

CLAIMS:

- ~~1. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides wherein the nucleobase sequence of the modified oligonucleotide is at least 90% complementary to an equal length portion of a FXII RNA, and wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.~~
- ~~2. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising at least 12, 13, 14, 15, 16, 17, 18, 19, or 20 contiguous nucleobases of any of SEQ ID NOs: 20-5042.~~
- ~~3. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising at least 12, 13, 14, 15, 16, 17, or 18 contiguous nucleobases of any of SEQ ID NOs: 3379 and 5006.~~
- ~~4. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 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 1,899-1,979 of SEQ ID NO: 1; or
an equal length portion of nucleobases 2,004-2,045 of SEQ ID NO: 1.~~
- ~~5. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 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:

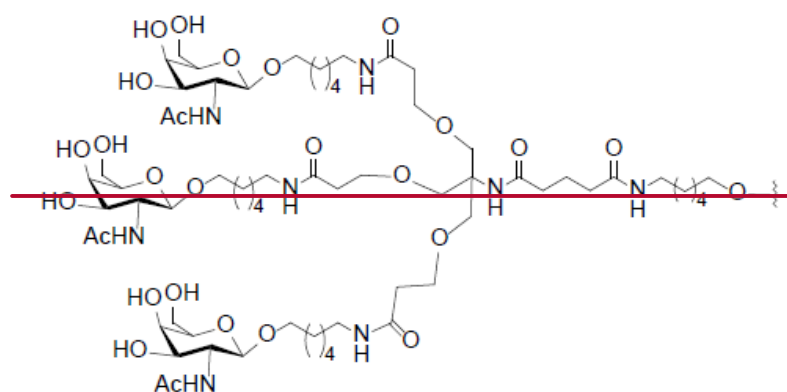
SEQ ID NOs: 92, 156, 270, 271, 345, 346, 420, 421, 496, 497, 571, 572, 653, 654, 728, 729, 802, 803, 877, 951, 1028, 1103, 1179, 1253, 1330, 1407, 1484, 1560, 1636, 1710, 1711, 1784, 1859, 1860, 1934, 1935, 2008, 2009, 2084, 2085, 2158, 2232, 2233, 2307, 2308, 2393, 2394, 2395, 2396, 2397, 2398, 2461, 2537, 2538, 2614, 2615, 2691, 2692, 2768, 2769, 2845, 2846, 2921, 2922, 2997, 2998, 3073, 3074, 3144, 3145, 3226, 3227, 3303, 3304, 3379, 3380, 3455, 3456, 3531, 3607, 3683, 3759, 3835, 3911, 4948, 4949, 4954, 4955, 4956, 4957, 4961, 4965, 4966, 4967, 4971, 4972, 4976, 4994, 4995, 4996, 4997, 4998, 4999, 5024, 5025, 5026, 5027, 5028, and 5029; or

SEQ ID NOs: 95, 159, 162, 163, 164, 165, 347, 422, 498, 573, 953, 1030, 1105, 1255, 1332, 1409, 1486, 1562, 2309, 2463, 2540, 2617, 2694, 2771, 2848, 2924, 3000, 3076, 3147, 3229, 3306, 3382, 3457, 3533, 3609, 3685, 3761, 3837, 3913, 5000, 5001, 5002, 5003, 5004, 5005, 5006, 5031, 5032, 5033, 5034, 5035, 5036, and 5037.~~

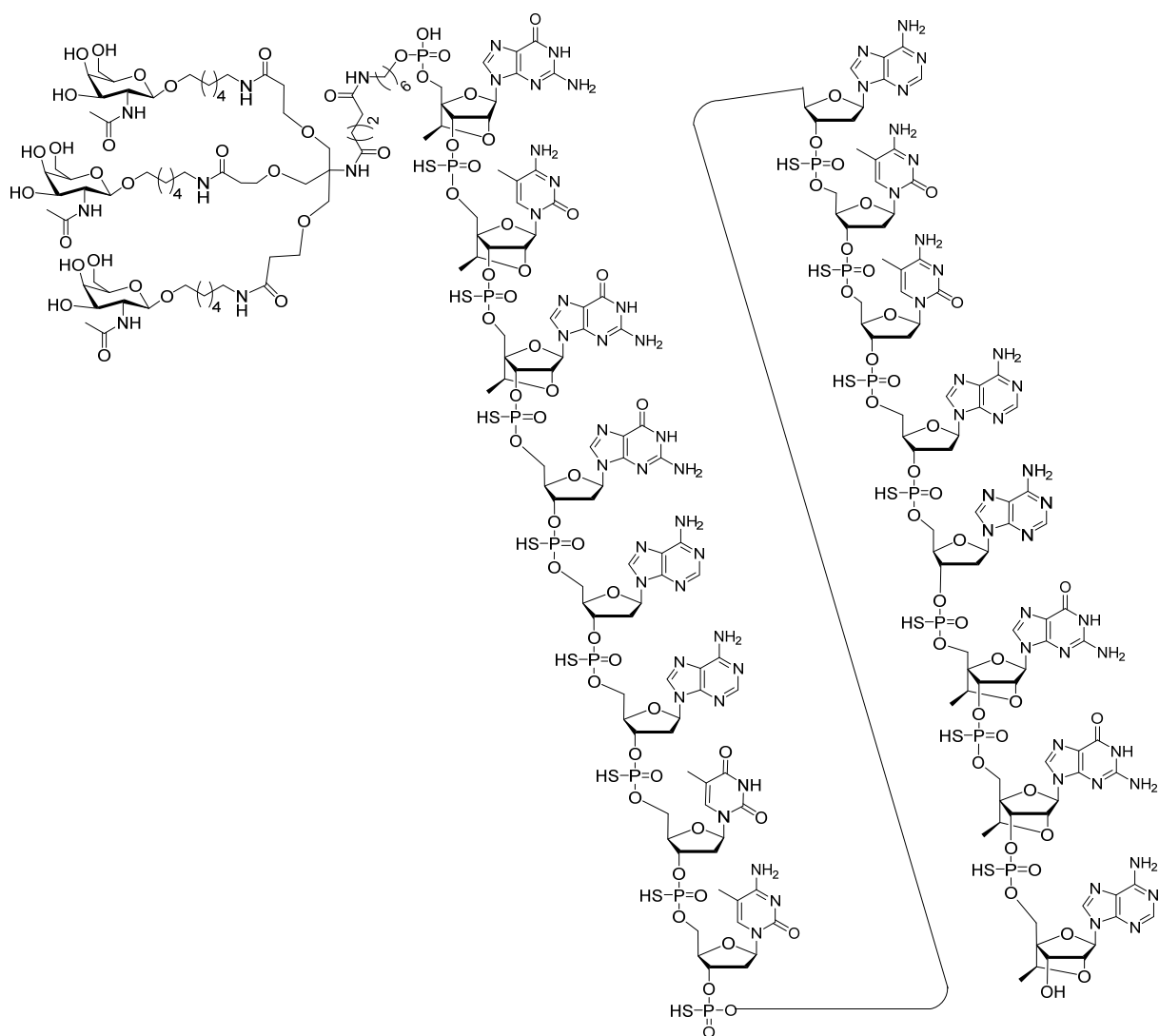
- ~~6. The oligomeric compound of any of claims 1-5, wherein the modified oligonucleotide has a nucleobase sequence that is at least 80%, 85%, 90%, 95%, or 100% complementary to the nucleobase sequence of any one of SEQ ID NOS: 1-4 when measured across the entire nucleobase sequence of the modified oligonucleotide.~~
- ~~7. The oligomeric compound of any of claims 1-6, wherein the modified oligonucleotide comprises at least one modified nucleoside.~~
- ~~8. The oligomeric compound of claim 7, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a modified sugar moiety.~~
- ~~9. The oligomeric compound of claim 8, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a bicyclic sugar moiety.~~
- ~~10. The oligomeric compound of claim 9, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a bicyclic sugar moiety having a 2'-4' bridge, wherein the 2'-4' bridge is selected from —O—CH₂—; and —O—CH(CH₃)—.~~
- ~~11. The oligomeric compound of any of claims 8-10, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a non-bicyclic modified sugar moiety.~~
- ~~12. The oligomeric compound of claim 11, wherein the non-bicyclic modified sugar moiety is a 2'-MOE sugar moiety or 2'-OMe sugar moiety.~~
- ~~13. The oligomeric compound of any of claims 7-8, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a sugar surrogate.~~
- ~~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 has a sugar motif comprising:
 - ~~a 5'-region consisting of 1-6 linked 5'-region nucleosides;~~
 - ~~a central region consisting of 6-10 linked central region nucleosides; and~~
 - ~~a 3'-region consisting of 1-6 linked 3'-region nucleosides,~~
 - ~~wherein each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety and each of the central region nucleosides comprises a 2'-β-D-deoxyribosyl sugar moiety.~~~~
- ~~16. The oligomeric compound of claim 15, wherein
 - ~~the 5'-region consists of 3 linked 5'-region nucleosides;~~~~

- the central region consists of 10 linked central region nucleosides; and
the 3' region consists of 3 linked 3' region nucleosides; and
wherein each of the 5' region nucleosides and each of the 3' region nucleosides comprises a cEt
modified sugar moiety.
17. The oligomeric compound of any of claims 1-16, wherein the modified oligonucleotide comprises at least
one modified internucleoside linkage.
18. The oligomeric compound of claim 17, wherein each internucleoside linkage of the modified
oligonucleotide is a modified internucleoside linkage.
19. The oligomeric compound of claim 17 or 18, wherein each internucleoside linkage is a phosphorothioate
internucleoside linkage.
20. The oligomeric compound of claim 17 or 18, wherein the modified oligonucleotide comprises at least one
phosphodiester internucleoside linkage.
21. The oligomeric compound of claim 17, wherein each internucleoside linkage is independently selected
from a phosphodiester internucleoside linkage or a phosphorothioate internucleoside linkage.
22. The oligomeric compound of any of claims 1-21, wherein the modified oligonucleotide comprises a
modified nucleobase.
23. The oligomeric compound of claim 22, wherein the modified nucleobase is a 5-methyl cytosine.
24. The oligomeric compound of any of claims 1-23, wherein the modified oligonucleotide consists of 12-30,
12-22, 12-20, 14-18, 14-20, 15-17, 15-25, 16-20, 18-22 or 18-20 linked nucleosides.
25. The oligomeric compound of any of claims 1-23, wherein the modified oligonucleotide consists of 16
linked nucleosides.
26. The oligomeric compound of any of claims 1-25, consisting of the modified oligonucleotide.
27. The oligomeric compound of any of claims 1-25, comprising a conjugate group comprising a conjugate
moiety and a conjugate linker.
28. The oligomeric compound of claim 27, wherein the conjugate linker consists of a single bond.
29. The oligomeric compound of claim 27, wherein the conjugate linker is cleavable.
30. The oligomeric compound of claim 27, wherein the conjugate linker comprises 1-3 linker nucleosides.

- ~~31. The oligomeric compound of 27, wherein the oligomeric compound does not comprise a linker-nucleoside.~~
- ~~32. The oligomeric compound of claim 27, wherein the conjugate linker is a phosphate.~~
- ~~33. The oligomeric compound of any of claims 29-32, wherein the conjugate group is attached to the modified oligonucleotide at the 5' end of the modified oligonucleotide.~~
- ~~34. The oligomeric compound of any of claims 29-32, wherein the conjugate group is attached to the modified oligonucleotide at the 3' end of the modified oligonucleotide.~~
- ~~35. The oligomeric compound of any of claims 1-34, comprising a terminal group.~~
- ~~36. The oligomeric compound of any one of claims 1-35, wherein the conjugate group comprises a GalNAc moiety.~~
- ~~37. The oligomeric compound of anyone of claims 1-36, wherein the conjugate group comprises a cell-targeting moiety, a conjugate linker and a cleavable moiety, and wherein the cell-targeting moiety and the conjugate linker together have the following chemical structure:~~



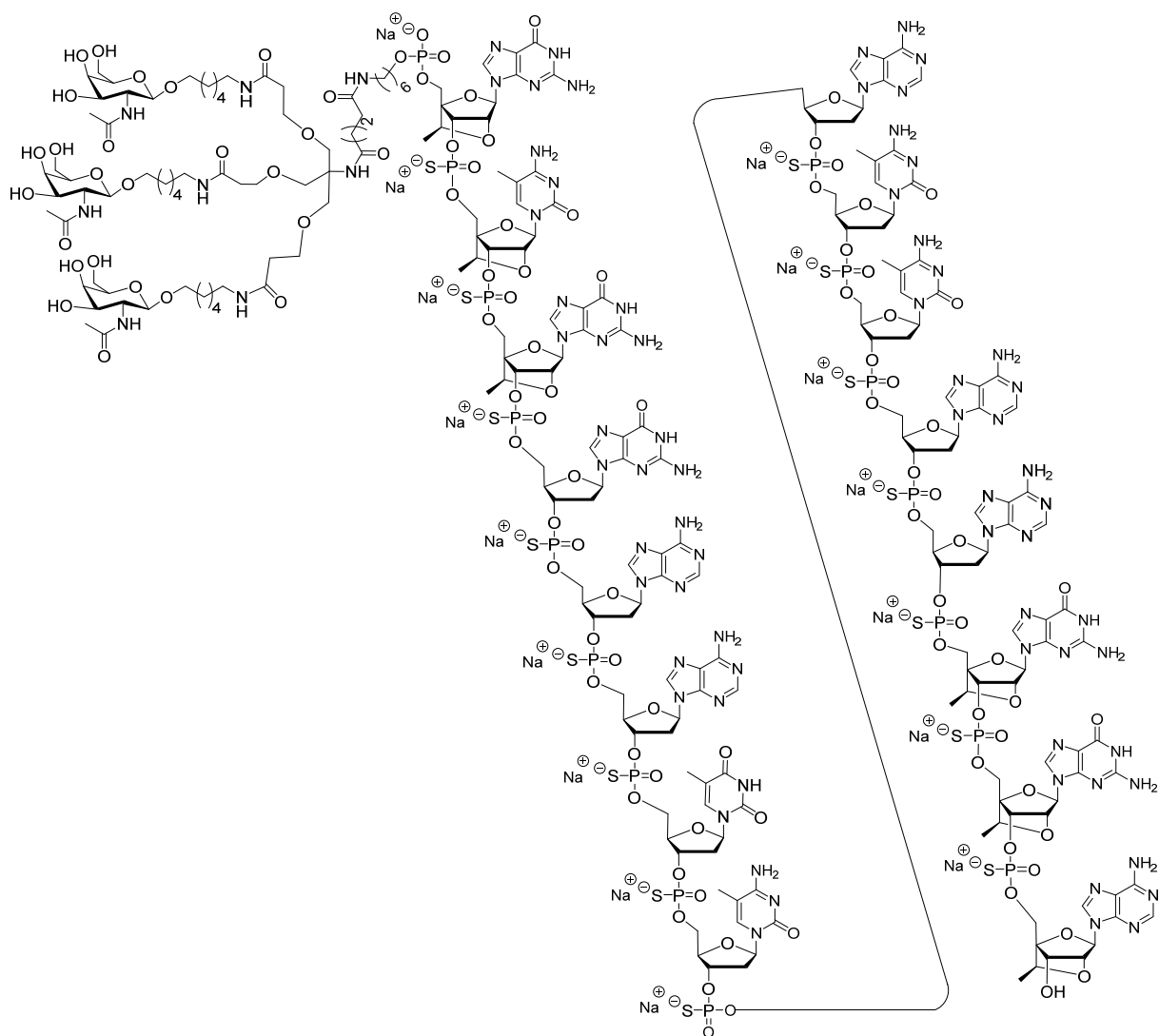
- ~~38. The oligomeric compound of any of claims 1-37 wherein the modified oligonucleotide is a single-stranded modified oligonucleotide.~~
139. An oligomeric compound according to the following chemical structure:



(SEQ ID NO: 3379), or a salt thereof.

~~40. The oligomeric compound of claim 39, which is the sodium salt or the potassium salt.~~

~~241.~~ An oligomeric compound according to the following chemical structure:



(SEQ ID NO: 3379).

3. An oligomeric compound comprising a modified oligonucleotide and a conjugate group according to the following chemical notation: (THA- GalNAc₃)_o Gks ^mCks Gks Gds Ads Ads Tds ^mCds Ads ^mCds ^mCds Ads Ads Gks Gks Ak (SEQ ID NO: 3379), wherein:

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

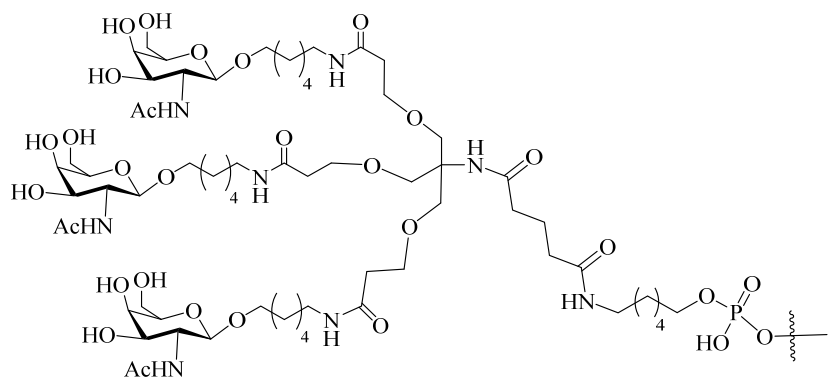
T = a thymine nucleobase,

k = a cEt modified sugar moiety,

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

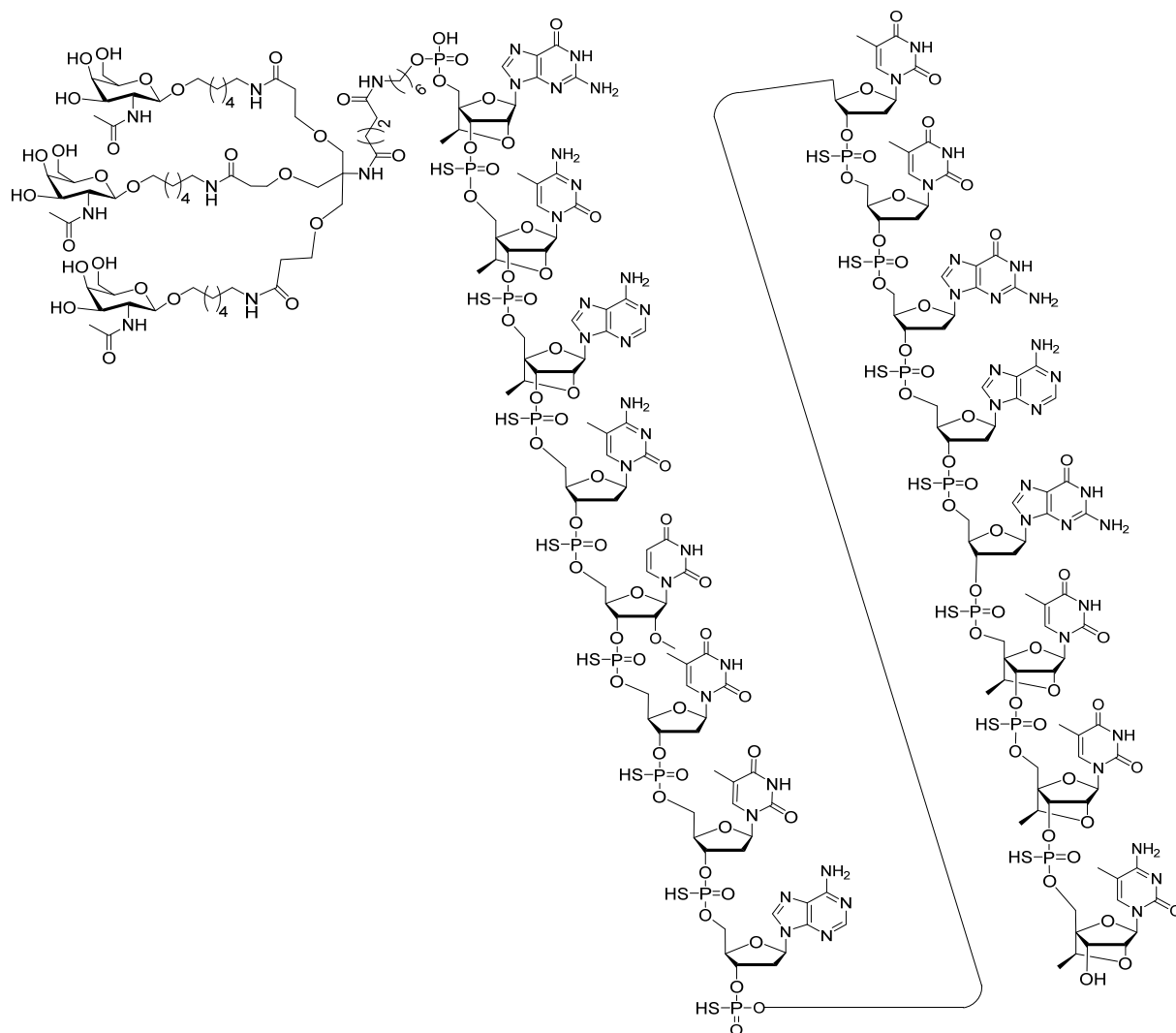
s = a phosphorothioate internucleoside linkage, and

(THA-GalNAc₃)_o =



4. The oligomeric compound of claim 1, which is the sodium salt or the potassium salt.

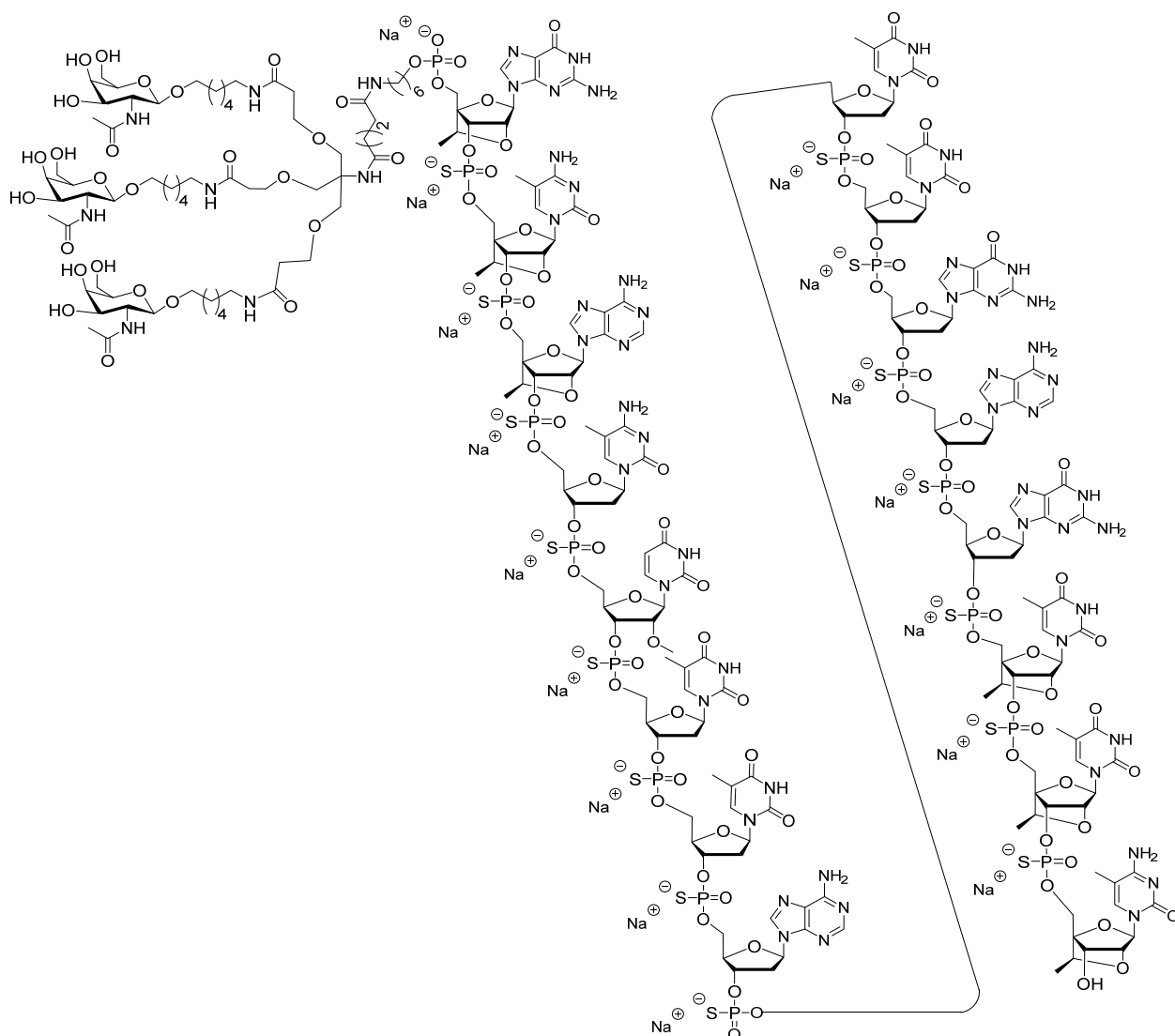
542. An oligomeric compound according to the following chemical structure:



(SEQ ID NO: 5006), or a salt thereof.

~~43. The oligomeric compound of claim 42, which is the sodium salt or the potassium salt.~~

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



(SEQ ID NO: 5006).

45. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: (THA-GalNAc₃)_o-Gks-^mCks-Gks-Gds-Ads-Ads-Tds-^mCds-Ads-^mCds-^mCds-Ads-Ads-Gks-Gks-Ak (SEQ ID NO: 3379), wherein:

—A = an adenine nucleobase;

—^mC = a 5-methyl cytosine nucleobase;

—G = a guanine nucleobase;

—T = a thymine nucleobase;

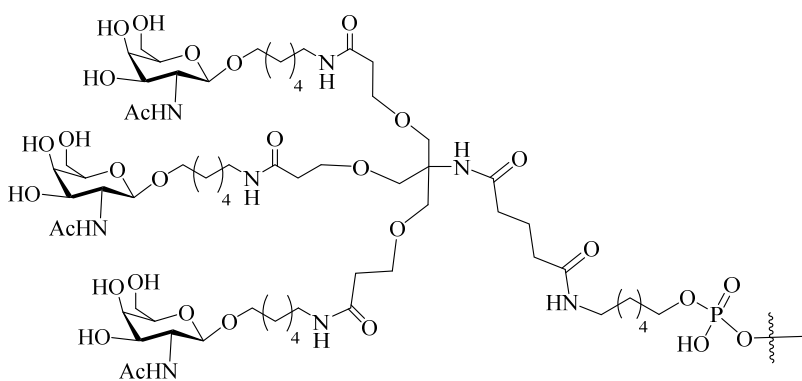
—k = a cEt modified sugar moiety,
 —d = a 2'-β-D-deoxyribosyl sugar moiety,
 —o = a phosphodiester linkage, and
 —s = a phosphorothioate internucleoside linkage.

7

746. An oligomeric compound comprising a modified oligonucleotide and a conjugate group according to the following chemical notation: (THA- GalNAc₃)_o Gks ^mCks Aks ^mCds Uys Tds Tds Ads Tds Tds Gds Ads Gds Tks Tks mCk (SEQ ID NO: 5006), wherein:

A = an adenine nucleobase,
 mC = a 5-methyl cytosine nucleobase,
 G = a guanine nucleobase,
 T = a thymine nucleobase,
 U = a uracil nucleobase,
 k = a cEt modified sugar moiety,
 y = a 2'-O-methyl modified ribosyl sugar moiety,
 -d = a 2'-β-D-deoxyribosyl sugar moiety,
~~-o = a phosphodiester linkage, and~~

-s = a phosphorothioate internucleoside linkage, and
(THA- GalNAc₃)_o =



8. The oligomeric compound of claim 5, which is the sodium salt or the potassium salt.

- ~~47. 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 to 37.~~
- ~~48. The oligomeric duplex of claim 47, 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.~~
- ~~49. The oligomeric duplex of claim 47 or 48, wherein the modified oligonucleotide of the first oligomeric compound comprises a 5'-stabilized phosphate group.~~
- ~~50. The oligomeric duplex of claim 49, wherein the stabilized phosphate group comprises a cyclopropyl phosphonate or a vinyl phosphonate.~~
- ~~51. The oligomeric duplex of any of claims 47 to 50, wherein at least one nucleoside of the second modified oligonucleotide comprises a modified sugar moiety.~~
- ~~52. The oligomeric duplex of claim 51, wherein the modified sugar moiety of the second modified oligonucleotide comprises a bicyclic sugar moiety.~~
- ~~53. The oligomeric duplex of claim 52, wherein the bicyclic sugar moiety of the second modified oligonucleotide comprises a 2'-4' bridge selected from $\text{O}-\text{CH}_2-$; and $\text{O}-\text{CH}(\text{CH}_3)-$.~~
- ~~54. The oligomeric duplex of claim 51, wherein the modified sugar moiety of the second modified oligonucleotide comprises a non-bicyclic modified sugar moiety.~~
- ~~55. The oligomeric duplex of claim 54, 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.~~
- ~~56. The oligomeric duplex of any of claims 47 to 55, wherein at least one nucleoside of the second modified oligonucleotide comprises a sugar surrogate.~~
- ~~57. The oligomeric duplex of any of claims 47 to 56, wherein at least one internucleoside linkage of the second modified oligonucleotide is a modified internucleoside linkage.~~
- ~~58. The oligomeric duplex of claim 57, wherein at least one modified internucleoside linkage of the second modified oligonucleotide is a phosphorothioate internucleoside linkage.~~
- ~~59. The oligomeric duplex of any of claims 47 to 58, wherein at least one internucleoside linkage of the second modified oligonucleotide is a phosphodiester internucleoside linkage.~~

- ~~60. The oligomeric duplex of any of claims 47 to 59, wherein each internucleoside linkage of the second modified oligonucleotide is independently selected from a phosphodiester or a phosphorothioate internucleoside linkage.~~
- ~~61. The oligomeric duplex of any of claims 47 to 60, wherein the second modified oligonucleotide comprises at least one modified nucleobase.~~
- ~~62. The oligomeric duplex of claim 61, wherein the modified nucleobase of the second modified oligonucleotide is 5-methylcytosine.~~
- ~~63. The oligomeric duplex of any of claims 47 to 62, wherein the second modified oligonucleotide comprises a conjugate group.~~
- ~~64. The oligomeric duplex of claim 63, wherein the conjugate group comprises a conjugate linker and a conjugate moiety.~~
- ~~65. The oligomeric duplex of claim 63 or 64, wherein the conjugate group is attached to the second modified oligonucleotide at the 5'-end of the second modified oligonucleotide.~~
- ~~66. The oligomeric duplex of claim 63 or 64, wherein the conjugate group is attached to the second modified oligonucleotide at the 3'-end of the second modified oligonucleotide.~~
- ~~67. The oligomeric duplex of any of claims 63 to 66, wherein the conjugate group comprises a GalNAc₃.~~
- ~~68. The oligomeric duplex of any of claims 47 to 62, wherein the second modified oligonucleotide comprises a terminal group.~~
- ~~69. The oligomeric duplex of claim 68, wherein the terminal group is an abasic sugar moiety.~~
- ~~70. The oligomeric duplex of any of claims 47 to 69, 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.~~
- ~~71. An antisense compound comprising or consisting of an oligomeric compound of any of claims 1-37 or an oligomeric duplex of claims 47-70.~~

- ~~72. A chirally enriched population of oligomeric compounds of any of claims 1-46, wherein the population is enriched for oligomeric compounds comprising at least one particular phosphorothioate internucleoside linkage having a particular stereochemical configuration.~~
- ~~73. The chirally enriched population of claim 72, wherein the population is enriched for oligomeric compounds comprising at least one particular phosphorothioate internucleoside linkage having the (*Sp*) configuration.~~
- ~~74. The chirally enriched population of claim 72, wherein the population is enriched for oligomeric compounds comprising at least one particular phosphorothioate internucleoside linkage having the (*Rp*) configuration.~~
- ~~75. The chirally enriched population of claim 72, wherein the population is enriched for oligomeric compounds having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage~~
- ~~76. The chirally enriched population of claim 72, wherein the population is enriched for oligomeric compounds having the (*Sp*) configuration at each phosphorothioate internucleoside linkage.~~
- ~~77. The chirally enriched population of claim 72, wherein the population is enriched for oligomeric compounds having the (*Rp*) configuration at each phosphorothioate internucleoside linkage.~~
- ~~78. The chirally enriched population of claim 72, 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.~~
- ~~79. The chirally enriched population of any one of claims 72-74, 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.~~
980. A population of oligomeric compounds of any one of claims 1-~~468~~, wherein all of the phosphorothioate internucleoside linkages ~~of the oligomeric compounds~~ are stereorandom.
1081. A pharmaceutical composition comprising ~~the~~an oligomeric compound of any one of claims 1-~~846~~, ~~an oligomeric duplex of any one of claims 47-70, an antisense compound of claim 71, or the~~a population of oligomeric compounds ~~of any one of claims 72-809~~; and a pharmaceutically acceptable ~~carrier or~~ diluent.
1182. The pharmaceutical composition of claim 1081, wherein the pharmaceutically acceptable diluent is sterile saline or sterile waterphosphate buffered saline.

1283. The pharmaceutical composition of claim 1182, wherein:

(i) the pharmaceutical composition consists ~~or consists essentially~~ of the ~~modified oligonucleotide~~oligomeric compound and sterile saline or sterile water~~phosphate buffered saline;~~ or

(ii) the pharmaceutical composition consists essentially of the oligomeric compound and sterile saline or sterile water.~~84. A method comprising administering to a subject a pharmaceutical composition of any of claims 81-83.~~

13. The oligomeric compound of any of claims 1-8, the population of oligomeric compounds of claim 9, or the pharmaceutical composition of any one of claims 10-12, for use in therapy.

8514. Use of the oligomeric compound of any of claims 1-8, the population of oligomeric compounds of claim 9, or the pharmaceutical composition of any one of claims 10-12, in the manufacture of a medicament for ~~A method of~~ ameliorating or preventing a thromboembolic condition, ~~comprising administering to a subject in need thereof wherein~~ a therapeutically effective amount of the oligomeric compound, the population of oligomeric compounds, or the pharmaceutical composition ~~according to any of claims 81-83~~ is to be administered to a subject in need thereof.

1586. The ~~method-use~~ of claim 1485, wherein the thromboembolic condition is selected from myocardial infarction (MI), stroke, limb ischemia and necrosis, venous thromboembolism (VTE), deep vein thrombosis (DVT), and pulmonary embolism (PE).

8716. The ~~use~~method of claim 14 or claim 15~~any of claims 84-86~~, wherein at least one symptom of the thromboembolic condition is ameliorated.

1788. The ~~method-use~~ of claim 1687, wherein the symptom is pain, shortness of breath, heart burn, cold sweat, fatigue, lightheadedness, dizziness, swelling, cramping, and death.

1889. The ~~method-use~~ of any one of claims 84-8814-17, further comprising identifying the subject as having the thromboembolic condition or as having a risk factor for having the thromboembolic condition.

9019. The ~~use~~method of claim 1889, wherein the risk factor is surgery, malignancy, pregnancy, aging, use of oral contraceptives, immobility, sepsis, a mechanical heart valve, valvular heart disease, atrial fibrillation, atherosclerosis, antiphospholipid syndrome, an inherited clotting disorder, or an acquired prothrombotic clotting disorder.

2094. Use of the oligomeric compound of any of claims 1-8, the population of oligomeric compounds of claim 9, or the pharmaceutical composition of any one of claims 10-12, in the manufacture of a

medicament for A method of ameliorating or preventing hereditary angioedema, comprising administering to a subject in need thereof wherein a therapeutically effective amount of the oligomeric compound, the population of oligomeric compounds, or the a pharmaceutical composition according to any of claims 81-83 is to be administered to a subject.

92. ~~The oligomeric compound of any of claims 1-46, the oligomeric duplex of any one of claims 47-70, the antisense compound of claim 71, or the population of any one of claims 72-80, for use in therapy.~~

93. ~~The oligomeric compound of any of claims 1-46, the oligomeric duplex of any one of claims 47-70, the antisense compound of claim 71, or the population of any one of claims 72-80, for use in ameliorating or preventing a thromboembolic condition.~~

94. ~~The oligomeric compound of any of claims 1-46, the oligomeric duplex of any one of claims 47-70, the antisense compound of claim 71, or the population of any one of claims 72-80, for use in ameliorating or preventing hereditary angioedema.~~