

CLAIMS:

1. An oligomeric compound comprising a modified oligonucleotide consisting of 8 to 80 linked nucleosides, wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to an equal length portion of a PLN nucleic acid, and wherein the modified oligonucleotide has at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.

2. The oligomeric compound of claim 1, wherein the PLN nucleic acid has the nucleobase sequence of SEQ ID NOs: 1 or 2.

3. The oligomeric compound of claim 1 or 2, wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to an equal length portion within nucleobases 3278-3293, 3281-3296, 3282-3297, 3284-3299, 3286-3301, 3287-3302, 3288-3303, 3327-3342, 3329-3344, 3332-3347, 3333-3348, 3336-3351, 3337-3352, 3338-3353, 3339-3354, 3340-3355, 3341-3356, 3343-3358, 3345-3360, 3348-3363, 3349-3364, 3350-3365, 3351-3366, 3352-3367, 3353-3368, 3354-3369, 3355-3370, 3356-3371, 3357-3372, 3358-3373, 3395-3410, 3396-3411, 3405-3420, 3406-3421, 3408-3423, 3409-3424, 3410-3425, 3412-3427, 3496-3511, 3497-3512, 3498-3513, 3499-3514, 3598-3613, 3612-3627, 3614-3629, 3615-3630, 3616-3631, 3617-3632, 3618-3633, 3619-3634, 3620-3635, 3622-3637, 3703-3718, 3704-3719, 3715-3730, 3716-3731, 3723-3738, 3724-3739, 3799-3814, 3801-3816, 3802-3817, 3803-3818, 3804-3819, 3805-3820, 3806-3821, 3807-3822, 3808-3823, 3809-3824, 3811-3826, 3814-3829, 3815-3830, 3816-3831, 3817-3832, 3821-3836, 3823-3838, 3830-3845, 3831-3846, 3848-3863, 3849-3864, 3850-3865, 3851-3866, 3861-3876, 3863-3878, 3864-3879, 3869-3884, 3871-3886, 3976-3991, 3977-3992, 3978-3993, 3980-3995, 3981-3996, 4116-4131, 4159-4174, 4204-4219, 4207-4222, 4208-4223, 4209-4224, 4210-4225, 4211-4226, 4212-4227, 4214-4229, 4221-4236, 4231-4246, 4232-4247, 4233-4248, 4234-4249, 4235-4250, 4236-4251, 4238-4253, 4252-4267, 4253-4268, 4266-4281, 4348-4363, 4349-4364, 4350-4365, 4367-4382, 4373-4388, 4374-4389, 4375-4390, 4510-4525, 4511-4526, 4513-4528, 4515-4530, 4516-4531, 4517-4532, 4518-4533, 4519-4534, 4530-4545, 4537-4552, 4539-4554, 4540-4555, 4541-4556, 4542-4557, 4543-4558, 4544-4559, 4545-4560, 4562-4577, 4614-4629, 4617-4632, 4619-4634, 4620-4635, 4621-4636, 4622-4637, 4623-4638, 4624-4639, 4638-4653, 4640-4655, 4641-4656, 4642-4657, 4643-4658, 4665-4680, 4672-4687, 4693-4708, 4694-4709, 4695-4710, 4696-4711, 4697-4712, 4750-4765, 4751-4766, 4752-4767, 4753-4768, 4774-4789, 4802-4817, 4804-4819, 4805-4820, 4806-4821, 4807-4822, 4823-4838, 4825-4840, 4826-4841, 4828-4843, 4860-4875, 4862-4877, 4869-4884, 4872-4887, 4874-4889, 4878-4893, 4881-4896, 4883-4898, 4884-4899, 4942-4957, 4943-4958, 4945-4960, 4946-4961, 4957-4972, 4958-4973, 4960-4975, 4961-4976, 4964-4979, 4965-4980, 4966-4981, 4968-4983, 4969-4984, 4971-4986, 4972-4987, 4974-4989, 4984-4999, 4985-5000, 4987-5002, 4988-5003, 5024-5039, 5127-5142, 5133-5148, 5134-5149, 5158-5173, 5159-5174, 5160-5175, 5163-5178, 5294-5309, 5341-5356, 5359-5374, 5394-5409, 5399-5414, 5400-5415, 5401-5416, 5402-5417, 5404-5419, 5411-5426, 5413-5428, 5414-5429, 5415-5430, 5416-5431, 5417-5432, 5418-5433, 5419-5434, 5421-5436, 5427-5442, 5428-5443, 5489-5504, 5494-5509, 5495-5510, 5497-5512, 5498-5513, 5498-5515, 5498-5517, 5499-5514, 5499-5515, 5499-5516, 5499-5518, 5500-5515, 5500-5516, 5500-5517, 5501-5516, 5501-5514, 5501-5517, 5502-5517, 5502-5515, 5503-5518, 5504-5519, 5505-5520, 5506-5521, 5511-5526, 5532-5547, 5533-5548, 5534-5549, 5547-5562, 5557-5572, 5558-5573, 5559-5574, 5560-5575, 5562-5577, 5563-5578, 5565-5580, 5599-5614, 5673-5688, 5674-5689, 5675-5690, 5676-5691, 5677-5692, 5678-5693, 5679-5694, 5694-5709, 5695-5710, 5696-5711, 5697-5712, 5698-5713, 5774-5789, 5827-5842, 5845-5860, 5847-5862, 5848-5863, 5850-5865, 5851-5866, 5855-5870, 5859-5874, 5924-5939, 5925-5940, 5926-5941, 5927-5942, 5929-5944, 5930-5945, 5931-5946,

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4. The oligomeric compound of any of claims 1-3, wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to an equal length portion within nucleobases 3341-3368, 4516-4533, 5498-5517, 14337-14357, 14569-14588, 14607-14631, 14683-14703, 14828-14848, 14939-14958, 15222-15243, or 15251-15273 of SEQ ID NO: 2.

5. The oligomeric compound of any of claims 1-4, wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to an equal length portion within nucleobases 5499-5514, 5500-5515, 5501-5516, 14686-14701, 14941-14956, 14942-14957, or 15224-15239 of SEQ ID NO: 2.

6. The oligomeric compound of any of claims 1-5, wherein the nucleobase sequence of the modified oligonucleotide is at least 85%, at least 90%, at least 95%, or 100% complementary to an equal length portion of the PLN nucleic acid.

7. An oligomeric compound, wherein the oligomeric compound comprises a modified oligonucleotide consisting of 8 to 80 linked nucleosides, wherein the nucleobase sequence of the modified oligonucleotide comprises 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 of any of the nucleobase sequences of any of SEQ ID NOs: 15-1712.

8. The oligomeric compound of claim 7, wherein the nucleobase sequence of the modified oligonucleotide comprises the nucleobase sequence of any of SEQ ID NOs: 15-1712.

9. The oligomeric compound of claim 8, wherein the modified oligonucleotide has a nucleobase sequence consisting of the nucleobase sequence of any of SEQ ID NOs: 15-1712.

10. The oligomeric compound of any of claims 7-9, wherein the modified oligonucleotide has 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, or at least 16 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 45, 120, 185, 609, 675, 737, or 752.

11. The oligomeric compound of claim 10, wherein the modified oligonucleotide consists of 16 to 80 linked nucleoside, wherein the nucleobase sequence of the modified oligonucleotide comprises the nucleobase sequence of any of SEQ ID NOs: 45, 120, 185, 609, 675, 737, or 752.

12. The oligomeric compound of claim 11, wherein the modified oligonucleotide consists of 16 linked nucleosides and has a nucleobase sequence consisting of the nucleobase sequence of any one of SEQ ID NOs: 45, 120, 185, 609, 675, 737, or 752.

13. The oligomeric compound of any of claims 7-11, wherein the nucleobase sequence of the modified oligonucleotide is at least 85%, at least 90%, at least 95%, or 100% complementary to an equal length portion of a PLN nucleic acid, wherein the PLN nucleic acid has the nucleobase sequence of SEQ ID NOs: 1 or 2.

14. The oligomeric compound of any of claims 1-13, wherein the modified oligonucleotide consists of 10 to 25, 10 to 30, 10 to 50, 12 to 20, 12 to 25, 12 to 30, 12 to 50, 13 to 20, 13 to 25, 13 to 30, 13 to 50, 14 to 20, 14 to 25, 14 to 30, 14 to 50, 15 to 20, 15 to 25, 15 to 30, 15 to 50, 16 to 18, 16 to 20, 16 to 25, 16 to 30, 16 to 50, 17 to 20, 17 to 25, 17 to 30, 17 to 50, 18 to 20, 18 to 25, 18 to 30, 18 to 50, 19 to 20, 19 to 25, 19 to 30, 19 to 50, 20 to 25, 20 to 30, 20 to 50, 21 to 25, 21 to 30, 21 to 50, 22 to 25, 22 to 30, 22 to 50, 23 to 25, 23 to 30, or 23 to 50 linked nucleosides.

15. The oligomeric compound of any of claims 1-14, wherein at least one nucleoside of the modified oligonucleotide comprises a modified sugar moiety.

16. The oligomeric compound of claim 15, wherein the modified sugar moiety comprises a bicyclic sugar moiety.

17. The oligomeric compound of claim 16, wherein the bicyclic sugar moiety comprises a 2'-4' bridge selected from -O-CH₂-; and -O-CH(CH₃)-.

18. The oligomeric compound of claim 15, wherein the modified sugar moiety comprises a non-bicyclic modified sugar moiety.

19. The oligomeric compound of claim 18, wherein the non-bicyclic modified sugar moiety is a 2'-MOE sugar moiety or 2'-OMe sugar moiety.

20. The oligomeric compound of any of claims 1-19, wherein at least one nucleoside of the modified oligonucleotide compound comprises a sugar surrogate.

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

22. The oligomeric compound of claim 21, wherein at least one modified internucleoside linkage is a phosphorothioate internucleoside linkage.

23. The oligomeric compound of claim 22, wherein each internucleoside linkage is a modified internucleoside linkage.

24. The oligomeric compound of claim 23, wherein the modified internucleoside linkage is a phosphorothioate internucleoside linkage.

25. The oligomeric compound of claim 23, wherein at least one modified internucleoside linkage of the second modified oligonucleotide is a mesyl phosphoramidate internucleoside linkage.

26. The oligomeric compound of any of claims 1-20, wherein each internucleoside linkage of the modified oligonucleotide is independently selected from a phosphodiester internucleoside linkage, a phosphorothioate internucleoside linkage, and a mesyl phosphoramidate internucleoside linkage.

27. The oligomeric compound of any of claims 1-26, wherein the modified oligonucleotide comprises at least one modified nucleobase.

28. The oligomeric compound of claim 27, wherein the modified nucleobase is 5-methylcytosine.

29. The oligomeric compound of claim 28, wherein each cytosine is a 5-methylcytosine.

30. The oligomeric compound of any of claims 1-29, wherein the modified oligonucleotide comprises a deoxy region consisting of 5-12 contiguous 2'-deoxynucleosides.

31. The oligomeric compound of claim 30, wherein each nucleoside of the deoxy region is a 2'-β-D-deoxynucleoside.

32. The oligomeric compound of claim 30 or 31, wherein the deoxy region consists of 6, 7, 8, 9, 10, or 6-10 linked nucleosides.

33. The oligomeric compound of any of claims 30-32, wherein each nucleoside immediately adjacent to the deoxy region comprises a modified sugar moiety.

34. The oligomeric compound of any of claims 30-33, 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

the 3'-most nucleoside of the 5' external region comprises a modified sugar moiety; and

the 5'-most nucleoside of the 3' external region comprises a modified sugar moiety.

35. The oligomeric compound of claim 34, wherein each nucleoside of the 3' external region comprises a modified sugar moiety.

36. The oligomeric compound of claim 34 or 35, wherein each nucleoside of the 5' external region comprises a modified sugar moiety.

37. The oligomeric compound of claim 36, wherein the modified oligonucleotide has:

a 5' external region consisting of 1-6 linked nucleosides;
a deoxy region consisting of 6-10 linked nucleosides; and
a 3' external region consisting of 1-6 linked nucleosides;

wherein each of the 5' external region nucleosides and each of the 3' external region nucleosides is a cEt nucleoside or a 2'-MOE nucleoside; and each of the deoxy region nucleosides is a 2'-β-D-deoxynucleoside.

38. The oligomeric compound of claim 36, wherein the modified oligonucleotide has a sugar motif comprising:

a 5' external region consisting of 3-6 linked nucleosides;
a deoxy region consisting of 7-8 linked nucleosides; and
a 3' external region consisting of 3-6 linked nucleosides; wherein

each of the 3' external region nucleosides is selected from a 2'-MOE nucleoside and a cEt nucleoside, and the 5' external region has the following formula:

(Nk)_n(Nd)(Nx)

wherein each Nk is a bicyclic nucleoside, Nx 2'-OMe nucleoside and Nd is a 2'-β-D-deoxynucleoside;

and n is from 1-4.

39. An oligomeric compound of any of claims 1-29, wherein the modified oligonucleotide has a sugar motif (5' to 3') selected from: kkkddddd kkk, kkkddddd kekek, kkkddddd kkkke, kkkdyddd kkk, kkkddddd kkk, kkkddddd keee, kkkddddd dkkee, kkkddddd kkkk, kkkkddddd kkk, kkkddddd keeee, kkkddddd kkeee, kkkkddddd kkkk, kkkkddddd kkkk, ekddddd kekek, ekddddd kkk, ekddddd kkkke, kedddd kekek, kedddd kkk, kekddddd kkkke, kedddd kkk, and kkedddd kkkke, wherein each "d" represents a 2'-β-D-deoxyribosyl sugar moiety, each "y" represents a 2'-OMe sugar moiety, each "e" represents a 2'-MOE sugar moiety, and each "k" represents a cEt modified sugar moiety.

40. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: ^mC_{ks}^mC_{ks}A_{ks}T_{ds}A_{ds}^mC_{ds}T_{ds}T_{ds}G_{ds}A_{ds}T_{ds}T_{ds}^mC_{ds}T_{ks}^mC_{ks}A_k (SEQ ID NO: 185), wherein:

A = an adenine nucleobase,

^mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

k = a cEt modified sugar moiety,

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

s = a phosphorothioate internucleoside linkage.

41. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: G_{ks}T_{ks}A_{ks}G_{ds}T_{ds}T_{ds}A_{ds}A_{ds}G_{ds}A_{ds}T_{ds}T_{ds}T_{ds}T_{ks}G_{ks}^mC_k (SEQ ID NO: 752), wherein:

A = an adenine nucleobase,

^mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,
 T = a thymine nucleobase,
 k = a cEt modified sugar moiety,
 d = a 2'-β-D-deoxyribosyl sugar moiety, and
 s = a phosphorothioate internucleoside linkage.

42. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $A_{ks}^m C_{ks} A_{ks}^m C_{ds} G_{ds} A_{ds} G_{ds} T_{ds} A_{ds} T_{ds} A_{ds} T_{ds} T_{ds} A_{ks} G_{ks} G_{ks}$ (SEQ ID NO: 609), wherein:

A = an adenine nucleobase,
 ^mC = a 5-methyl cytosine nucleobase,
 G = a guanine nucleobase,
 T = a thymine nucleobase,
 k = a cEt modified sugar moiety,
 d = a 2'-β-D-deoxyribosyl sugar moiety, and
 s = a phosphorothioate internucleoside linkage.

43. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $A_{ks} A_{ks} G_{ds} A_{ds} T_{ds} A_{ds} T_{ds} A_{ds} G_{ds} T_{ds} A_{ds} T_{ks} G_{es} G_{ks} T_{es} A_k$ (SEQ ID NO: 45), wherein:

A = an adenine nucleobase,
 G = a guanine nucleobase,
 T = a thymine nucleobase,
 e = a 2'-MOE sugar moiety,
 k = a cEt modified sugar moiety
 d = a 2'-β-D-deoxyribosyl sugar moiety, and
 s = a phosphorothioate internucleoside linkage.

44. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $A_{ks}^m C_{ks} G_{ds} A_{ds} G_{ds} T_{ds} A_{ds} T_{ds} A_{ds} T_{ds} T_{ds} A_{ks} G_{es} G_{ks} A_{es} A_k$ (SEQ ID NO: 737), 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,
 k = a cEt modified sugar moiety
 d = a 2'-β-D-deoxyribosyl sugar moiety, and
 s = a phosphorothioate internucleoside linkage.

45. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: A_{ks}A_{ks}A_{ds}G_{ds}A_{ds}T_{ds}A_{ds}T_{ds}A_{ds}G_{ds}T_{ds}A_{ks}T_{es}G_{ks}G_{es}T_k (SEQ ID NO: 120), wherein:

A = an adenine nucleobase,
G = a guanine nucleobase,
T = a thymine nucleobase,
e = a 2'-MOE sugar moiety,
k = a cEt modified sugar moiety
d = a 2'-β-D-deoxyribosyl sugar moiety, and
s = a phosphorothioate internucleoside linkage.

46. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: ^mC_{ks}A_{ks}^mC_{ks}G_{ds}A_{ds}G_{ds}T_{ds}A_{ds}T_{ds}A_{ds}T_{ds}A_{ks}G_{ks}G_{ks}A_e (SEQ ID NO: 675), 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,
k = a cEt modified sugar moiety
d = a 2'-β-D-deoxyribosyl sugar moiety, and
s = a phosphorothioate internucleoside linkage.

47. The oligomeric compound of any of claims 1-46, wherein the oligomeric compound comprises a conjugate group.

48. The oligomeric compound of claim 47, wherein the conjugate group comprises a conjugate linker and a conjugate moiety.

49. The oligomeric compound of claim 47 or 48, wherein the conjugate linker consists of a single bond.

50. The oligomeric compound of any of claims 47-49, wherein the conjugate linker is cleavable.

51. The oligomeric compound of any of claims 47-50, wherein the conjugate linker comprises 1-3 linker-nucleosides.

52. The oligomeric compound of any of claims 47-50, wherein the conjugate linker does not comprise any linker nucleosides.

53. The oligomeric compound of any of claims 47-52, wherein the conjugate group is attached to the modified oligonucleotide at the 5'-end of the modified oligonucleotide.

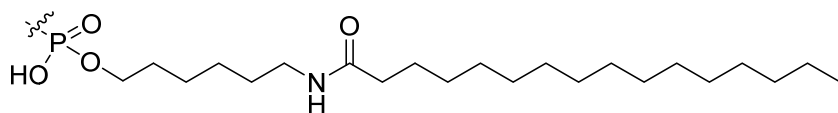
54. The oligomeric compound of any of claims 47-52, wherein the conjugate group is attached to the modified oligonucleotide at the 3'-end of the modified oligonucleotide.

55. The oligomeric compound of any of claims 47-54, wherein the conjugate group comprises a C22 alkyl, C20 alkyl, C16 alkyl, C10 alkyl, C21 alkyl, C19 alkyl, C18 alkyl, C15 alkyl, C14 alkyl, C13 alkyl, C12 alkyl, C11 alkyl, C9 alkyl, C8 alkyl, C7 alkyl, C6 alkyl, C5 alkyl, C22 alkenyl, C20 alkenyl, C16 alkenyl, C10 alkenyl, C21

alkenyl, C19 alkenyl, C18 alkenyl, C15 alkenyl, C14 alkenyl, C13 alkenyl, C12 alkenyl, C11 alkenyl, C9 alkenyl, C8 alkenyl, C7 alkenyl, C6 alkenyl, or C5 alkenyl.

56. The oligomeric compound of any of claims 47-55, wherein the conjugate moiety is a 6-palmitamidohexyl conjugate moiety.

57. The oligomeric compound of any of claims 47-54, wherein the conjugate group has the following structure:



58. The oligomeric compound of any of claims 47-57, wherein the conjugate group comprises a cell-targeting moiety.

59. The oligomeric compound of claim 58, wherein the cell-targeting moiety has an affinity for TfR1.

60. The oligomeric compound of claim 59, wherein the cell-targeting moiety comprises an anti-TfR1 antibody or fragment thereof.

61. The oligomeric compound of claim 59, wherein the cell-targeting moiety comprises a protein or peptide capable of binding TfR1.

62. The oligomeric compound of claim 59, wherein the cell-targeting moiety comprises an aptamer capable of binding TfR1.

63. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: [C16-HA]_oA_{ks}A_{ks}G_{ds}A_{ds}T_{ds}A_{ds}T_{ds}A_{ds}G_{ds}T_{ds}A_{ds}T_{ks}G_{es}G_{ks}T_{es}A_k (SEQ ID NO: 45), wherein:

A = an adenine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

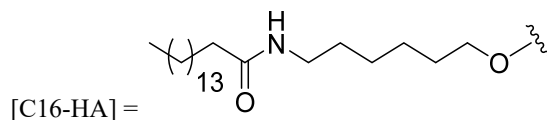
e = a 2'-MOE sugar moiety,

k = a cEt modified sugar moiety

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

o = a phosphodiester linkage,

s = a phosphorothioate internucleoside linkage, and



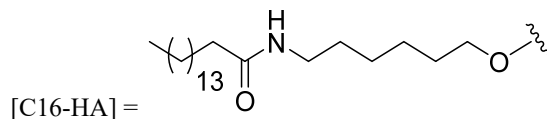
64. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: [C16-HA]_oA_{ks}^mC_{ks}A_{ks}^mC_{ds}G_{ds}A_{ds}G_{ds}T_{ds}A_{ds}T_{ds}A_{ds}T_{ds}A_{ks}G_{ks}G_k (SEQ ID NO: 609), wherein:

A = an adenine nucleobase,

^mC = a 5-methyl cytosine nucleobase,

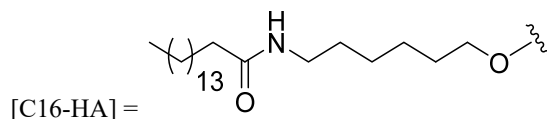
G = a guanine nucleobase,

T = a thymine nucleobase,
 k = a cEt modified sugar moiety
 d = a 2'-β-D-deoxyribosyl sugar moiety,
 o = a phosphodiester linkage,
 s = a phosphorothioate internucleoside linkage, and



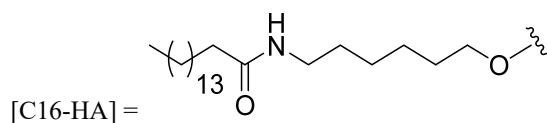
65. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: [C16-HA]_oG_{ks}T_{ks}A_{ks}G_{ds}T_{ds}T_{ds}A_{ds}A_{ds}G_{ds}A_{ds}T_{ds}T_{ds}T_{ds}T_{ks}G_{ks}^mC_k (SEQ ID NO: 752), wherein:

A = an adenine nucleobase,
^mC = a 5-methyl cytosine nucleobase,
 G = a guanine nucleobase,
 T = a thymine nucleobase,
 k = a cEt modified sugar moiety
 d = a 2'-β-D-deoxyribosyl sugar moiety,
 o = a phosphodiester linkage,
 s = a phosphorothioate internucleoside linkage, and

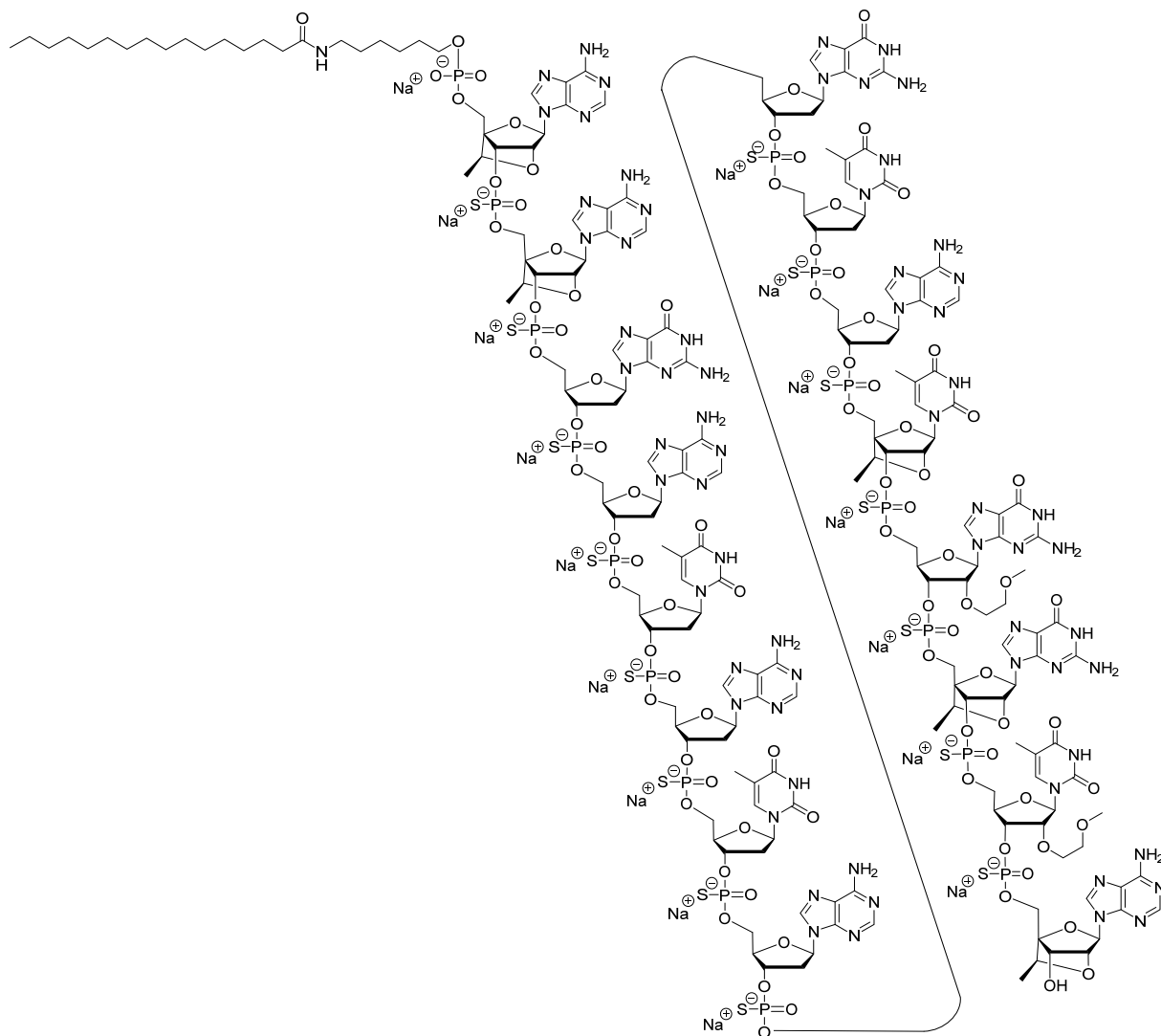


66. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: [C16-HA]_oA_{ks}A_{ks}A_{ds}G_{ds}A_{ds}T_{ds}A_{ds}T_{ds}A_{ds}G_{ds}T_{ds}A_{ks}T_{es}G_{ks}G_{es}T_k (SEQ ID NO: 120), wherein:

A = an adenine nucleobase,
 G = a guanine nucleobase,
 T = a thymine nucleobase,
 e = a 2'-MOE sugar moiety,
 k = a cEt modified sugar moiety
 d = a 2'-β-D-deoxyribosyl sugar moiety,
 o = a phosphodiester linkage,
 s = a phosphorothioate internucleoside linkage, and

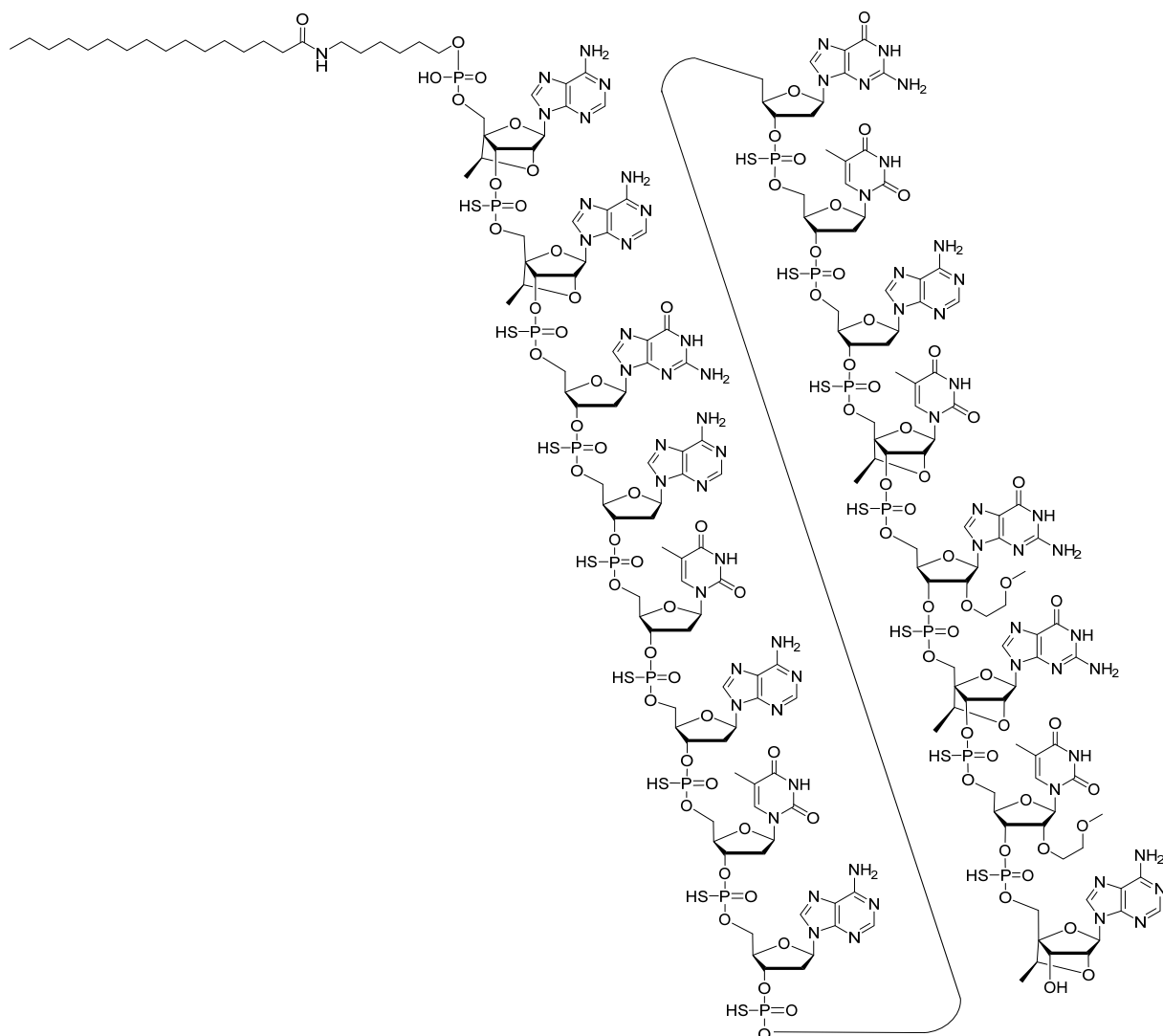


67. The oligomeric compound of any of claims 1 to 66, wherein the oligomeric compound comprises a terminal group.
68. The oligomeric compound of claim 67, wherein the terminal group is an abasic sugar moiety.
69. An oligomeric compound according to the following chemical structure:



(SEQ ID NO: 45).

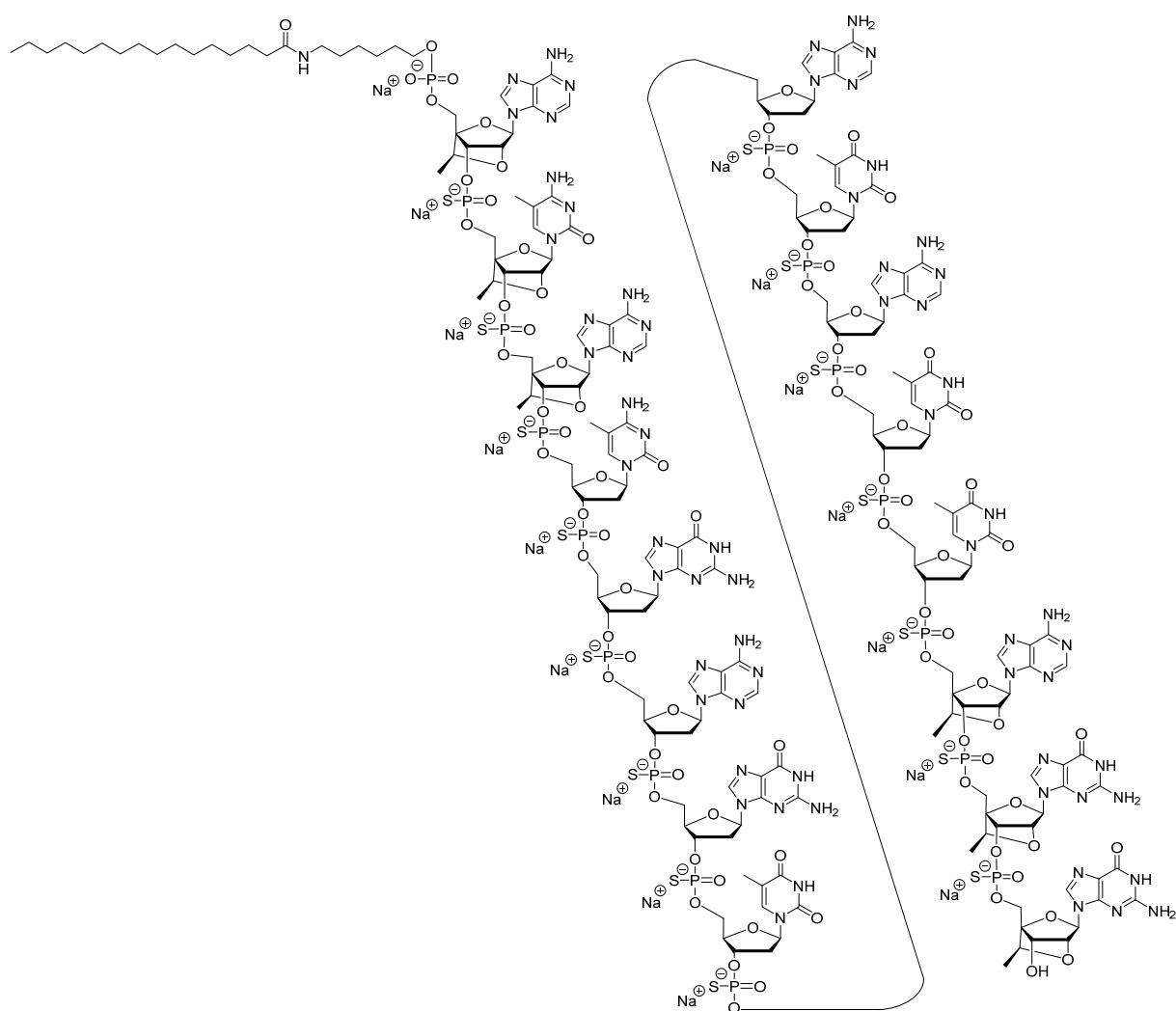
70. An oligomeric compound according to the following chemical structure:



(SEQ ID NO: 45), or a salt thereof.

71. The oligomeric compound of claim 70, which is the sodium salt or potassium salt.

72. An oligomeric compound according to the following chemical structure:

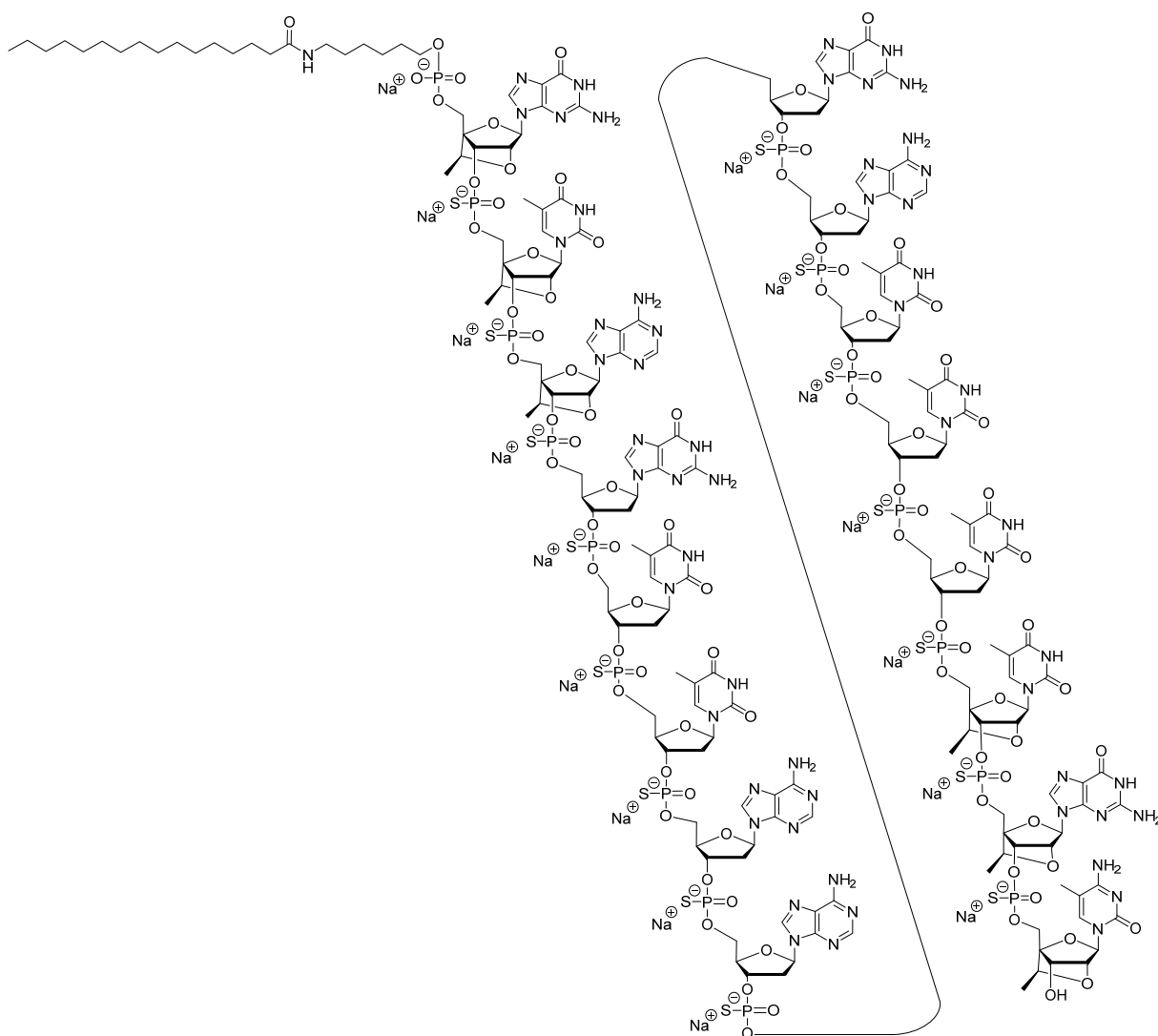


(SEQ ID NO: 609).

The image displays a complex chemical structure of a long-chain polyphosphate derivative. The structure features a long, straight alkyl chain at the top left, which is connected to a series of phosphate groups. These phosphate groups are linked to a chain of nucleoside units. Each nucleoside unit consists of a sugar ring (likely ribose or deoxyribose) attached to a nitrogenous base (adenine, guanine, or cytosine). The phosphate groups are shown as HO-P=O and HS-P=O groups, indicating the presence of hydroxyl and thiol groups. The structure is highly branched and complex, with multiple phosphate groups and nucleoside units connected in a chain-like fashion. A large, curved line is drawn across the middle of the structure, possibly indicating a break or a specific conformational change. The overall structure is highly detailed, showing the connectivity of atoms and the presence of various functional groups.

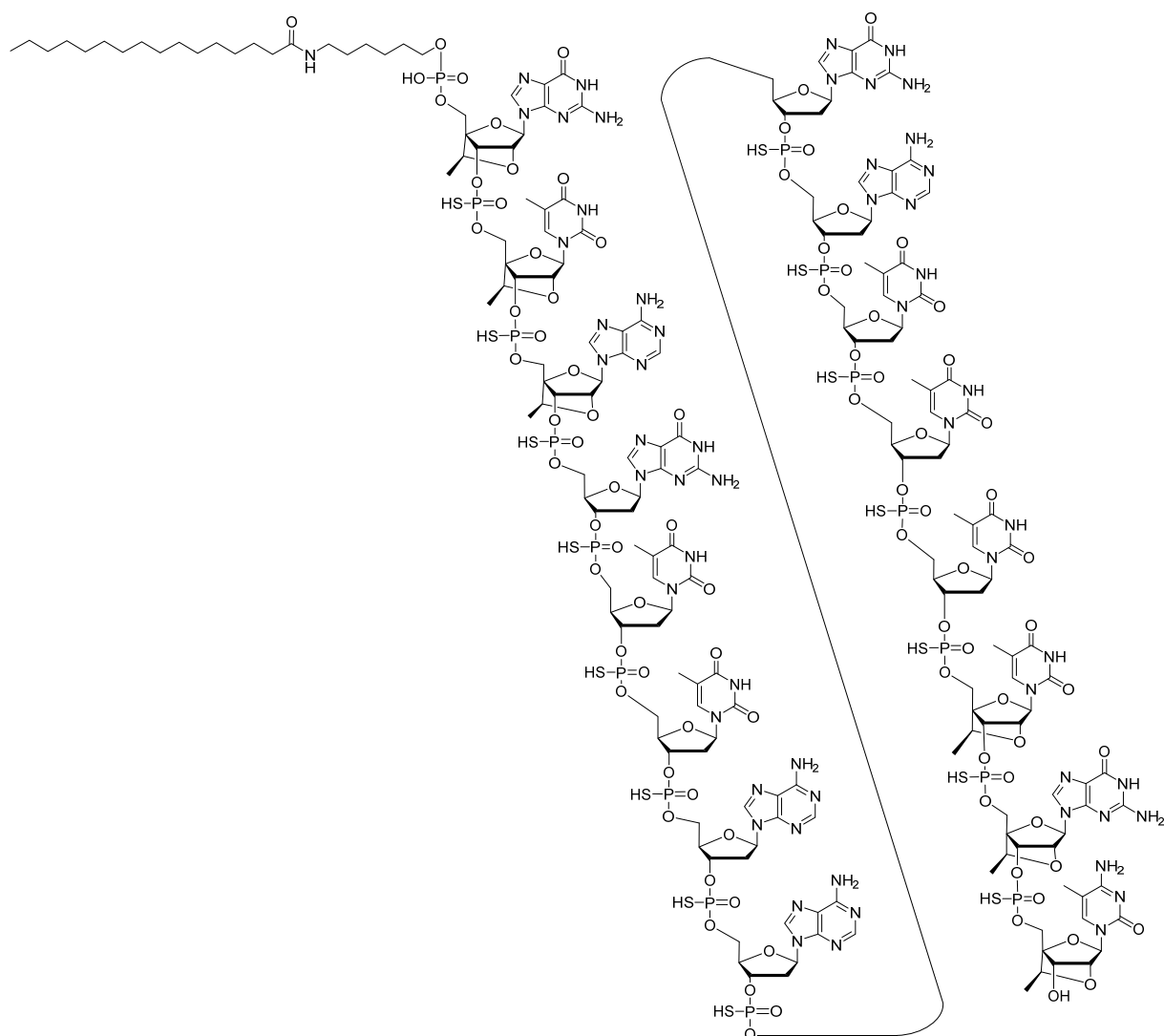
74. The oligomeric compound of claim 73, which is the sodium salt or potassium salt.

75. An oligomeric compound according to the following chemical structure:



(SEQ ID NO: 752).

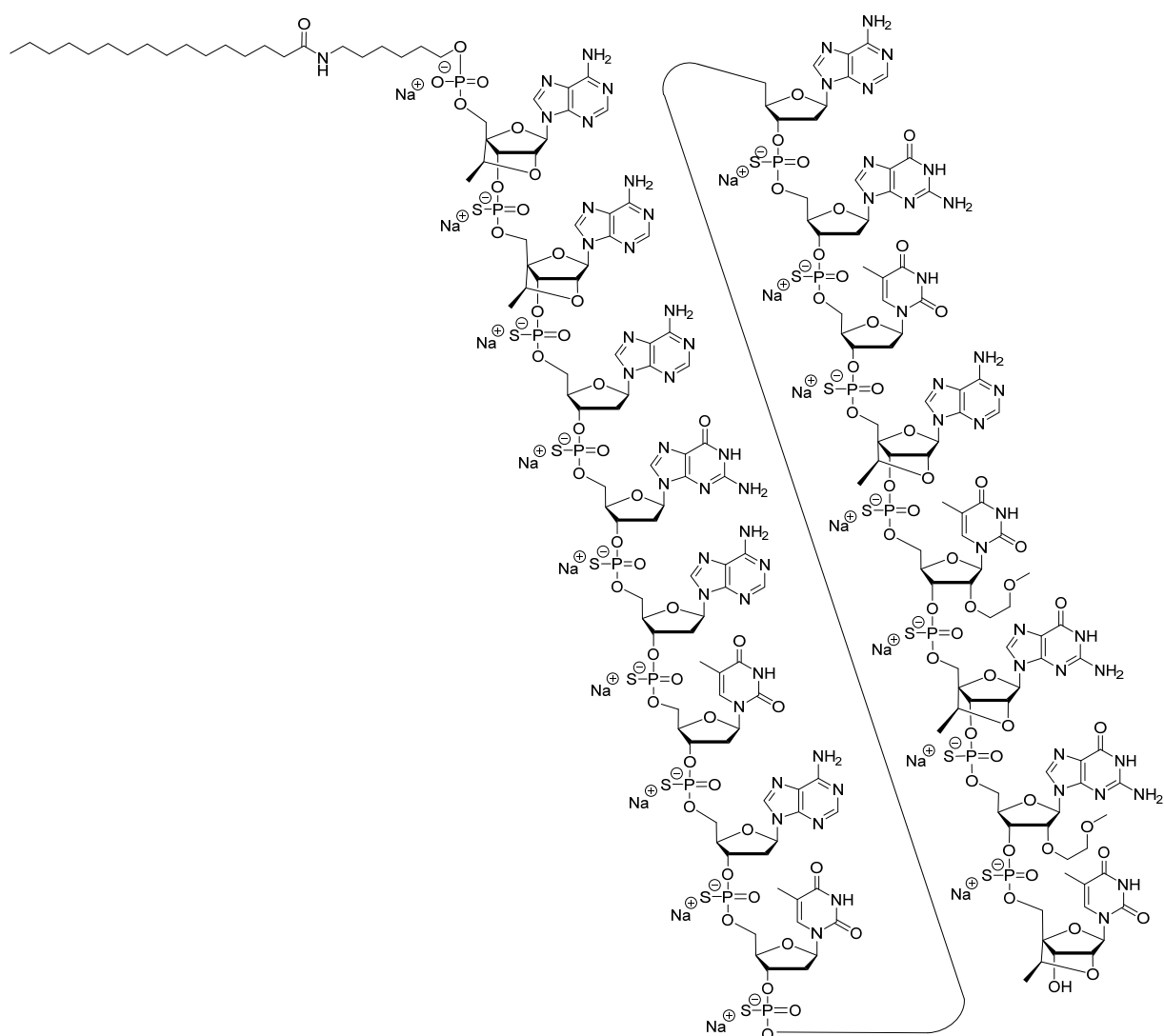
76. An oligomeric compound according to the following chemical structure:



(SEQ ID NO: 752), or a salt thereof.

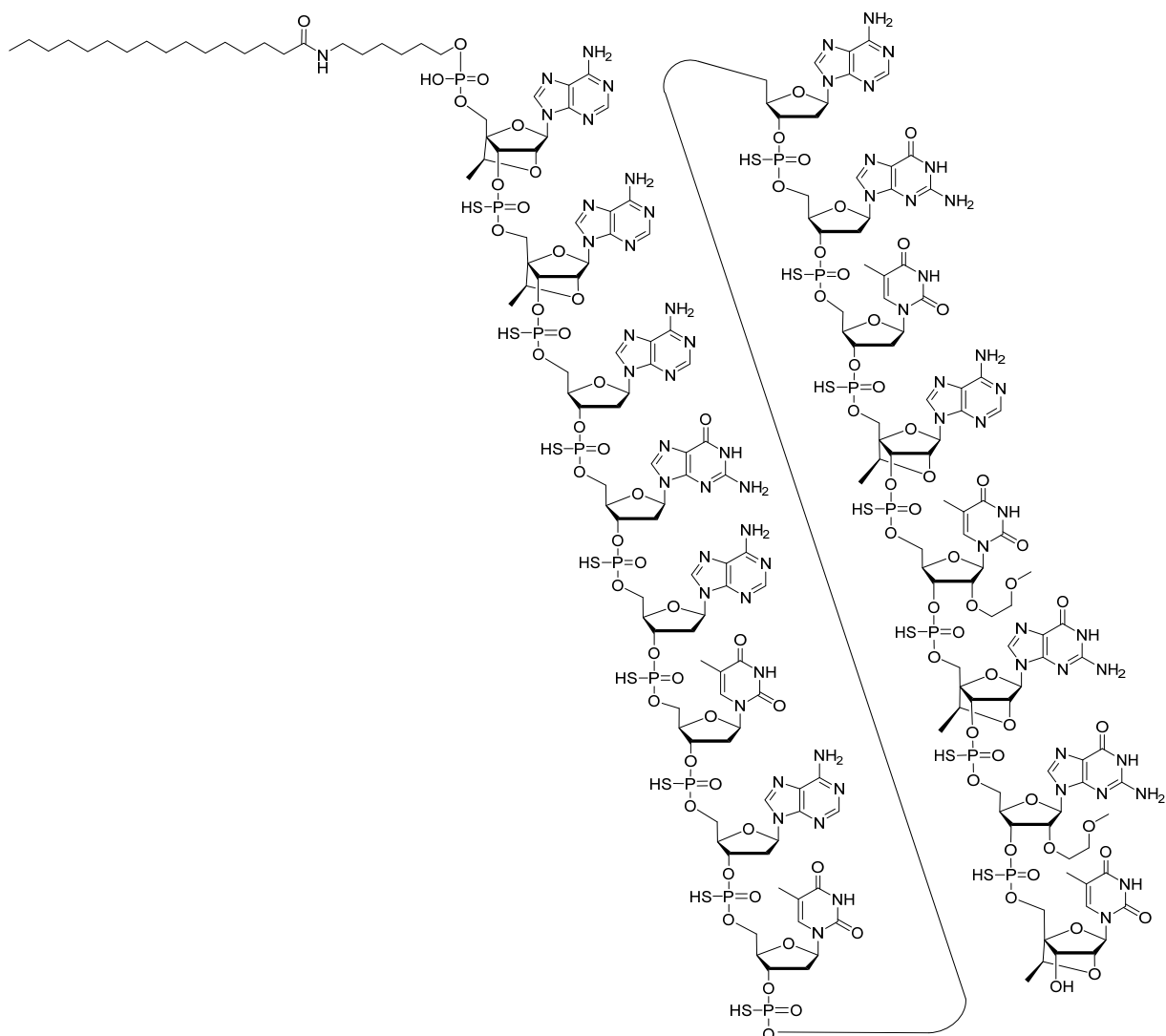
77. The oligomeric compound of claim 76, which is the sodium salt or potassium salt.

78. An oligomeric compound according to the following chemical structure:



(SEQ ID NO: 120).

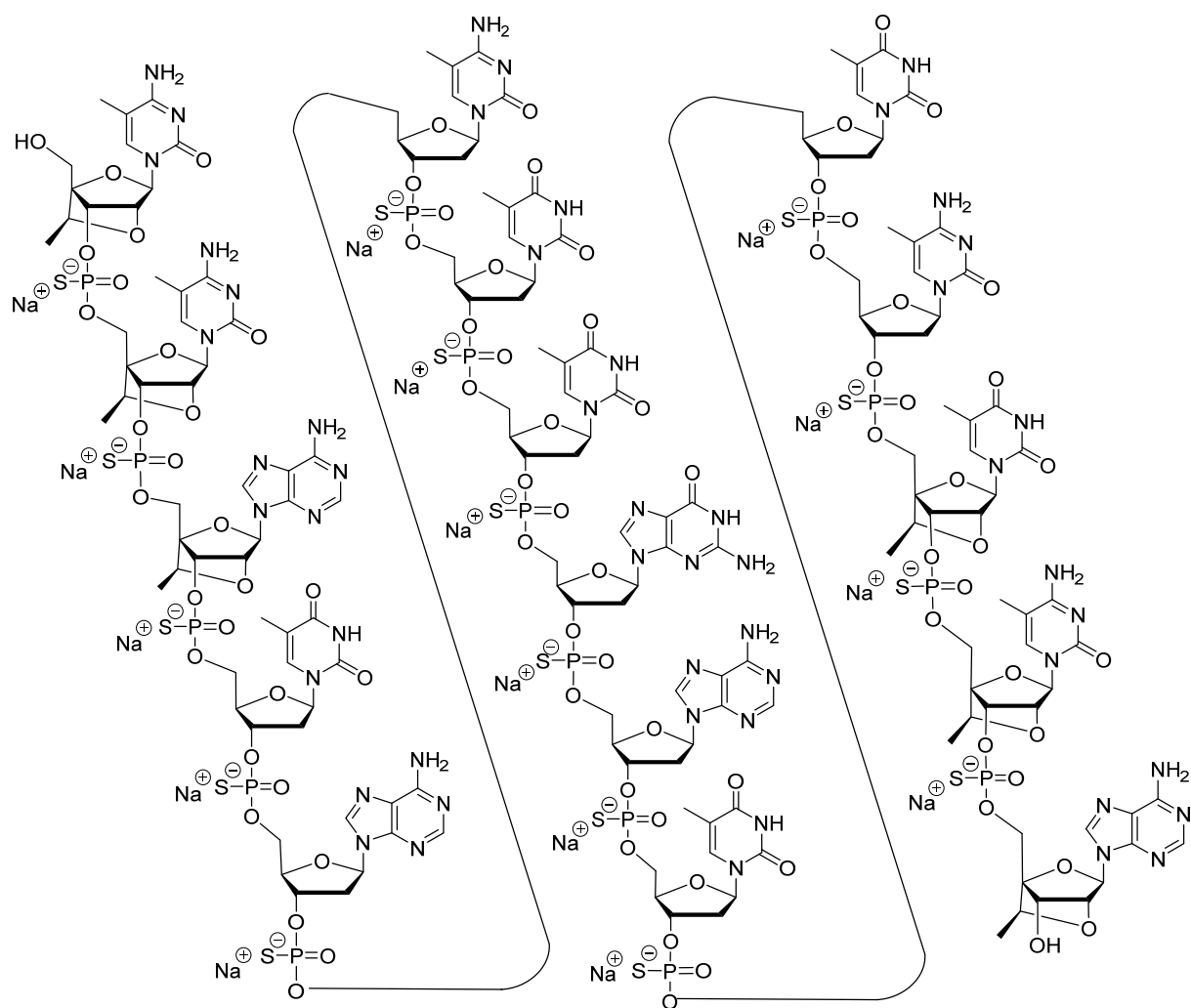
79. An oligomeric compound according to the following chemical structure:



(SEQ ID NO: 120), or a salt thereof.

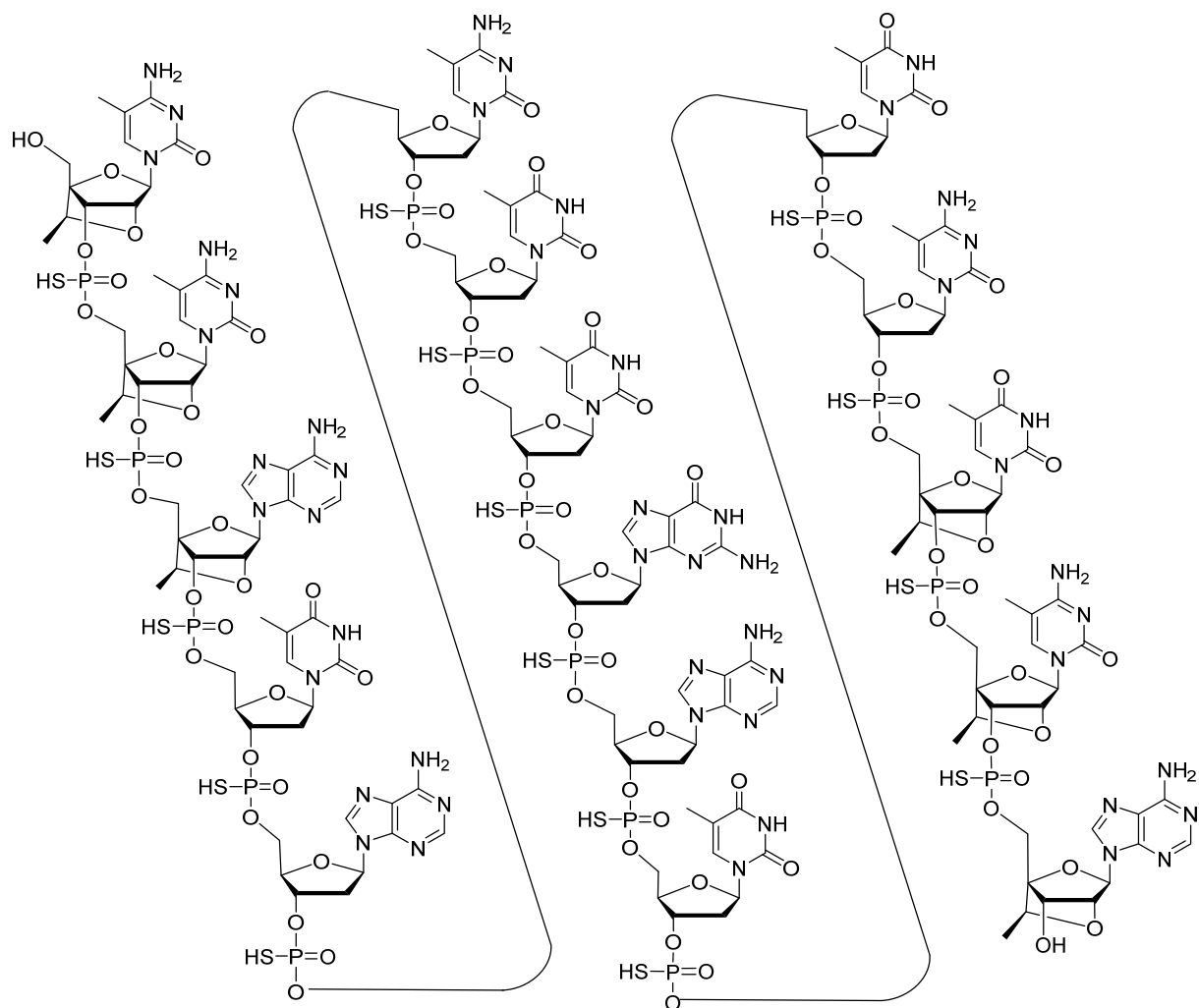
80. The oligomeric compound of claim 79, which is the sodium salt or potassium salt.

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



(SEQ ID NO: 185).

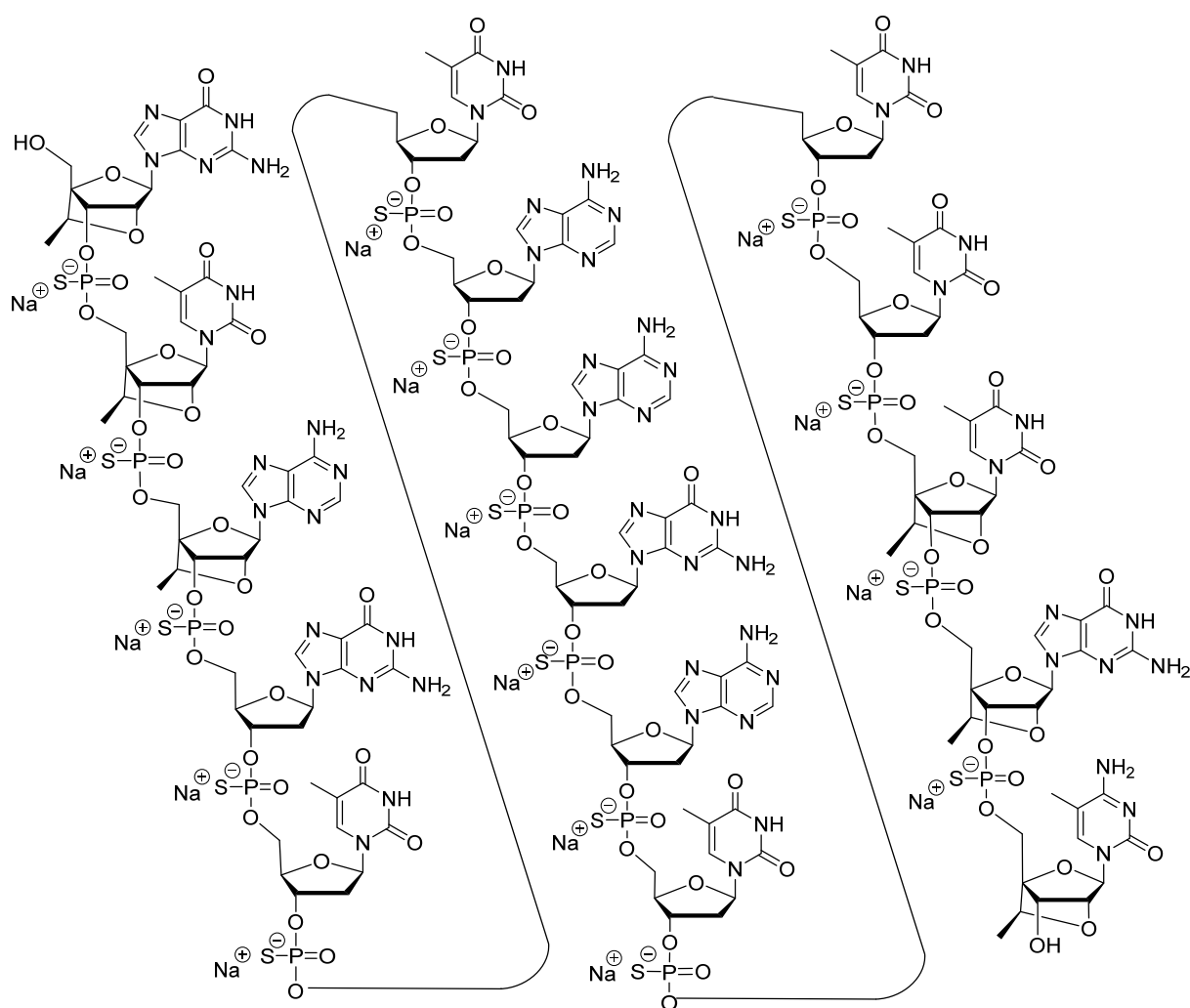
82. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 185), or a salt thereof.

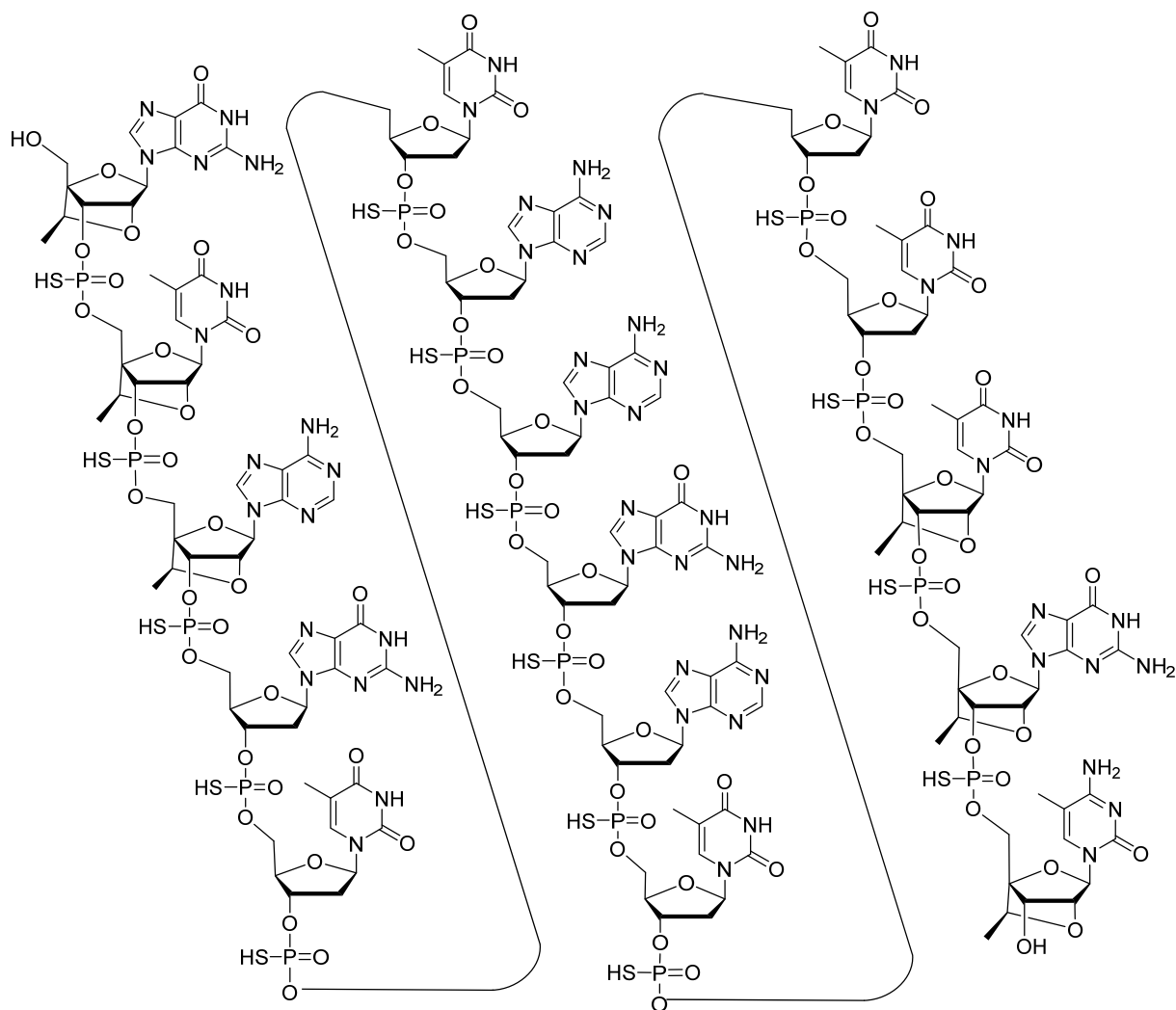
83. The modified oligonucleotide of claim 82, which is the sodium salt or potassium salt.

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



(SEQ ID NO: 752).

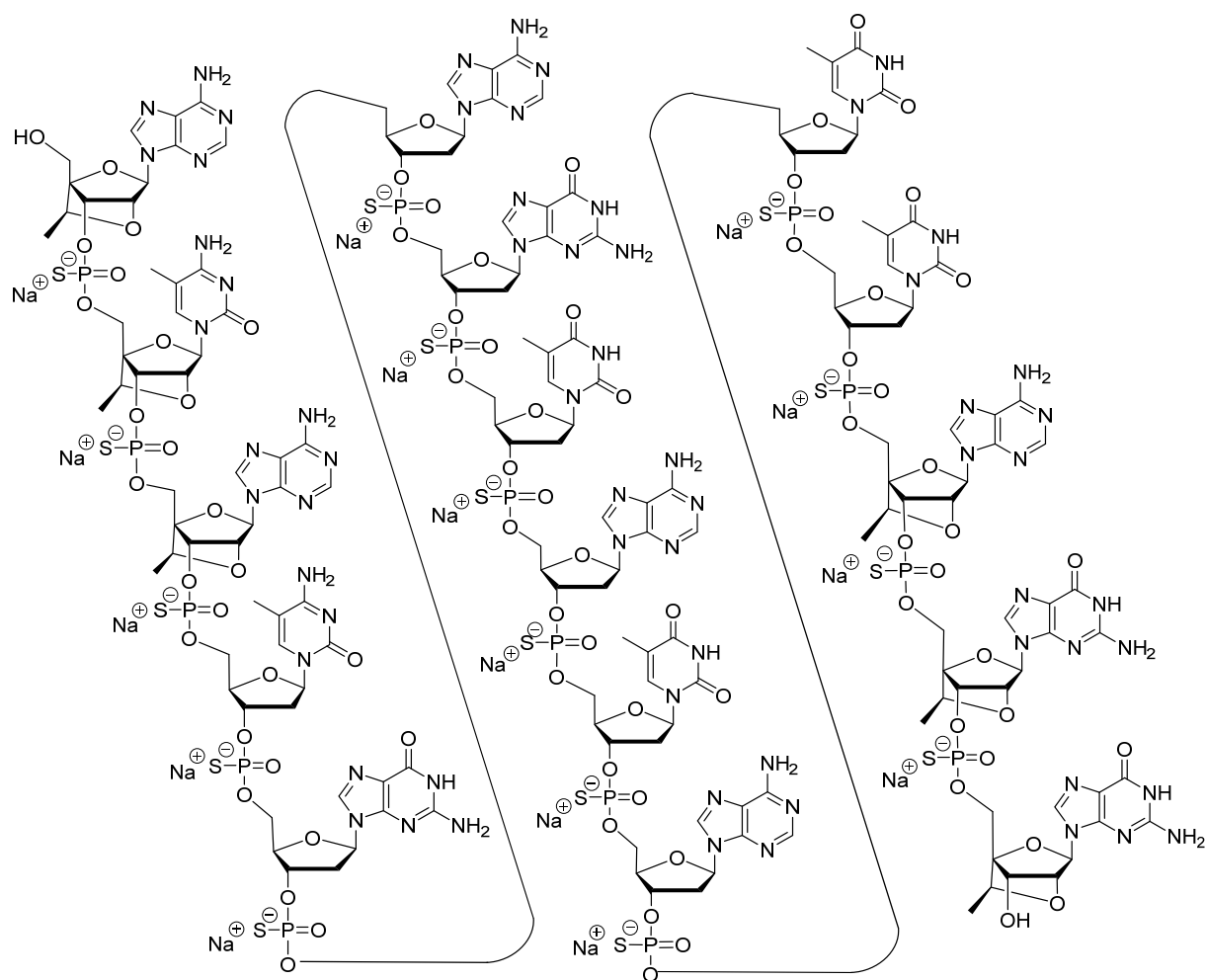
85. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 752), or a salt thereof.

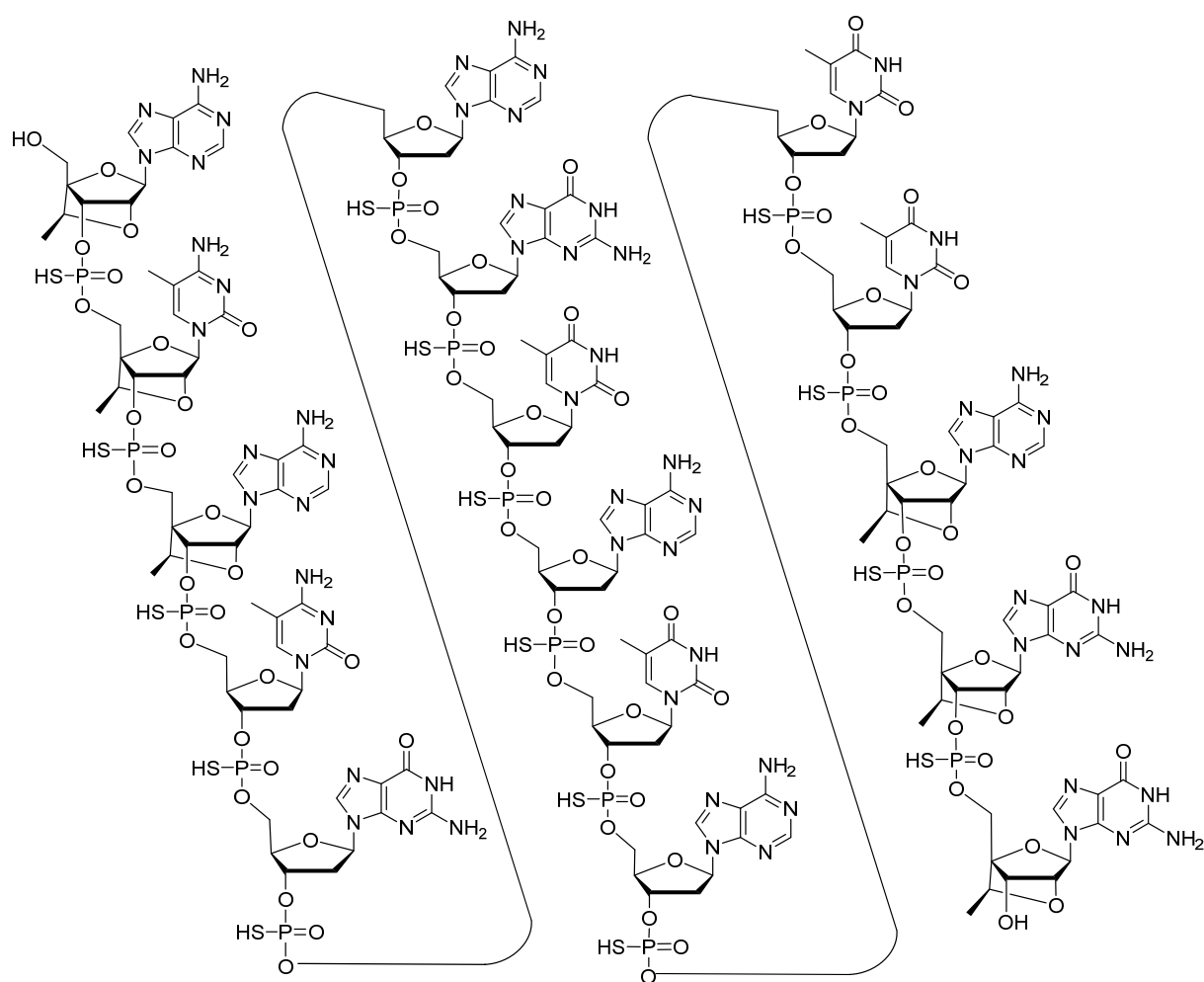
86. The modified oligonucleotide of claim 85, which is the sodium salt or potassium salt.

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



(SEQ ID NO: 609).

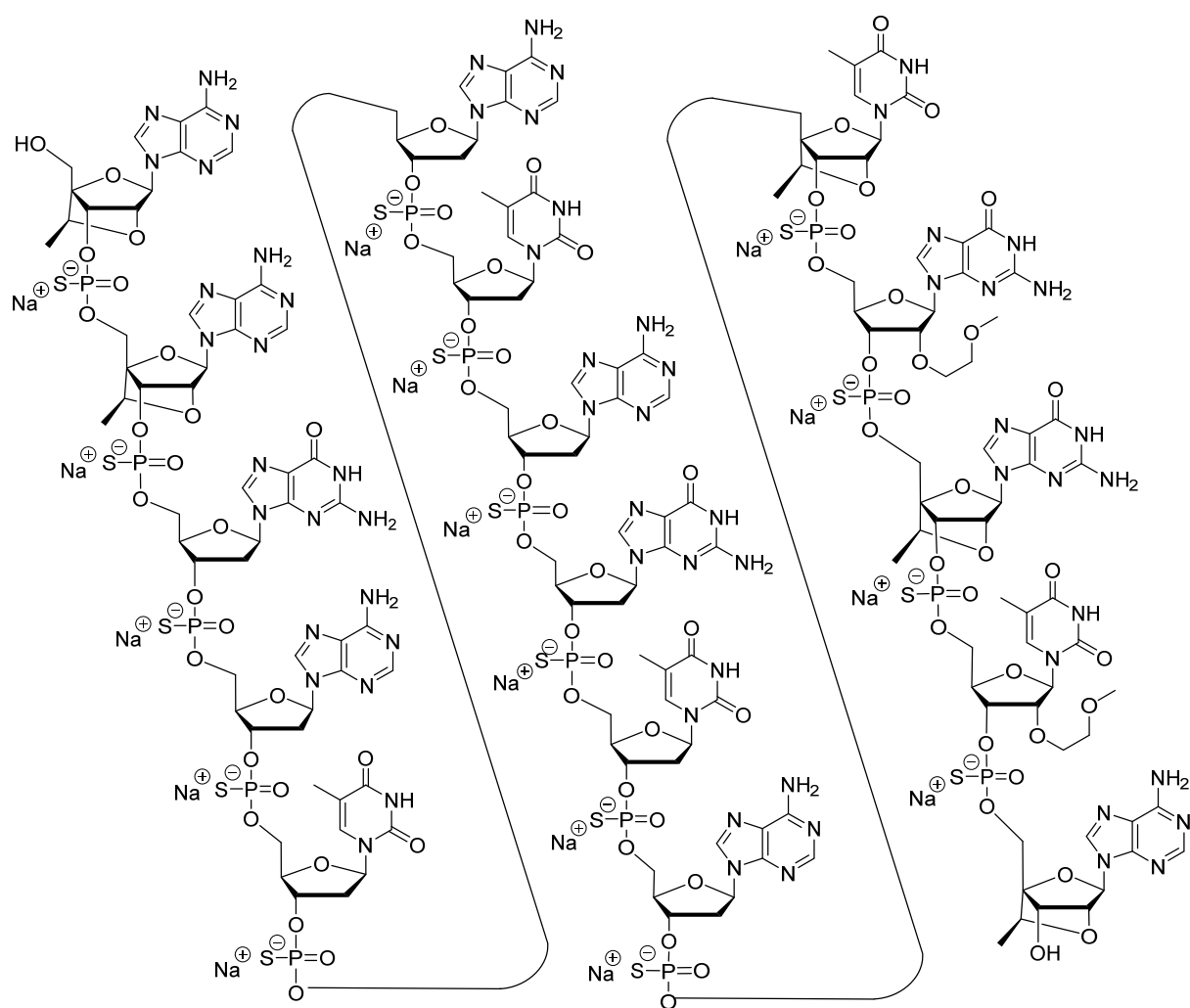
88. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 609), or a salt thereof.

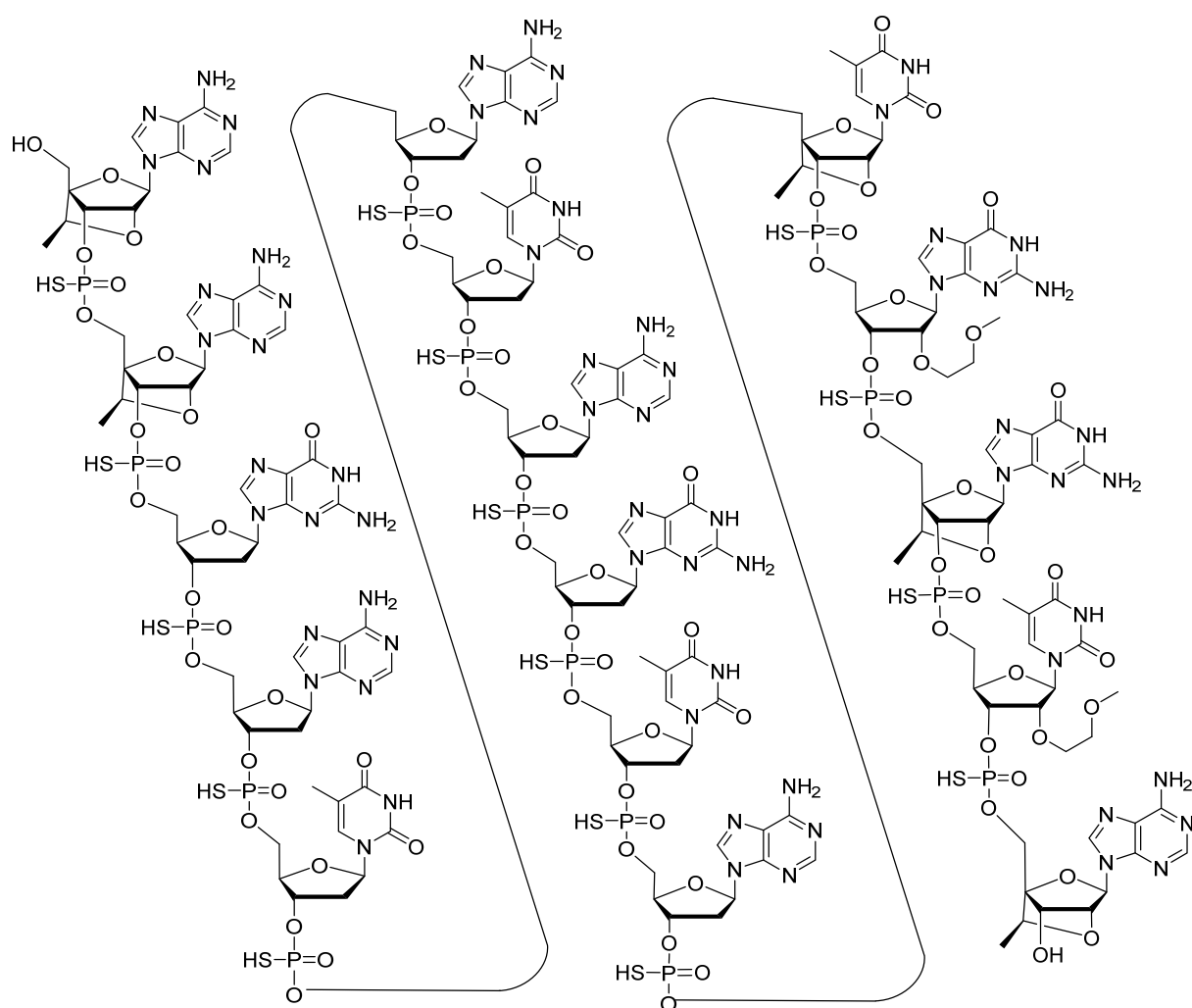
89. The modified oligonucleotide of claim 88, which is the sodium salt or potassium salt.

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



(SEQ ID NO: 45).

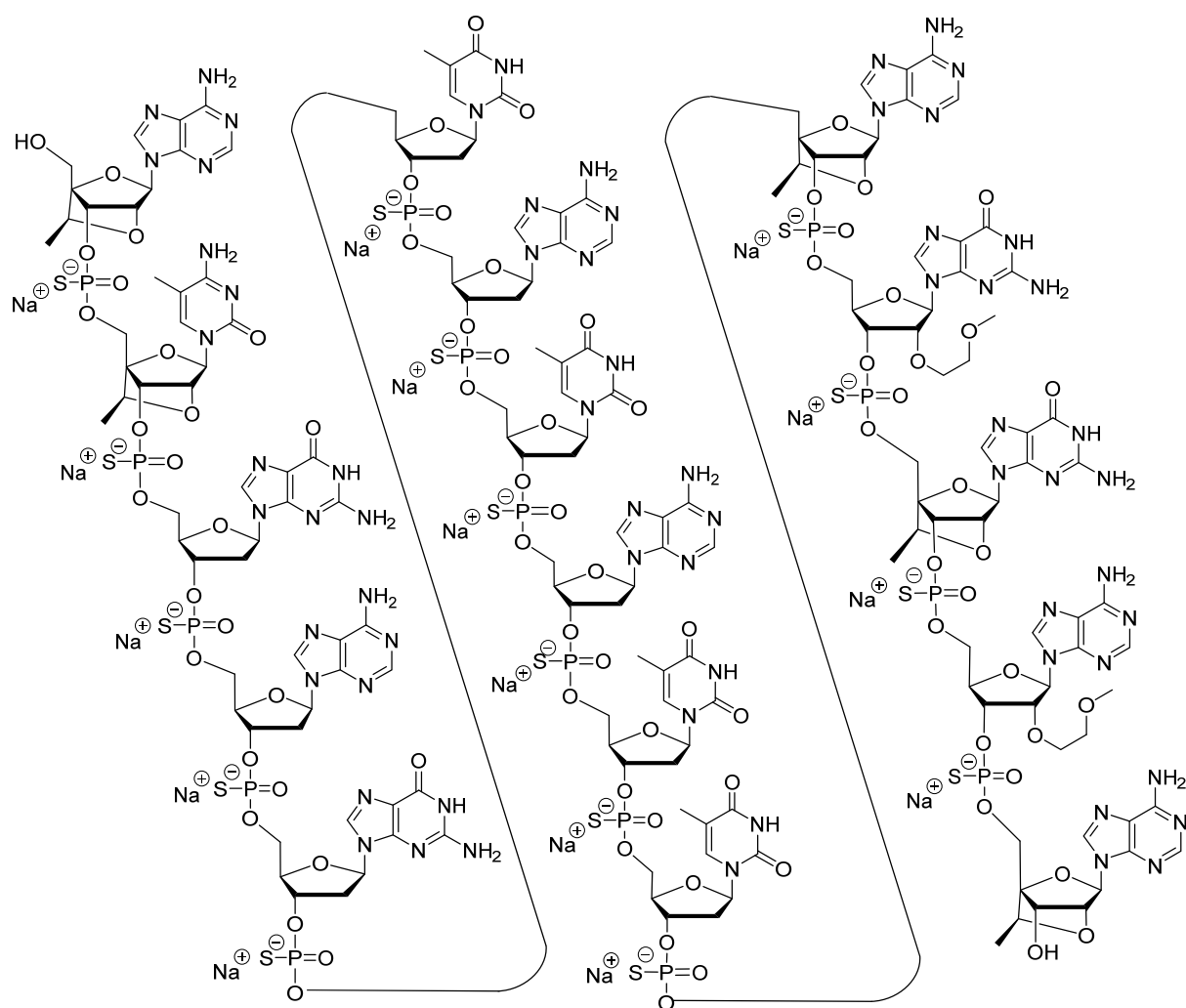
91. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 45), or a salt thereof.

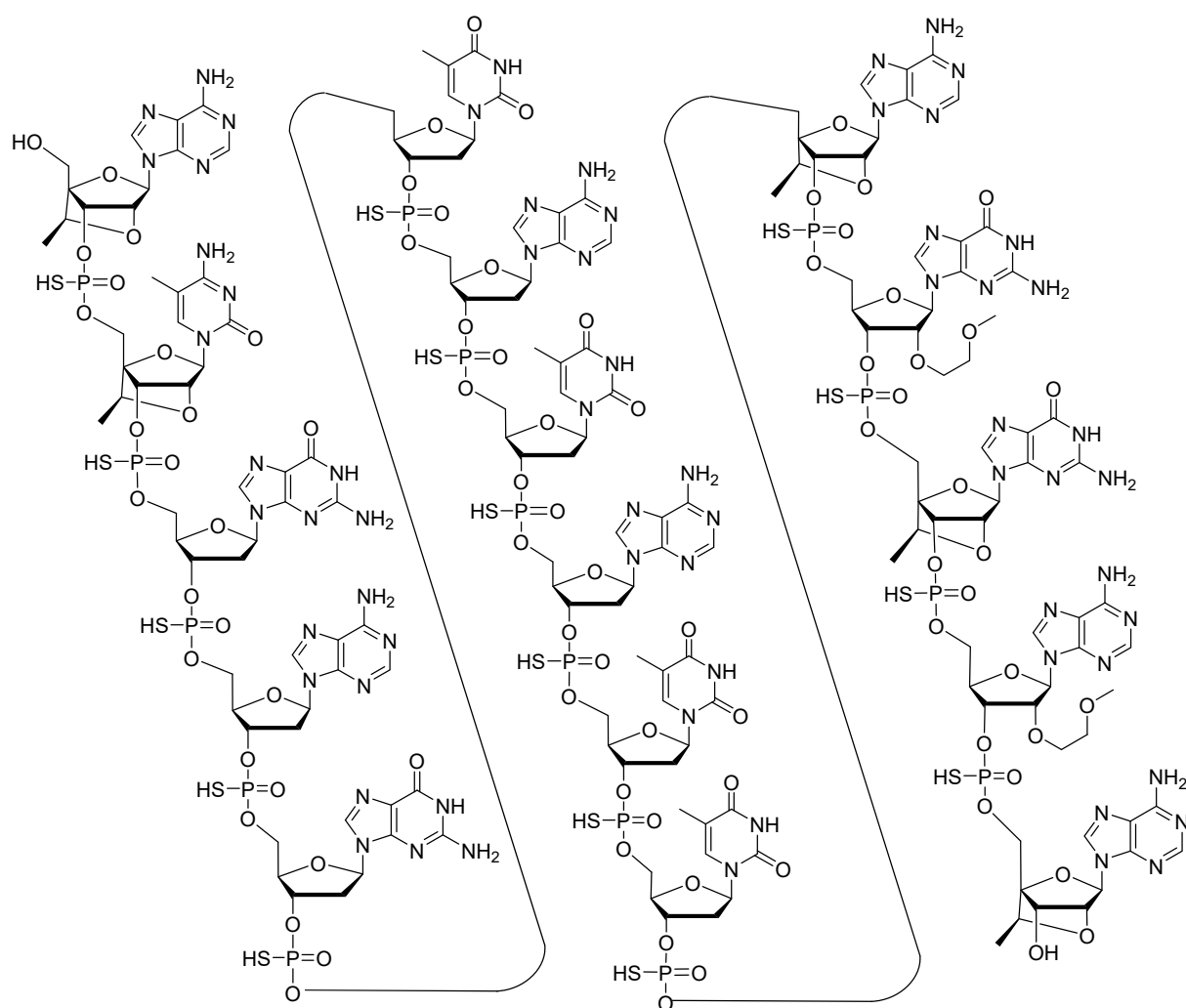
92. The modified oligonucleotide of claim 91, which is the sodium salt or potassium salt.

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



(SEQ ID NO: 737).

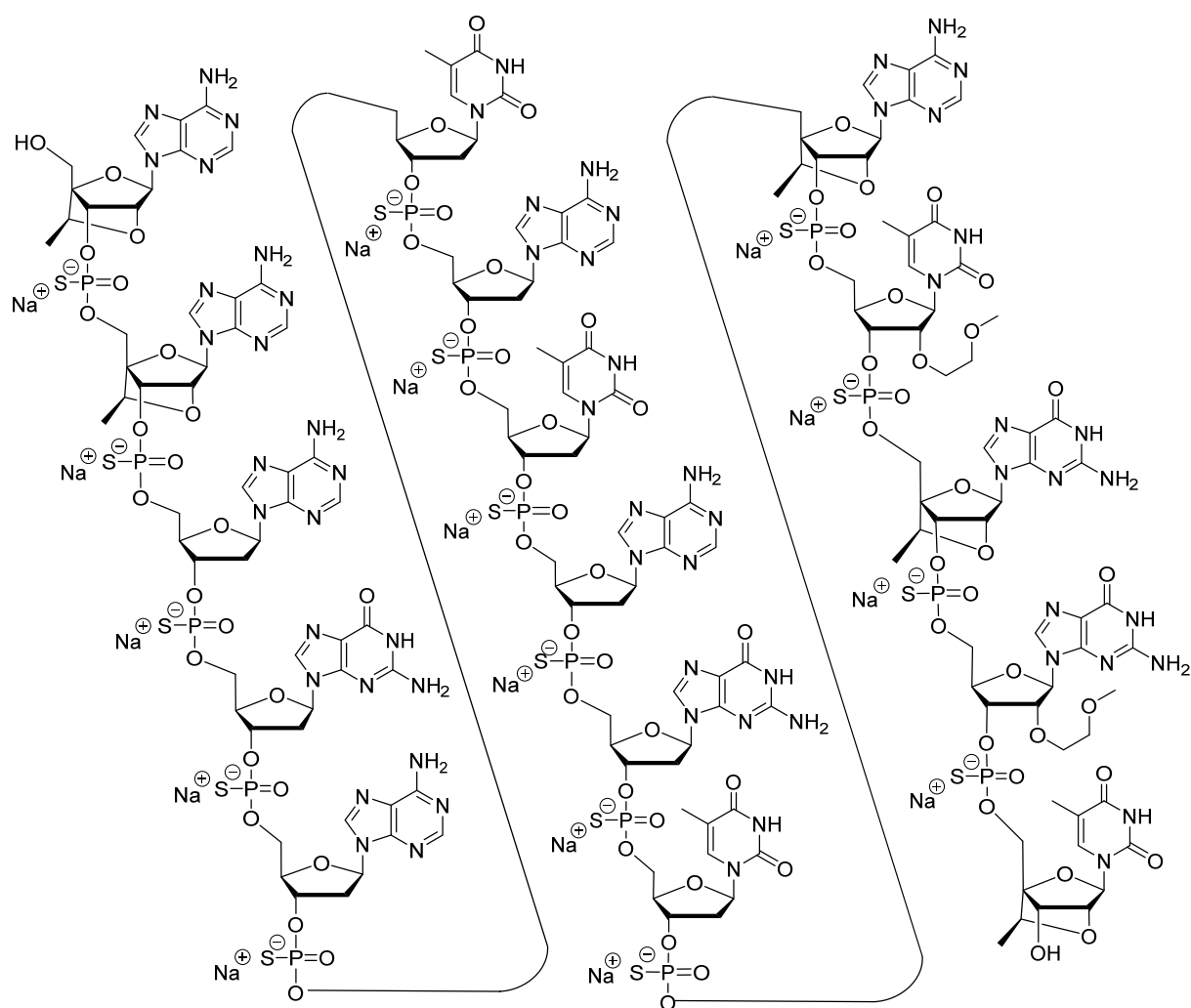
94. A modified oligonucleotide according to the following chemical structure:



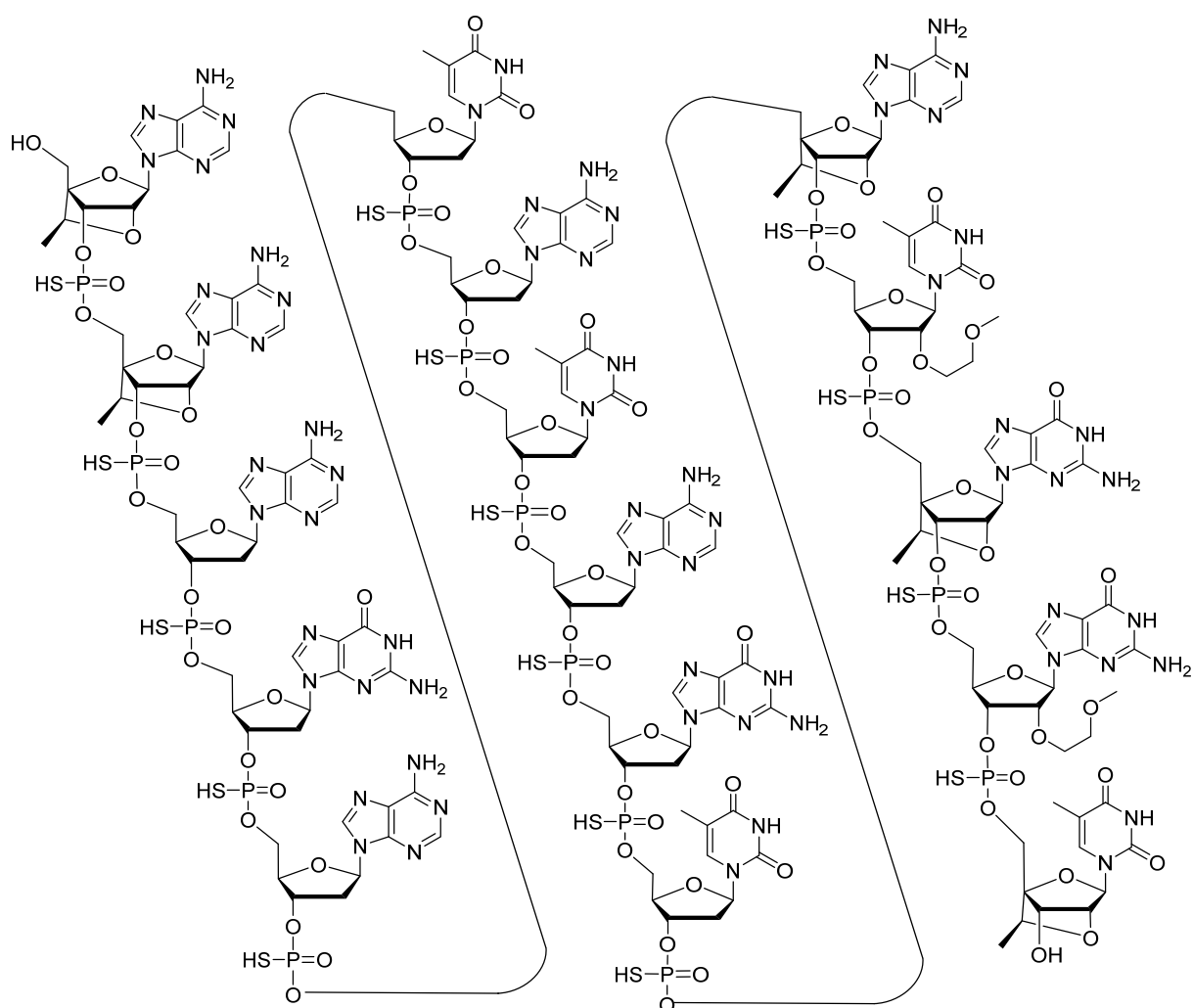
(SEQ ID NO: 737), or a salt thereof.

95. The modified oligonucleotide of claim 94, which is the sodium salt or potassium salt.

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



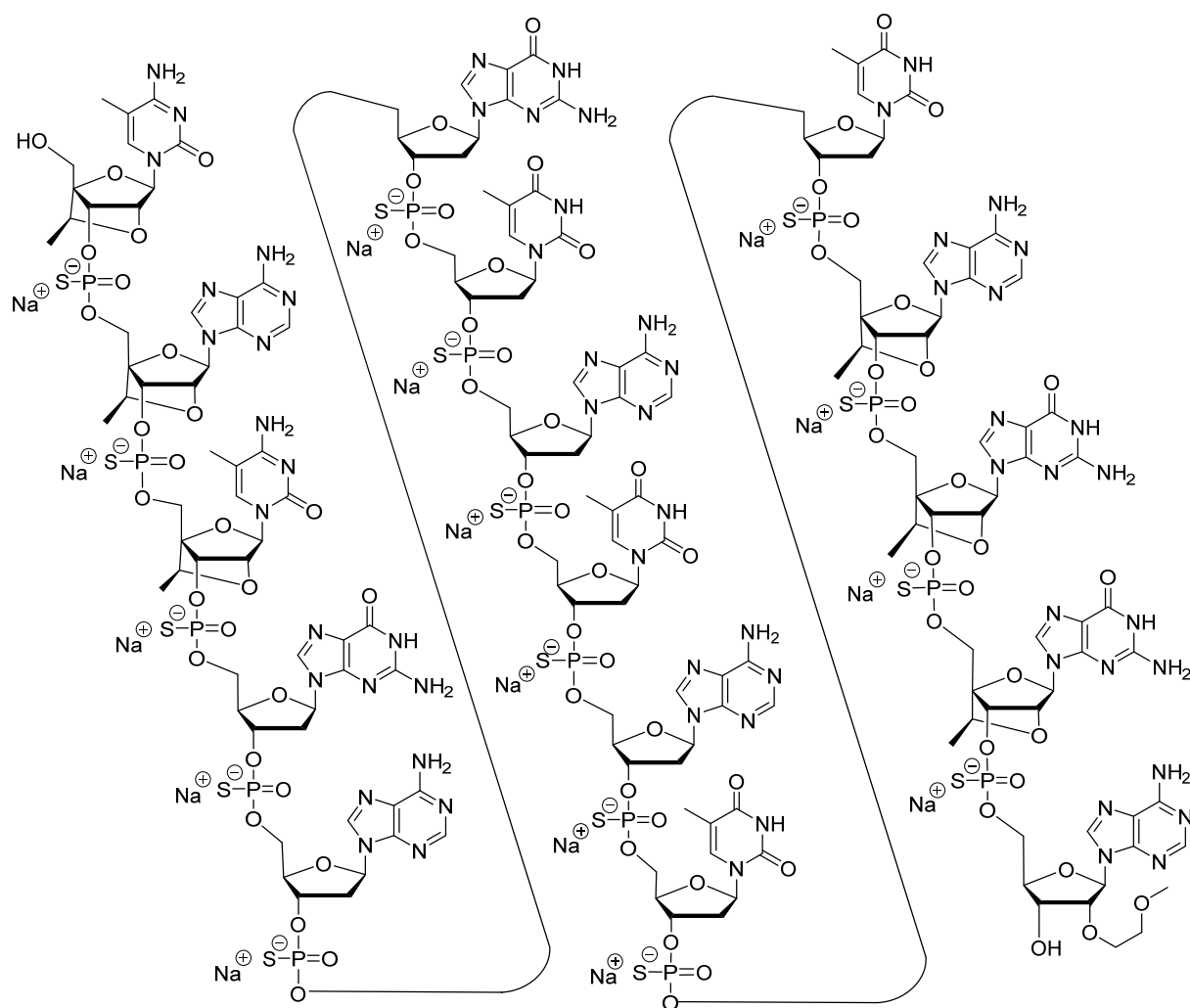
97. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 120), or a salt thereof.

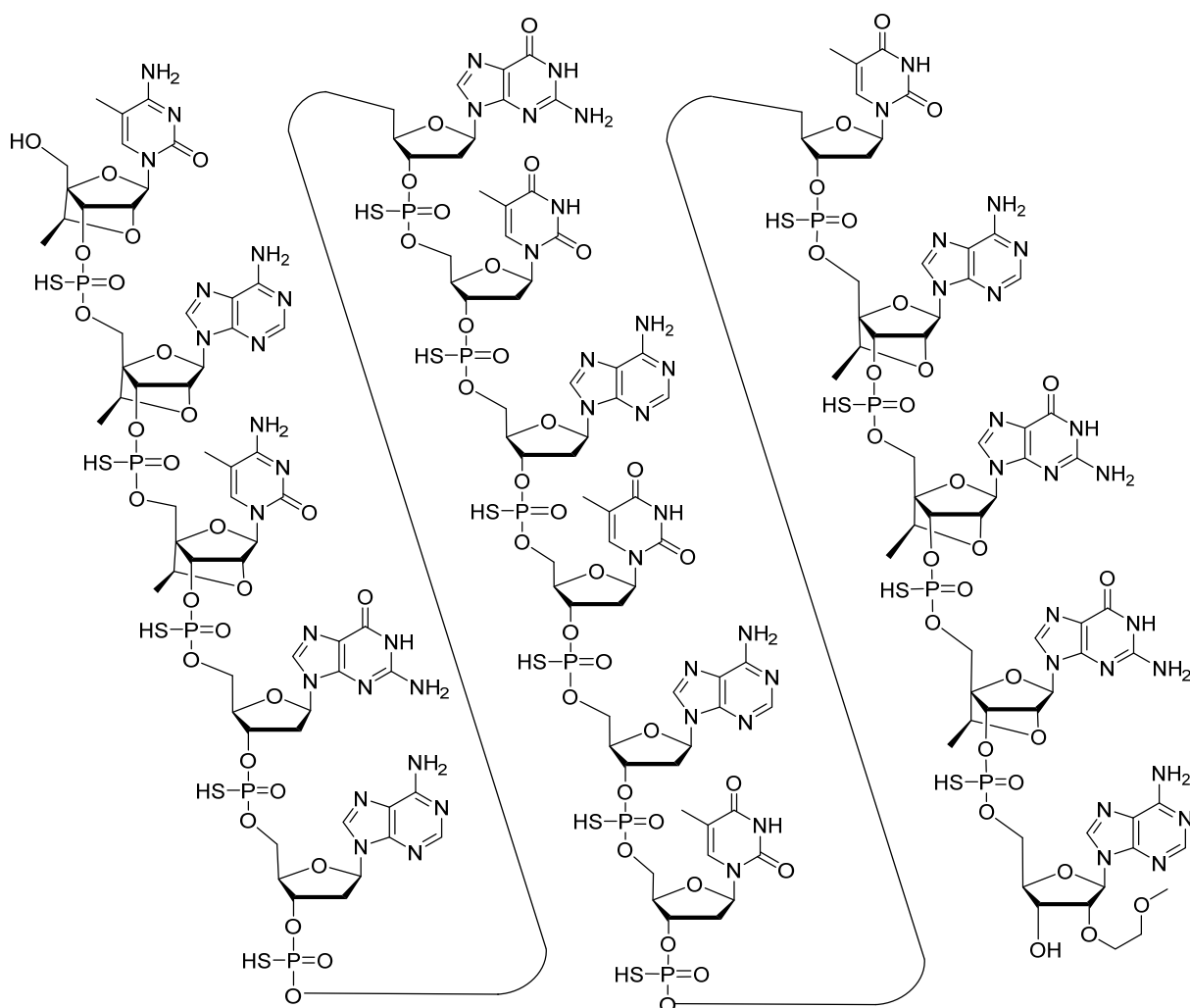
98. The modified oligonucleotide of claim 97, which is the sodium salt or potassium salt.

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



(SEQ ID NO: 675).

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



(SEQ ID NO: 675), or a salt thereof.

101. The modified oligonucleotide of claim 100, which is the sodium salt or potassium salt.

102. A chirally enriched population of oligomeric compounds of any of claims 1-80 or modified oligonucleotide of claims 81-101, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having a particular stereochemical configuration.

103. The chirally enriched population of claim 102, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (*Sp*) or (*Rp*) configuration.

104. The chirally enriched population of claim 102, wherein the population is enriched for modified oligonucleotides having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage.

105. The chirally enriched population of claim 102, 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.

106. The chirally enriched population of claim 102, 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.

107. A population of oligomeric compounds comprising the modified oligonucleotides of any of claims 1-80, or a population of modified oligonucleotides of claims 81-101, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

108. The oligomeric compound of claim 1 or 2, wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to an equal length portion within nucleobases 34-56, 44-66, 54-76, 64-86, 74-96, 84-106, 94-116, 104-126, 114-136, 124-146, 134-156, 144-166, 154-176, 164-186, 174-196, 184-206, 194-216, 204-226, 214-236, 224-246, 234-256, 244-266, 254-276, 264-286, 274-296, 284-306, 294-316, 304-326, 314-336, 324-346, 334-356, 344-366, 354-376, 364-386, 374-396, 384-406, 394-416, 404-426, 414-436, 424-446, 434-456, 444-466, 454-476, 464-486, 474-496, 484-506, 494-516, 504-526, 514-536, 524-546, 534-556, 544-566, 554-576, 564-586, 574-596, 584-606, 594-616, 604-626, 614-636, 624-646, 634-656, 644-666, 654-676, 664-686, 674-696, 684-706, 694-716, 704-726, 714-736, 724-746, 734-756, 744-766, 754-776, 764-786, 774-796, 784-806, 794-816, 804-826, 814-836, 819-841, 834-856, 844-866, 854-876, 864-886, 874-896, 884-906, 894-916, 904-926, 914-936, 924-946, 934-956, 944-966, 954-976, 964-986, 974-996, 984-1006, 994-1016, 1004-1026, 1014-1036, 1024-1046, 1034-1056, 1044-1066, 1054-1076, 1064-1086, 1074-1096, 1084-1106, 1094-1116, 1104-1126, 1114-1136, 1124-1146, 1134-1156, 1144-1166, 1154-1176, 1164-1186, 1174-1196, 1184-1206, 1194-1216, 1204-1226, 1214-1236, 1224-1246, 1234-1256, 1238-1260, 1243-1265, 1248-1270, 1254-1276, 1264-1286, 1274-1296, 1279-1301, 1284-1306, 1294-1316, 1304-1326, 1314-1336, 1324-1346, 1334-1356, 1344-1366, 1354-1376, 1364-1386, 1374-1396, 1384-1406, 1394-1416, 1404-1426, 1414-1436, 1424-1446, 1434-1456, 1444-1466, 1454-1476, 1464-1486, 1474-1496, 1484-1506, 1494-1516, 1499-1521, 1504-1526, 1514-1536, 1522-1544, 1534-1556, 1544-1566, 1554-1576, 1564-1586, 1574-1596, 1584-1606, 1594-1616, 1604-1626, 1614-1636, 1624-1646, 1634-1656, 1644-1666, 1654-1676, 1664-1686, 1674-1696, 1684-1706, 1694-1716, 1704-1726, 1714-1736, 1724-1746, 1734-1756, 1744-1766, 1754-1776, 1764-1786, 1774-1796, 1784-1806, 1794-1816, 1804-1826, 1814-1836, 1824-1846, 1834-1856, 1844-1866, 1854-1876, 1864-1886, 1874-1896, 1884-1906, 1894-1916, 1904-1926, 1914-1936, 1924-1946, 1934-1956, 1944-1966, 1954-1976, 1964-1986, 1974-1996, 1984-2006, 1994-2016, 2004-2026, 2014-2036, 2019-2041, 2024-2046, 2034-2056, 2044-2066, 2054-2076, 2064-2086, 2074-2096, 2084-2106, 2094-2116, 2104-2126, 2114-2136, 2124-2146, 2134-2156, 2144-2166, 2154-2176, 2164-2186, 2174-2196, 2184-2206, 2194-2216, 2204-2226, 2214-2236, 2219-2241, 2224-2246, 2234-2256, 2244-2266, 2254-2276, 2264-2286, 2274-2296, 2284-2306, 2294-2316, 2304-2326, 2314-2336, 2324-2346, 2334-2356, 2344-2366, 2354-2376, 2364-2386, 2374-2396, 2379-2401, 2384-2406, 2394-2416, 2404-2426, 2414-2436, 2424-2446, 2434-2456, 2444-2466, 2454-2476, 2464-2486, 2474-2496, 2479-2501, 2484-2506, 2494-2516, 2504-2526, 2514-2536, 2524-2546, 2534-2556, 2544-2566, 2554-2576, 2564-2586, 2574-2596, 2584-2606, 2594-2616, 2604-2626, 2614-2636, 2619-2641, 2624-2646, 2634-2656, 2644-2666, 2654-2676, 2664-2686, 2674-2696, 2684-2706, 2694-2716, 2699-2721, 2704-2726, 2714-2736, 2724-2746, 2734-2756, 2744-2766, 2754-2776, 2759-2781, 2764-2786, 2774-2796, 2784-2806, 2794-2816, 2804-2826,

2814-2836, 2824-2846, 2834-2856, 2844-2866, 2854-2876, 2864-2886, 2874-2896, 2879-2901, 2884-2906, 2894-2916, 2904-2926, 2914-2936, 2919-2941, 2924-2946, 2934-2956, 2944-2966, 2954-2976, 2964-2986, 2974-2996, 2981-3003, 2987-3009, or 2994-3016, of SEQ ID NO: 1.

109. 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 1-80 or 108, or the modified oligonucleotide of any of claims 81-101.

110. The oligomeric duplex of claim 109, wherein the second oligomeric compound comprises a second modified oligonucleotide consisting of 8 to 80 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.

111. An oligomeric duplex comprising:

a first oligomeric compound comprising a first modified oligonucleotide consisting of 19 to 29 linked nucleosides wherein the nucleobase sequence of the first modified oligonucleotide comprises 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, at least 20, at least 21, at least 22, or at least 23 contiguous nucleobases of the nucleobase sequence of any of SEQ ID NOs: 1713-2024; and

a second oligomeric compound comprising a second modified oligonucleotide consisting of 15 to 29 linked nucleosides 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.

112. An oligomeric duplex comprising:

a first oligomeric compound comprising a first modified oligonucleotide consisting of 19 to 29 linked nucleosides wherein the nucleobase sequence of the first modified oligonucleotide comprises 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, at least 20, at least 21, at least 22, or at least 23 contiguous nucleobases of the nucleobase sequence of any of SEQ ID NOs: 1713-2024; and

a second oligomeric compound comprising a second modified oligonucleotide consisting of 15 to 29 linked nucleosides wherein the nucleobase sequence of the second modified oligonucleotide comprises 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, at least 20, or at least 21 contiguous nucleobases of the nucleobase sequence of any of SEQ ID NOs: 2025-2336, wherein the nucleobase sequence of the second modified oligonucleotide is at least 90% complementary to an equal length portion of the first modified oligonucleotide.

113. An oligomeric duplex comprising:

a first oligomeric compound comprising a first modified oligonucleotide consisting of 23 linked nucleosides wherein the nucleobase sequence of the first modified oligonucleotide comprises or consists of the nucleobase sequence of any of SEQ ID NOs: 1713-2024; and

a second oligomeric compound comprising a second modified oligonucleotide consisting of 21 linked nucleosides wherein the nucleobase sequence of the second modified oligonucleotide comprises or consists of

the nucleobase sequence of any of SEQ ID NOs: 2025-2336, wherein the nucleobase sequence of the second modified oligonucleotide is at least 90% complementary to an equal length portion of the first modified oligonucleotide.

114. The oligomeric duplex of any of claims 109-113, wherein the modified oligonucleotide of the first oligomeric compound comprises a 5'-stabilized phosphate group.

115. The oligomeric duplex of claim 114, wherein the 5'-stabilized phosphate group comprises a cyclopropyl phosphonate or a vinyl phosphonate.

116. The oligomeric duplex of any of claims 109-115, wherein the modified oligonucleotide of the first oligomeric compound comprises a glycol nucleic acid (GNA) sugar surrogate.

117. The oligomeric duplex of any of claims 109-116, wherein the modified oligonucleotide of the first oligomeric compound comprises a 2'-NMA sugar moiety.

118. The oligomeric duplex of any of claims 109-117, wherein at least one nucleoside of the second modified oligonucleotide comprises a modified sugar moiety.

119. The oligomeric duplex of claim 118, wherein the modified sugar moiety of the second modified oligonucleotide comprises a bicyclic sugar moiety.

120. The oligomeric duplex of claim 119, wherein the bicyclic sugar moiety of the second modified oligonucleotide comprises a 2'-4' bridge selected from $-O-CH_2-$; and $-O-CH(CH_3)-$.

121. The oligomeric duplex of claim 118, wherein the modified sugar moiety of the second modified oligonucleotide comprises a non-bicyclic modified sugar moiety.

122. The oligomeric duplex of claim 121, wherein the non-bicyclic modified sugar moiety of the second modified oligonucleotide is a 2'-MOE sugar moiety, a 2'-F sugar moiety, or 2'-OMe sugar moiety.

123. The oligomeric duplex of any of claims 109-122, wherein at least one nucleoside of the second modified oligonucleotide comprises a sugar surrogate.

124. The oligomeric duplex of any of claims 109-123, wherein the first and/or the second modified oligonucleotide comprises at least one modified internucleoside linkage.

125. The oligomeric duplex of claim 124, wherein the at least one modified internucleoside linkage is a phosphorothioate internucleoside linkage.

126. The oligomeric duplex of claim 124, wherein the at least one modified internucleoside linkage is a mesyl phosphoramidate internucleoside linkage.

127. The oligomeric duplex of any of claims 109-126, wherein the first and/or the second modified oligonucleotide comprises at least one phosphodiester internucleoside linkage.

128. The oligomeric duplex of any of claims 109-127, wherein each internucleoside linkage of the first and/or the second modified oligonucleotide is independently selected from a phosphodiester, a phosphorothioate, or a mesyl phosphoramidate internucleoside linkage.

129. The oligomeric duplex of any of claims 109-128, wherein the internucleoside linkage motif of the first modified oligonucleotide is $ssoooooooooooooooooss$ and the internucleoside linkage motif of the second modified oligonucleotide is $ssoooooooooooooooooss$, wherein each "o" represents a phosphodiester internucleoside linkage and each "s" represents a phosphorothioate internucleoside linkage.

130. The oligomeric duplex of any of claims 109-129, wherein the first and/or the second modified oligonucleotide comprises at least one modified nucleobase.

131. The oligomeric duplex of claim 130, wherein the modified nucleobase is 5-methylcytosine.

132. The oligomeric duplex of any of claims 109-131, wherein the second modified oligonucleotide comprises a conjugate group.

133. The oligomeric duplex of claim 132, wherein the conjugate group comprises a conjugate linker and a conjugate moiety.

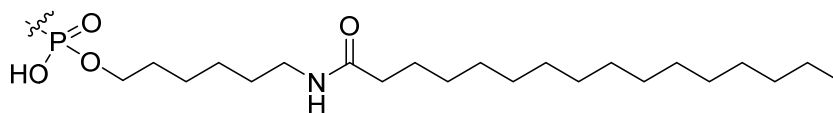
134. The oligomeric duplex of claim 132 or 133, wherein the conjugate group is attached to the second modified oligonucleotide at the 5'-end of the second modified oligonucleotide.

135. The oligomeric duplex of claim 132 or 133, wherein the conjugate group is attached to the second modified oligonucleotide at the 3'-end of the modified oligonucleotide.

136. The oligomeric duplex of any of claims 132-135, wherein the conjugate group comprises a C22 alkyl, C20 alkyl, C16 alkyl, C10 alkyl, C21 alkyl, C19 alkyl, C18 alkyl, C15 alkyl, C14 alkyl, C13 alkyl, C12 alkyl, C11 alkyl, C9 alkyl, C8 alkyl, C7 alkyl, C6 alkyl, C5 alkyl, C22 alkenyl, C20 alkenyl, C16 alkenyl, C10 alkenyl, C21 alkenyl, C19 alkenyl, C18 alkenyl, C15 alkenyl, C14 alkenyl, C13 alkenyl, C12 alkenyl, C11 alkenyl, C9 alkenyl, C8 alkenyl, C7 alkenyl, C6 alkenyl, or C5 alkenyl.

137. The oligomeric duplex of any of claims 132-136, wherein the conjugate moiety is a 6-palmitamidohexyl conjugate moiety.

138. The oligomeric duplex of any of claims 132-135, wherein the conjugate group has the following structure:



139. The oligomeric duplex of any of claims 132-136, wherein the conjugate group comprises a cell-targeting moiety.

140. The oligomeric duplex of claim 139, wherein the cell-targeting moiety has an affinity for TfR1.

141. The oligomeric duplex of claim 140, wherein the cell-targeting moiety comprises an anti-TfR1 antibody or fragment thereof.

142. The oligomeric duplex of claim 140, wherein the cell-targeting moiety comprises a protein or peptide capable of binding TfR1.

143. The oligomeric duplex of claim 140, wherein the cell-targeting moiety comprises an aptamer capable of binding TfR1.

144. The oligomeric duplex of any of claims 109-143, wherein the second modified oligonucleotide comprises a terminal group.

145. The oligomeric duplex of claim 144, wherein the terminal group is an abasic sugar moiety.

146. The oligomeric duplex of any of claims 109-145, wherein the second modified oligonucleotide consists of 10 to 25, 10 to 30, 10 to 50, 12 to 20, 12 to 25, 12 to 30, 12 to 50, 13 to 20, 13 to 25, 13 to 30, 13 to 50, 14 to 20, 14 to 25, 14 to 30, 14 to 50, 15 to 20, 15 to 25, 15 to 30, 15 to 50, 16 to 18, 16 to 20, 16 to 25, 16 to 30, 16 to 50, 17

to 20, 17 to 25, 17 to 30, 17 to 50, 18 to 20, 18 to 25, 18 to 30, 18 to 50, 19 to 20, 19 to 25, 19 to 30, 19 to 50, 20 to 25, 20 to 30, 20 to 50, 21 to 25, 21 to 30, 21 to 50, 22 to 25, 22 to 30, 22 to 50, 23 to 25, 23 to 30, or 23 to 50 linked nucleosides.

147. The oligomeric duplex of any of claims 109-146, wherein the modified oligonucleotide of the first oligomeric compound consists of 23 linked nucleosides and the second modified oligonucleotide consists of 21 linked nucleosides.

148. The oligomeric duplex of claim 147, wherein the modified oligonucleotide of the first oligomeric compound has a sugar motif (from 5' to 3') of: yfyfyfyfyfyfyfyfyfy and the second modified oligonucleotide has a sugar motif (from 5' to 3') of: fyfyfyfyfyfyfyfyfyf, wherein each "y" represents a 2'-OMe sugar moiety and each "f" represents a 2'-F sugar moiety.

149. An antisense agent comprising an antisense compound, wherein the antisense compound is the oligomeric compound of any of claims 1-80 or 108 or the modified oligonucleotide of any of claims 81-101.

150. An antisense agent, wherein the antisense agent is the oligomeric duplex of any of claims 109-148.

151. The antisense agent of claim 149 or 150, wherein the antisense agent is:

- i. an RNase H agent capable of reducing the amount of PLN nucleic acid through the activation of RNase H; or
- ii. an RNAi agent capable of reducing the amount of PLN nucleic acid through the activation of RISC/Ago2.

152. The antisense agent of any of claims 149-151, comprising a cell-targeting moiety.

153. A pharmaceutical composition comprising the oligomeric compound of any of claims 1-80 or 108, the modified oligonucleotide of any of claims 81-101, the population of any of claims 102-107, the oligomeric duplex of any of claims 109-148, or the antisense agent of any of claims 149-152, and a pharmaceutically acceptable diluent or carrier.

154. The pharmaceutical composition of claim 153, wherein the pharmaceutically acceptable diluent is water or phosphate-buffered saline.

155. The pharmaceutical composition of claim 154, wherein the pharmaceutical composition consists essentially of the oligomeric compound, the modified oligonucleotide, the population, the oligomeric duplex, or the antisense agent, and water or phosphate-buffered saline.

~~156. — A method comprising administering to a subject the oligomeric compound of any of claims 1-80 or 108, the modified oligonucleotide of any of claims 81-101, the population of any of claims 102-107, the oligomeric duplex of any of claims 109-148, the antisense agent of any of claims 149-152, or the pharmaceutical composition of any of claims 153-155.~~

~~157. — A method of treating a disease associated with PLN comprising administering to a subject having a disease associated with PLN a therapeutically effective amount of the oligomeric compound of any of claims 1-80 or 108, the modified oligonucleotide of any of claims 81-101, the population of any of claims 102-107, the oligomeric duplex of any of claims 109-148, the antisense agent of any of claims 149-152, or the pharmaceutical composition of any of claims 153-155; thereby treating the disease associated with PLN.~~

~~158. — The method of claim 157, wherein the disease associated with PLN is cardiomyopathy, heart failure, or arrhythmia.~~

- ~~159. The method of claim 158, wherein the cardiomyopathy is genetic cardiomyopathy.~~
- ~~160. The method of claim 159, wherein the genetic cardiomyopathy is associated with p.Arg14del, Arg9Cys (R9C), or Arg25Cys (R25C) genetic mutations.~~
- ~~161. The method of claim 158, wherein the cardiomyopathy is dilated cardiomyopathy (DCM).~~
- ~~162. The method of claim 161, wherein the DCM is genetic DCM.~~
- ~~163. The method of claim 162, wherein the genetic DCM is associated with TTN, LMNA, RBM20, SCN5A, MYH7, TNNT2, and TPM1 mutations.~~
- ~~164. The method of claim 161, wherein the DCM is arrhythmogenic DCM.~~
- ~~165. The method of claim 158, wherein the heart failure is heart failure with preserved ejection fraction (HFpEF), heart failure with reduced ejection fraction (HFrEF), acute heart failure, or worsening of chronic heart failure.~~
- ~~166. The method of claim 158, wherein the arrhythmia is ventricular tachycardia (Vtac) or ventricular fibrillation (Vfib).~~
- ~~167. The method of any of claims 158-166, wherein administering the oligomeric compound of any of claims 1-80 or 108, the modified oligonucleotide of any of claims 81-101, the population of any of claims 102-107, the oligomeric duplex of any of claims 109-148, the antisense agent of any of claims 149-152, or the pharmaceutical composition of any of claims 153-155 improves cardiac function, cardiovascular death, cardiac dilation, cardiac fibrosis, low voltage ECG, diastolic calcium uptake, ejection fraction (EF), left ventricular ejection fraction (LVEF), left ventricular end systolic volume (LVESV), left ventricular end diastolic volume (LVEDV), mitral valve flow profile, left ventricle (LV) strain, left ventricle (LV) strain rate, infarct size, heart failure hospitalization, 6 minute walk test (6MWT), the Kansas City Cardiomyopathy Questionnaire Score (KCCQS), heart rate, or heart rhythm in the subject.~~
- ~~168-156. AAn in vitro or ex vivo~~ method of reducing expression of PLN in a cell comprising contacting the cell with the oligomeric compound of any of claims 1-80 or 108, the modified oligonucleotide of any of claims 81-101, the population of any of claims 102-107, the oligomeric duplex of any of claims 109-148, the antisense agent of any of claims 149-152, or the pharmaceutical composition of any of claims 153-155.
- ~~169-157. The in vitro or ex vivo~~ method of claim ~~156~~168, wherein the cell is a heart cell.
- ~~170-158. Use of the The~~ oligomeric compound of any of claims 1-80 or 108, the modified oligonucleotide of any of claims 81-101, the population of any of claims 102-107, the oligomeric duplex of any of claims 109-148, the antisense agent of any of claims 149-152, or the pharmaceutical composition of any of claims 153-155 for use as a medicament~~treating a disease associated with PLN.~~
- ~~171-159. Use of the~~ oligomeric compound of any of claims 1-80 or 108, the modified oligonucleotide of any of claims 81-101, the population of any of claims 102-107, the oligomeric duplex of any of claims 109-148, the antisense agent of any of claims 149-152, or the pharmaceutical composition of any of claims 153-155 in the manufacture of a medicament for treating a disease associated with PLN.
- ~~172-160. The use of claim 159~~170 ~~or 171,~~ wherein the disease associated with PLN is cardiomyopathy, heart failure, or arrhythmia.
- ~~173-161. The use of claim 160~~172, wherein the cardiomyopathy is genetic cardiomyopathy.

~~174,162.~~ The use of claim ~~161173~~, wherein the genetic cardiomyopathy is associated with p.Arg14del, Arg9Cys (R9C), or Arg25Cys (R25C) genetic mutations.

~~175,163.~~ The use of claim ~~160172~~, wherein the cardiomyopathy is dilated cardiomyopathy (DCM).

~~176,164.~~ The use of claim ~~163175~~, wherein the DCM is genetic DCM.

~~177,165.~~ The use of claim ~~164176~~, wherein the genetic DCM is associated with TTN, LMNA, RBM20, SCN5A, MYH7, TNNT2, and TPM1 mutations.

~~178,166.~~ The use of claim ~~163175~~, wherein the DCM is arrhythmogenic DCM.

~~179,167.~~ The use of claim ~~160172~~, wherein the heart failure is heart failure with preserved ejection fraction (HFpEF), heart failure with reduced ejection fraction (HFrEF), acute heart failure, or worsening of chronic heart failure.

~~180,168.~~ The use of claim ~~160172~~, wherein the arrhythmia is ventricular tachycardia (Vtac) or ventricular fibrillation (Vfib).