_{\text{eo}} \text{A}_{\text{es}} {}^m\text{C}_{\text{es}} \text{A}_{\text{e}}$ (SEQ ID NO: 3646), wherein
 A = an adenine,
 ${}^m\text{C}$ = a 5-methylcytosine,
 G = a guanine,
 T = a thymine,
 e = a 2'-O-methoxyethylribose modified sugar,
 d = a 2'-deoxyribose sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

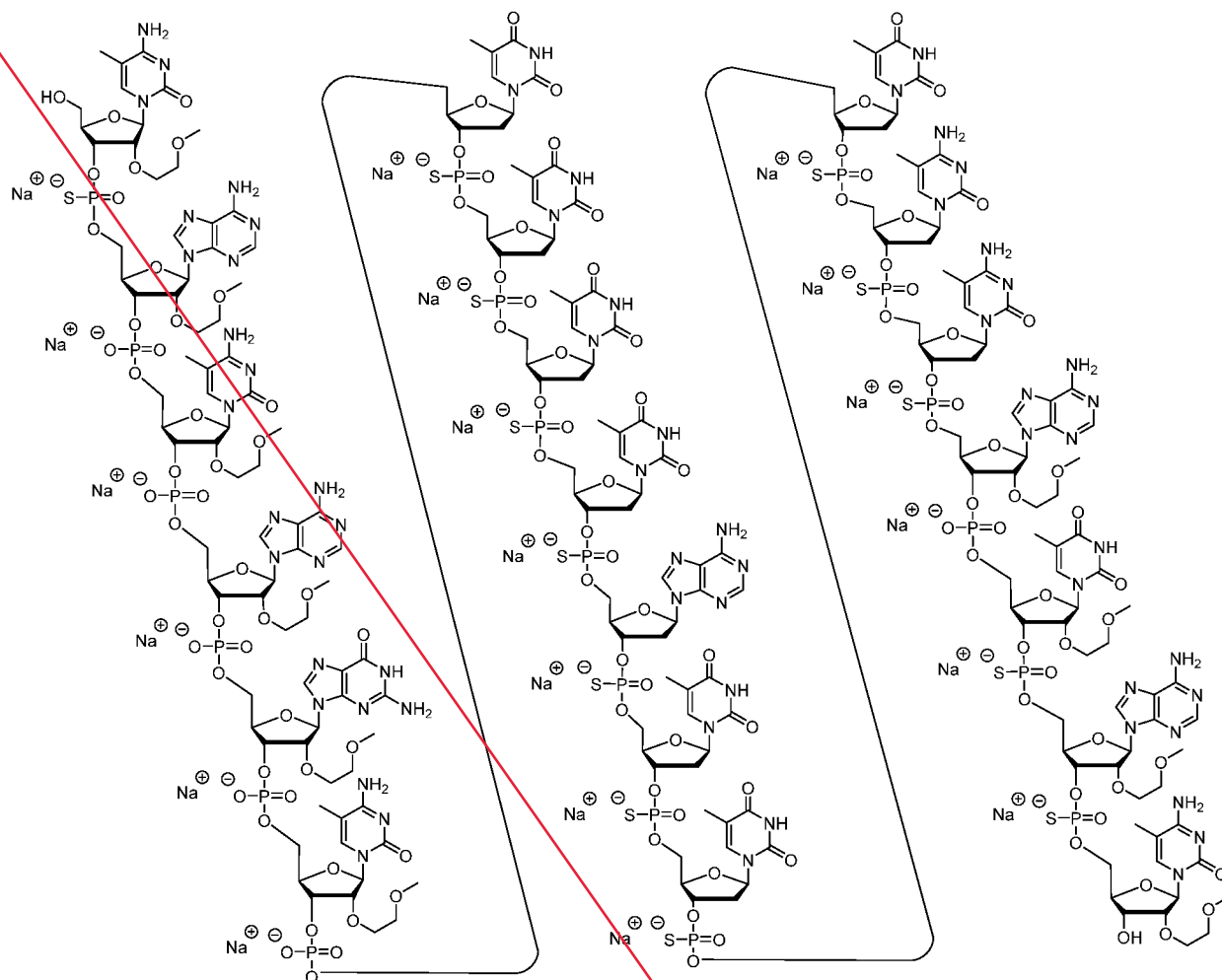
60. The oligomeric compound of any of claims 57-59, wherein the modified oligonucleotide is a pharmaceutically acceptable salt.
61. The oligomeric compound of claim 60, which is a pharmaceutically acceptable salt comprising one or more cations selected from sodium, potassium, calcium, and magnesium.
62. The oligomeric compound of any of claims 57-61, wherein the oligomeric compound is a single-stranded oligomeric compound.
63. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3619), or a pharmaceutically acceptable salt thereof.

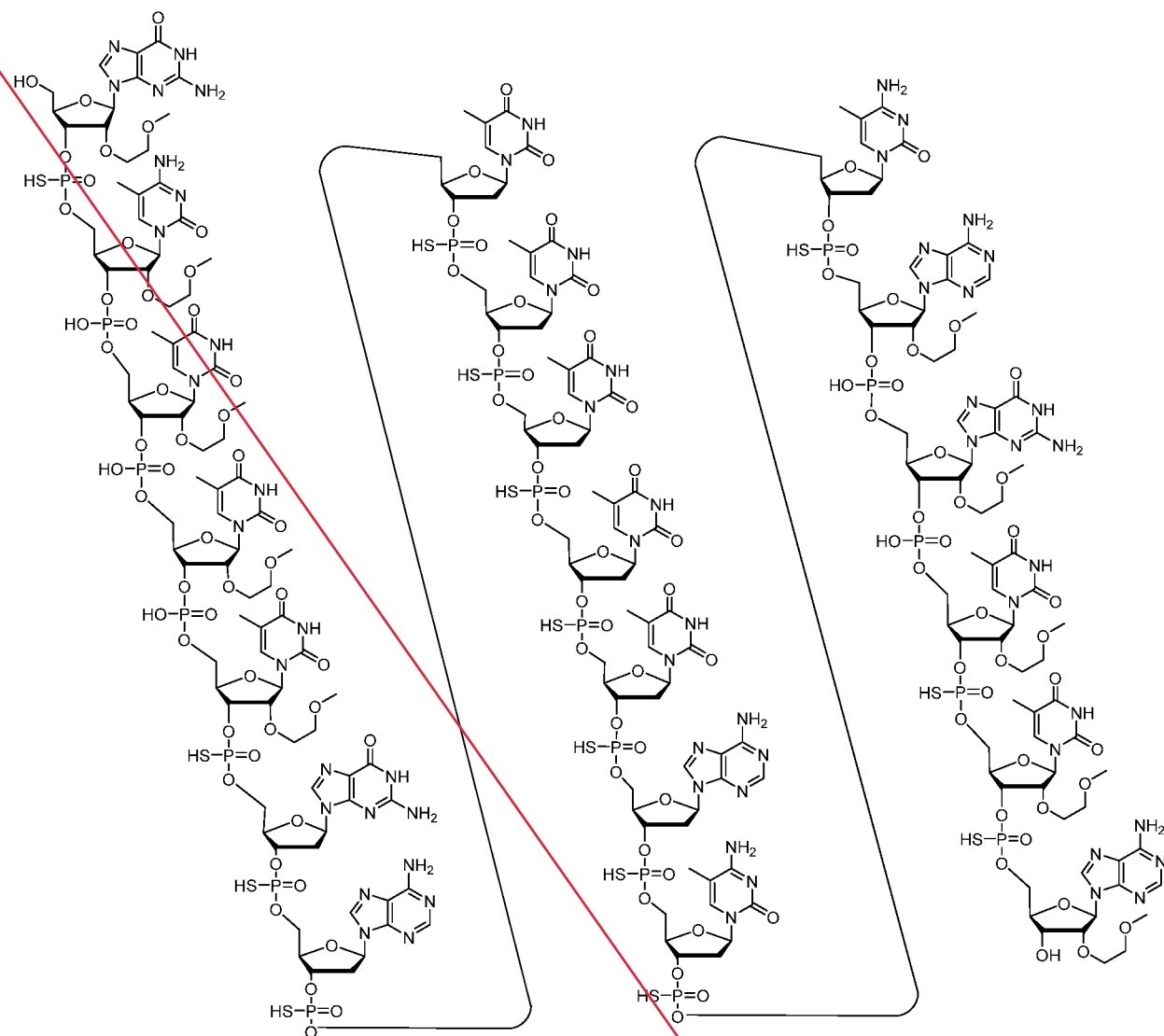
64. The modified oligonucleotide of claim 63, which is a pharmaceutically acceptable salt comprising one or more cations selected from sodium, potassium, calcium, and magnesium.

65. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3619).

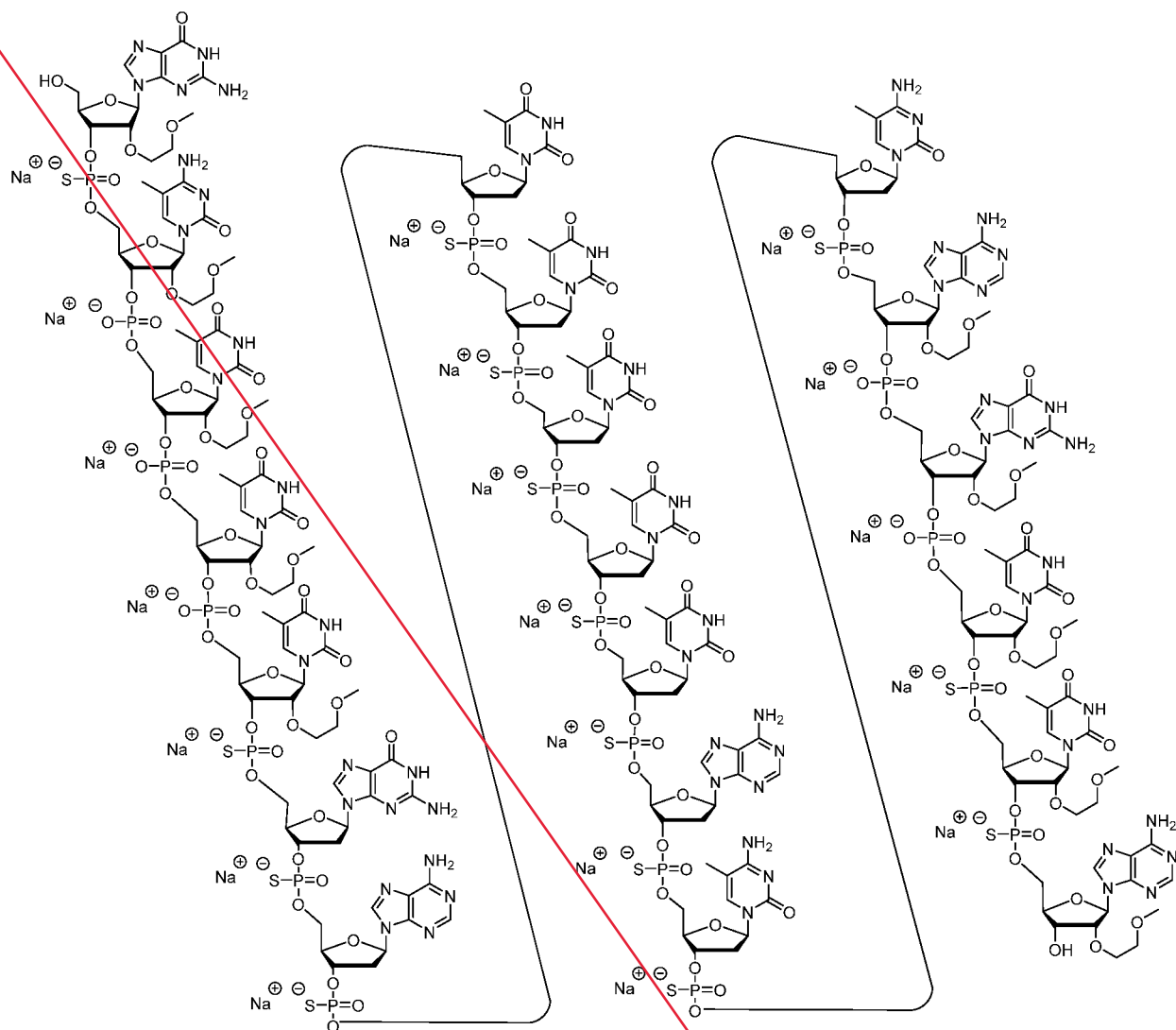
66. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 1502), or a pharmaceutically acceptable salt thereof.

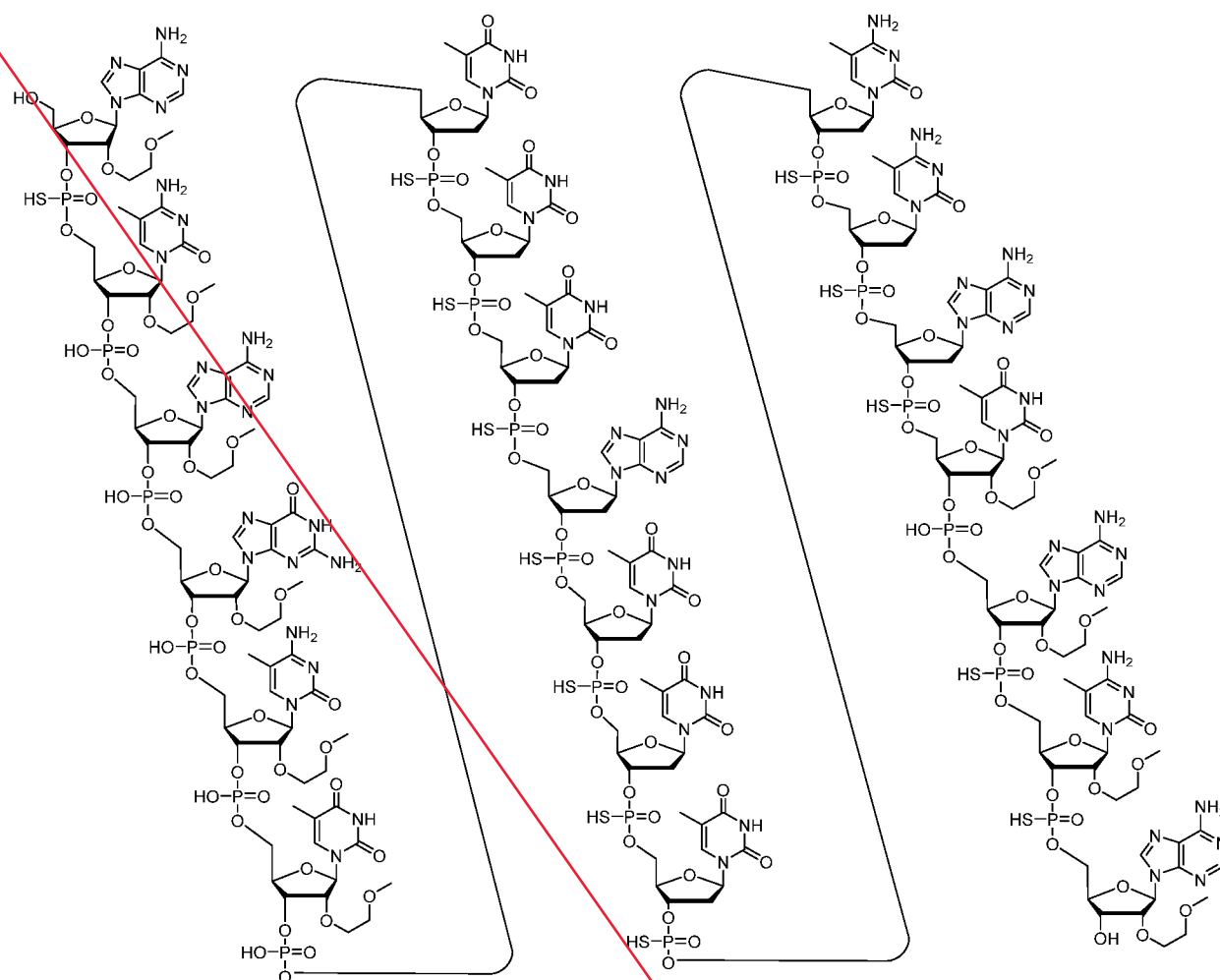
67. The modified oligonucleotide of claim 66, which is a pharmaceutically acceptable salt comprising one or more cations selected from sodium, potassium, calcium, and magnesium.

68. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 1502).

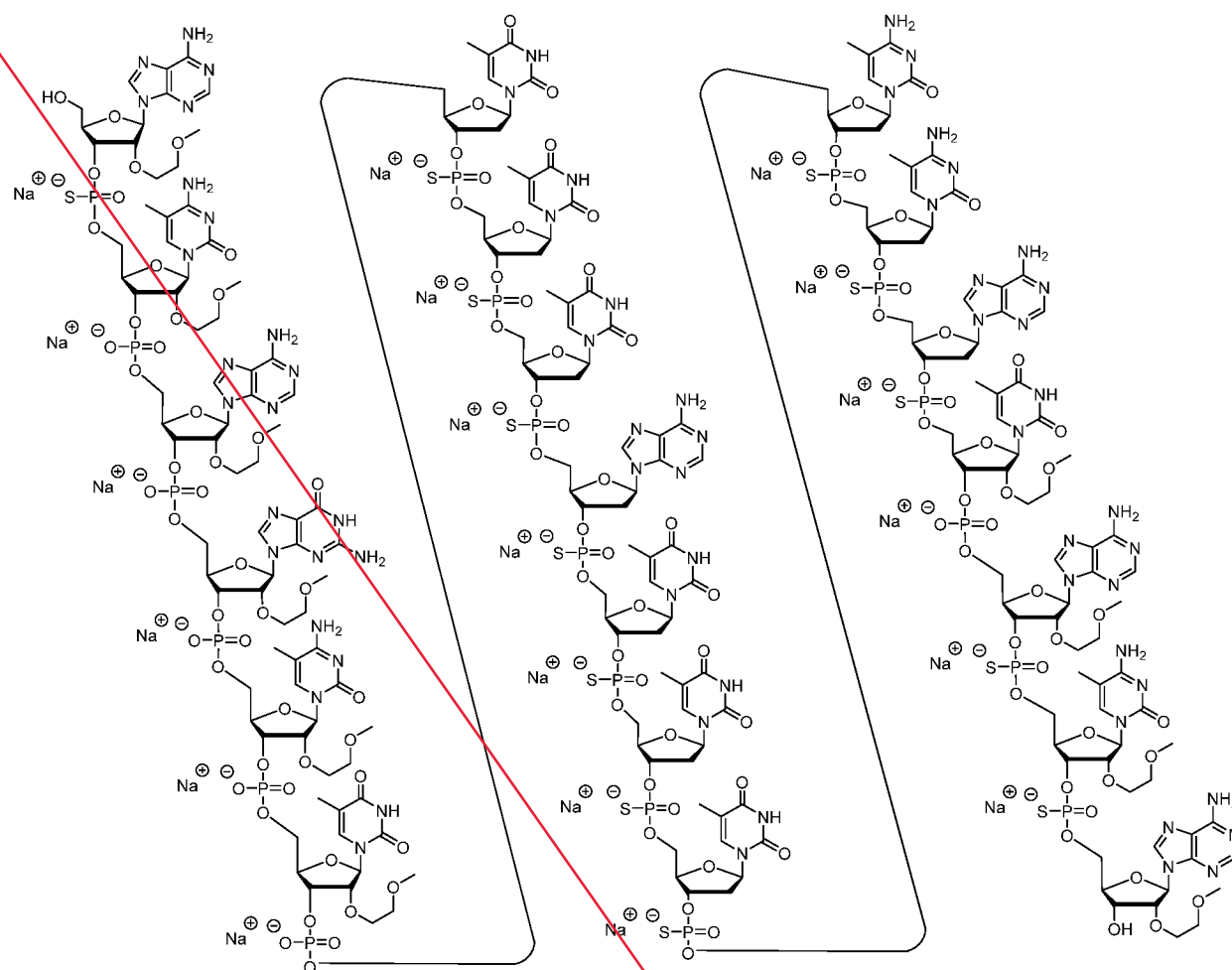
69. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3646), or a pharmaceutically acceptable salt thereof.

70. The modified oligonucleotide of claim 69, which is a pharmaceutically acceptable salt comprising one or more cations selected from sodium, potassium, calcium, and magnesium.

71. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3646).

72. A chirally enriched population of oligomeric compounds of any of claims 1-62 or modified oligonucleotides of any of claims 63-71, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having a particular stereochemical configuration.
73. The chirally enriched population of claim 72, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (*Sp*) configuration.
74. The chirally enriched population of claim 72, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (*Rp*) configuration.
75. The chirally enriched population of claim 72, wherein the population is enriched for modified oligonucleotides having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage
76. The chirally enriched population of claim 72, wherein the population is enriched for modified oligonucleotides having the (*Sp*) configuration at each phosphorothioate internucleoside linkage.

77. The chirally enriched population of claim 72, wherein the population is enriched for modified oligonucleotides having the (*Rp*) configuration at each phosphorothioate internucleoside linkage.
78. The chirally enriched population of claim 72, wherein the population is enriched for modified oligonucleotides having the (*Rp*) configuration at one particular phosphorothioate internucleoside linkage and the (*Sp*) configuration at each of the remaining phosphorothioate internucleoside linkages.
79. The chirally enriched population of claim 72, wherein the population is enriched for modified oligonucleotides having at least 3 contiguous phosphorothioate internucleoside linkages in the *Sp*, *Sp*, and *Rp* configurations, in the 5' to 3' direction.
80. A population of oligomeric compounds of any of claims 1-62 or modified oligonucleotides of any of claims 63-71, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.
81. An oligomeric duplex, comprising a first oligomeric compound and a second oligomeric compound comprising a second modified oligonucleotide, wherein the first oligomeric compound is an oligomeric compound of any of claims 1-62.
82. The oligomeric duplex of claim 81, wherein the second modified oligonucleotide consists of 12 to 30 linked nucleosides, and wherein the nucleobase sequence of the second modified oligonucleotide comprises a complementary region of at least 8 nucleobases that is at least 90% complementary to an equal length portion of the first modified oligonucleotide.
83. The oligomeric duplex of claim 81 or claim 82, wherein the modified oligonucleotide of the first oligomeric compound comprises a 5'-stabilized phosphate group.
84. The oligomeric duplex of claim 83, wherein the stabilized phosphate group comprises a cyclopropyl phosphonate or a vinyl phosphonate.
85. The oligomeric duplex of any of claims 81-84, wherein at least one nucleoside of the second modified oligonucleotide comprises a modified sugar moiety.
86. The oligomeric duplex of claim 85, wherein the modified sugar moiety of the second modified oligonucleotide comprises a bicyclic sugar moiety.
87. The oligomeric duplex of claim 86, wherein the bicyclic sugar moiety of the second modified oligonucleotide comprises a 2'-4' bridge selected from -O-CH₂-; and -O-CH(CH₃)-.
88. The oligomeric duplex of claim 85, wherein the modified sugar moiety of the second modified oligonucleotide comprises a non-bicyclic modified sugar moiety.
89. The oligomeric duplex of claim 88, wherein the non-bicyclic modified sugar moiety of the second modified oligonucleotide is a 2'-MOE sugar moiety, a 2'-cEt sugar moiety, a 2'-F sugar moiety, or a 2'-OMe sugar moiety.
90. The oligomeric duplex of any of claims 81-89, wherein at least one internucleoside linkage of the second modified oligonucleotide is a modified internucleoside linkage.
91. The oligomeric duplex of claim 90, wherein at least one modified internucleoside linkage of the second modified oligonucleotide is a phosphorothioate internucleoside linkage.

92. The oligomeric duplex of any of claims 81-91, wherein at least one internucleoside linkage of the second modified oligonucleotide is a phosphodiester internucleoside linkage.
93. The oligomeric duplex of any of claims 81-92, wherein each internucleoside linkage of the second modified oligonucleotide is independently selected from a phosphodiester or a phosphorothioate internucleoside linkage.
94. The oligomeric duplex of any of claims 81-93, wherein the second modified oligonucleotide comprises at least one modified nucleobase.
95. The oligomeric duplex of claim 94, wherein the at least one modified nucleobase of the second modified oligonucleotide is 5-methylcytosine.
96. The oligomeric duplex of any of claims 81-95, wherein the second modified oligonucleotide comprises a conjugate group.
97. The oligomeric duplex of claim 96, wherein the conjugate group comprises a conjugate linker and a conjugate moiety.
98. The oligomeric duplex of claim 96 or claim 97, wherein the conjugate group is attached to the 5'-end of the second modified oligonucleotide.
99. The oligomeric duplex of claim 96 or claim 97, wherein the conjugate group is attached to the 3'-end of the second modified oligonucleotide.
100. The oligomeric duplex of any of claims 96-99, wherein the conjugate group comprises a lipid.
101. The oligomeric duplex of any of claims 81-100, wherein the second modified oligonucleotide comprises a terminal group.
102. The oligomeric duplex of claim 101, wherein the terminal group is an abasic sugar moiety.
103. The oligomeric duplex of any of claims 81-102, wherein the second modified oligonucleotide consists of 12 to 20, 12 to 25, 12 to 30, 13 to 20, 13 to 25, 13 to 30, 14 to 20, 14 to 25, 14 to 30, 15 to 20, 15 to 25, 15 to 30, 16 to 18, 16 to 20, 16 to 25, 16 to 30, 17 to 20, 17 to 25, 17 to 30, 18 to 20, 18 to 22, 18 to 25, 18 to 30, 19 to 20, 19 to 25, 19 to 30, 20 to 25, 20 to 30, 21 to 25, 21 to 30, 22 to 25, 22 to 30, 23 to 25, or 23 to 30 linked nucleosides.
104. An antisense agent comprising an antisense compound, wherein the antisense compound is an oligomeric compound of any of claims 1-62.
105. An antisense agent comprising an antisense compound, wherein the antisense compound is an oligomeric duplex of any of claims 81-103.
106. The antisense agent of claim 104 or claim 105, wherein the antisense agent is:
 - a) an RNase H agent capable of reducing the amount of HTT nucleic acid through the activation of RNase H; or
 - b) an RNAi agent capable of reducing the amount of HTT nucleic acid through the activation of RISC/Ago2.
107. A pharmaceutical composition comprising an oligomeric compound of any of claims 1-62, a modified oligonucleotide of any of claims 63-71, a population of any of claims 72-79, an

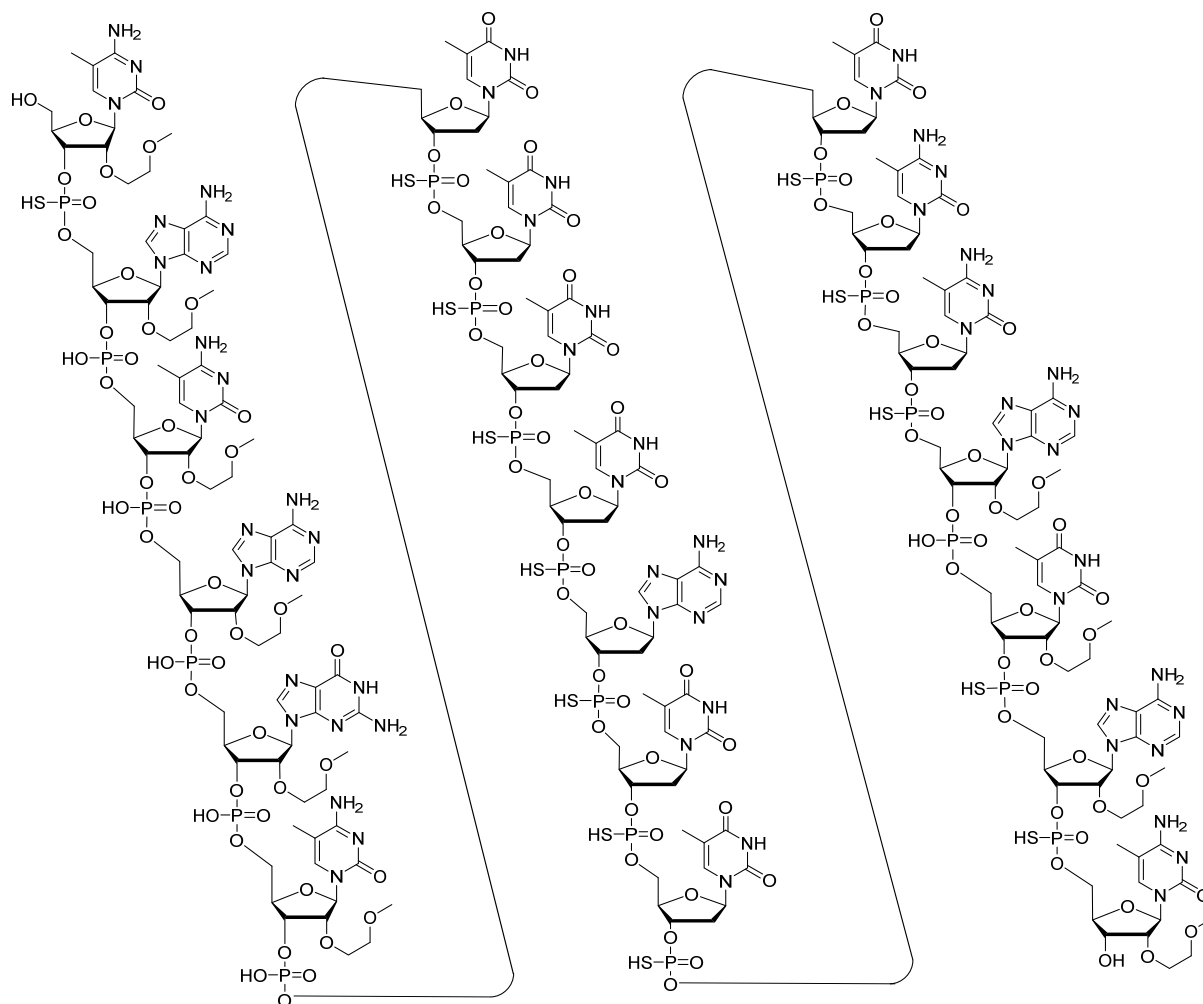
- oligomeric duplex of any of claims 81-103, or an antisense agent of any of claims 104-106; and a pharmaceutically acceptable carrier or diluent.
108. The pharmaceutical composition of claim 107, wherein the pharmaceutically acceptable diluent comprises phosphate buffered saline (PBS) or artificial cerebrospinal fluid (aCSF).
109. The pharmaceutical composition of claim 108, wherein the pharmaceutical composition consists essentially of the oligomeric compound of any of claims 1-62, the modified oligonucleotide of any of claims 63-71, the population of any of claims 72-79, the oligomeric duplex of any of claims 81-103, or the antisense agent of any of claims 104-106, and PBS.
110. The pharmaceutical composition of claim 108, wherein the pharmaceutical composition consists essentially of the oligomeric compound of any of claims 1-62, the modified oligonucleotide of any of claims 63-71, the population of any of claims 72-79, the oligomeric duplex of any of claims 81-103, or the antisense agent of any of claims 104-106, and aCSF.
111. A method comprising administering to a subject an oligomeric compound of any of claims 1-62, a modified oligonucleotide of any of claims 63-71, a population of any of claims 72-79, an oligomeric duplex of any of claims 81-103, an antisense agent of any of claims 104-106, or a pharmaceutical composition of any of claims 107-110.
112. A method of ameliorating or preventing a repeat expansion disease, comprising administering to a subject in need thereof a therapeutically effective amount of an oligomeric compound of any of claims 1-62, a modified oligonucleotide of any of claims 63-71, a population of any of claims 72-79, an oligomeric duplex of any of claims 81-103, an antisense agent of any of claims 104-106, or a pharmaceutical composition of any of claims 107-110.
113. The method of claim 112, wherein the repeat expansion disease is selected from myotonic dystrophy (DM1 and DM2), amyotrophic lateral sclerosis, frontotemporal dementia, Huntington's disease, a polyglutamine disorder, Fragile X syndrome, and a spinocerebellar ataxia.
114. The method of claim 112, wherein the repeat expansion disease is Huntington's disease.
115. The method of claim 112, wherein the repeat expansion disease is a spinocerebellar ataxia.
116. The method of any of claims 112-115, wherein at least one symptom or hallmark of the repeat expansion disease is ameliorated.
117. The method of claim 116, wherein the symptom or hallmark is selected from brain atrophy, reduced brain activity, reduced brain connectivity, muscle atrophy, muscle weakness, muscle cramping, difficulty swallowing, seizure, tremor, nerve degeneration, cardiac failure, impaired glucose tolerance, weight loss, osteoporosis, testicular atrophy, impaired global function, impaired motor function, impaired cognitive function, impaired daily function, impaired attention, impaired visuoperceptual processing, impaired working memory, impaired psychomotor speed, impaired verbal motor output, impaired degree of independence, impaired apathy, impaired learning ability, impaired mental concentration, impaired speech, depression,

- irritability, anger, impaired mobility, impaired self-care, pain, discomfort, anxiety, suicidal ideation, suicidal behavior, and a combination thereof.
118. The method of any of claims 116-117, wherein administering the oligomeric compound of any of claims 1-62, the modified oligonucleotide of any of claims 63-71, the population of any of claims 72-79, the oligomeric duplex of any of claims 81-103, the antisense agent of any of claims 104-106, or the pharmaceutical composition of any of claims 107-110 reduces or delays the onset or progression of brain atrophy, reduced brain activity, reduced brain connectivity, muscle atrophy, muscle weakness, muscle cramping, difficulty swallowing, seizure, tremor, nerve degeneration, cardiac failure, impaired glucose tolerance, weight loss, osteoporosis, testicular atrophy, impaired global function, impaired motor function, impaired cognitive function, impaired daily function, impaired attention, impaired visuoperceptual processing, impaired working memory, impaired psychomotor speed, impaired verbal motor output, impaired degree of independence, impaired apathy, impaired learning ability, impaired mental concentration, impaired speech, depression, irritability, anger, impaired mobility, impaired self-care, pain, discomfort, anxiety, suicidal ideation, or suicidal behavior.
119. The method of any of claims 111-118, comprising identifying the subject as having the repeat expansion disease or at risk for having the repeat expansion disease.
120. The method of any of claims 111-119, wherein the oligomeric compound of any of claims 1-62, the modified oligonucleotide of any of claims 63-71, the population of any of claims 72-79, the oligomeric duplex of any of claims 81-103, the antisense agent of any of claims 104-106, or the pharmaceutical composition of any of claims 107-110 is administered to the central nervous system or systemically.
121. The method of any of claims 111-119, wherein the oligomeric compound of any of claims 1-62, the modified oligonucleotide of any of claims 63-71, the population of any of claims 72-79, the oligomeric duplex of any of claims 81-103, the antisense agent of any of claims 104-106, or the pharmaceutical composition of any of claims 107-110 is administered intrathecally.
122. The method of any of claims 111-121, wherein the subject is a human.
123. A method of reducing expression of HTT in a cell comprising contacting the cell with an oligomeric compound of any of claims 1-62, a modified oligonucleotide of any of claims 63-71, a population of any of claims 72-79, an oligomeric duplex of any of claims 81-103, an antisense agent of any of claims 104-106, or a pharmaceutical composition of any of claims 107-110.
124. The method of claim 123, wherein the cell is from a brain tissue, optionally from the cortex, substantia nigra, striatum, midbrain, brainstem, or spinal cord.
125. The method of claim 123 or claim 124, wherein the cell is a human cell.
126. Use of an oligomeric compound of any of claims 1-62, a modified oligonucleotide of any of claims 63-71, a population of any of claims 72-79, an oligomeric duplex of any of claims 81-103, an antisense agent of any of claims 104-106, or a pharmaceutical composition of any of claims 107-110 for ameliorating or preventing a repeat expansion disease.

127. Use of an oligomeric compound of any of claims 1-62, a modified oligonucleotide of any of claims 63-71, a population of any of claims 72-79, an oligomeric duplex of any of claims 81-103, an antisense agent of any of claims 104-106, or a pharmaceutical composition of any of claims 107-110 in the manufacture of a medicament for ameliorating or preventing a repeat expansion disease.
128. The use of claim 126 or claim 127, wherein the repeat expansion disease is Huntington's disease.

CLAIMS

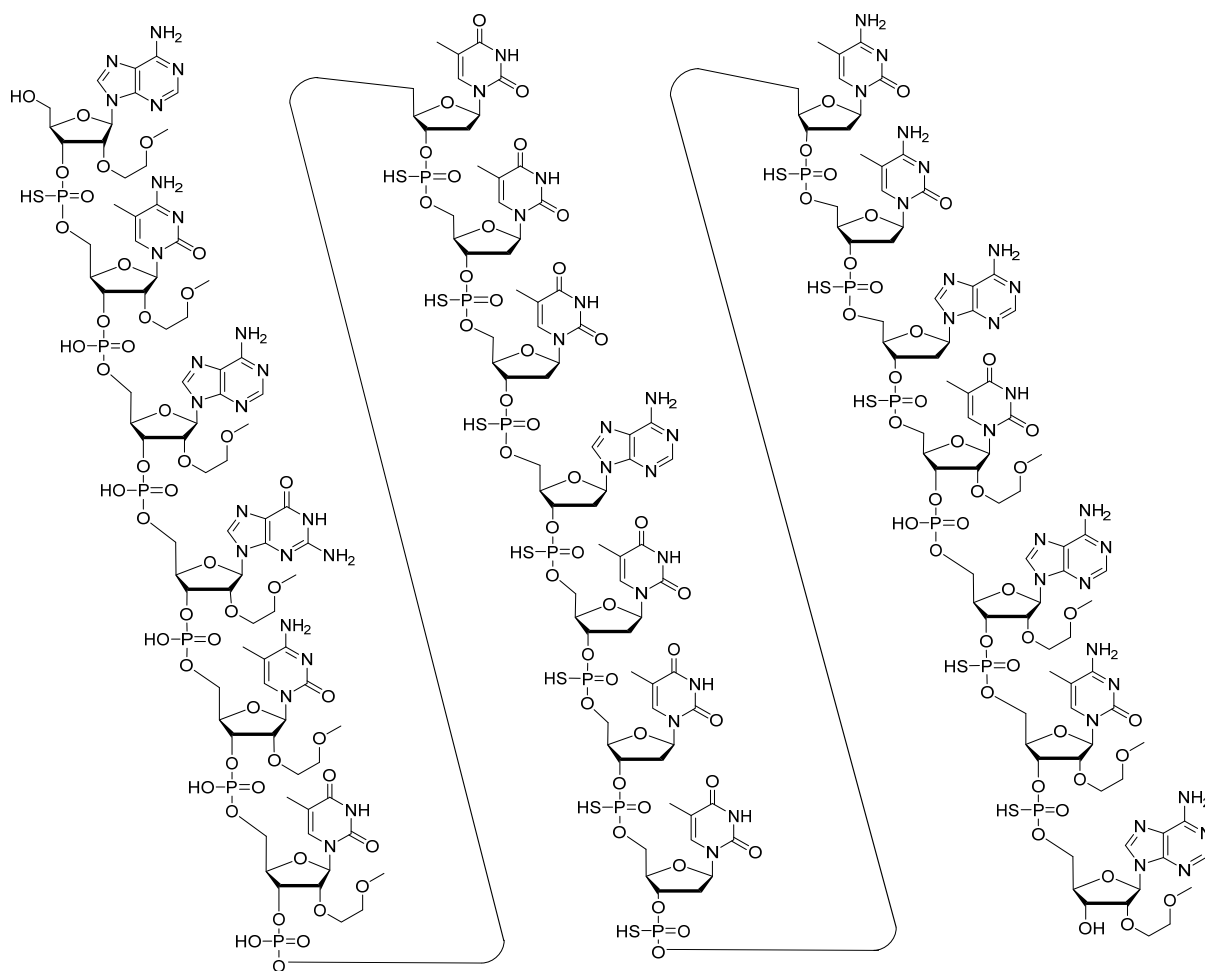
1. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3619), or a pharmaceutically acceptable salt thereof.

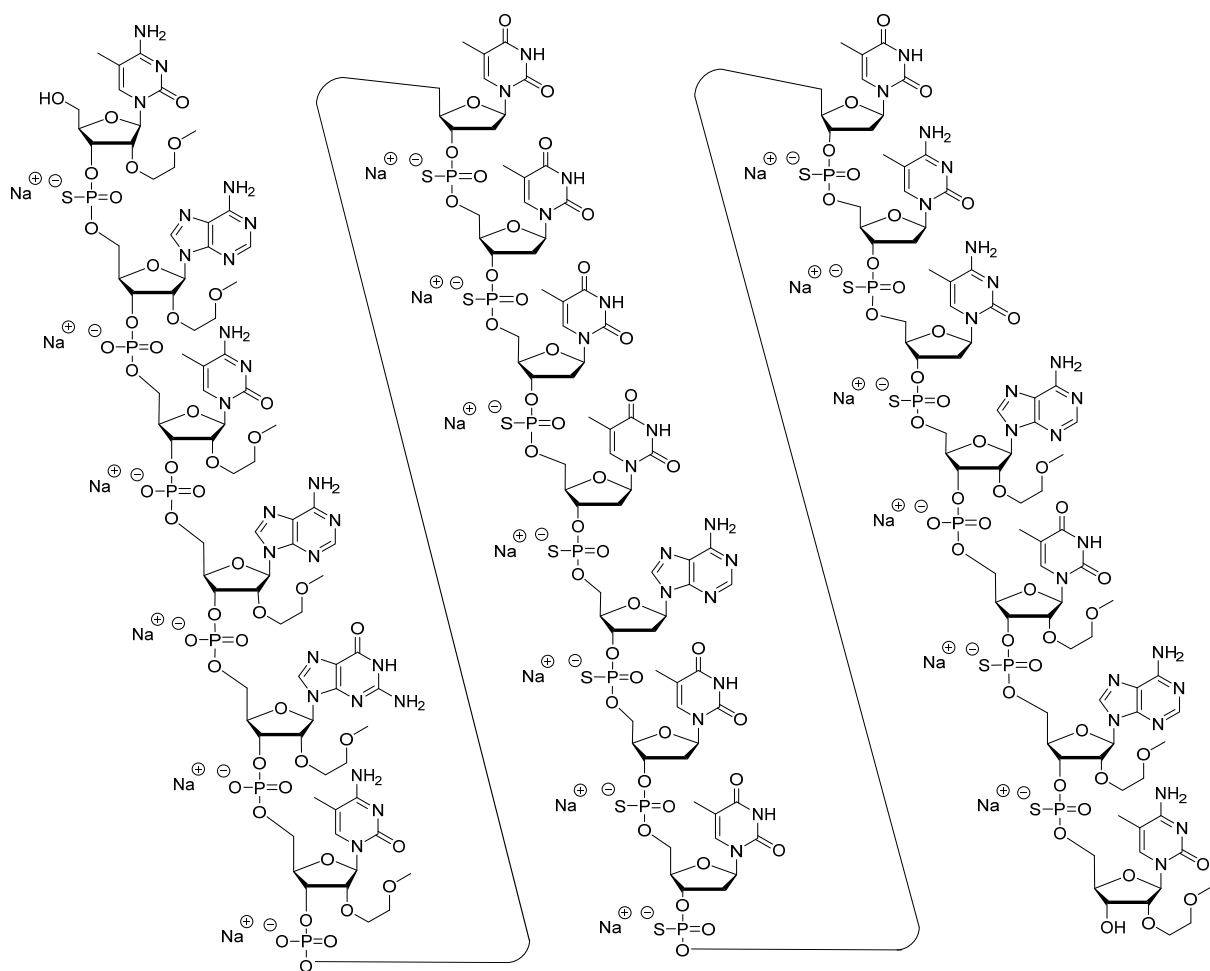
-

3. A modified oligonucleotide according to the following chemical structure:



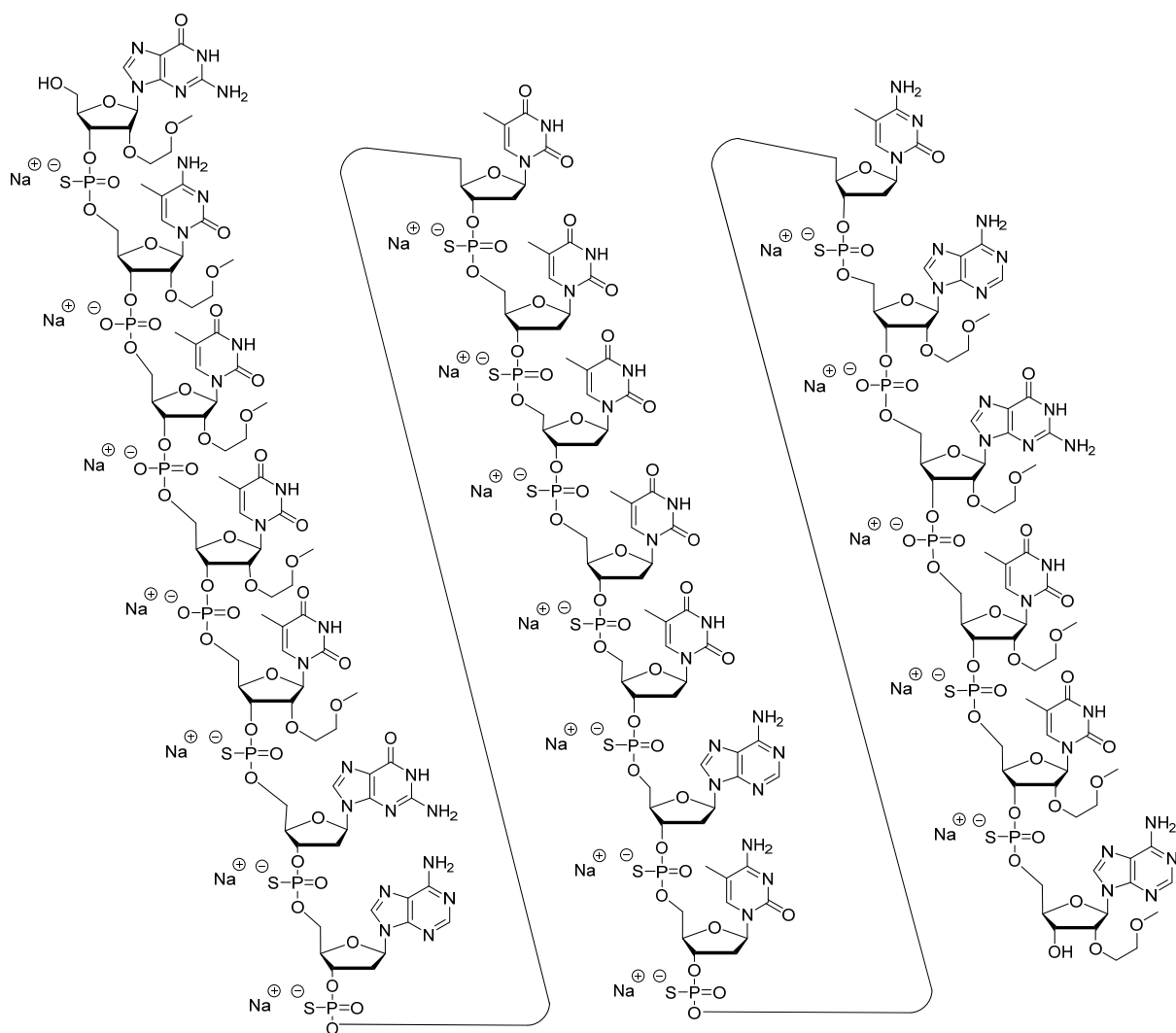
(SEQ ID NO: 3646), or a pharmaceutically acceptable salt thereof.

4. The modified oligonucleotide of any of claims 1-3, which is a pharmaceutically acceptable salt comprising one or more cations selected from sodium, potassium, calcium, and magnesium.
5. A modified oligonucleotide according to the following chemical structure:



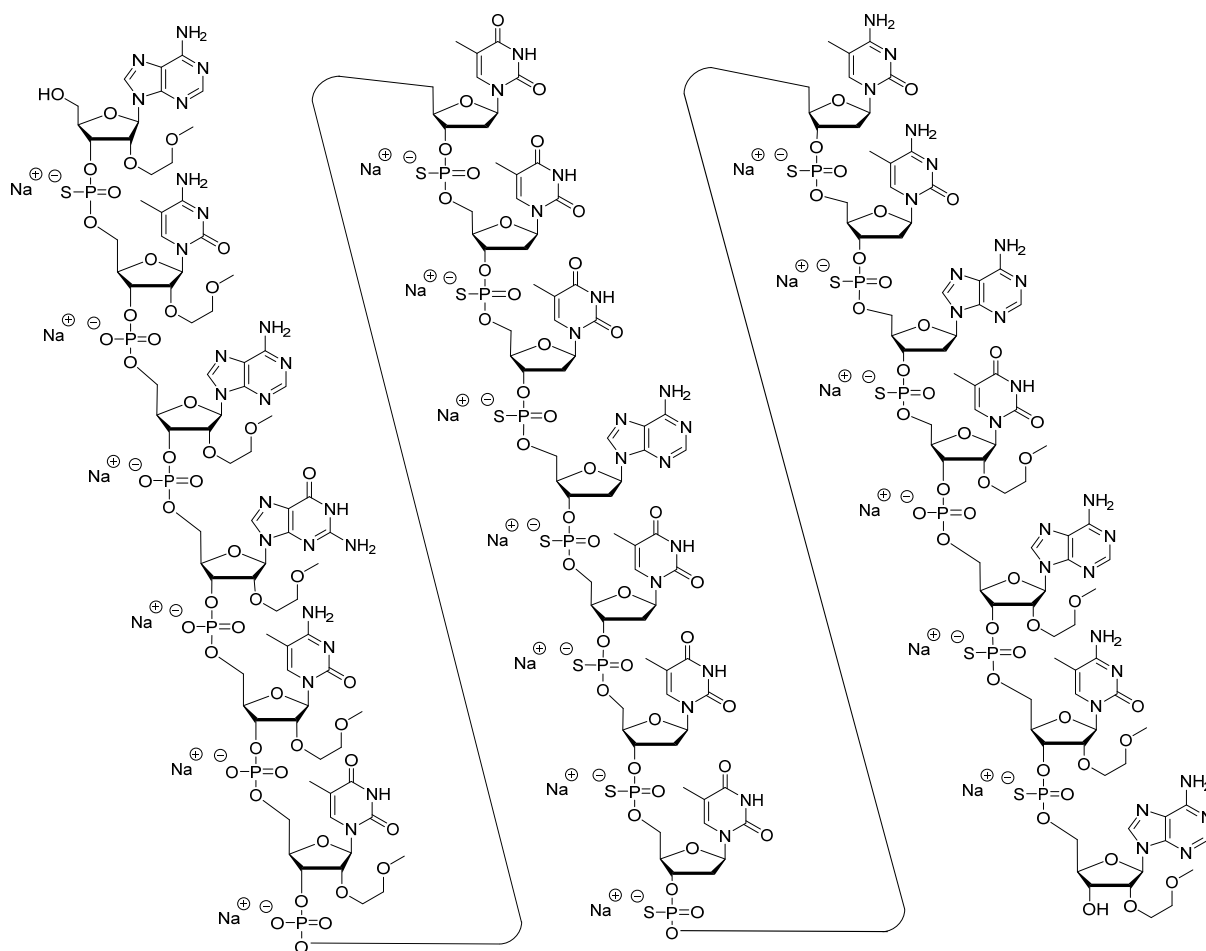
(SEQ ID NO: 3619).

6. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 1502).

7. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3646).

8. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation:

${}^m\text{C}_{\text{es}} \text{A}_{\text{eo}} {}^m\text{C}_{\text{eo}} \text{A}_{\text{eo}} \text{G}_{\text{eo}} {}^m\text{C}_{\text{eo}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{A}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} \text{T}_{\text{ds}} {}^m\text{C}_{\text{ds}} {}^m\text{C}_{\text{ds}} \text{A}_{\text{eo}} \text{T}_{\text{es}} \text{A}_{\text{es}} {}^m\text{C}_{\text{e}}$ (SEQ ID NO: 3619), wherein

A = an adenine nucleobase,

${}^m\text{C}$ = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-O-methoxyethylribose modified sugar,

d = a 2'-deoxyribose sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

9. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation:

$G_{es} {}^mC_{eo} T_{eo} T_{es} G_{ds} A_{ds} T_{ds} T_{ds} T_{ds} T_{ds} T_{ds} A_{ds} {}^mC_{ds} {}^mC_{ds} A_{eo} G_{eo} T_{es} T_{es} A_e$ (SEQ ID NO: 1502),
wherein

A = an adenine nucleobase,

${}^mC$ = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-O-methoxyethylribose modified sugar,

d = a 2'-deoxyribose sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

10. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation:

$A_{es} {}^mC_{eo} A_{eo} G_{eo} {}^mC_{eo} T_{eo} T_{ds} T_{ds} T_{ds} A_{ds} T_{ds} T_{ds} T_{ds} {}^mC_{ds} {}^mC_{ds} A_{ds} T_{eo} A_{es} {}^mC_{es} A_e$ (SEQ ID NO: 3646), wherein

A = an adenine nucleobase,

${}^mC$ = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-O-methoxyethylribose modified sugar,

d = a 2'-deoxyribose sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

11. A population of modified oligonucleotides of any of claims 1-7, or a population of oligomeric compounds of any of claims 8-10, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

12. A pharmaceutical composition comprising the modified oligonucleotide of any of claims 1-7, the oligomeric compound of any of claims 8-10, the population of modified oligonucleotides of claim 11, or the population of oligomeric compounds of claim 11, and a pharmaceutically acceptable diluent.

13. The pharmaceutical composition of claim 12, wherein the pharmaceutically acceptable diluent comprises artificial cerebrospinal fluid (aCSF) or phosphate-buffered saline (PBS).

14. The pharmaceutical composition of claim 13, wherein the pharmaceutical composition consists or consists essentially of the modified oligonucleotide or oligomeric compound and aCSF.

15. The pharmaceutical composition of claim 13, wherein the pharmaceutical composition consists or consists essentially of the modified oligonucleotide or oligomeric compound and PBS.
16. The pharmaceutical composition of claim 13, wherein the pharmaceutical composition consists or consists essentially of the population of modified oligonucleotides or population of oligomeric compounds and aCSF.
17. The pharmaceutical composition of claim 13, wherein the pharmaceutical composition consists or consists essentially of the population of modified oligonucleotides or population of oligomeric compounds and PBS.