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 85% complementary to an equal length portion of a PLP1 nucleic acid, 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 the nucleobase sequences of SEQ ID NOs: 20-2155, wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.

3. 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 at least 20 contiguous nucleobases complementary to:

an equal length portion of nucleobases 9198-9222 of SEQ ID NO: 2;
an equal length portion of nucleobases 13702-13766 of SEQ ID NO: 2;
an equal length portion of nucleobases 14037-14062 of SEQ ID NO: 2;
an equal length portion of nucleobases 16761-16800 of SEQ ID NO: 2;
an equal length portion of nucleobases 17558-17602 of SEQ ID NO: 2;
an equal length portion of nucleobases 17615-17667 of SEQ ID NO: 2;
an equal length portion of nucleobases 17853-17883 of SEQ ID NO: 2;
an equal length portion of nucleobases 18097-18160 of SEQ ID NO: 2;
an equal length portion of nucleobases 18206-18237 of SEQ ID NO: 2;
an equal length portion of nucleobases 18237-18340 of SEQ ID NO: 2;
an equal length portion of nucleobases 18350-18387 of SEQ ID NO: 2;
an equal length portion of nucleobases 18412-18469 of SEQ ID NO: 2;
an equal length portion of nucleobases 18461-18506 of SEQ ID NO: 2;
an equal length portion of nucleobases 18539-18579 of SEQ ID NO: 2;
an equal length portion of nucleobases 18697-18727 of SEQ ID NO: 2;
an equal length portion of nucleobases 18755-18793 of SEQ ID NO: 2;
an equal length portion of nucleobases 18797-18819 of SEQ ID NO: 2;
an equal length portion of nucleobases 18839-18862 of SEQ ID NO: 2;
an equal length portion of nucleobases 18974-19021 of SEQ ID NO: 2;
an equal length portion of nucleobases 19028-19080 of SEQ ID NO: 2;
an equal length portion of nucleobases 19146-19173 of SEQ ID NO: 2;
an equal length portion of nucleobases 19228-19253 of SEQ ID NO: 2;
an equal length portion of nucleobases 19347-19393 of SEQ ID NO: 2;

an equal length portion of nucleobases 19500-19523 of SEQ ID NO: 2; or

an equal length portion of nucleobases 19512-19534 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.

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, or at least 18 contiguous nucleobases of a sequence selected from:

SEQ ID NOs: 1050, 1124, 2145, 2151, 2152, 2153;

SEQ ID NOs: 36, 86, 114, 164, 191, 242, 269, 426, 523, 602, 691, 780;

SEQ ID NOs: 89, 167, 245, 322, 323;

SEQ ID NOs: 720, 808, 904, 937, 1058, 1097, 1184, 1278, 1340;

SEQ ID NOs: 40, 41, 117, 118, 195, 196, 273, 274, 588, 690;

SEQ ID NOs: 42, 43, 119, 120, 197, 198, 275, 276, 373, 460, 1431, 1542, 1645, 1850, 1965, 2109;

SEQ ID NOs: 1451, 1499, 1543, 1654, 1733, 2154, 2155,

SEQ ID NOs: 200, 420, 504, 620, 646, 709, 823, 980, 1029, 1149, 1196, 1253, 1323, 1423, 1476, 1605, 1613, 1728, 1832;

SEQ ID NOs: 45, 46, 123, 124, 201, 202, 279, 280, 538, 562, 2091;

SEQ ID NOs: 48, 49, 50, 51, 52, 53, 125, 126, 127, 128, 129, 130, 131, 203, 204, 205, 206, 207, 208, 281, 282, 283, 284, 285, 286, 414, 459, 485, 503, 579, 580, 693, 724, 840, 873, 911, 1034, 1081, 1125, 1159, 1318, 1413, 1513, 1548, 1672, 1701, 1794, 1868, 1958, 2002;

SEQ ID NOs: 209, 287, 335, 439, 506, 606, 659, 1922, 2033, 2104;

SEQ ID NOs: 784, 842, 869, 978, 1082, 1131, 1218, 1250, 1320, 1453, 1529, 1538, 1616, 1712, 1821;

SEQ ID NOs: 54, 55, 132, 133, 210, 288, 419, 499, 564, 665, 764, 800, 881, 993, 1059, 1200, 1295, 1354, 1422, 1465, 1544, 1705, 1802, 2149;

SEQ ID NOs: 338, 438, 525, 604, 658, 758, 813, 887, 977, 1043, 1108, 1199, 1258, 1336, 1395, 1514, 1557, 1668, 1697, 2089;

SEQ ID NOs: 875, 934, 1047, 1110, 1229, 1243, 1373, 1438, 2146, 2147;

SEQ ID NOs: 761, 798, 890, 946, 1022, 1120, 1198, 1293, 1358, 1398, 1463;

SEQ ID NOs: 56, 134, 683, 718;

SEQ ID NOs: 1610, 1663, 1702, 1786;

SEQ ID NOs: 212, 1060, 1090, 1181, 1277, 1446, 1510, 1589, 1646, 1693, 1772, 2148;

SEQ ID NOs: 57, 586, 666, 714, 812, 914, 951, 1052, 1138, 1162, 1248, 1363, 1455;

SEQ ID NOs: 385, 416, 545, 621, 682, 1968, 2055, 2101, 2150;

SEQ ID NOs: 363, 467, 541, 2008, 2111;

SEQ ID NOs: 58, 59, 136, 213, 214, 291, 292, 383, 417, 519, 612, 671, 730, 900, 986, 1019, 1136, 1353, 1457, 1504, 1546, 2093;

SEQ ID NOs: 398, 435, 2095, 2010, 2144; or

SEQ ID NOs: 1201, 1238, 1341, 1435,

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

5. The oligomeric compound of any of claims 1-4, wherein the modified oligonucleotide has a nucleobase sequence that is at least 80%, at least 85%, at least 90%, at least 95%, or 100% complementary to the nucleobase sequence of SEQ ID NO: 1 or SEQ ID NO: 2 when measured across the entire nucleobase sequence of the modified oligonucleotide.

6. The oligomeric compound of any of claims 1-5, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a modified sugar moiety.

7. The oligomeric compound of claim 6, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a bicyclic sugar moiety.

8. The oligomeric compound of claim 7, wherein the bicyclic sugar moiety comprises a 4'-2' bridge, wherein the 4'-2' bridge is selected from $-CH_2-O-$, and $-CH(CH_3)-O-$.

9. The oligomeric compound of any of claims 6-8, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a non-bicyclic modified sugar moiety.

10. The oligomeric compound of claim 9, wherein the non-bicyclic modified sugar moiety is a 2'-MOE sugar moiety or a 2'-OMe sugar moiety.

11. The oligomeric compound of any of claims 6-10, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a sugar surrogate.

12. The oligomeric compound of claim 11, wherein the sugar surrogate is any of morpholino, modified morpholino, PNA, THP, and F-HNA.

13. The oligomeric compound of any of claims 1-6 or 9-12, wherein the modified oligonucleotide does not comprise a bicyclic sugar moiety.

14. The oligomeric compound of any of claims 1-13, wherein the modified oligonucleotide is a gapmer.

15. The oligomeric compound of any of claims 1-14, wherein the modified oligonucleotide comprises:
a 5'-region consisting of 1-7 linked 5'-region nucleosides;
a central region consisting of 6-10 linked central region nucleosides; and
a 3'-region consisting of 1-7 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'-deoxyfuranosyl sugar moiety.

16. The oligomeric compound of claim 15, wherein the modified oligonucleotide comprises:
a 5'-region consisting of 5 linked 5'-region nucleosides;
a central region consisting of 10 linked central region nucleosides; and
a 3'-region consisting of 5 linked 3'-region nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides is a 2'-MOE nucleoside, and each of the central region nucleosides is a 2'-β-D-deoxynucleoside.

17. The oligomeric compound of claim 15, wherein the modified oligonucleotide comprises:

a 5'-region consisting of 6 linked 5'-region nucleosides;

a central region consisting of 10 linked central region nucleosides; and

a 3'-region consisting of 4 linked 3'-region nucleosides; wherein

each of the 5'-region nucleosides and each of the 3'-region nucleosides is a 2'-MOE nucleoside, and each of the central region nucleosides is a 2'-β-D-deoxynucleoside.

18. The oligomeric compound of any of claims 1-17, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage.

19. The oligomeric compound of claim 18, wherein each internucleoside linkage of the modified oligonucleotide is a modified internucleoside linkage.

20. The oligomeric compound of claim 18 or claim 19, wherein at least one internucleoside linkage is a phosphorothioate internucleoside linkage.

21. The oligomeric compound of claim 18 or claim 20 wherein the modified oligonucleotide comprises at least one phosphodiester internucleoside linkage.

22. The oligomeric compound of any of claims 18, 20, or 21, wherein each internucleoside linkage is either a phosphodiester internucleoside linkage or a phosphorothioate internucleoside linkage.

23. The oligomeric compound of claim 19, wherein each internucleoside linkage is a phosphorothioate internucleoside linkage.

24. The oligomeric compound of any of claims 1-18 or 20-22, wherein the modified oligonucleotide has an internucleoside linkage motif of soooosssssssssssooss or sooooossssssssssoss; wherein,

s = a phosphorothioate internucleoside linkage and o = a phosphodiester internucleoside linkage.

25. The oligomeric compound of any of claims 1-24, wherein the modified oligonucleotide comprises at least one modified nucleobase.

26. The oligomeric compound of claim 25, wherein the modified nucleobase is a 5-methyl cytosine.

27. The oligomeric compound of any of claims 1-26, wherein the modified oligonucleotide consists of 12-30, 12-22, 12-20,14-18, 14-20, 15-17, 15-25, 16-18, 16-20, 17-20, 18-20 or 18-22 linked nucleosides.

28. The oligomeric compound of any of claims 1-26, wherein the modified oligonucleotide consists of 16, 17, 18, 19, or 20 linked nucleosides.

29. The oligomeric compound of claim 28, wherein the modified oligonucleotide consists of 20 linked nucleosides.

30. The oligomeric compound of claim 28, wherein the modified oligonucleotide consists of 18 linked nucleosides.

31. An oligomeric compound comprising a modified oligonucleotide according to any of the following chemical notations:

$^{m}C_{es}{}^{m}C_{eo}{}^{m}C_{eo}A_{eo}A_{eo}T_{ds}A_{ds}G_{ds}A_{ds}T_{ds}T_{ds}{}^{m}C_{ds}A_{ds}A_{ds}{}^{m}C_{ds}T_{eo}A_{eo}G_{es}{}^{m}C_{es}{}^{m}C_{e}$ (SEQ ID NO: 134);

$A_{es}{}^{m}C_{eo}A_{eo}{}^{m}C_{eo}A_{eo}A_{ds}{}^{m}C_{ds}T_{ds}{}^{m}C_{ds}T_{ds}T_{ds}T_{ds}A_{ds}{}^{m}C_{ds}A_{ds}A_{eo}{}^{m}C_{eo}A_{es}A_{es}A_{e}$ (SEQ ID NO: 411);

$T_{es}{}^{m}C_{eo}T_{eo}{}^{m}C_{eo}{}^{m}C_{eo}A_{ds}G_{ds}A_{ds}{}^{m}C_{ds}A_{ds}T_{ds}T_{ds}T_{ds}{}^{m}C_{ds}T_{ds}G_{eo}A_{eo}T_{es}G_{es}{}^{m}C_{e}$ (SEQ ID NO: 934);

$G_{es}T_{eo}G_{eo}T_{eo}G_{eo}T_{ds}T_{ds}A_{ds}A_{ds}A_{ds}A_{ds}A_{ds}T_{ds}T_{ds}G_{ds}{}^{m}C_{ds}A_{eo}A_{eo}T_{es}T_{es}{}^{m}C_{e}$ (SEQ ID NO: 1238);

$A_{es}T_{eo}T_{eo}G_{eo}{}^{m}C_{eo}A_{ds}A_{ds}T_{ds}T_{ds}{}^{m}C_{ds}T_{ds}A_{ds}T_{ds}A_{ds}T_{ds}{}^{m}C_{eo}A_{eo}G_{es}A_{es}A_{e}$ (SEQ ID NO: 2010);

$A_{es}T_{eo}G_{eo}T_{eo}G_{eo}A_{ds}T_{ds}{}^{m}C_{ds}T_{ds}A_{ds}T_{ds}A_{ds}T_{ds}{}^{m}C_{ds}A_{ds}G_{eo}G_{eo}A_{es}G_{es}A_{e}$ (SEQ ID NO: 1772); or

$A_{es}{}^{m}C_{eo}{}^{m}C_{eo}A_{eo}G_{eo}A_{ds}G_{ds}G_{ds}G_{ds}{}^{m}C_{ds}{}^{m}C_{ds}A_{ds}T_{ds}{}^{m}C_{ds}T_{ds}{}^{m}C_{eo}A_{eo}G_{es}G_{es}T_{e}$ (SEQ ID NO: 881)

$T_{es}G_{eo}T_{eo}A_{eo}G_{eo}T_{ds}A_{ds}{}^{m}C_{ds}A_{ds}A_{ds}A_{ds}T_{ds}{}^{m}C_{ds}T_{ds}T_{ds}T_{eo}{}^{m}C_{eo}{}^{m}C_{es}T_{es}T_{e}$ (SEQ ID NO: 2101);

$G_{es}{}^{m}C_{eo}A_{eo}T_{eo}{}^{m}C_{eo}A_{ds}G_{ds}A_{ds}T_{ds}G_{ds}T_{ds}T_{ds}{}^{m}C_{ds}A_{ds}T_{ds}{}^{m}C_{eo}T_{eo}{}^{m}C_{es}T_{es}T_{e}$ (SEQ ID NO: 1050);

$^{m}C_{es}{}^{m}C_{eo}T_{eo}{}^{m}C_{eo}{}^{m}C_{eo}A_{ds}T_{ds}T_{ds}{}^{m}C_{ds}{}^{m}C_{ds}T_{ds}T_{ds}T_{ds}G_{ds}T_{ds}G_{eo}A_{eo}{}^{m}C_{es}T_{es}T_{e}$ (SEQ ID NO: 1449),

wherein:

A = an adenine nucleobase,

^{m}C = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

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

$T_{es}G_{eo}T_{eo}A_{eo}G_{eo}T_{ds}A_{ds}{}^{m}C_{ds}A_{ds}A_{ds}A_{ds}T_{ds}{}^{m}C_{ds}T_{ds}T_{ds}T_{eo}{}^{m}C_{eo}{}^{m}C_{es}T_{es}T_{e}$ (SEQ ID NO: 2101), wherein:

A = an adenine nucleobase,

^{m}C = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

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

$A_{es}{}^{m}C_{eo}A_{eo}A_{eo}A_{eo}T_{eo}{}^{m}C_{ds}T_{ds}T_{ds}T_{ds}{}^{m}C_{ds}{}^{m}C_{ds}T_{ds}T_{ds}{}^{m}C_{ds}A_{ds}A_{eo}T_{es}T_{es}A_{e}$ (SEQ ID NO: 682), wherein:

A = an adenine nucleobase,

^{m}C = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

34. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $^{m}C_{es}A_{eo}G_{eo}A_{eo}T_{eo}G_{eo}T_{ds}T_{ds}{}^{m}C_{ds}A_{ds}T_{ds}{}^{m}C_{ds}T_{ds}{}^{m}C_{ds}T_{ds}T_{ds}{}^{m}C_{eo}A_{es}{}^{m}C_{es}A_{e}$ (SEQ ID NO: 1124), wherein:

A = an adenine nucleobase,

^{m}C = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

35. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $^{m}C_{es}A_{eo}T_{eo}{}^{m}C_{eo}A_{eo}G_{eo}A_{ds}T_{ds}G_{ds}T_{ds}T_{ds}{}^{m}C_{ds}A_{ds}T_{ds}{}^{m}C_{ds}T_{ds}{}^{m}C_{eo}T_{es}T_{es}{}^{m}C_{e}$ (SEQ ID NO: 2145), wherein:

A = an adenine nucleobase,

^{m}C = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

36. The oligomeric compound of any of claims 1-35 wherein the oligomeric compound is a singled-stranded oligomeric compound.

37. The oligomeric compound of any of claims 1-36, consisting of the modified oligonucleotide.

38. The oligomeric compound of any of claims 1-36, further comprising a conjugate group.

39. The oligomeric compound of claim 38, wherein the conjugate group comprises a conjugate moiety and a conjugate linker.

40. The oligomeric compound of claim 38, wherein the conjugate group comprises a GalNAc cluster comprising 1-3 GalNAc ligands.

41. The oligomeric compound of claim 38 or claim 39, wherein the conjugate linker consists of a single bond.

42. The oligomeric compound of and of claims 39 or claim 41, wherein the conjugate linker is cleavable.

43. The oligomeric compound of claim 39 or claim 42, wherein the conjugate linker comprises 1-3 linker-nucleosides.

44. The oligomeric compound of any of claims 38-43, wherein the conjugate group is attached to the modified oligonucleotide at the 5'-end of the modified oligonucleotide.

45. The oligomeric compound of any of claims 38-43, wherein the conjugate group is attached to the modified oligonucleotide at the 3'-end of the modified oligonucleotide.

46. The oligomeric compound of any of claims 1-36 or 38-45 further comprising a terminal group.

47. The oligomeric compound of any of claims 1-42 or 44-46, wherein the oligomeric compound does not comprise linker-nucleosides.

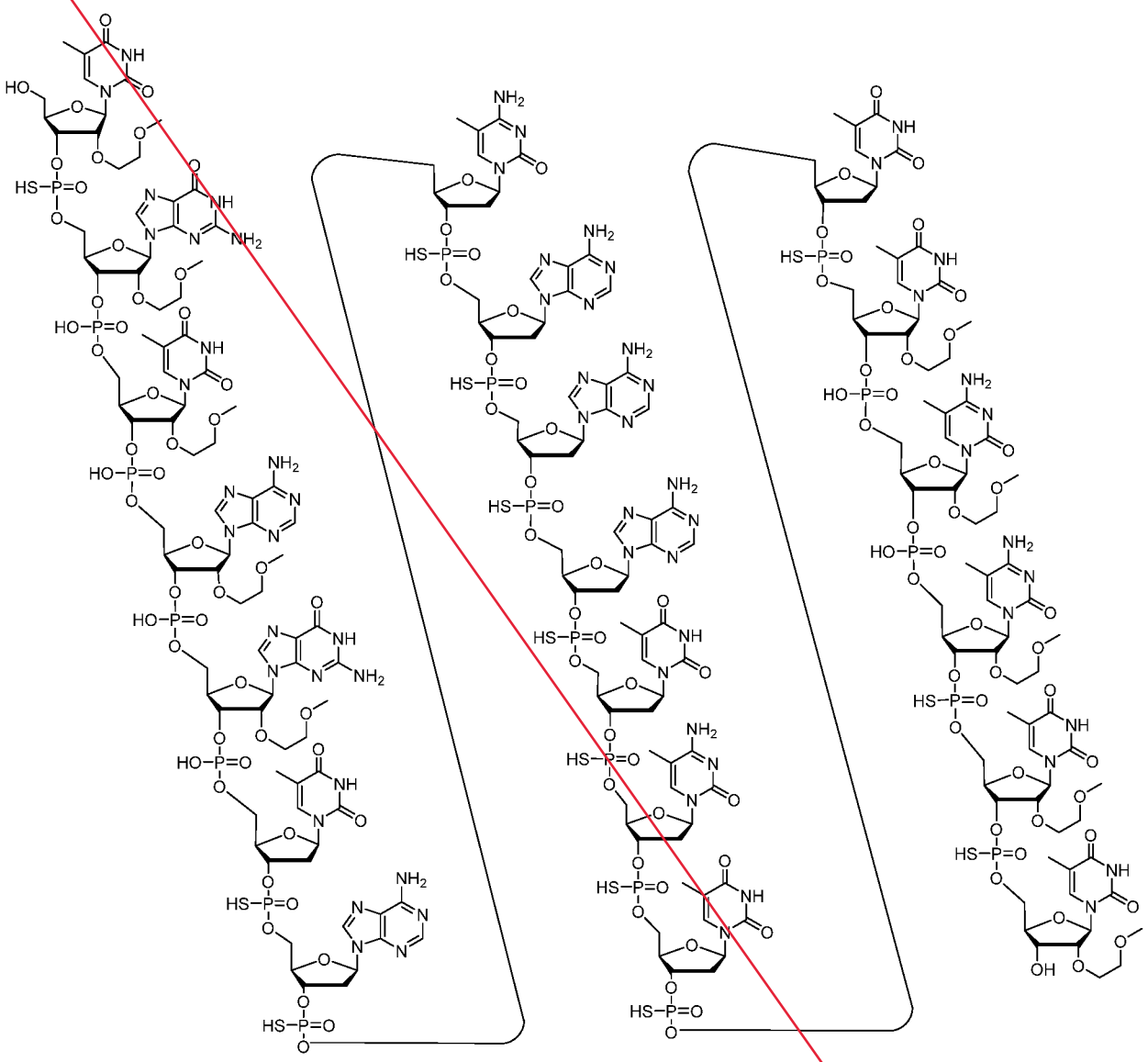
48. The oligomeric compound of any of claims 1-47, wherein the modified oligonucleotide of the oligomeric compound is a salt, and wherein the salt is a sodium salt or a potassium salt.

49. The oligomeric compound of any of claims 1-48, wherein the modified oligonucleotide is an RNAi compound.

50. An oligomeric duplex comprising an oligomeric compound of any of claims 1-35 or 37-49.

51. An antisense compound comprising or consisting of an oligomeric compound of any of claims 1-49 or an oligomeric duplex of claim 50.

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

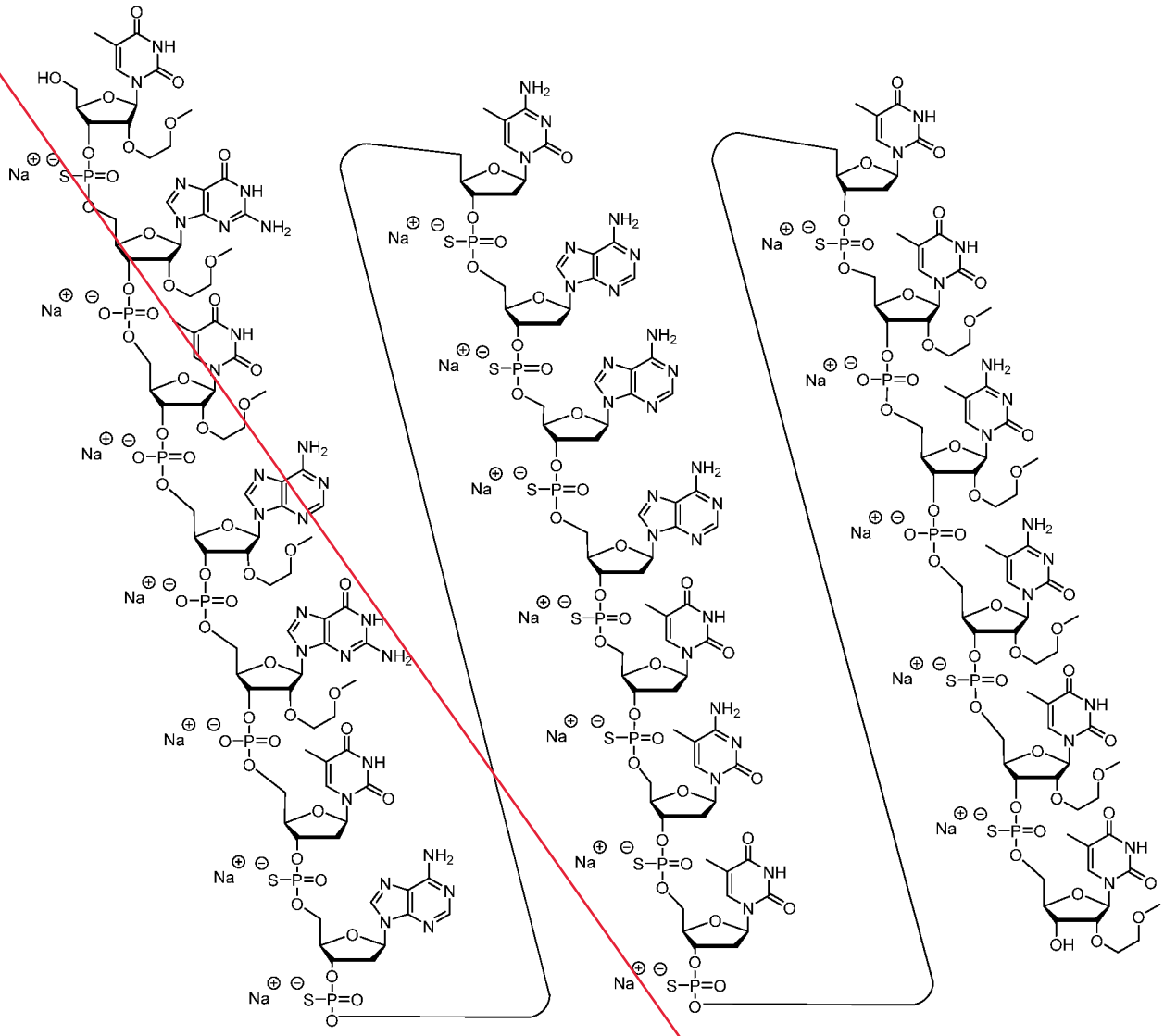


(SEQ ID NO: 2101)

or a salt thereof.

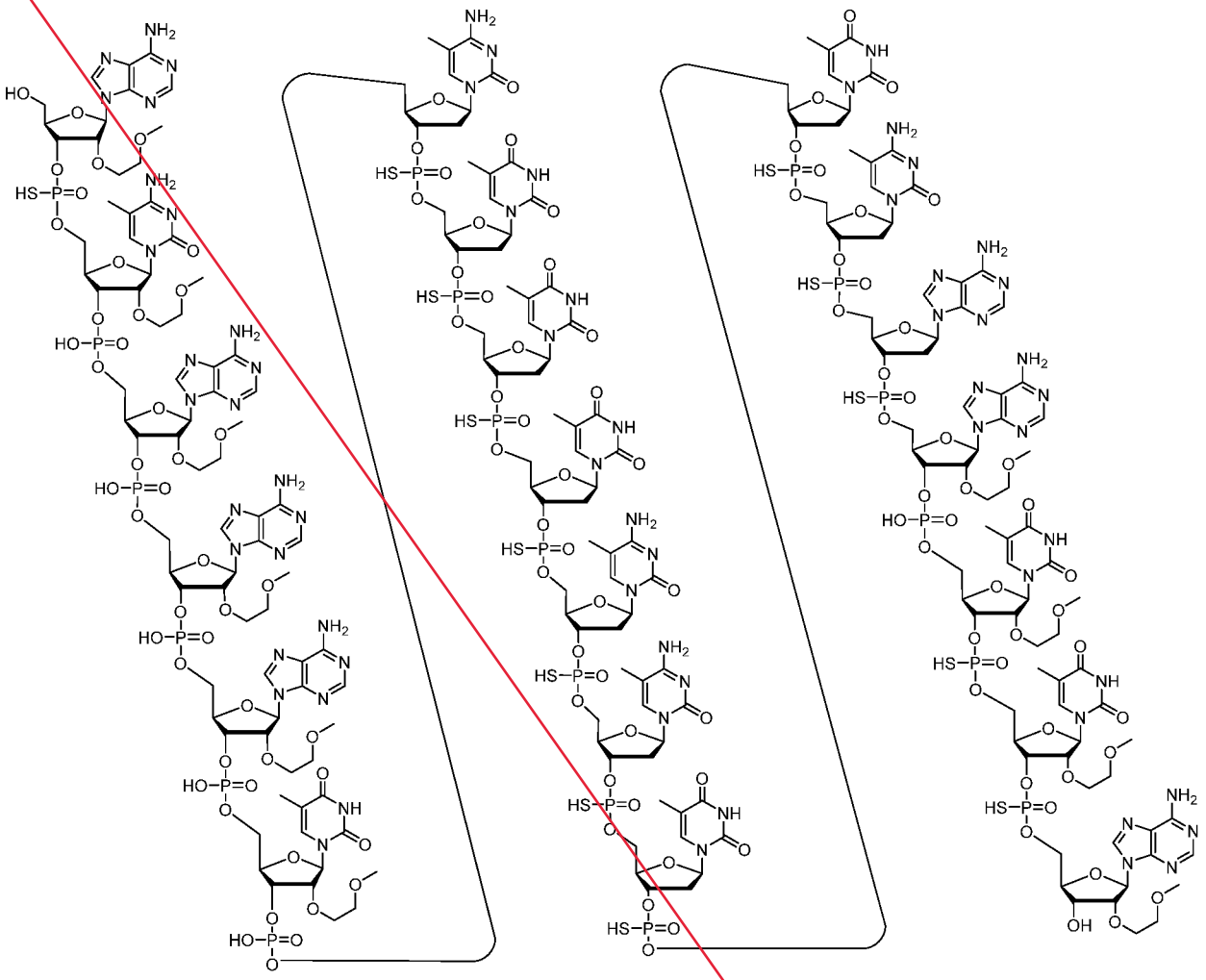
53. The modified oligonucleotide of claim 52, which is the sodium salt or the potassium salt.

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



(SEQ ID NO: 2101).

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

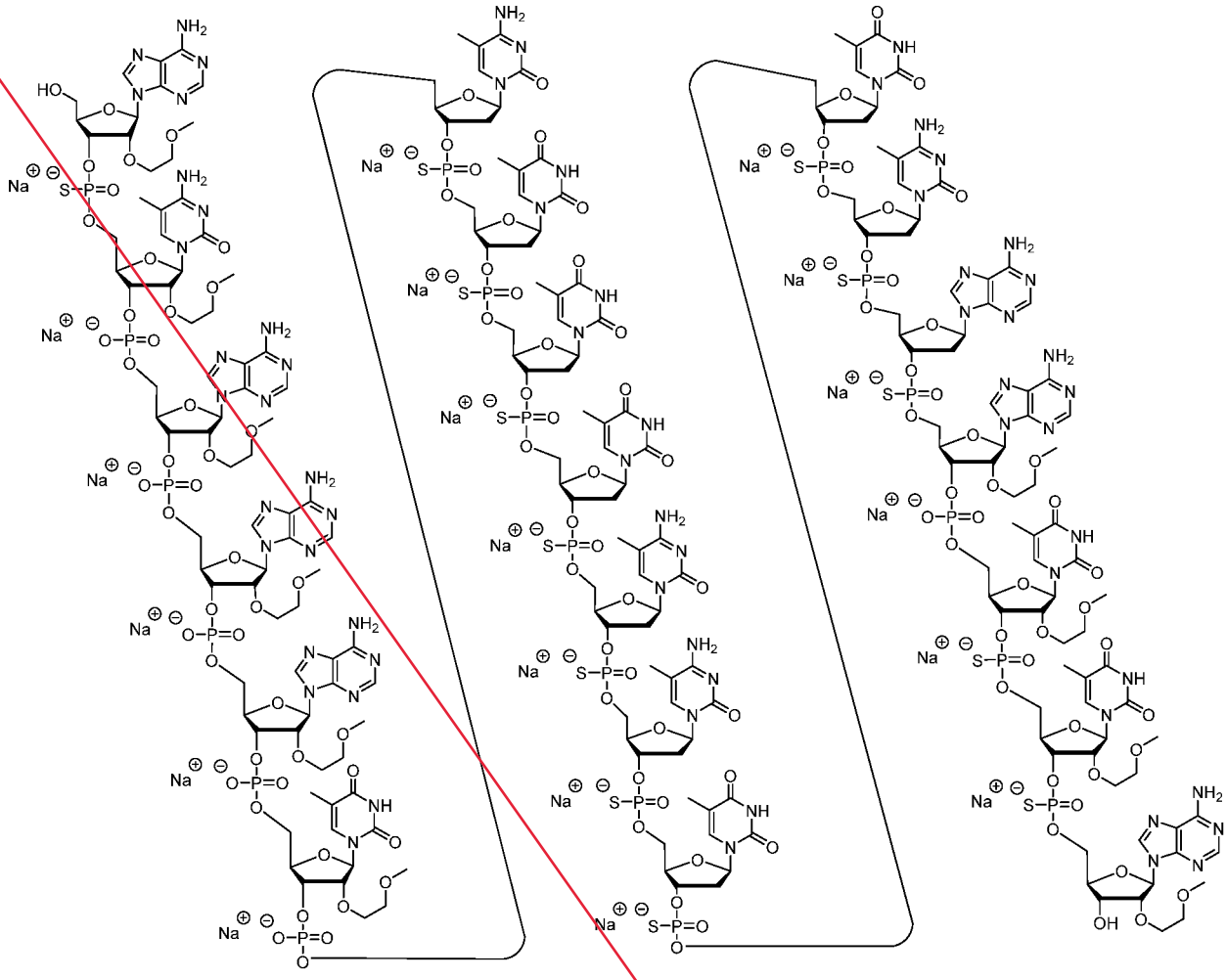


(SEQ ID NO: 682)

or a salt thereof.

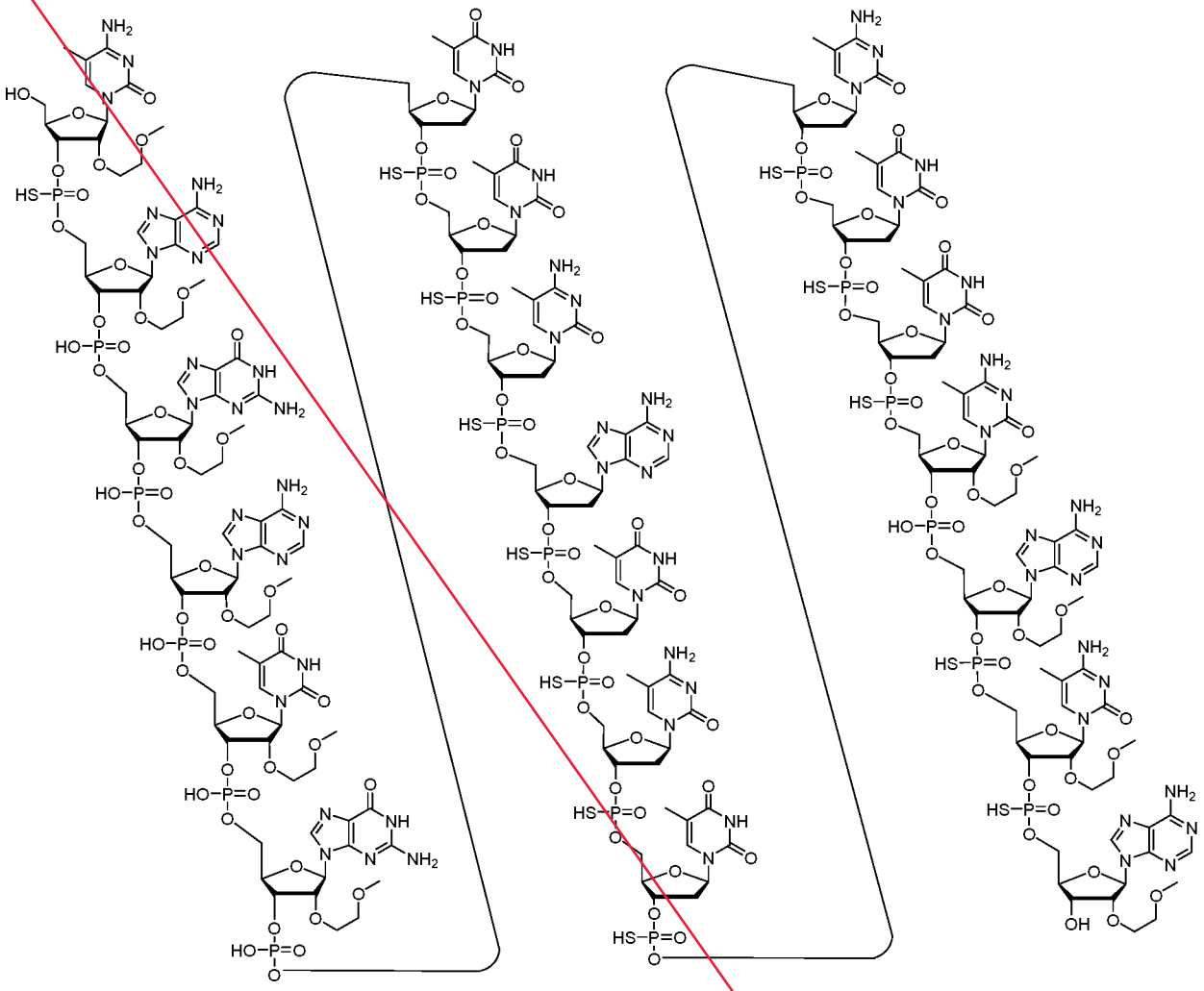
56. The modified oligonucleotide of claim 55, which is the sodium salt or the potassium salt.

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



(SEQ ID NO: 682).

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

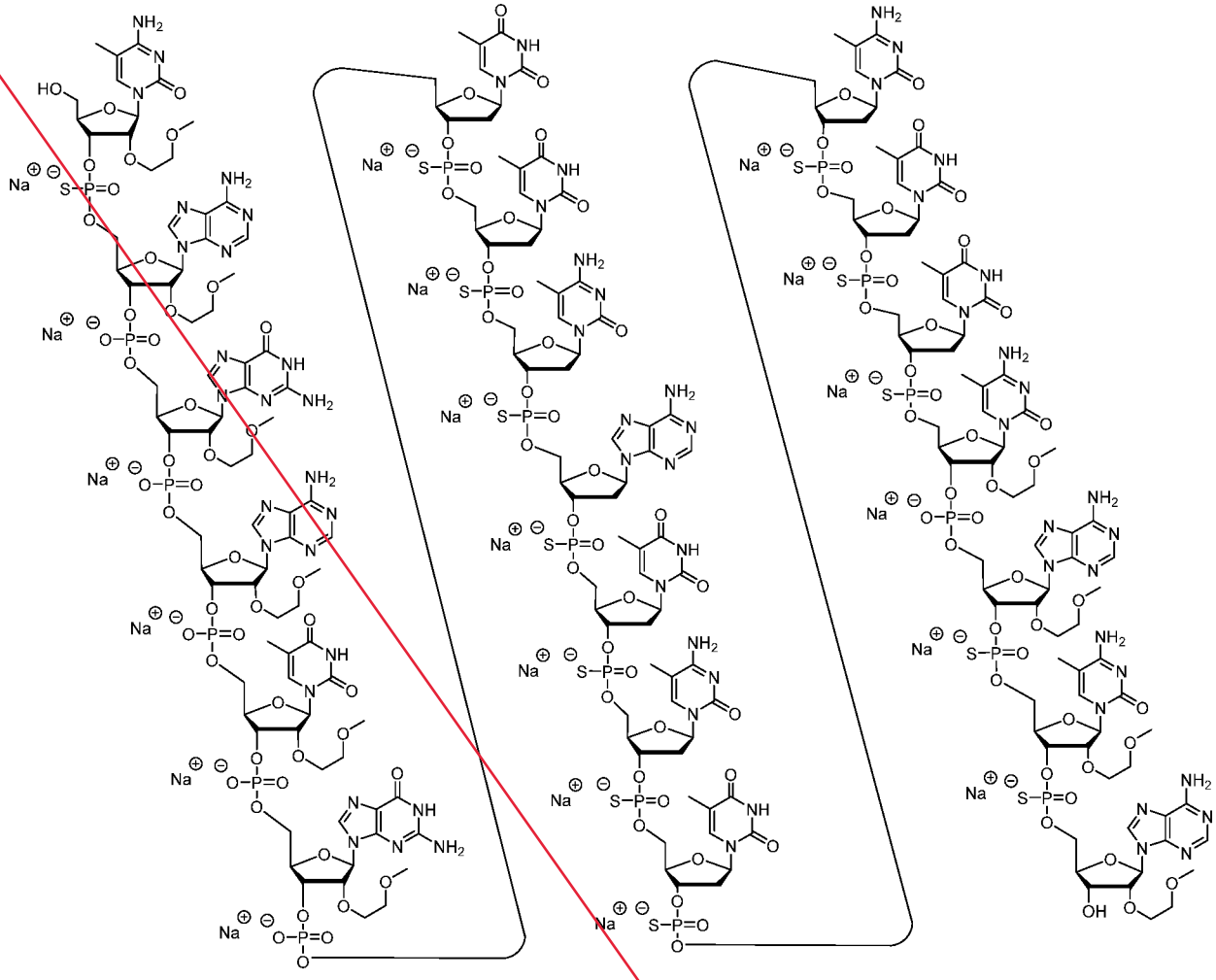


(SEQ ID NO: 1124)

or a salt thereof.

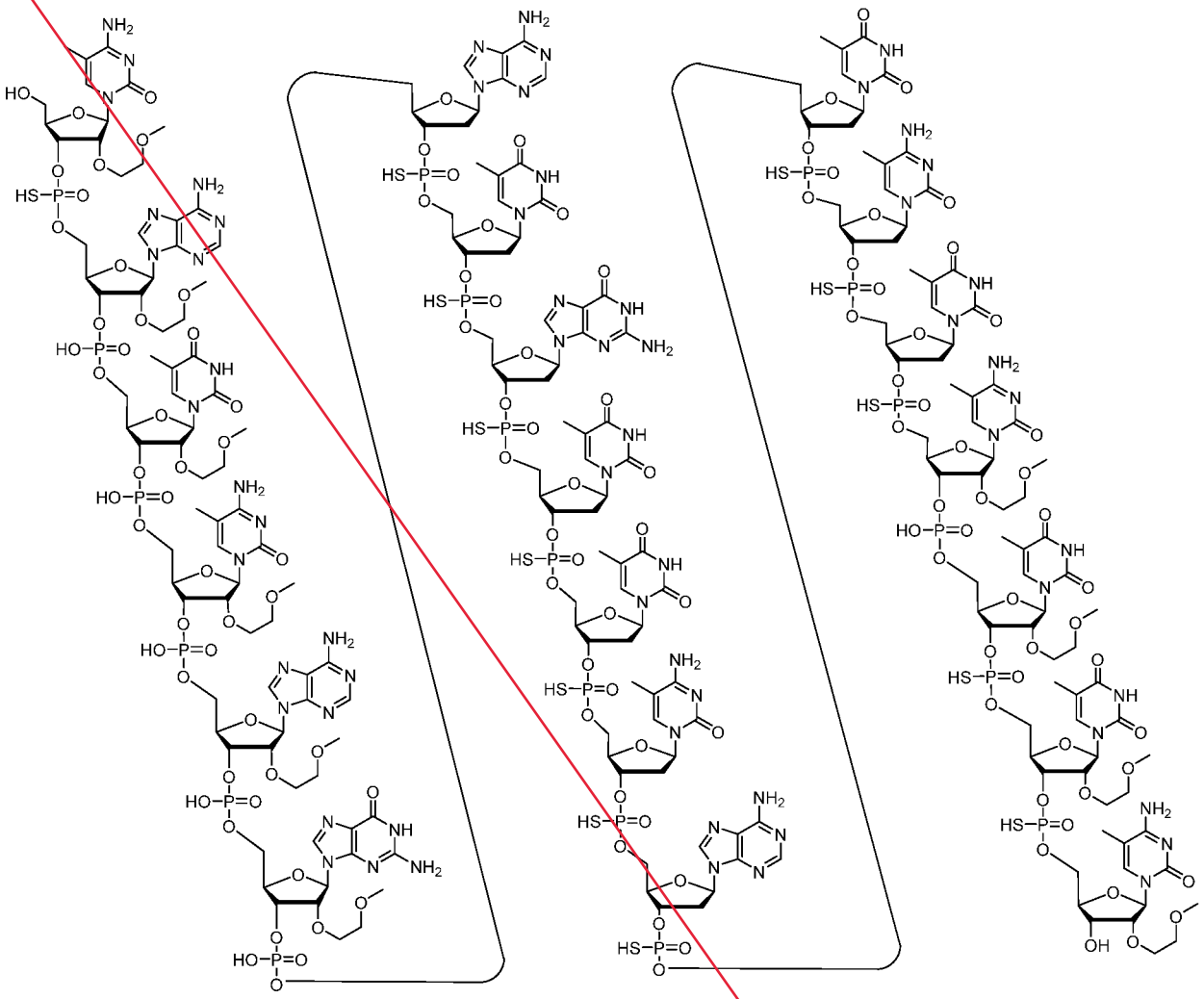
59. The modified oligonucleotide of claim 58, which is the sodium salt or the potassium salt.

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



(SEQ ID NO: 1124).

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

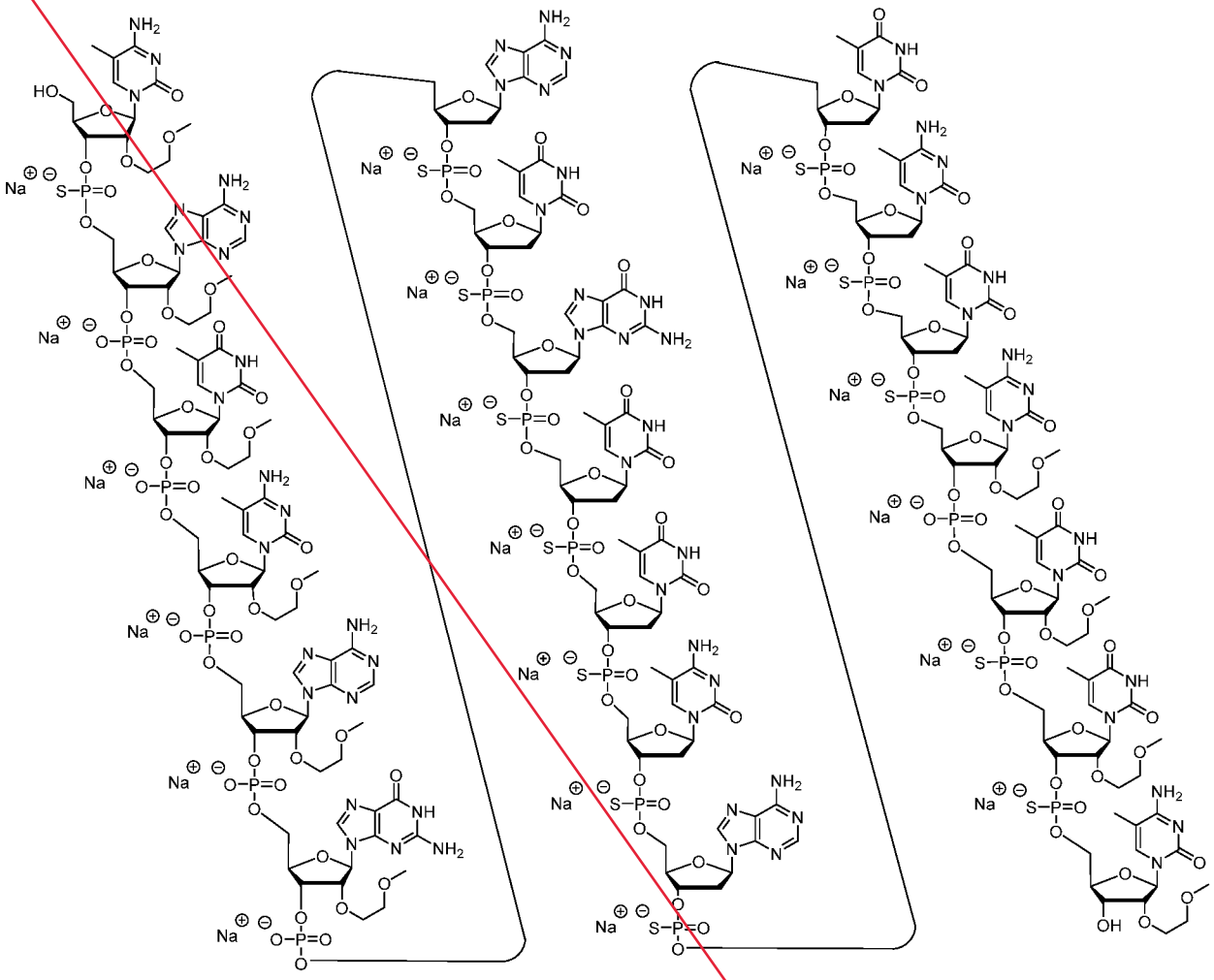


(SEQ ID NO: 2145)

or a salt thereof.

62. The modified oligonucleotide of claim 61, which is the sodium salt or the potassium salt.

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



(SEQ ID NO: 2145).

64. A pharmaceutical composition comprising the oligomeric compound of any of claims 1-49, the oligomeric duplex of claim 50, the antisense compound of claim 51, or the modified oligonucleotide of any of claims 52-63 and a pharmaceutically acceptable diluent or carrier.

65. The pharmaceutical composition of claim 64, comprising a pharmaceutically acceptable diluent and wherein the pharmaceutically acceptable diluent is artificial cerebrospinal fluid (aCSF) or phosphate-buffered saline (PBS).

66. The pharmaceutical composition of claim 65, wherein the pharmaceutical composition consists essentially of the oligomeric compound or the modified oligonucleotide and aCSF.

67. The pharmaceutical composition of claim 65, wherein the pharmaceutical composition consists essentially of the oligomeric compound or the modified oligonucleotide and PBS.

68. A pharmaceutical composition comprising a modified oligonucleotide of any of claims 52-63 and a pharmaceutically acceptable diluent.

69. The pharmaceutical composition of claim 68, wherein the pharmaceutically acceptable diluent is artificial cerebrospinal fluid (aCSF) or phosphate-buffered saline (PBS).

70. The pharmaceutical composition of claim 69, wherein the pharmaceutical composition consists essentially of the modified oligonucleotide and aCSF.

71. The pharmaceutical composition of claim 69, wherein the pharmaceutical composition consists essentially of the modified oligonucleotide and PBS.

72. A pharmaceutical composition comprising an oligomeric compound of any of claims 32-35 and a pharmaceutically acceptable diluent.

73. The pharmaceutical composition of claim 72, wherein the pharmaceutically acceptable diluent is artificial cerebrospinal fluid (aCSF) or phosphate-buffered saline (PBS).

74. The pharmaceutical composition of claim 73, wherein the pharmaceutical composition consists essentially of the oligomeric compound and aCSF.

75. The pharmaceutical composition of claim 73, wherein the pharmaceutical composition consists essentially of the oligomeric compound and PBS.

76. A chirally enriched population of modified oligonucleotides of any of claims 52-63, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having a particular stereochemical configuration.

77. The chirally enriched population of claim 76, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (*S*p) configuration.

78. The chirally enriched population of claim 76, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (*R*p) configuration.

79. The chirally enriched population of claim 76, wherein the population is enriched for modified oligonucleotides having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage.

80. The chirally enriched population of claim 79, wherein the population is enriched for modified oligonucleotides having the (*S*p) configuration at each phosphorothioate internucleoside linkage or for modified oligonucleotides having the (*R*p) configuration at each phosphorothioate internucleoside linkage.

81. The chirally enriched population of claim 79, 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.

82. The chirally enriched population of claim 79, 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.

83. A population of modified oligonucleotides of any of claims 52-63, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

84. A chirally enriched population of oligomeric compounds of any of claims 32-35, wherein the population is enriched for oligomeric compounds comprising at least one particular phosphorothioate internucleoside linkage having a particular stereochemical configuration.

85. The chirally enriched population of claim 84, wherein the population is enriched for oligomeric compounds comprising at least one particular phosphorothioate internucleoside linkage having the (*S*p) configuration.

86. The chirally enriched population of claim 84, wherein the population is enriched for oligomeric compounds comprising at least one particular phosphorothioate internucleoside linkage having the (*R*p) configuration.

87. The chirally enriched population of claim 84, wherein the population is enriched for oligomeric compounds having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage.

88. The chirally enriched population of claim 87, wherein the population is enriched for oligomeric compounds having the (*S*p) configuration at each phosphorothioate internucleoside linkage or for modified oligonucleotides having the (*R*p) configuration at each phosphorothioate internucleoside linkage.

89. The chirally enriched population of claim 87, wherein the population is enriched for oligomeric compounds having the (Rp) configuration at one particular phosphorothioate internucleoside linkage and the (Sp) configuration at each of the remaining phosphorothioate internucleoside linkages.

90. The chirally enriched population of claim 87, wherein the population is enriched for oligomeric compounds having at least 3 contiguous phosphorothioate internucleoside linkages in the Sp, Sp, and Rp configurations, in the 5' to 3' direction.

91. A population of oligomeric compounds of any of claims 32-35, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

92. A pharmaceutical composition comprising the chirally enriched population of any of claims 76-82 or 84-90, the population of claim 83, or the population of claim 91 and a pharmaceutically acceptable diluent.

93. The pharmaceutical composition of claim 92, wherein the pharmaceutically acceptable diluent is artificial CSF (aCSF) or phosphate-buffered saline (PBS).

94. The pharmaceutical composition of claim 93, wherein the pharmaceutical composition consists essentially of the oligomeric compounds or the modified oligonucleotides and artificial CSF (aCSF).

95. The pharmaceutical composition of claim 93, wherein the pharmaceutical composition consists essentially of the oligomeric compounds or the modified oligonucleotides and PBS.

96. A method comprising administering to an animal the pharmaceutical composition of any of claims 64-75 or 92-95.

97. A method of treating a disease or disorder associated with PLP1, comprising administering to a subject having or at risk for developing a disease or disorder associated with PLP1 a therapeutically effective amount of a pharmaceutical composition according to any of claims 64-75 or 92-95, and thereby treating the disease or disorder associated with PLP1.

98. A method of reducing PLP1 protein in the CSF of a subject having or at risk for developing a disease or disorder associated with PLP1 a therapeutically effective amount of a pharmaceutical composition according any of claims 64-75 or 92-95, and thereby reducing PLP1 protein in the CSF.

99. The method of claim 97 or claim 98, wherein the disease or disorder associated with PLP1 is a neurodegenerative disease.

100. The method of any of claims 97-99, wherein the disease or disorder associated with PLP1 is a leukodystrophy.

101. The method of claim 100, wherein the leukodystrophy is PMD.

102. The method of claim 101, wherein the PMD is any of connatal PMD, classic PMD, transitional PMD.

103. The method of claim 101, wherein the PMD is caused by overexpression of PLP1 protein.

104. The method of claim 101, wherein the PMD is caused by multiple copies of the PLP1 gene.

105. The method of claim 101, wherein the PMD is caused by the expression of duplicate copies of the PLP1 gene.

106. The method of any of claims 100-105, wherein at least one symptom or hallmark of the leukodystrophy is ameliorated.

107. The method of claim 97 or claim 98, wherein the disease or disorder associated with PLP1 is SPG2.

108. The method of claim 107, wherein at least one symptom or hallmark of SPG2 is ameliorated.

109. The method of claim 106 or claim 108, wherein the symptom or hallmark is any of hypotonia, nystagmus, optic atrophy, respiratory distress, motor delays, cognitive dysfunction, speech dysfunction, spasticity, ataxia, seizures, choreiform movements, and death.

110. The method of any of claims 96-109 wherein administering the modified oligonucleotide reduces hypotonia, nystagmus, optic atrophy, respiratory distress, motor delays, cognitive dysfunction, speech dysfunction, spasticity, ataxia, seizures, or choreiform movements, or delays death in the subject.

111. The method of any of claims 96-110, wherein the pharmaceutical composition is administered to the central nervous system or systemically.

112. The method of claim 111, wherein the pharmaceutical composition is administered to the central nervous system and systemically.

113. The method of any of claims 96-110, wherein the pharmaceutical composition is administered any of intrathecally, systemically, subcutaneously, or intramuscularly.

114. A method of reducing PLP1 RNA in a cell comprising contacting the cell with an oligomeric compound of any of claims 1-49, an oligomeric duplex according to claim 50, an antisense compound according to claim 51, or a modified oligonucleotide of any of claims 52-63, and thereby reducing PLP1 RNA in the cell.

115. A method of reducing PLP1 protein in a cell comprising contacting the cell with an oligomeric compound of any of claims 1-49, an oligomeric duplex according to claim 50, an antisense compound according to claim 51, or a modified oligonucleotide of any of claims 52-63, and thereby reducing PLP1 protein in the cell.

116. The method of claim 114 or claim 115, wherein the cell is an oligodendrocyte or an oligodendrocyte progenitor cell.

117. The method of claim 114 or claim 115, wherein the cell is a Schwann cell or a Schwann cell progenitor.

118. The method of any of claims 114-117, wherein the cell is in an animal.

119. The method of claim 96 or claim 117, wherein the animal is human.

120. A method comprising administering to a subject a pharmaceutical composition of any of claims 68-71.

121. A method of treating a disease or disorder associated with PLP1, comprising administering to an subject having or at risk for developing a disease or disorder associated with PLP1 a therapeutically effective amount of a pharmaceutical composition according to any of claims 68-71 and thereby treating the disease or disorder associated with PLP1.

122. The method of claim 121, wherein the disease associated with PLP1 is a neurodegenerative disease.

123. The method of claim 122, wherein the neurodegenerative disease is a leukodystrophy.

124. The method of claim 123, wherein the leukodystrophy is PMD.

125. The method of claim 124, wherein the PMD is any of connatal PMD, classic PMD, transitional PMD.

126. The method of claim 124, wherein the PMD is caused by overexpression of PLP1 protein.

127. The method of claim 124, wherein the PMD is caused by multiple copies of the PLP1 gene.

128. The method of claim 124, wherein the PMD is caused by the expression of duplicate copies of the PLP1 gene.

129. The method of any of claims 122-128, wherein at least one symptom or hallmark of the neurodegenerative disease is ameliorated.

130. The method of claim 129, wherein the symptom or hallmark is any of hypotonia, nystagmus, optic atrophy, respiratory distress, motor delays, cognitive dysfunction, speech dysfunction, spasticity, ataxia, seizures, choreiform movements, and death.

131. The method of any of claims 121-130 wherein administering the pharmaceutical composition reduces hypotonia, nystagmus, optic atrophy, respiratory distress, motor delays, cognitive dysfunction, speech dysfunction, spasticity, ataxia, seizures, or choreiform movements, or delays death in the subject.

132. The method of any of claims 121-131, wherein the subject is human.

133. A method of reducing expression of PLP1 in a cell comprising contacting the cell with a modified oligonucleotide of any of claims 52-63.

134. The method of claim 134, wherein the cell is a human cell.

135. Use of an oligomeric compound any of claims 1-49, an oligomeric duplex according to claim 50, an antisense compound according to claim 51, or a modified oligonucleotide of any of claims 52-63 for reducing PLP1 expression in a cell.

136. The use of claim 135, wherein the level of PLP1 RNA in the cell is reduced.

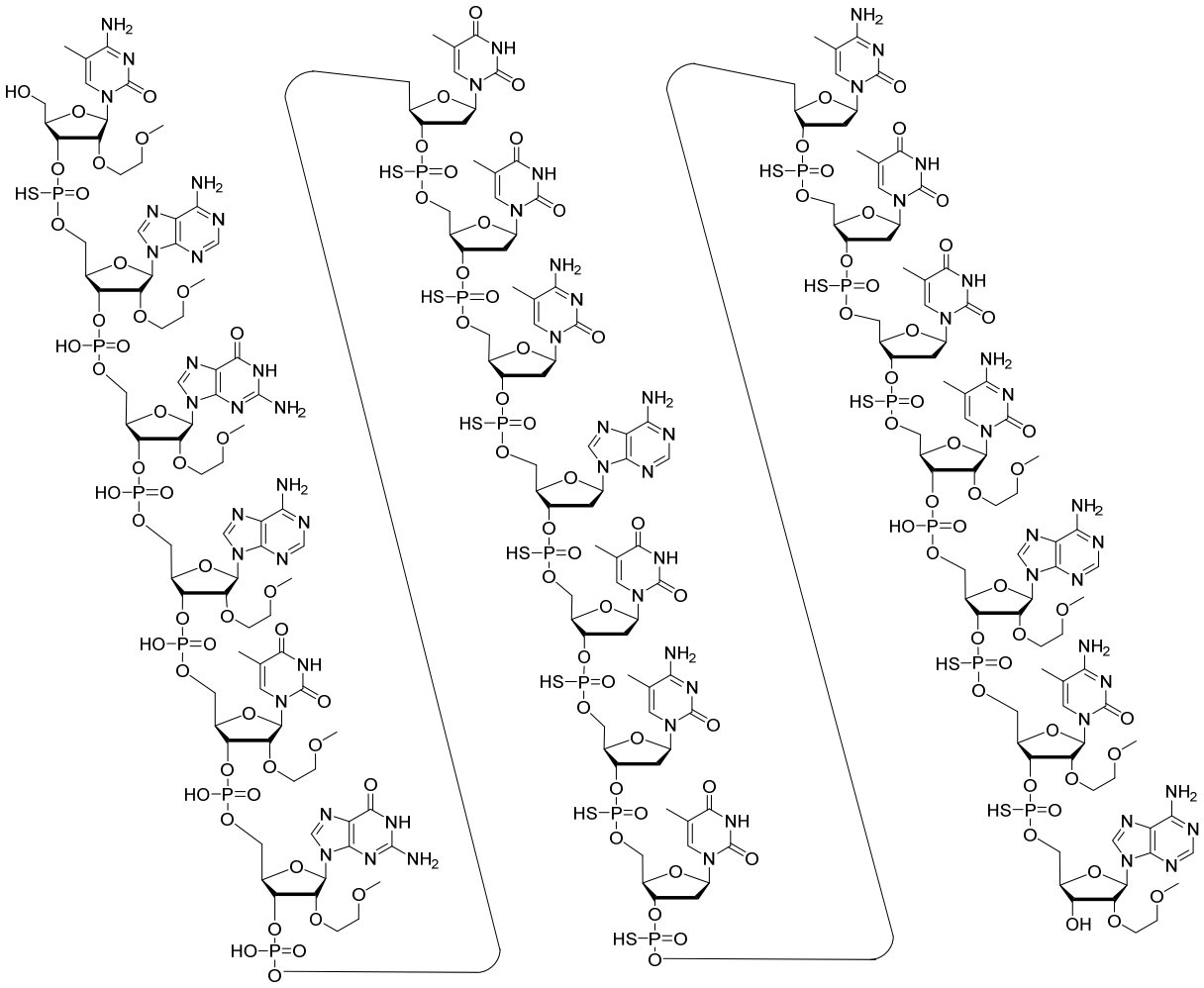
137. The use of claim 135, wherein the level of PLP1 protein in the cell is reduced.

138. The use of any of claims 135-137, wherein the cell is an oligodendrocyte or an oligodendrocyte progenitor cell.

139. The use of any of claims 135-137, wherein the cell is a Schwann cell or a Schwann cell progenitor.

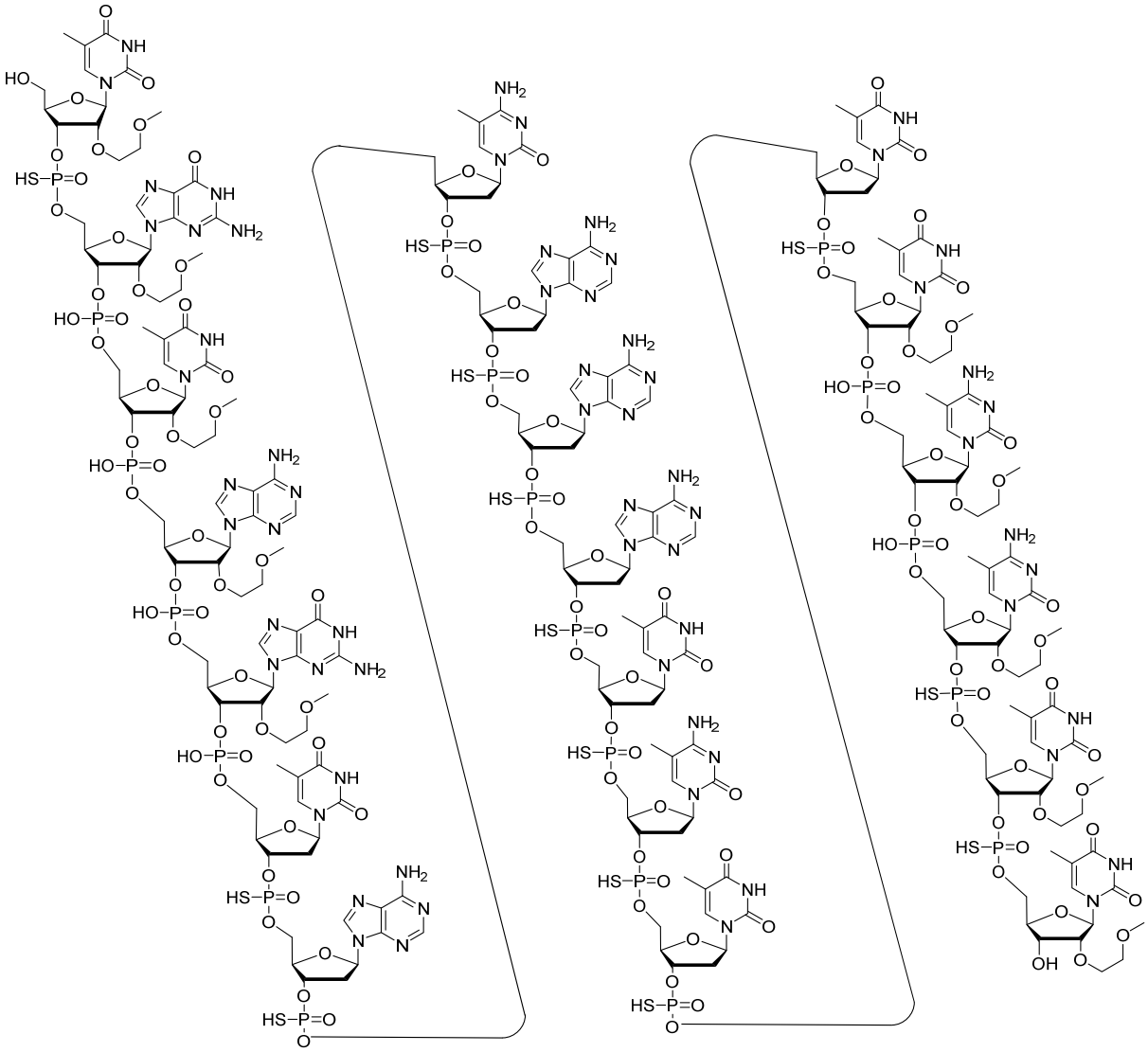
CLAIMS

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



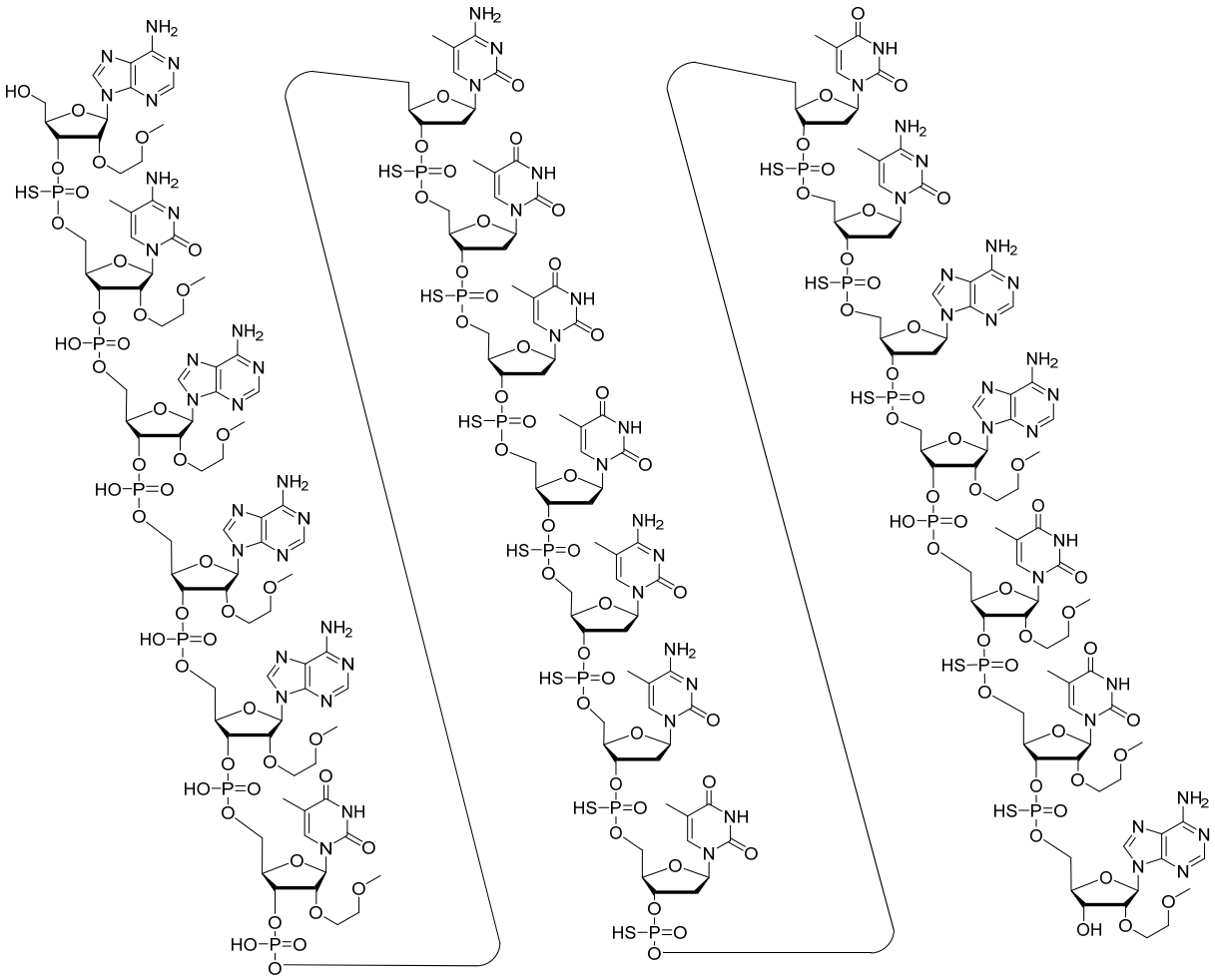
(SEQ ID NO: 1124), or a salt thereof.

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



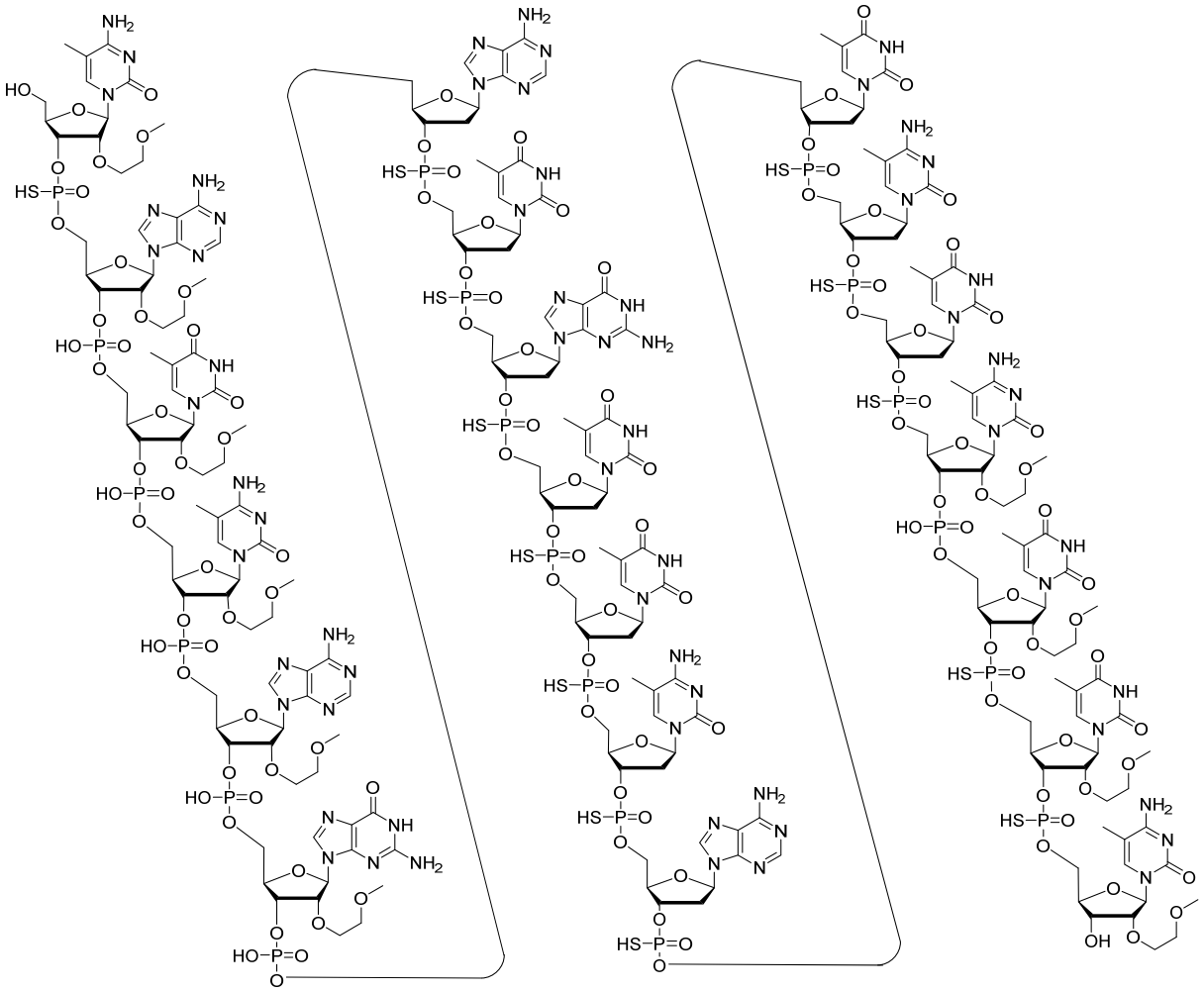
(SEQ ID NO: 2101), or a salt thereof.

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



(SEQ ID NO: 682), or a salt thereof.

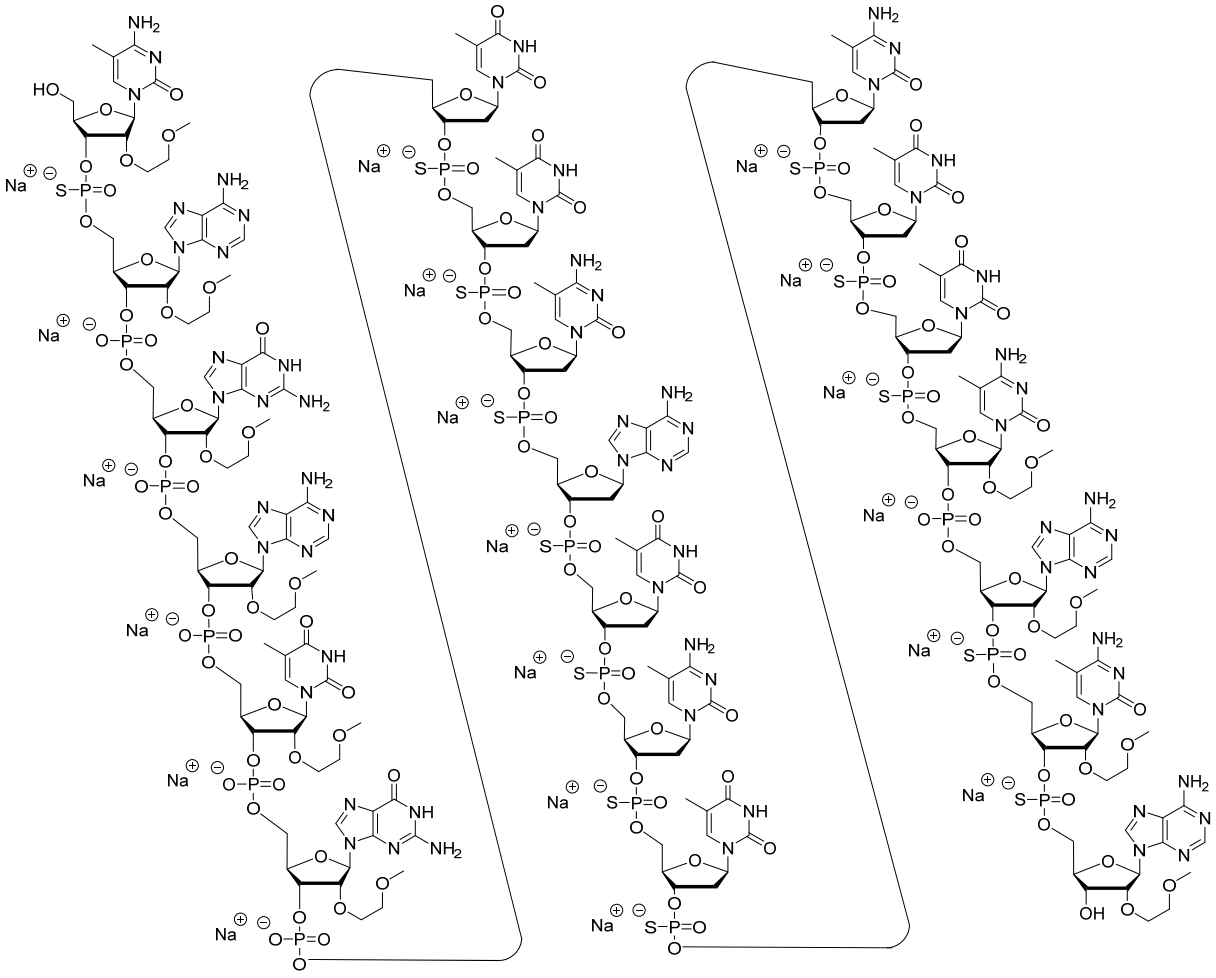
4. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 2145), or a salt thereof.

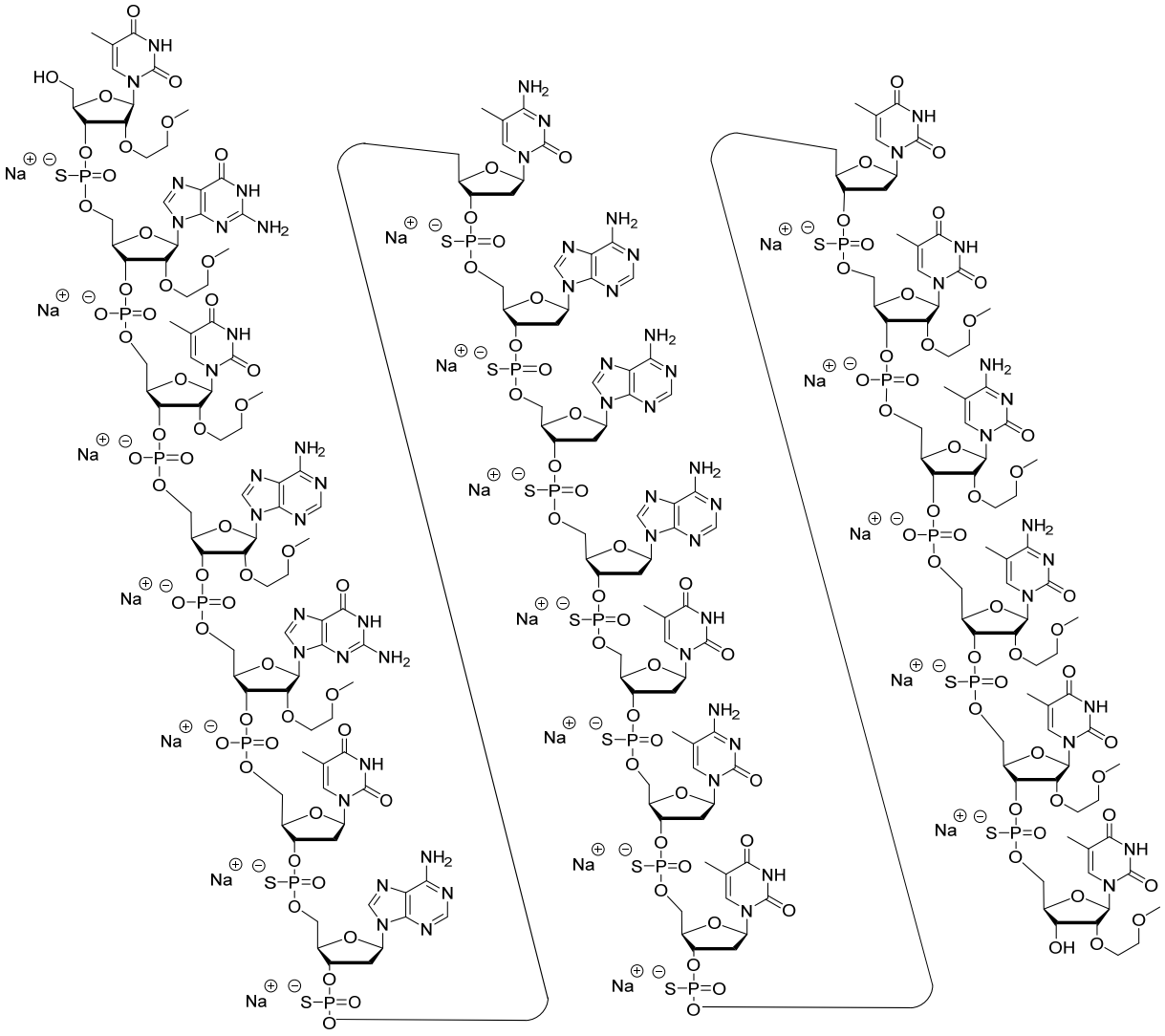
5. The modified oligonucleotide of any of claims 1-4, which is the sodium salt or the potassium salt.

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



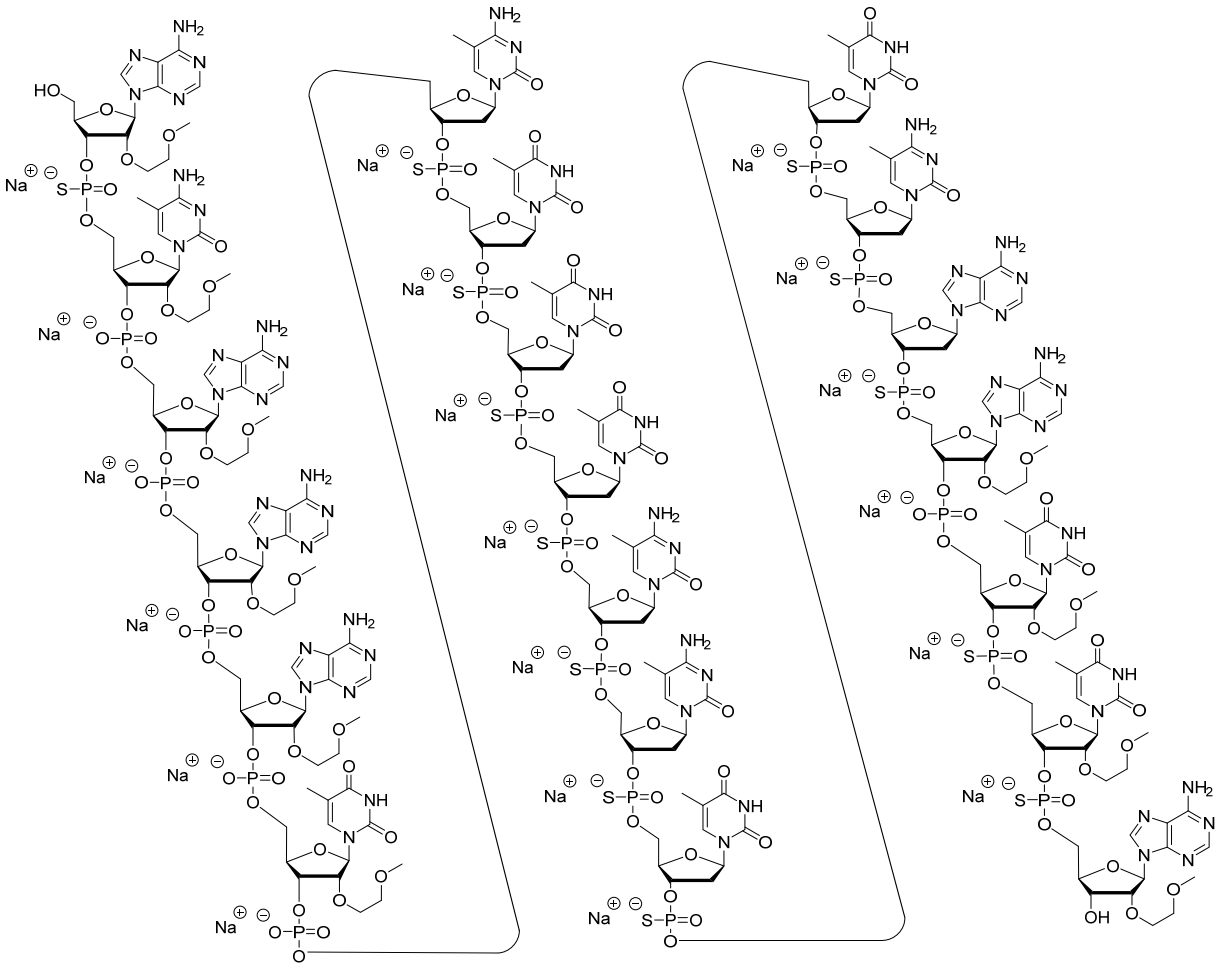
(SEQ ID NO: 1124).

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



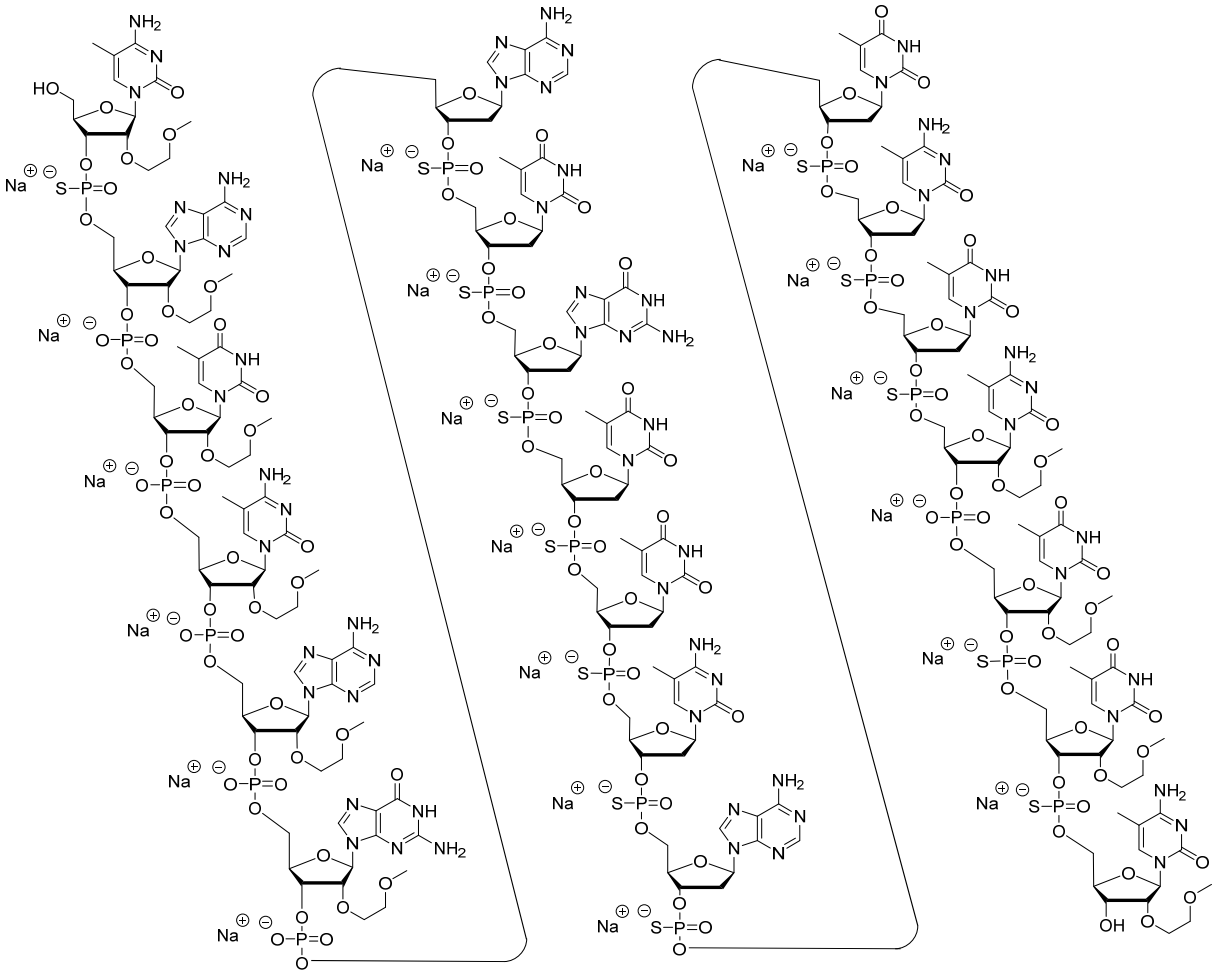
(SEQ ID NO: 2101).

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



(SEQ ID NO: 682).

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



(SEQ ID NO: 2145).

10. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $^{m}C_{es}A_{eo}G_{eo}A_{eo}T_{eo}G_{eo}T_{ds}T_{ds}{}^{m}C_{ds}A_{ds}T_{ds}{}^{m}C_{ds}T_{ds}{}^{m}C_{ds}T_{ds}T_{ds}{}^{m}C_{eo}A_{es}{}^{m}C_{es}A_{e}$ (SEQ ID NO: 1124), wherein:

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

11. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $T_{es}G_{eo}T_{eo}A_{eo}G_{eo}T_{ds}A_{ds}{}^{m}C_{ds}A_{ds}A_{ds}A_{ds}T_{ds}{}^{m}C_{ds}T_{ds}T_{ds}T_{eo}{}^{m}C_{eo}{}^{m}C_{es}T_{es}T_{e}$ (SEQ ID NO: 2101), wherein:

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

12. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $A_{es}{}^{m}C_{eo}A_{eo}A_{eo}A_{eo}T_{eo}{}^{m}C_{ds}T_{ds}T_{ds}T_{ds}{}^{m}C_{ds}{}^{m}C_{ds}T_{ds}T_{ds}{}^{m}C_{ds}A_{ds}A_{eo}T_{es}T_{es}A_{e}$ (SEQ ID NO: 682), wherein:

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

13. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $^{m}C_{es}A_{eo}T_{eo}{}^{m}C_{eo}A_{eo}G_{eo}A_{ds}T_{ds}G_{ds}T_{ds}T_{ds}{}^{m}C_{ds}A_{ds}T_{ds}{}^{m}C_{ds}T_{ds}{}^{m}C_{eo}T_{es}T_{es}{}^{m}C_{e}$ (SEQ ID NO: 2145), wherein:

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

14. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $^{m}C_{es}{}^{m}C_{eo}{}^{m}C_{eo}A_{eo}A_{eo}T_{ds}A_{ds}G_{ds}A_{ds}T_{ds}T_{ds}{}^{m}C_{ds}A_{ds}A_{ds}{}^{m}C_{ds}T_{eo}A_{eo}G_{es}{}^{m}C_{es}{}^{m}C_{e}$ (SEQ ID NO: 134), wherein:

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

15. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $A_{es}{}^{m}C_{eo}A_{eo}{}^{m}C_{eo}A_{eo}A_{ds}{}^{m}C_{ds}T_{ds}{}^{m}C_{ds}T_{ds}T_{ds}T_{ds}A_{ds}{}^{m}C_{ds}A_{ds}A_{eo}{}^{m}C_{eo}A_{es}A_{es}A_{e}$ (SEQ ID NO: 411), wherein:

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

16. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $T_{es}{}^{m}C_{eo}T_{eo}{}^{m}C_{eo}{}^{m}C_{eo}A_{ds}G_{ds}A_{ds}{}^{m}C_{ds}A_{ds}T_{ds}T_{ds}T_{ds}{}^{m}C_{ds}T_{ds}G_{eo}A_{eo}T_{es}G_{es}{}^{m}C_{e}$ (SEQ ID NO: 934), wherein:

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

17. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $G_{es}T_{eo}G_{eo}T_{eo}G_{eo}T_{ds}T_{ds}A_{ds}A_{ds}A_{ds}A_{ds}T_{ds}T_{ds}G_{ds}{}^{m}C_{ds}A_{eo}A_{eo}T_{es}T_{es}{}^{m}C_{e}$ (SEQ ID NO: 1238), wherein:

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

18. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $A_{es}T_{eo}T_{eo}G_{eo}{}^{m}C_{eo}A_{ds}A_{ds}T_{ds}T_{ds}{}^{m}C_{ds}T_{ds}A_{ds}T_{ds}A_{ds}T_{ds}{}^{m}C_{eo}A_{eo}G_{es}A_{es}A_{e}$ (SEQ ID NO: 2010), wherein:

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

19. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $A_{es}T_{eo}G_{eo}T_{eo}G_{eo}A_{ds}T_{ds}{}^{m}C_{ds}T_{ds}A_{ds}T_{ds}A_{ds}T_{ds}{}^{m}C_{ds}A_{ds}G_{eo}G_{eo}A_{es}G_{es}A_{e}$ (SEQ ID NO: 1772), wherein:

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

20. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $A_{es}{}^{m}C_{eo}{}^{m}C_{eo}A_{eo}G_{eo}A_{ds}G_{ds}G_{ds}G_{ds}{}^{m}C_{ds}{}^{m}C_{ds}A_{ds}T_{ds}{}^{m}C_{ds}T_{ds}{}^{m}C_{eo}A_{eo}G_{es}G_{es}T_{e}$ (SEQ ID NO: 881), wherein:

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

21. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $G_{es}{}^{m}C_{eo}A_{eo}T_{eo}{}^{m}C_{eo}A_{ds}G_{ds}A_{ds}T_{ds}G_{ds}T_{ds}T_{ds}{}^{m}C_{ds}A_{ds}T_{ds}{}^{m}C_{eo}T_{eo}{}^{m}C_{es}T_{es}T_{e}$ (SEQ ID NO: 1050), wherein:

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

22. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $^{m}C_{es}{}^{m}C_{eo}T_{eo}{}^{m}C_{eo}{}^{m}C_{eo}A_{ds}T_{ds}T_{ds}{}^{m}C_{ds}{}^{m}C_{ds}T_{ds}T_{ds}T_{ds}G_{ds}T_{ds}G_{eo}A_{eo}{}^{m}C_{es}T_{es}T_{e}$ (SEQ ID NO: 1449), wherein:

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

23. A population of modified oligonucleotides of any of claims 1-9, or a population of oligomeric

compounds of any of claims 10-22, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

24. A pharmaceutical composition comprising the modified oligonucleotide of any of claims 1-9, the oligomeric compound of any of claims 10-22, the population of modified oligonucleotides of claim 23, or the population of oligomeric compounds of claim 23, and a pharmaceutically acceptable diluent.

25. The pharmaceutical composition of claim 24, wherein the pharmaceutically acceptable diluent is artificial CSF (aCSF) or phosphate-buffered saline (PBS).

26. The pharmaceutical composition of claim 25, wherein the pharmaceutical composition consists or consists essentially of the modified oligonucleotide or oligomeric compound and aCSF.

27. The pharmaceutical composition of claim 25, wherein the pharmaceutical composition consists or consists essentially of the modified oligonucleotide or oligomeric compound and PBS.

28. The pharmaceutical composition of claim 25, wherein the pharmaceutical composition consists or consists essentially of the population of modified oligonucleotides or population of oligomeric compounds and aCSF.

29. The pharmaceutical composition of claim 25, wherein the pharmaceutical composition consists or consists essentially of the population of modified oligonucleotides or population of oligomeric compounds and PBS.