

[illegible]

8. The oligomeric compound of any of claims 1-6, wherein the modified oligonucleotide has an internucleoside linkage motif selected from: sssssssssssssxs and ssssssssssssssx, wherein 's' represents a phosphorothioate internucleoside linkage, 'o' represents a phosphodiester internucleoside linkage, and 'x' represents a methoxypropylphosphonate internucleoside linkage.

9. The oligomeric compound of any of claims 1-6, wherein the modified oligonucleotide has an internucleoside linkage motif selected from: *zzzzzzzzzzzzzzzzzzzz*, *sssssssssszzzzzzzz*, *sssszzzzzzssssss*, *zzoooooooooooooooozz*, *zzzzoooooooooooooooozz*, *zzzzzzoooooooooooooooozz*, and *ssooooooooooooooooss*, wherein 's' represents a phosphorothioate internucleoside linkage, 'o' represents a phosphodiester internucleoside linkage, and "z" represents a mesyl phosphoramidate internucleoside linkage.

[illegible]

kekekekekekeeeeee,eeeeeekekekekeek, kekekekeeeeee, eeeeeeekekekeek, kekekeeeeee, eeeeeeekekeek, eeeeeeeeee, eeeeeeeeee, ennnnnnnnnnnnnnnnnnnnn, and ennnnnnnnnnnnnnnnnnnne; wherein 'e' represents a 2'-MOE sugar moiety, 'n' represents a 2'-NMA sugar moiety, 'k' represents a cEt sugar moiety, 'd' represents a 2'-β-D-deoxyribosyl sugar moiety, and 'y' represents a 2'-OMe sugar moiety.

11. The oligomeric compound of any of claims 1-9, wherein the modified oligonucleotide has a sugar motif (5' to 3') selected from nnnnnnnnnnnnnnnenn and nnnnnnnnnnnnnnnnen, wherein 'e' represents a 2'-MOE sugar moiety and 'n' represents a 2'-NMA sugar moiety.

12. The oligomeric compound of any of claims 1-9, wherein the modified oligonucleotide has a sugar motif (5' to 3') of qqnqqqqnqnqnqnn, wherein in each 'n' represents a 2'-NMA sugar moiety, and each 'q' is independently selected from a 2'-O-(N,N-dimethyl) acetamide sugar moiety, a 2'-O-(N-ethyl) acetamide sugar moiety, a 2'-O-(N-propyl) acetamide sugar moiety, a 2'-O-(N-cyclopropyl) acetamide sugar moiety, and a 2'-O-(N-cyclopropylmethyl) acetamide sugar moiety.

13. The oligomeric compound of any of claims 1-9, wherein the modified oligonucleotide comprises at least one modified sugar moiety.

14. The oligomeric compound of claim 13, wherein the modified oligonucleotide comprises at least one bicyclic sugar moiety.

15. The oligomeric compound of claim 14, wherein the bicyclic sugar moiety has a 4'-2' bridge, wherein the 4'-2' bridge is selected from -CH₂-O-; and -CH(CH₃)-O-.

16. The oligomeric compound of claim 13, wherein the modified oligonucleotide comprises at least one non-bicyclic modified sugar moiety.

17. The oligomeric compound of claim 16, wherein the non-bicyclic modified sugar moiety is any of a 2'-MOE sugar moiety, a 2'-NMA sugar moiety, a 2'-OMe sugar moiety, or a 2'-F sugar moiety.

18. The oligomeric compound of claim 13, wherein the modified oligonucleotide comprises at least one sugar surrogate.

19. The oligomeric compound of claim 18, wherein the sugar surrogate is any of morpholino, modified morpholino, PNA, THP, and F-HNA.

20. The oligomeric compound of any of claims 1-6 and 10-16, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage.

21. The oligomeric compound of claim 20, wherein each internucleoside linkage of the modified oligonucleotide is a modified internucleoside linkage.

22. The oligomeric compound of claim 20 or claim 21, wherein the modified internucleoside linkage is a phosphorothioate internucleoside linkage.

23. The oligomeric compound of any of claims 1-20 or 22, wherein the modified oligonucleotide comprises at least one phosphodiester internucleoside linkage.

24. The oligomeric compound of any of claims 20, 22, or 23, wherein each internucleoside linkage is independently selected from a phosphodiester internucleoside linkage and a phosphorothioate internucleoside linkage.
25. The oligomeric compound of any of claims 10-16, wherein the modified oligonucleotide has an internucleoside linkage motif (5' to 3') selected from: sosososososososos, soososososososos, soososososososos, soososososososos, soososososososos, ssoosososososos, ssoosososososos, ssoosososososos, ssoosososososos, and ssoosososososos; wherein 's' represents a phosphorothioate internucleoside linkage and 'o' represents a phosphodiester internucleoside linkage.
26. The oligomeric compound of any of claims 1-25, wherein the modified oligonucleotide comprises a modified nucleobase.
27. The oligomeric compound of claim 26, wherein the modified nucleobase is a 5-methyl cytosine.
28. The oligomeric compound of any of claims 1-27, wherein the modified oligonucleotide consists of 16, 17, 18, 19, or 20 linked nucleosides.
29. The oligomeric compound of any of claims 1-28, wherein the modified oligonucleotide comprises 1 or 2 non-complementary nucleobases.
30. The oligomeric compound of any of claims 1-29, wherein the modified oligonucleotide comprises 1 or 2 cleavable moieties.
31. The oligomeric compound of claim 30, wherein the cleavable moiety is a phosphodiester internucleoside linkage.
32. The oligomeric compound of any of claims 1-31, consisting of the modified oligonucleotide.
33. The oligomeric compound of any of claims 1-32, wherein the oligomeric compound is a single-stranded oligomeric compound.
34. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: ${}^m\text{C}_{\text{es}} \text{A}_{\text{eo}} {}^m\text{C}_{\text{es}} \text{T}_{\text{eo}} \text{T}_{\text{es}} \text{T}_{\text{es}} {}^m\text{C}_{\text{es}} \text{A}_{\text{es}} \text{T}_{\text{es}} \text{A}_{\text{es}} \text{A}_{\text{es}} \text{T}_{\text{es}} \text{G}_{\text{es}} {}^m\text{C}_{\text{es}} \text{T}_{\text{es}} \text{G}_{\text{es}} \text{G}_{\text{es}} {}^m\text{C}_{\text{e}}$ (SEQ ID NO: 21), wherein:
A = an adenine nucleobase,
 ${}^m\text{C}$ = a 5-methyl cytosine nucleobase,
G = a guanine nucleobase,
T = a thymine nucleobase,
e = a 2'-MOE 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: $\text{T}_{\text{eo}} \text{T}_{\text{es}} {}^m\text{C}_{\text{es}} \text{A}_{\text{es}} {}^m\text{C}_{\text{es}} \text{T}_{\text{es}} \text{T}_{\text{es}} \text{T}_{\text{es}} {}^m\text{C}_{\text{es}} \text{A}_{\text{es}} \text{T}_{\text{es}} \text{A}_{\text{es}} \text{A}_{\text{es}} \text{T}_{\text{es}} \text{G}_{\text{es}} {}^m\text{C}_{\text{es}} \text{T}_{\text{es}} \text{G}_{\text{es}} \text{G}_{\text{eo}} {}^m\text{C}_{\text{e}}$ (SEQ ID NO: 22), wherein:
A = an adenine nucleobase,
 ${}^m\text{C}$ = a 5-methyl cytosine nucleobase,
G = a guanine nucleobase,
T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,
 s = a phosphorothioate internucleoside linkage, and
 o = a phosphodiester internucleoside linkage.

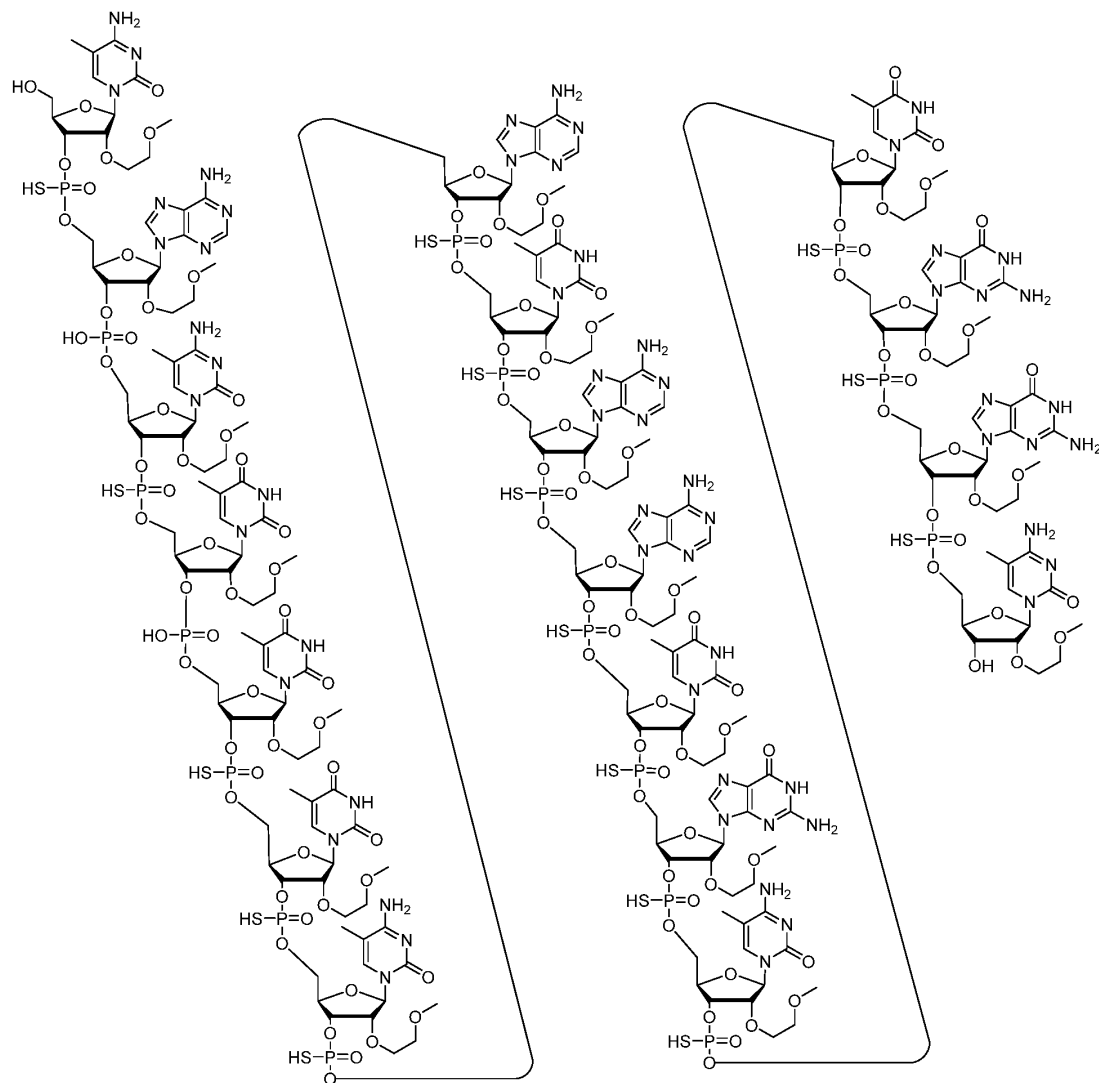
36. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $T_{eo} T_{ns} {}^mC_{ns} A_{ns} {}^mC_{ns} T_{ns} T_{ns} T_{ns} {}^mC_{ns} A_{ns} T_{ns} A_{ns} A_{ns} T_{ns} G_{ns} {}^mC_{ns} T_{ns} G_{ns} G_{no} {}^mC_e$ (SEQ ID NO: 22), wherein:

A = an adenine nucleobase,
 ${}^mC$ = a 5-methyl cytosine nucleobase,
 G = a guanine nucleobase,
 T = a thymine nucleobase,
 e = a 2'-MOE sugar moiety,
 n = a 2'-NMA sugar moiety,
 s = a phosphorothioate internucleoside linkage, and
 o = a phosphodiester internucleoside linkage.

37. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: ${}^mC_{ns} A_{no} {}^mC_{ns} T_{no} T_{ns} T_{ns} {}^mC_{ns} A_{ns} T_{ns} A_{ns} A_{ns} T_{ns} G_{ns} {}^mC_{ns} T_{ns} G_{ns} G_{ns} {}^mC_n$ (SEQ ID NO: 21), wherein:

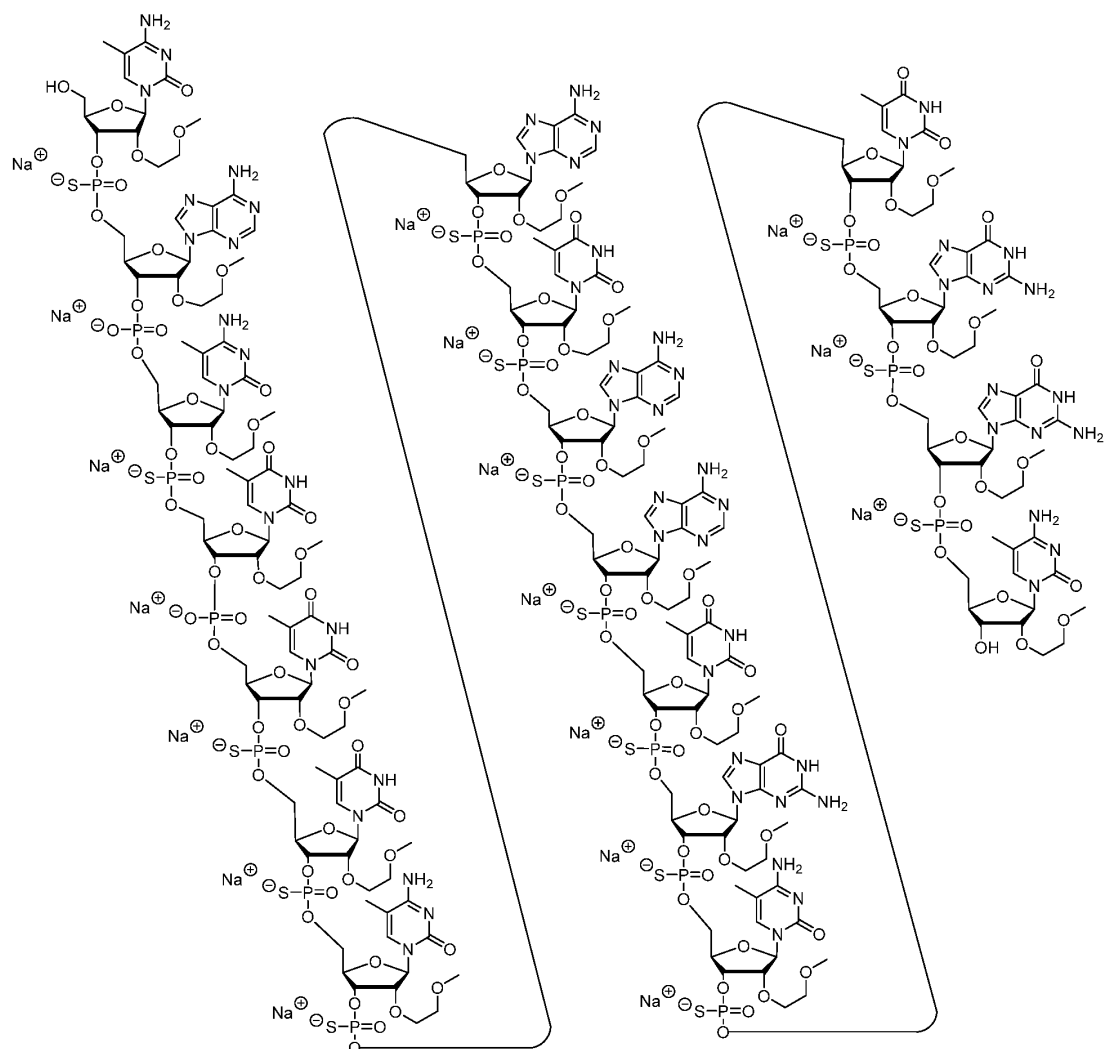
A = an adenine nucleobase,
 ${}^mC$ = a 5-methyl cytosine nucleobase,
 G = a guanine nucleobase,
 T = a thymine nucleobase,
 n = a 2'-NMA sugar moiety,
 s = a phosphorothioate internucleoside linkage, and
 o = a phosphodiester internucleoside linkage.

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



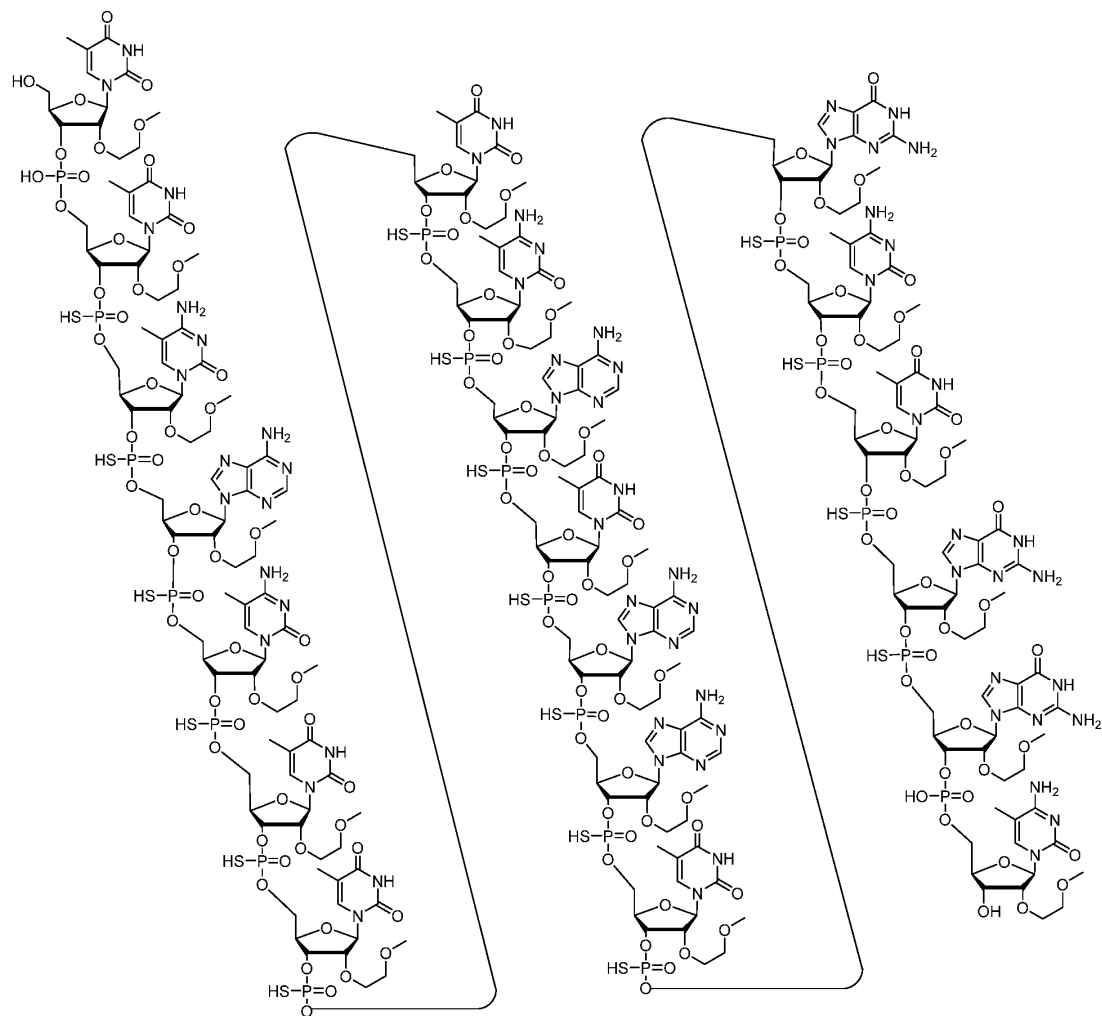
(SEQ ID NO: 21), or a salt thereof.

39. The modified oligonucleotide of claim 38, which is the sodium salt or the potassium salt.
40. A modified oligonucleotide according to the following chemical structure:



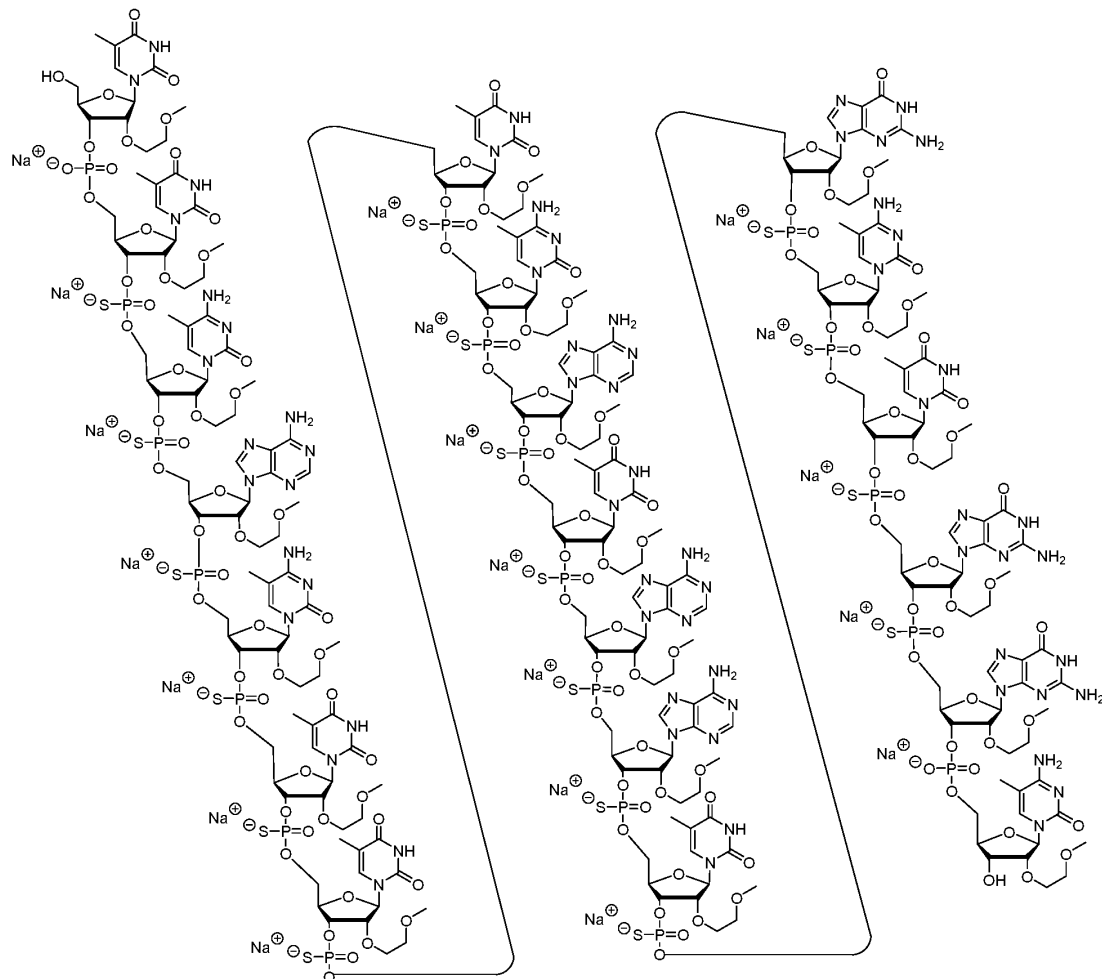
(SEQ ID NO: 21).

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



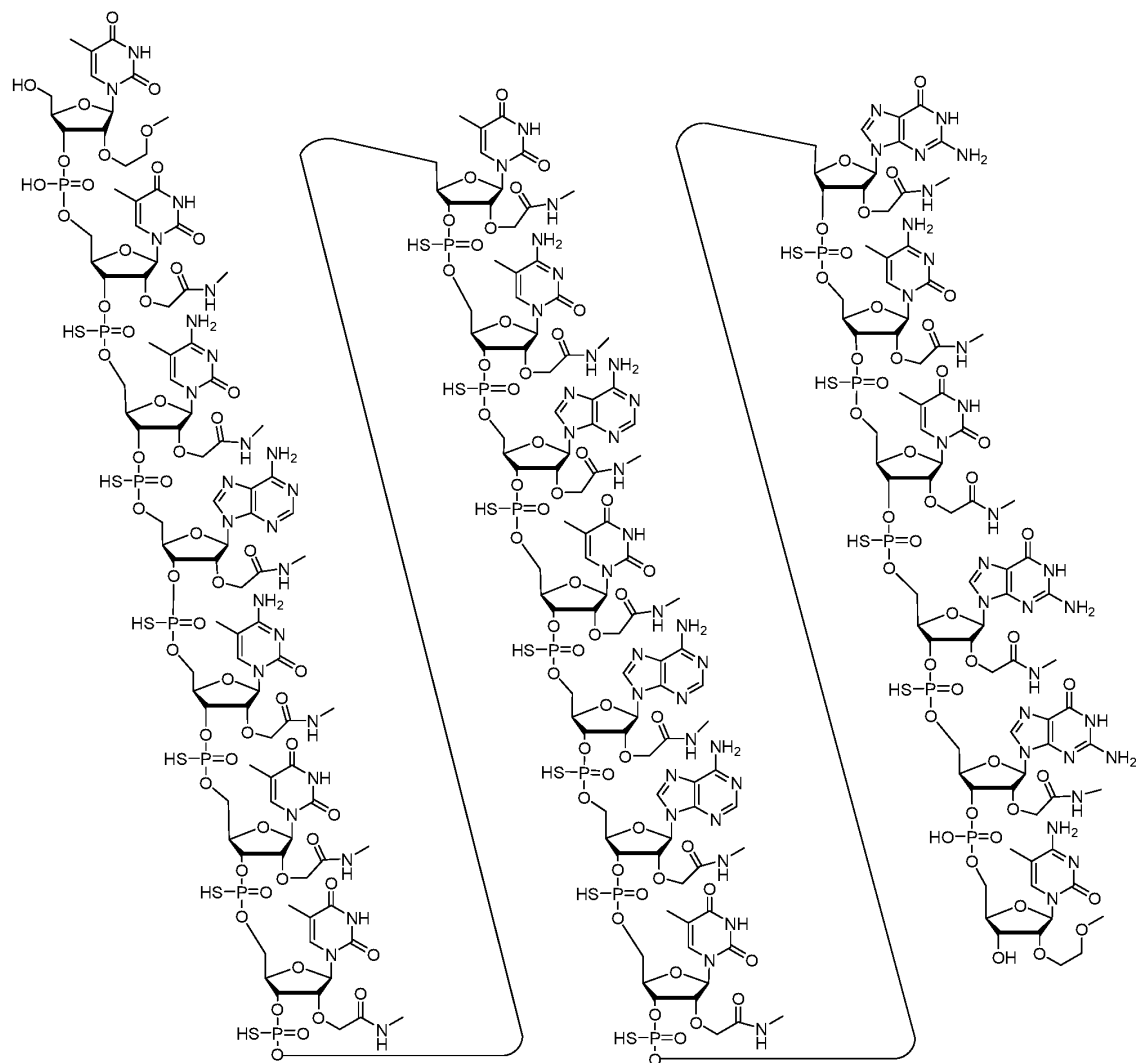
(SEQ ID NO: 22), or a salt thereof.

42. The modified oligonucleotide of claim 41, which is the sodium salt or the potassium salt.
43. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 22).

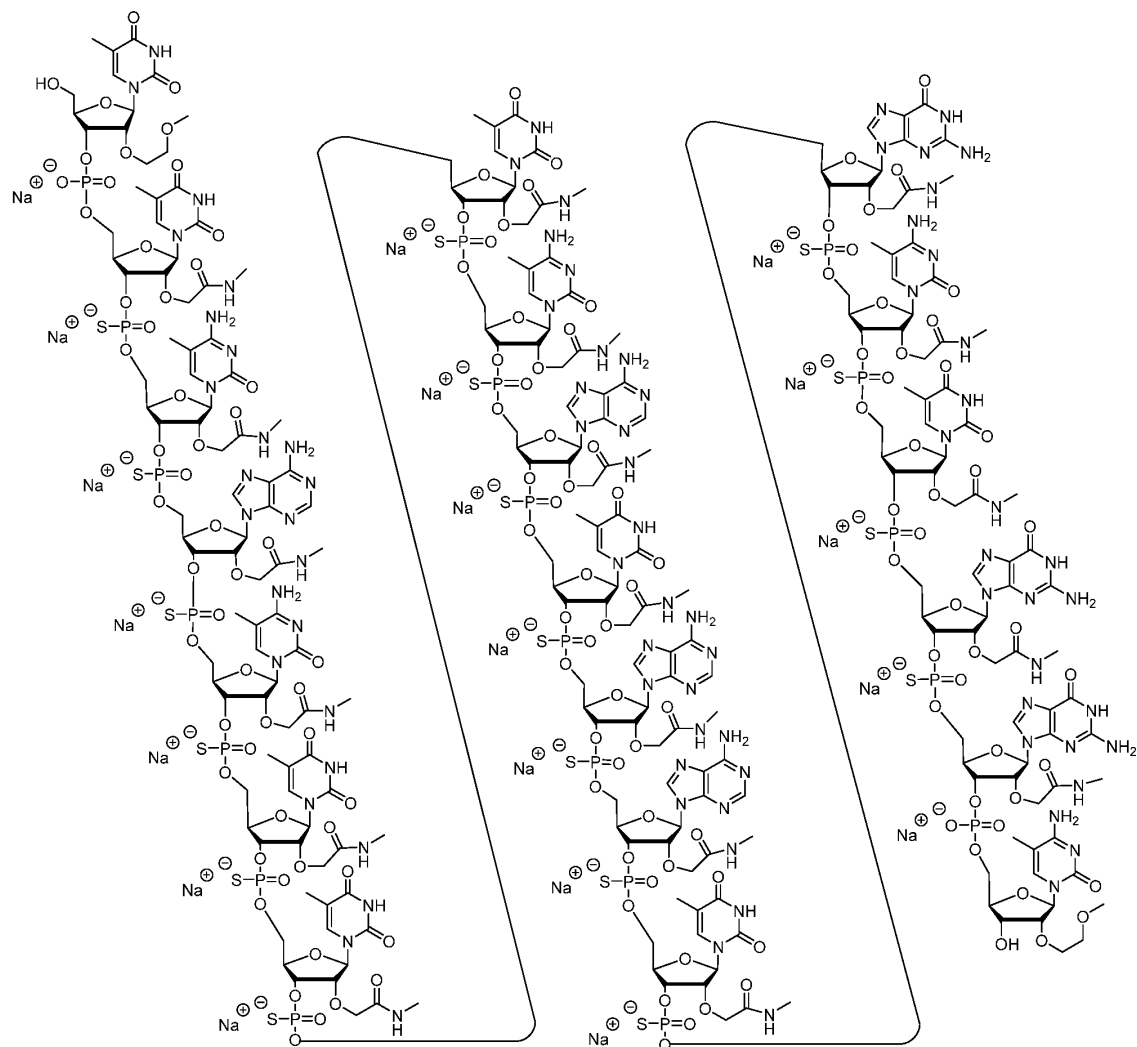
44. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 22), or a salt thereof.

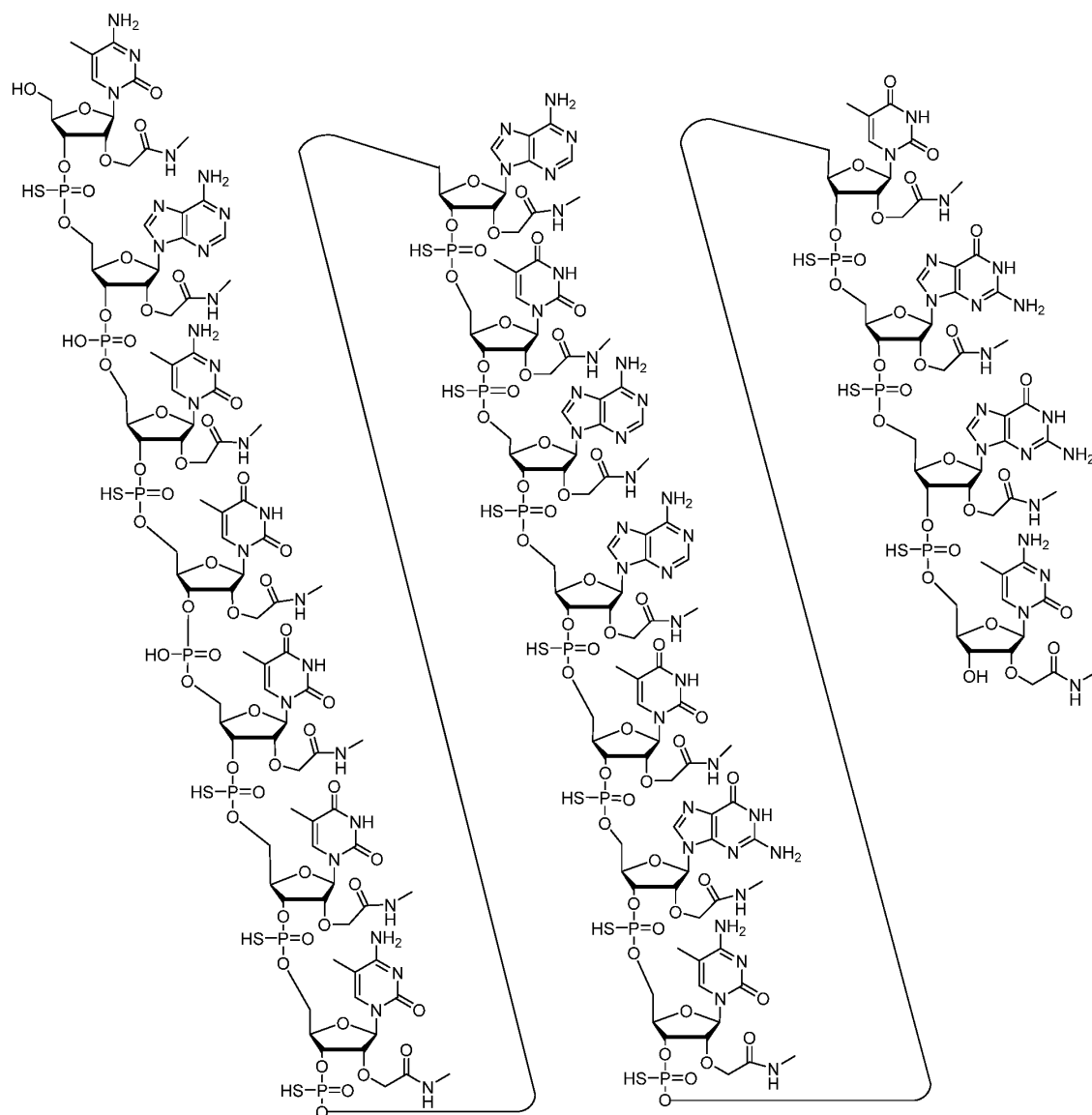
45. The modified oligonucleotide of claim 44, which is the sodium salt or the potassium salt.

46. A modified oligonucleotide corresponding to the following chemical structure:



(SEQ ID NO: 22).

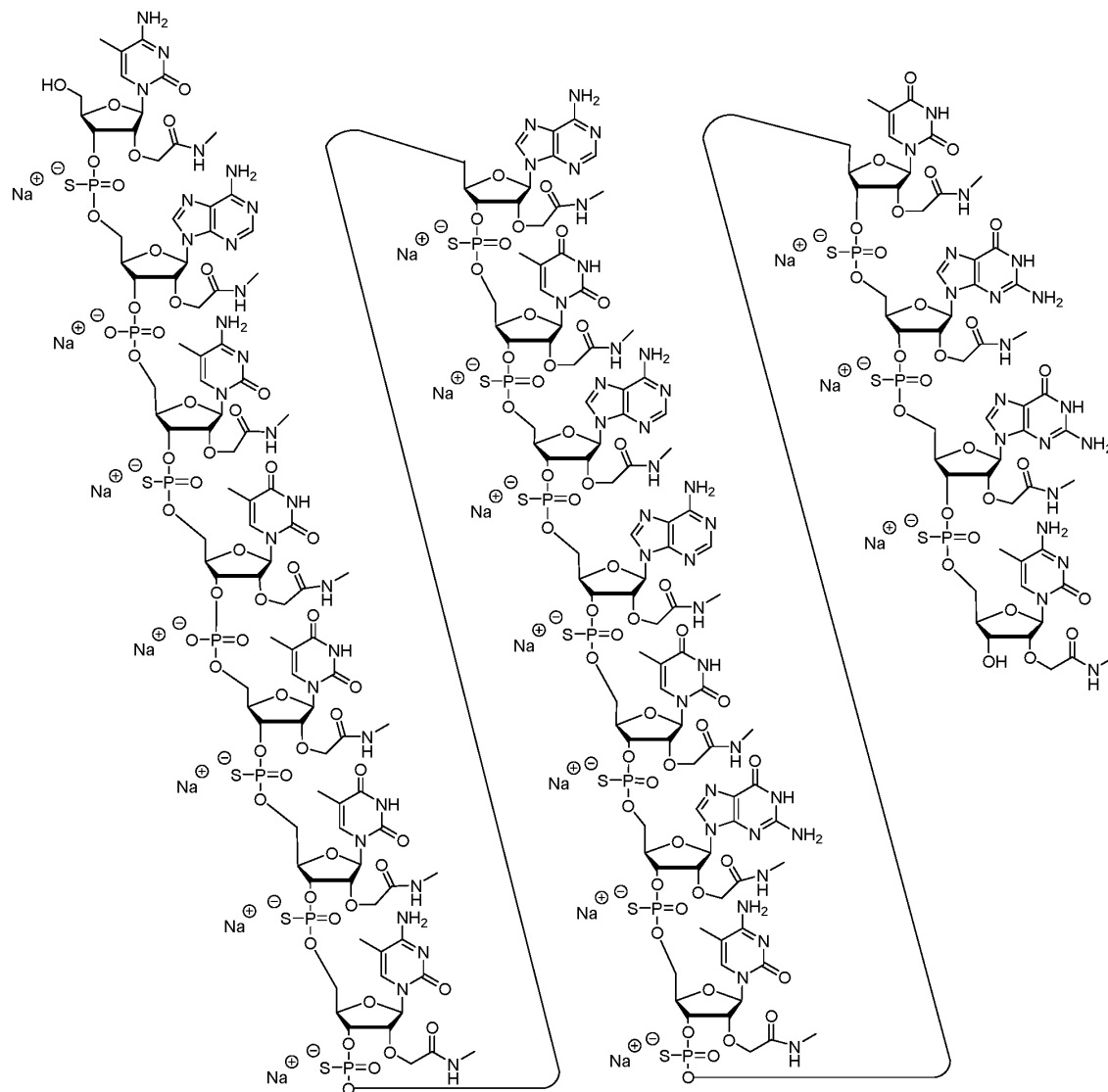
47. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 21), or a salt thereof.

48. The modified oligonucleotide of claim 47, which is the sodium salt or the potassium salt.

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



(SEQ ID NO: 21).

50. A pharmaceutical composition comprising the oligomeric compound of any of claims 1-37 or the modified oligonucleotide of any of claims 38-49, and a pharmaceutically acceptable diluent or carrier.

51. The pharmaceutical composition of claim 50, comprising a pharmaceutically acceptable diluent and wherein the pharmaceutically acceptable diluent is artificial CSF (aCSF) or PBS.

52. The pharmaceutical composition of claim 51, wherein the pharmaceutical composition consists essentially of the modified oligonucleotide and artificial CSF (aCSF).

53. The pharmaceutical composition of claim 52, wherein the pharmaceutical composition consists essentially of the modified oligonucleotide and PBS.
54. A chirally enriched population of modified oligonucleotides of any of claims 38-49, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having a particular stereochemical configuration.
55. The chirally enriched population of claim 54, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (*Sp*) configuration.
56. The chirally enriched population of claim 54, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (*Rp*) configuration.
57. The chirally enriched population of claim 54, wherein the population is enriched for modified oligonucleotides having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage.
58. The chirally enriched population of claim 57, wherein the population is enriched for modified oligonucleotides having the (*Sp*) configuration at each phosphorothioate internucleoside linkage or for modified oligonucleotides having the (*Rp*) configuration at each phosphorothioate internucleoside linkage.
59. The chirally enriched population of claim 57, 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.
60. The chirally enriched population of claim 57, 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.
61. A population of modified oligonucleotides of any of claims 38-49, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.
62. A method of treating a disease associated with SMN1 or SMN2 comprising administering to a subject having or at risk for developing a disease associated with SMN1 or SMN2 a therapeutically effective amount of a pharmaceutical composition according to any of claims 50-53; and thereby treating the disease associated with SMN1 or SMN2.
63. The method of claim 62, wherein the disease associated with SMN1 or SMN2 is a neurodegenerative disease.
64. The method of claim 63, wherein the neurodegenerative disease is Spinal Muscular Atrophy (SMA).
65. The method of claim 64, wherein the SMA is any of Type I SMA, Type II SMA, Type III SMA, or Type IV SMA.
66. The method of claim 64 or claim 65, wherein at least one symptom of SMA is ameliorated.
67. The method of claim 66, wherein the symptom is any of reduced muscle strength; inability or reduced ability to sit upright, to stand, and/or walk; reduced neuromuscular activity; reduced electrical activity in one or more muscles;

reduced respiration; inability or reduced ability to eat, drink, and/or breathe without assistance; loss of weight or reduced weight gain; and/or decreased survival.

68. The method of any of claims 62-67, wherein the pharmaceutical composition is administered to the central nervous system or systemically.

69. The method of claim 68, wherein the pharmaceutical composition is administered to the central nervous system and systemically.

70. The method of any of claim 62-67, wherein the pharmaceutical composition is administered any of intrathecally, systemically, subcutaneously, or intramuscularly.

71. A method of increasing SMN2 RNA including exon 7 comprising contacting a cell, tissue, or organ with an oligomeric compound of any of claims 1-37, a modified oligonucleotide of any of claims 38-49, or a pharmaceutical composition of any of claims 50-53.