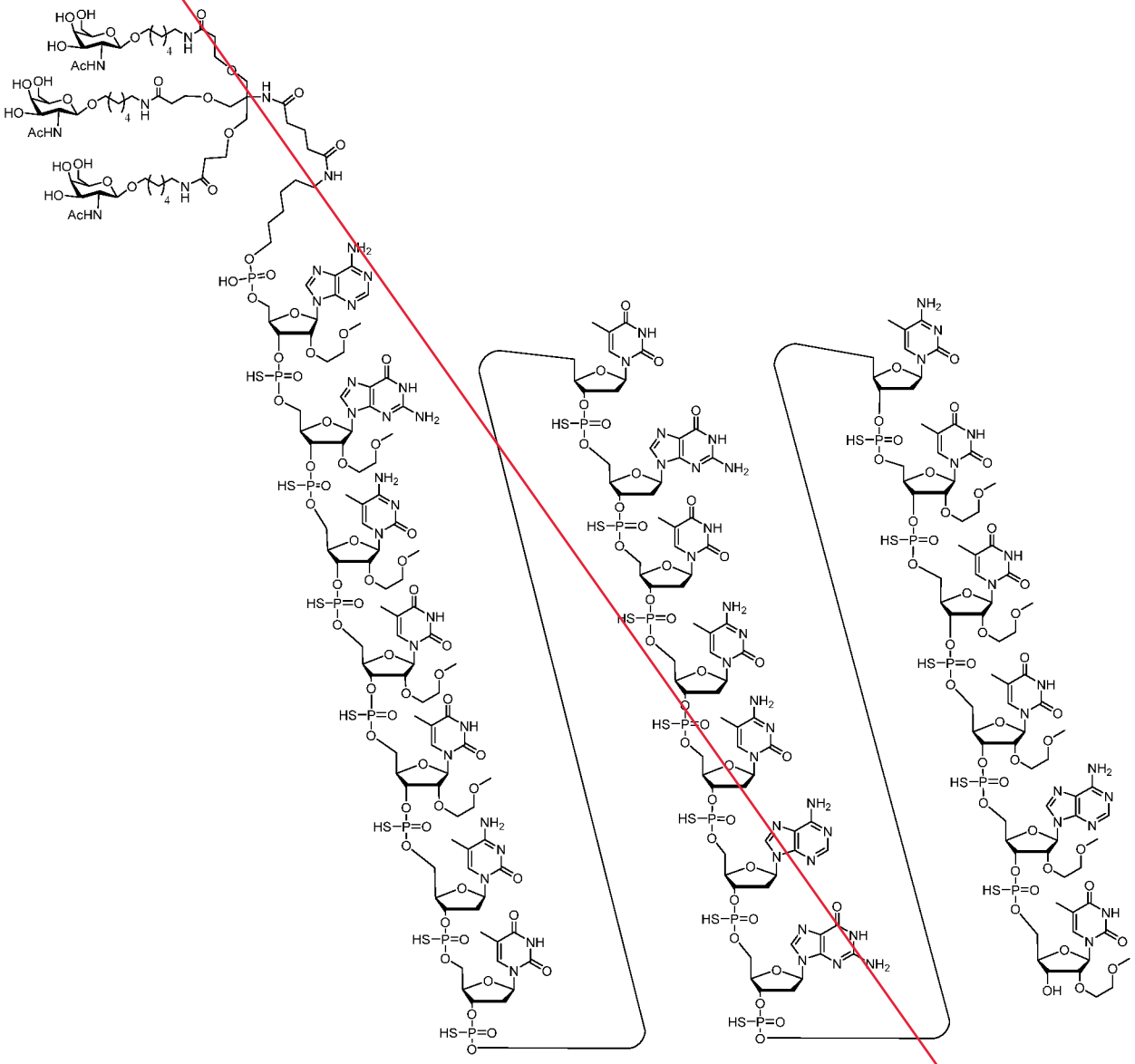
CLAIMS:

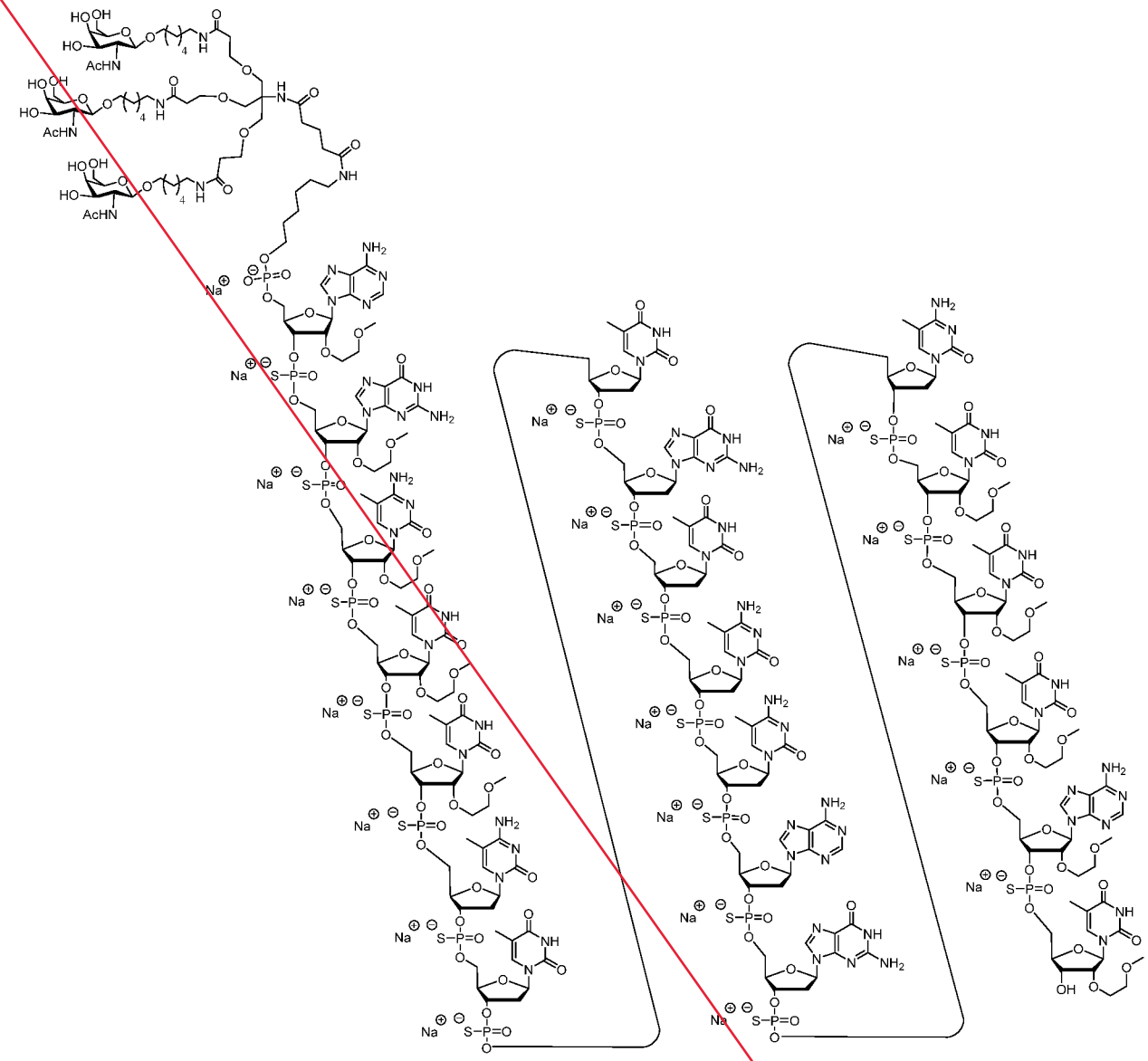
1. A method of ameliorating Familial Chylomicronemia Syndrome (FCS) in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of a compound according to the following chemical structure:



(SEQ ID NO: 3), or a salt thereof.

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

3. A method of ameliorating FCS in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of a compound according to the following chemical structure:



(SEQ ID NO: 3).

4. A method of ameliorating FCS in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of a compound, wherein the compound comprises a modified oligonucleotide having the following chemical notation (5' to 3'):

$A_{es}G_{es}{}^{m}C_{es}T_{es}T_{es}{}^{m}C_{ds}T_{ds}T_{ds}G_{ds}T_{ds}{}^{m}C_{ds}{}^{m}C_{ds}A_{ds}G_{ds}{}^{m}C_{ds}T_{es}T_{es}T_{es}A_{es}T_{e}$ (SEQ ID NO: 3); wherein,

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

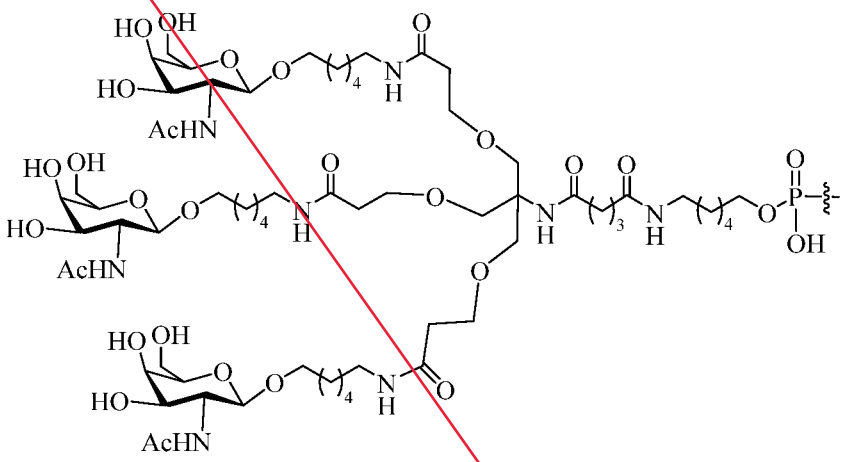
T = a thymine nucleobase,

e = a 2'- $OCH_2CH_2OCH_3$ modified ribosyl sugar moiety,

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

s = a phosphorothioate internucleoside linkage,

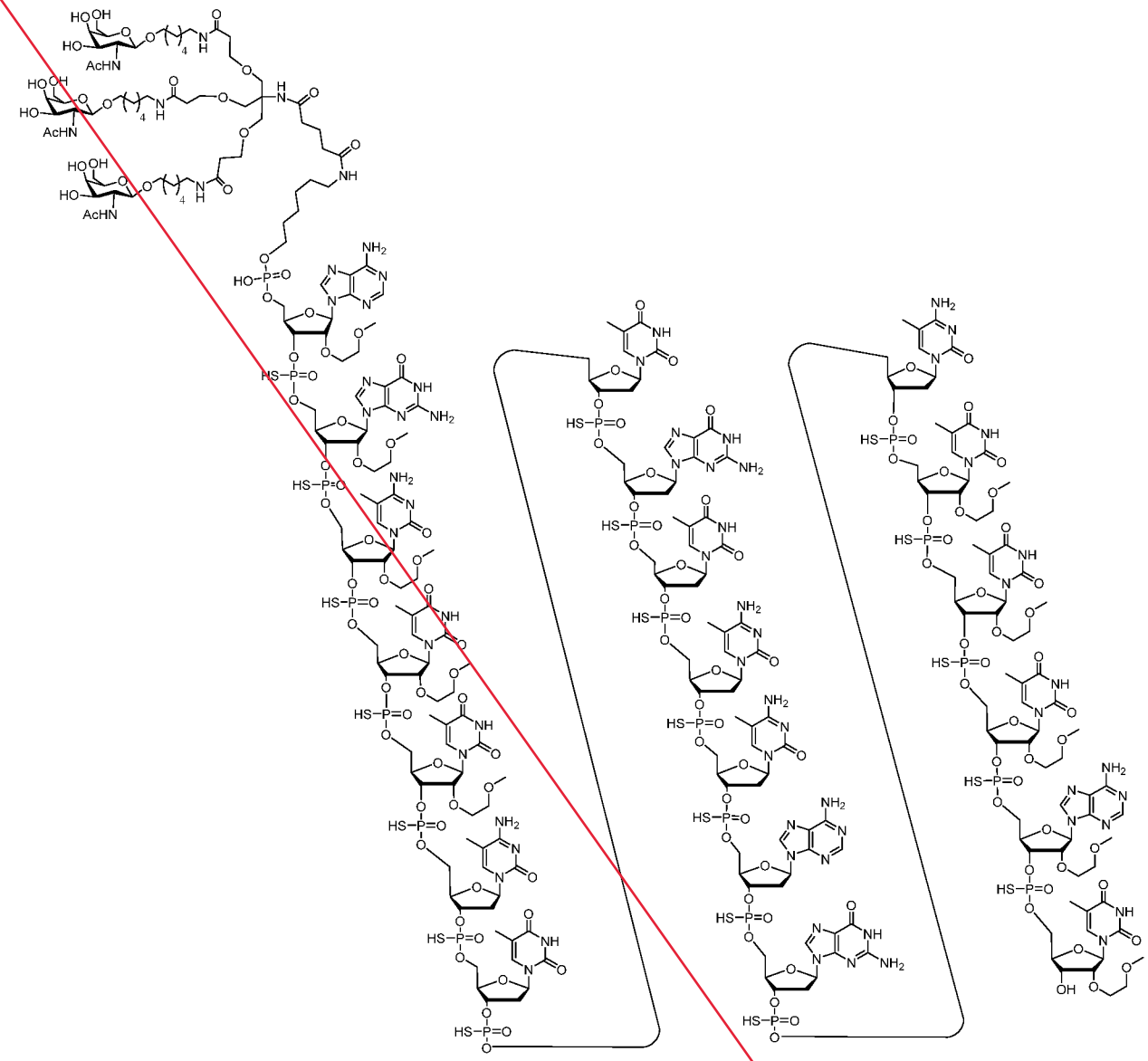
and wherein the modified oligonucleotide has a 5'-trishexylamino-(THA)-C_6GalNAc$_3$ endcap, represented by the structure below, wherein the phosphate group is attached to the 5'-oxygen atom of the 5'-nucleoside:



5. The method of any one of claims 1-4, wherein at least one symptom of FCS is ameliorated.

6. The method of claim 5, wherein the at least one symptom comprises severe elevations in chylomicrons and extremely elevated TG levels (always reaching well above 1000 mg/dL and not infrequently rising as high as 10,000 mg/dL or more) with episodes of abdominal pain, physical fatigue, difficulty thinking, diarrhea, recurrent acute pancreatitis, eruptive cutaneous xanthomata, and hepatosplenomegaly or a combination thereof.

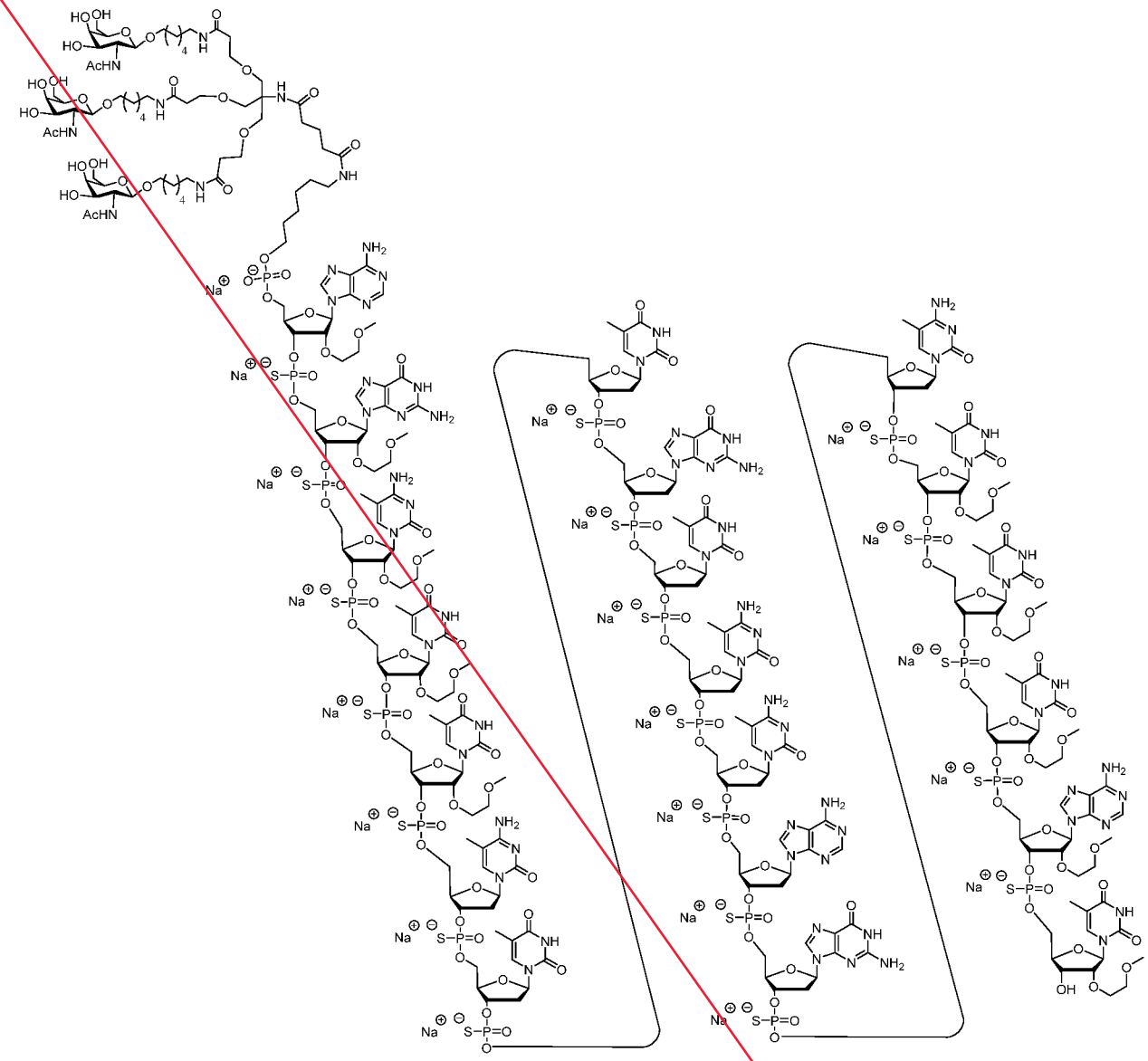
7. A method of reducing APOCIII RNA in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of a compound according to the following chemical structure:



(SEQ ID NO: 3), or a salt thereof.

8. The compound of claim 7, which is the sodium salt or the potassium salt.

9. A method of reducing APOCIII RNA in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of a compound according to the following chemical structure:



(SEQ ID NO: 3).

10. A method of reducing APOCIII RNA in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of a compound, wherein the compound comprises a modified oligonucleotide having the following chemical notation (5' to 3'):

$A_{es}G_{es}{}^{m}C_{es}T_{es}T_{es}{}^{m}C_{ds}T_{ds}T_{ds}G_{ds}T_{ds}{}^{m}C_{ds}{}^{m}C_{ds}A_{ds}G_{ds}{}^{m}C_{ds}T_{es}T_{es}T_{es}A_{es}T_{e}$ (SEQ ID NO: 3); wherein,

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

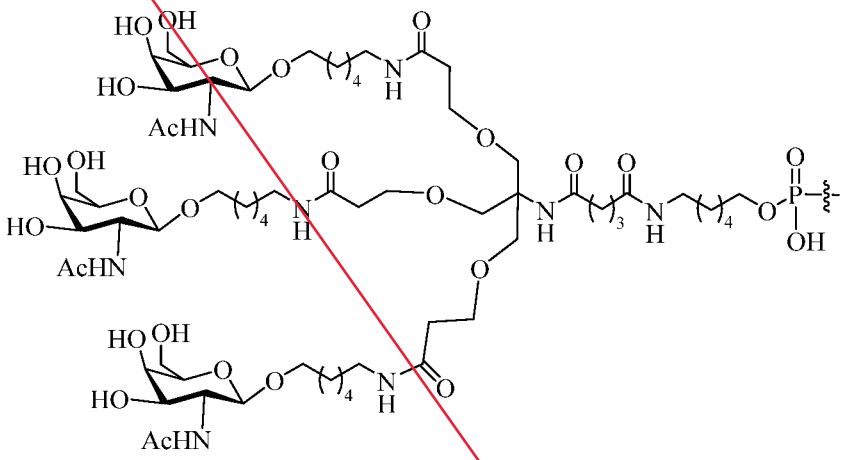
T = a thymine nucleobase,

e = a 2'- $OCH_2CH_2OCH_3$ modified ribosyl sugar moiety,

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

s = a phosphorothioate internucleoside linkage,

and wherein the modified oligonucleotide has a 5'-trishexylamino-(THA)-C_6GalNAc$_3$ endcap, represented by the structure below, wherein the phosphate group is attached to the 5'-oxygen atom of the 5'-nucleoside:



11. The method of any one of claims 1-10, wherein the therapeutically effective amount is 50 mg.

12. The method of any one of claims 1-10, wherein the therapeutically effective amount is 60 mg.

13. The method of any one of claims 1-10, wherein the therapeutically effective amount is 70 mg.

14. The method of any one of claims 1-10, wherein the therapeutically effective amount is 80 mg.

15. The method of any one of claims 1-10, wherein the therapeutically effective amount is any of 40 mg, 45 mg, 50 mg, 55 mg, 60 mg, 65 mg, 70 mg, 75 mg, 80 mg, 85 mg, 90 mg, 95 mg, and 100 mg.

16. The method of any one of claims 1-10, wherein the therapeutically effective amount is any of about 40 mg, about 45 mg, about 50 mg, about 55 mg, about 60 mg, about 65 mg, about 70 mg, about 75 mg, about 80 mg, about 85 mg, about 90 mg, about 95 mg, and about 100 mg.

17. The method of any one of claims 1-10, wherein the therapeutically effective amount is any of 40.0 mg, 40.1 mg, 40.2 mg, 40.3 mg, 40.4 mg, 40.5 mg, 40.6 mg, 40.7 mg, 40.8 mg, 40.9 mg, 41.0 mg, 41.1 mg, 41.2 mg, 41.3 mg, 41.4 mg, 41.5 mg, 41.6 mg, 41.7 mg, 41.8 mg, 41.9 mg, 42.0 mg, 42.1 mg, 42.2 mg, 42.3 mg, 42.4 mg, 42.5 mg, 42.6 mg, 42.7 mg, 42.8 mg, 42.9 mg, 43.0 mg, 43.1 mg, 43.2 mg, 43.3 mg, 43.4 mg, 43.5 mg, 43.6 mg, 43.7 mg, 43.8 mg, 43.9 mg, 44.0 mg, 44.1 mg, 44.2 mg, 44.3 mg, 44.4 mg, 44.5 mg, 44.6 mg, 44.7 mg, 44.8 mg, 44.9 mg, 45.0 mg, 45.1 mg, 45.2 mg, 45.3 mg, 45.4 mg, 45.5 mg, 45.6 mg, 45.7 mg, 45.8 mg, 45.9 mg, 46.0 mg, 46.1 mg, 46.2 mg, 46.3 mg, 46.4 mg, 46.5 mg, 46.6 mg, 46.7 mg, 46.8 mg, 46.9 mg, 47.0 mg, 47.1 mg, 47.2 mg, 47.3 mg, 47.4 mg, 47.5 mg, 47.6 mg, 47.7 mg, 47.8 mg, 47.9 mg, 48.0

mg, 48.1 mg, 48.2 mg, 48.3 mg, 48.4 mg, 48.5 mg, 48.6 mg, 48.7 mg, 48.8 mg, 48.9 mg, 49.0 mg, 49.1 mg, 49.2 mg, 49.3 mg, 49.4 mg, 49.5 mg, 49.6 mg, 49.7 mg, 49.8 mg, 49.9 mg, 50.0 mg, 50.1 mg, 50.2 mg, 50.3 mg, 50.4 mg, 50.5 mg, 50.6 mg, 50.7 mg, 50.8 mg, 50.9 mg, 51.0 mg, 51.1 mg, 51.2 mg, 51.3 mg, 51.4 mg, 51.5 mg, 51.6 mg, 51.7 mg, 51.8 mg, 51.9 mg, 52.0 mg, 52.1 mg, 52.2 mg, 52.3 mg, 52.4 mg, 52.5 mg, 52.6 mg, 52.7 mg, 52.8 mg, 52.9 mg, 53.0 mg, 53.1 mg, 53.2 mg, 53.3 mg. 53.4 mg, 53.5 mg, 53.6 mg, 53.7 mg, 53.8 mg, 53.9 mg, 54.0 mg, 54.1 mg, 54.2 mg, 54.3 mg, 54.4 mg, 54.5 mg, 54.6 mg, 54.7 mg, 54.8 mg, 54.9 mg, 55.0 mg, 50.0 mg, 50.1 mg, 50.2 mg, 50.3 mg, 50.4 mg, 50.5 mg, 50.6 mg, 50.7 mg, 50.8 mg, 50.9 mg, 51.0 mg, 51.1 mg, 51.2 mg, 51.3 mg, 51.4 mg, 51.5 mg, 51.6 mg, 51.7 mg, 51.8 mg, 51.9 mg, 52.0 mg, 52.1 mg, 52.2 mg, 52.3 mg, 52.4 mg, 52.5 mg, 52.6 mg, 52.7 mg, 52.8 mg, 52.9 mg, 53.0 mg, 53.1 mg, 53.2 mg, 53.3 mg. 53.4 mg, 53.5 mg, 53.6 mg, 53.7 mg, 53.8 mg, 53.9 mg, 54.0 mg, 54.1 mg, 54.2 mg, 54.3 mg, 54.4 mg, 54.5 mg, 54.6 mg, 54.7 mg, 54.8 mg, 54.9 mg, 55.0 mg, 55.1 mg, 55.2 mg, 55.3 mg. 55.4 mg, 55.5 mg, 55.6 mg, 55.7 mg, 55.8 mg, 55.9 mg, 55.0 mg, 55.1 mg, 55.2 mg, 55.3 mg, 55.4 mg, 55.5 mg, 55.6 mg, 55.7 mg, 55.8 mg, 55.9 mg, 56.0 mg, 56.1 mg, 56.2 mg, 56.3 mg. 56.4 mg, 56.5 mg, 56.6 mg, 56.7 mg, 56.8 mg, 56.9 mg, 57.0 mg, 57.1 mg, 57.2 mg, 57.3 mg, 57.4 mg, 57.5 mg, 57.6 mg, 57.7 mg, 57.8 mg, 57.9 mg, 58.0 mg, 58.1 mg, 58.2 mg, 58.3 mg. 58.4 mg, 58.5 mg, 58.6 mg, 58.7 mg, 58.8 mg, 58.9 mg, 59.0 mg, 59.1 mg, 59.2 mg, 59.3 mg, 59.4 mg, 59.5 mg, 59.6 mg, 59.7 mg, 59.8 mg, 59.9 mg, 60.0 mg, 60.1 mg, 60.2 mg, 60.3 mg, 60.4 mg, 60.5 mg, 60.6 mg, 60.7 mg, 60.8 mg, 60.9 mg, 61.0 mg, 61.1 mg, 61.2 mg, 61.3 mg, 61.4 mg, 61.5 mg, 61.6 mg, 61.7 mg, 61.8 mg, 61.9 mg, 62.0 mg, 62.1 mg, 62.2 mg, 62.3 mg, 62.4 mg, 62.5 mg, 62.6 mg, 62.7 mg, 62.8 mg, 62.9 mg, 63.0 mg, 63.1 mg, 63.2 mg, 63.3 mg, 63.4 mg, 63.5 mg, 63.6 mg, 63.7 mg, 63.8 mg, 63.9 mg, 64.0 mg, 64.1 mg, 64.2 mg, 64.3 mg, 64.4 mg, 64.5 mg, 64.6 mg, 64.7 mg, 64.8 mg, 64.9 mg, 65.0 mg, 65.1 mg, 65.2 mg, 65.3 mg, 65.4 mg, 65.5 mg, 65.6 mg, 65.7 mg, 65.8 mg, 65.9 mg, 66.0 mg, 66.1 mg, 66.2 mg, 66.3 mg, 66.4 mg, 66.5 mg, 66.6 mg, 66.7 mg, 66.8 mg, 66.9 mg, 67.0 mg, 67.1 mg, 67.2 mg, 67.3 mg, 67.4 mg, 67.5 mg, 67.6 mg, 67.7 mg, 67.8 mg, 67.9 mg, 68.0 mg, 68.1 mg, 68.2 mg, 68.3 mg, 68.4 mg, 68.5 mg, 68.6 mg, 68.7 mg, 68.8 mg, 68.9 mg, 69.0 mg, 69.1 mg, 69.2 mg, 69.3 mg, 69.4 mg, 69.5 mg, 69.6 mg, 69.7 mg, 69.8 mg, 69.9 mg, 70.0 mg, 70.1 mg, 70.2 mg, 70.3 mg, 70.4 mg, 70.5 mg, 70.6 mg, 70.7 mg, 70.8 mg, 70.9 mg, 71.0 mg, 71.1 mg, 71.2 mg, 71.3 mg, 71.4 mg, 71.5 mg, 71.6 mg, 71.7 mg, 71.8 mg, 71.9 mg, 72.0 mg, 72.1 mg, 72.2 mg, 72.3 mg, 72.4 mg, 72.5 mg, 72.6 mg, 72.7 mg, 72.8 mg, 72.9 mg, 73.0 mg, 73.1 mg, 73.2 mg, 73.3 mg, 73.4 mg, 73.5 mg, 73.6 mg, 73.7 mg, 73.8 mg, 73.9 mg, 74.0 mg, 74.1 mg, 74.2 mg, 74.3 mg, 74.4 mg, 74.5 mg, 74.6 mg, 74.7 mg, 74.8 mg, 74.9 mg, 75.0 mg, 75.1 mg, 75.2 mg, 75.3 mg, 75.4 mg, 75.5 mg, 75.6 mg, 75.7 mg, 75.8 mg, 75.9 mg, 76.0 mg, 76.1 mg, 76.2 mg, 76.3 mg, 76.4 mg, 76.5 mg, 76.6 mg, 76.7 mg, 76.8 mg, 76.9 mg, 77.0 mg, 77.1 mg, 77.2 mg, 77.3 mg, 77.4 mg, 77.5 mg, 77.6 mg, 77.7 mg, 77.8 mg, 77.9 mg, 78.0 mg, 78.1 mg, 78.2 mg, 78.3 mg, 78.4 mg, 78.5 mg, 78.6 mg, 78.7 mg, 78.8 mg, 78.9 mg, 79.0 mg, 79.1 mg, 79.2 mg, 79.3 mg, 79.4 mg, 79.5 mg, 79.6 mg, 79.7 mg, 79.8 mg, 79.9 mg, 80.0 mg, 80.1 mg, 80.2 mg, 80.3 mg, 80.4 mg, 80.5 mg, 80.6 mg, 80.7 mg, 80.8 mg, 80.9 mg, 81.0 mg, 81.1 mg, 81.2 mg, 81.3 mg, 81.4 mg, 81.5 mg, 81.6 mg, 81.7 mg, 81.8 mg, 81.9 mg, 82.0 mg, 82.0 mg, 82.1 mg, 82.2 mg, 82.3 mg, 82.4 mg, 82.5 mg, 82.6 mg, 82.7 mg, 82.8 mg, 82.9 mg, 83.0 mg, 83.1 mg, 83.2

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18. The method of any one of claims 1-10, wherein the therapeutically effective amount is any of about 40.0 mg, about 40.1 mg, about 40.2 mg, about 40.3 mg, about 40.4 mg, about 40.5 mg, about 40.6 mg, about 40.7 mg, about 40.8 mg, about 40.9 mg, about 41.0 mg, about 41.1 mg, about 41.2 mg, about 41.3 mg, about 41.4 mg, about 41.5 mg, about 41.6 mg, about 41.7 mg, about 41.8 mg, about 41.9 mg, about 42.0 mg, about 42.1 mg, about 42.2 mg, about 42.3 mg, about 42.4 mg, about 42.5 mg, about 42.6 mg, about 42.7 mg, about 42.8 mg, about 42.9 mg, about 43.0 mg, about 43.1 mg, about 43.2 mg, about 43.3 mg, about 43.4 mg, about 43.5 mg, about 43.6 mg, about 43.7 mg, about 43.8 mg, about 43.9 mg, about 44.0 mg, about 44.1 mg, about 44.2 mg, about 44.3 mg, about 44.4 mg, about 44.5 mg, about 44.6 mg, about 44.7 mg, about 44.8 mg, about 44.9 mg, about 45.0 mg, about 45.1 mg, about 45.2 mg, about 45.3 mg, about 45.4 mg, about 45.5 mg, about 45.6 mg, about 45.7 mg, about 45.8 mg, about 45.9 mg, about 46.0 mg, about 46.1 mg, about 46.2 mg, about 46.3 mg, about 46.4 mg, about 46.5 mg, about 46.6 mg, about 46.7 mg, about 46.8 mg, about 46.9 mg, about 47.0 mg, about 47.1 mg, about 47.2 mg, about 47.3 mg, about 47.4 mg, about 47.5 mg, about 47.6 mg, about 47.7 mg, about 47.8 mg, about 47.9 mg, about 48.0 mg, about 48.1 mg, about 48.2 mg, about 48.3 mg, about 48.4 mg, about 48.5 mg, about 48.6 mg, about 48.7 mg, about 48.8 mg, about 48.9 mg, about 49.0 mg, about 49.1 mg, about 49.2 mg, about 49.3 mg, about 49.4 mg, about 49.5 mg, about 49.6 mg, about 49.7 mg, about 49.8 mg, about 49.9 mg, about 50.0 mg, about 50.1 mg, about 50.2 mg, about 50.3 mg, about 50.4 mg, about 50.5 mg, about 50.6 mg, about 50.7 mg, about 50.8 mg, about 50.9 mg, about 51.0 mg, about 51.1 mg, about 51.2 mg, about 51.3 mg, about 51.4 mg, about 51.5 mg, about 51.6 mg, about 51.7 mg, about 51.8 mg, about 51.9 mg, about 52.0 mg, about 52.1 mg, about 52.2 mg, about 52.3 mg, about 52.4 mg, about 52.5 mg, about 52.6 mg, about 52.7 mg, about 52.8 mg, about 52.9 mg, about 53.0 mg, about 53.1 mg, about 53.2 mg,

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19. The method of any one of claims 1-10, wherein the therapeutically effective amount is within the range of any of 40 mg to 100 mg, 40 mg to 80 mg, 40 mg to 70 mg, 40 mg to 60 mg, 40 mg to 50 mg, 50 mg

to 100 mg, 50 mg to 80 mg, 50 mg to 70 mg, 50 mg to 60 mg, 60 mg to 100 mg, 60 mg to 80 mg, 60 mg to 70 mg, 70 mg to 100 mg, 70 mg to 80 mg, 80 mg to 100 mg, 80 mg to 90 mg, and 90 mg to 100 mg.

20. The method of any one of claims 1-10, wherein the therapeutically effective amount is any of less than 100 mg, less than 95 mg, less than 90 mg, less than 85 mg, less than 80 mg, less than 75 mg, less than 70 mg, less than 65 mg, less than 60 mg, less than 55 mg, less than 50 mg, less than 45 mg, and less than 40 mg.

21. The method of any one of claims 1-10, wherein the therapeutically effective amount is any of less than about less than about 100 mg, less than about 95 mg, less than about 90 mg, less than about 85 mg, less than about 80 mg, less than about 75 mg, less than about 70 mg, less than about 65 mg, less than about 60 mg, less than about 55 mg, less than about 50 mg, less than about 45 mg, and less than about 40 mg.

22. The method of any one of claims 1-10, wherein the therapeutically effective amount is any of at least 40 mg, at least 45 mg, at least 50 mg, at least 55 mg, at least 60 mg, at least 65 mg, at least 70 mg, at least 75 mg, at least 80 mg, at least 85 mg, at least 90 mg, at least 95 mg, and at least about 100 mg.

23. The method of any one of claims 1-10, wherein the therapeutically effective amount is any of at least about 40 mg, at least about 45 mg, at least about 50 mg, at least about 55 mg, at least about 60 mg, at least about 65 mg, at least about 70 mg, at least about 75 mg, at least about 80 mg, at least about 85 mg, at least about 90 mg, at least about 95 mg, and at least about 100 mg.

24. The method of any one of claims 1-23, comprising administering the modified oligonucleotide once every 4 weeks.

25. The method of any one of claims 1-23, comprising administering the modified oligonucleotide once every 8 weeks.

26. The method of any one of claims 1-23, comprising administering the modified oligonucleotide once every 12 weeks.

27. The method of any one of claims 1-23, comprising administering the modified oligonucleotide once every 16 weeks.

28. The method of any one of claims 1-23, comprising administering the modified oligonucleotide once every 20 weeks.

29. The method of any one of claims 1-23, comprising administering the modified oligonucleotide about once every 4 weeks.

30. The method of any one of claims 1-23, comprising administering the modified oligonucleotide about once every 8 weeks.

31. The method of any one of claims 1-23, comprising administering the modified oligonucleotide about once every 12 weeks.

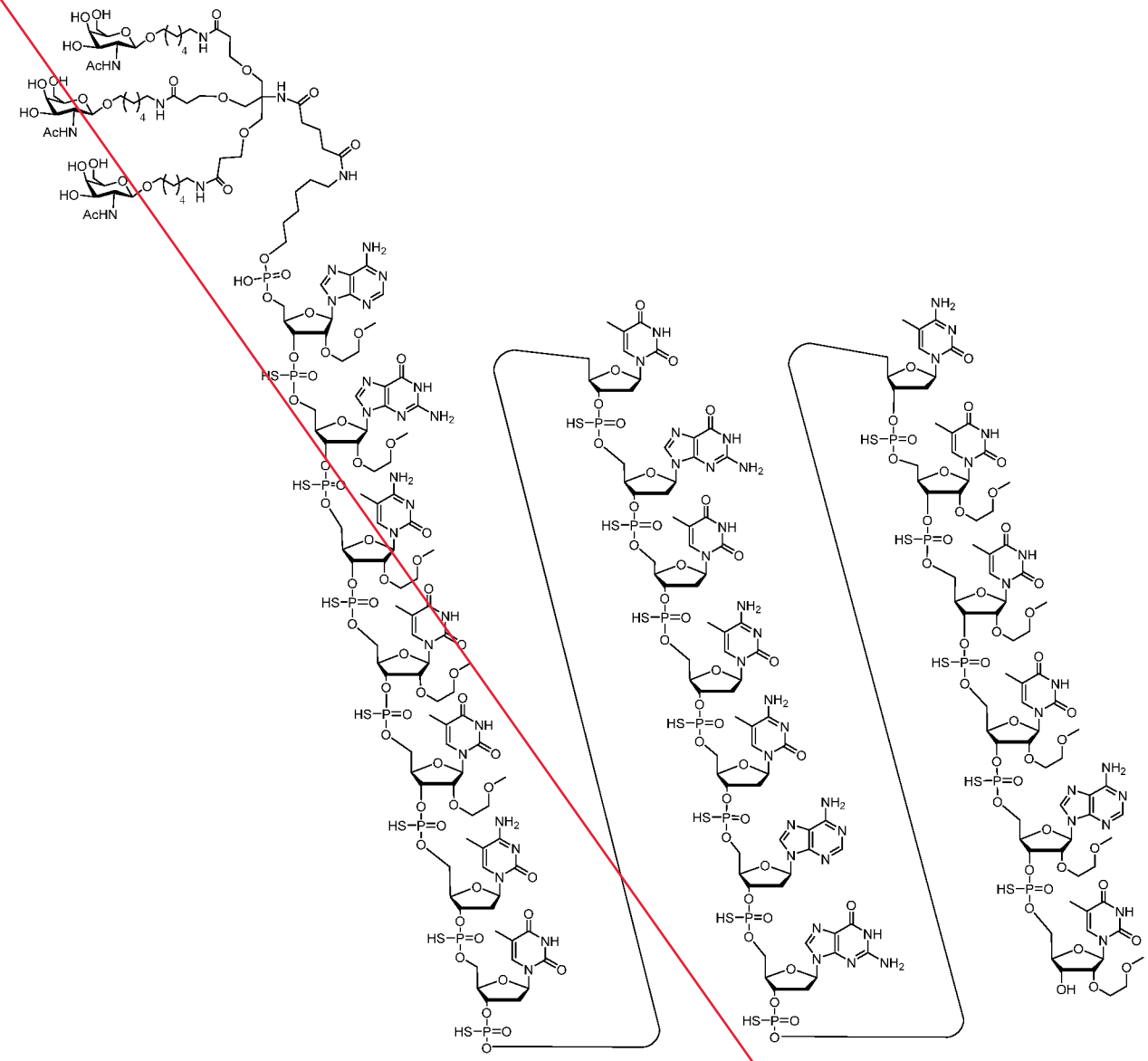
32. The method of any one of claims 1-23, comprising administering the modified oligonucleotide about once every 16 weeks.

33. The method of any one of claims 1-23, comprising administering the modified oligonucleotide about once every 20 weeks.

34. The method of any one of claims 1-23, comprising administering the modified oligonucleotide any of once every 1 week, once every 2 weeks, once every 3 weeks, once every 4 weeks, once every 5 weeks, once every 6 weeks, once every 7 weeks, once every 8 weeks, once every 9 weeks, once every 10 weeks, once every 11 weeks, once every 12 weeks, once every 13 weeks, once every 14 weeks, once every 15 weeks, once every 16 weeks, once every 17 weeks, once every 18 weeks, once every 19 weeks, and once every 20 weeks.

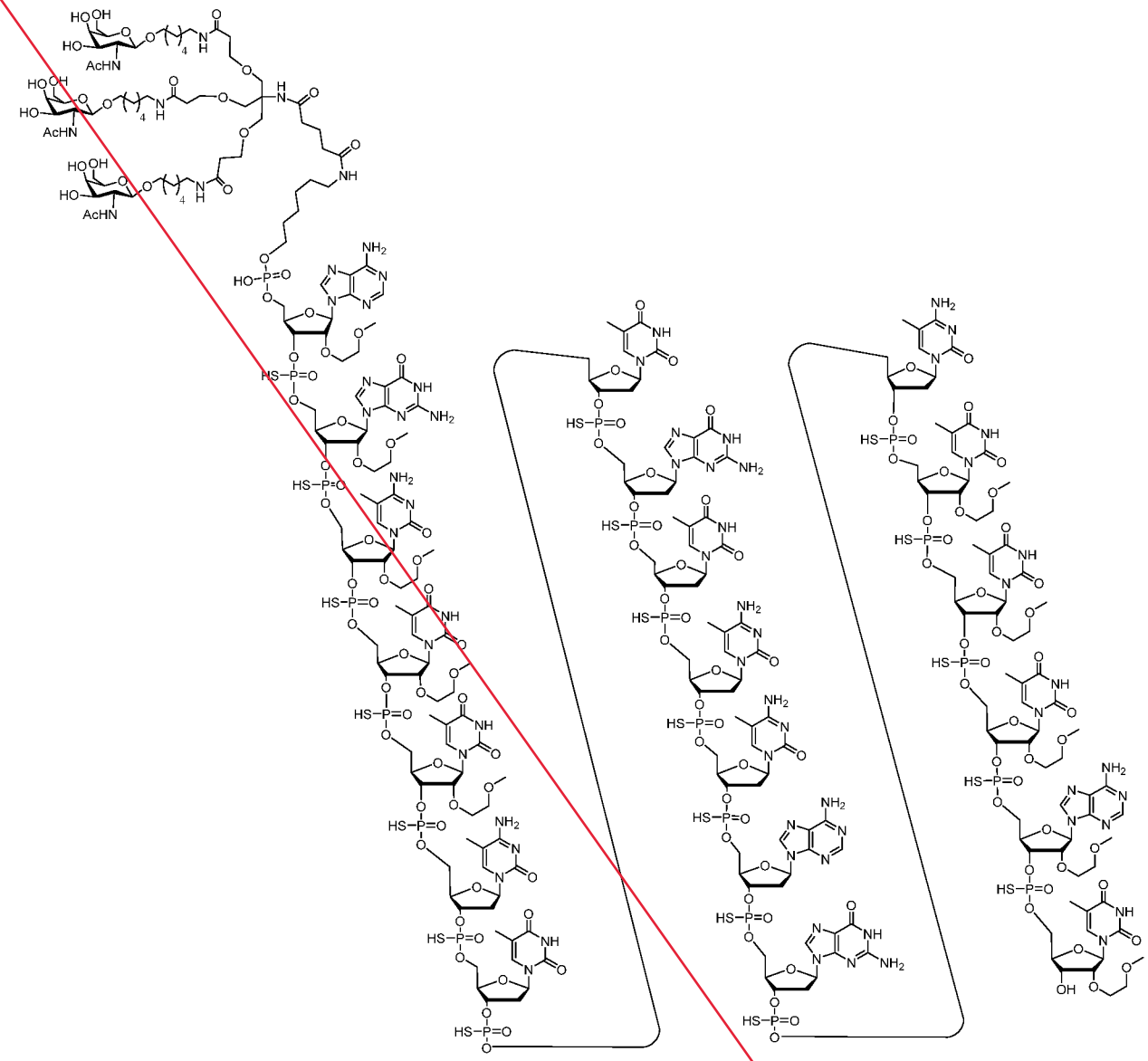
35. The method of any one of claims 1-23, comprising administering the modified oligonucleotide any of once about every 1 week, once about every 2 weeks, once about every 3 weeks, once about every 4 weeks, once about every 5 weeks, once about every 6 weeks, once about every 7 weeks, once about every 8 weeks, once about every 9 weeks, once about every 10 weeks, once about every 11 weeks, once about every 12 weeks, once about every 13 weeks, once about every 14 weeks, once about every 15 weeks, once about every 16 weeks, once about every 17 weeks, once about every 18 weeks, once about every 19 weeks, and once about every 20 weeks.

36. A method of ameliorating FCS, reducing APOCIII RNA, or reducing APOCIII protein, in a human subject in need thereof, the method comprising subcutaneously administering to the human subject a therapeutically effective amount of 50 mg or about 50 mg of a compound according to the following chemical structure:



(SEQ ID NO: 3), or a salt thereof.

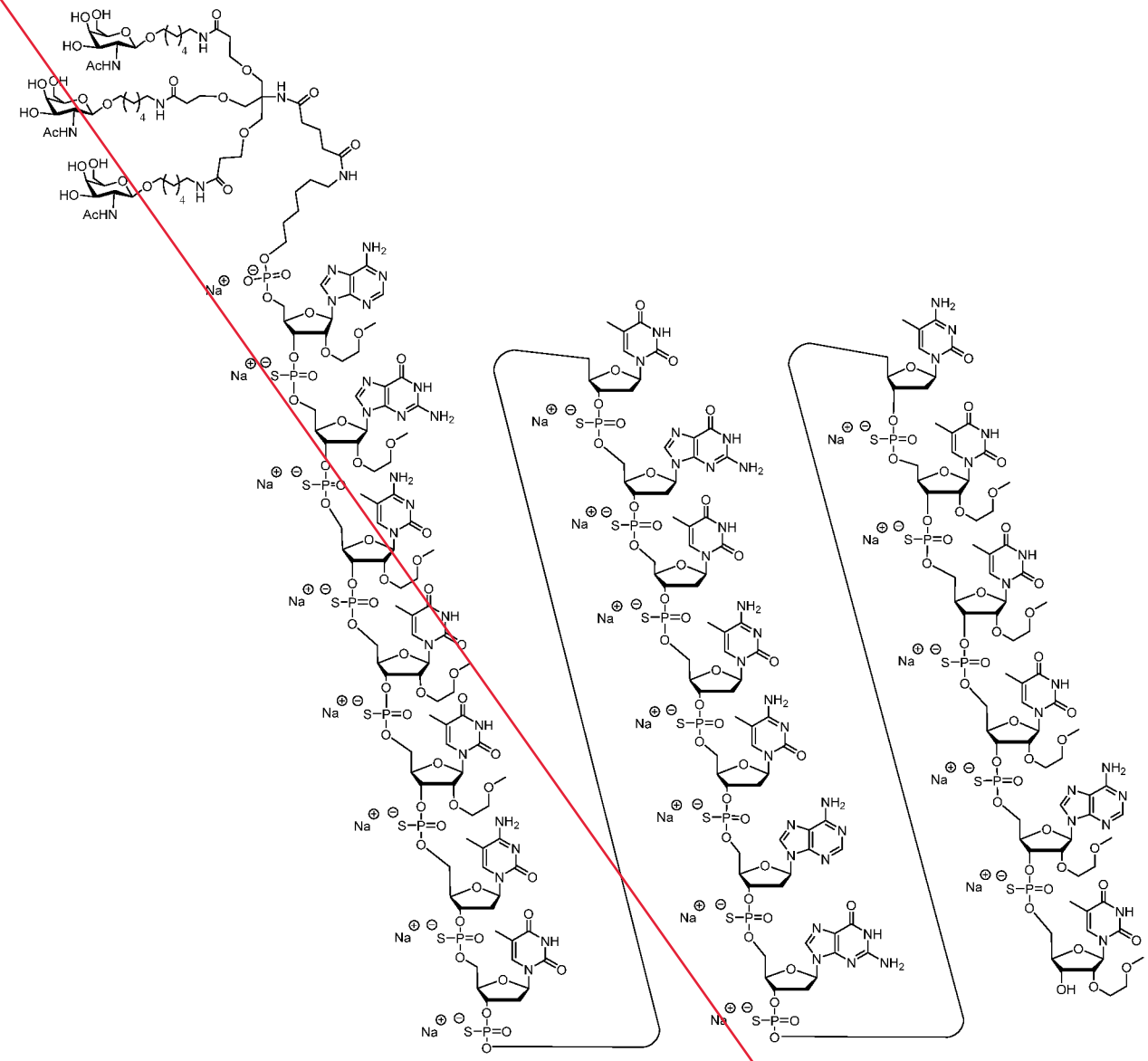
37. A method of ameliorating FCS, reducing APOCIII RNA, or reducing APOCIII protein, in a human subject in need thereof, the method comprising subcutaneously administering to the human subject a therapeutically effective amount of 80 mg or about 80 mg of a compound according to the following chemical structure:



(SEQ ID NO: 3), or a salt thereof.

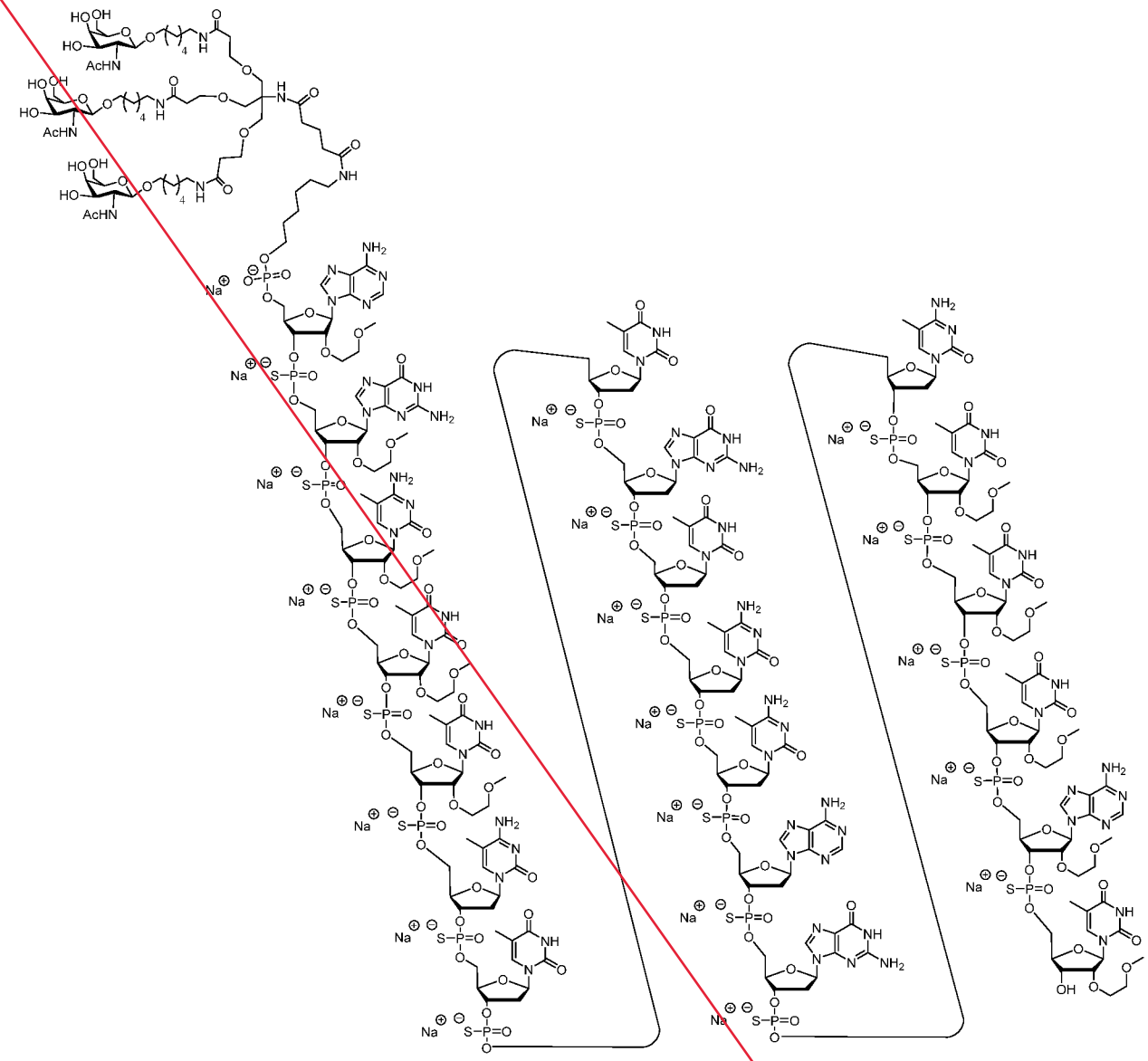
38. The modified oligonucleotide of claim 36 or claim 37, which is the sodium salt or the potassium salt.

39. A method of ameliorating FCS, reducing APOCIII RNA, or reducing APOCIII protein, in a human subject in need thereof, the method comprising intrathecally administering to the human subject a therapeutically effective amount of 50 mg or about 50 mg of a compound according to the following chemical structure:



(SEQ ID NO: 3).

40. A method of ameliorating FCS, reducing APOCIII RNA, or reducing APOCIII protein, in a human subject in need thereof, the method comprising subcutaneously administering to the human subject a therapeutically effective amount of 80 mg or about 80 mg of a compound according to the following chemical structure:



(SEQ ID NO: 3).

41. A method of ameliorating FCS, reducing APOCIII RNA, or reducing APOCIII protein in a human subject in need thereof, the method comprising subcutaneously administering to the human subject a therapeutically effective amount of 50 mg or about 50 mg of a compound, wherein the compound comprises a modified oligonucleotide having the following chemical notation (5' to 3'):

$A_{es}G_{es}{}^{m}C_{es}T_{es}T_{es}{}^{m}C_{ds}T_{ds}T_{ds}G_{ds}T_{ds}{}^{m}C_{ds}{}^{m}C_{ds}A_{ds}G_{ds}{}^{m}C_{ds}T_{es}T_{es}T_{es}A_{es}T_{e}$ (SEQ ID NO: 3); wherein,

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

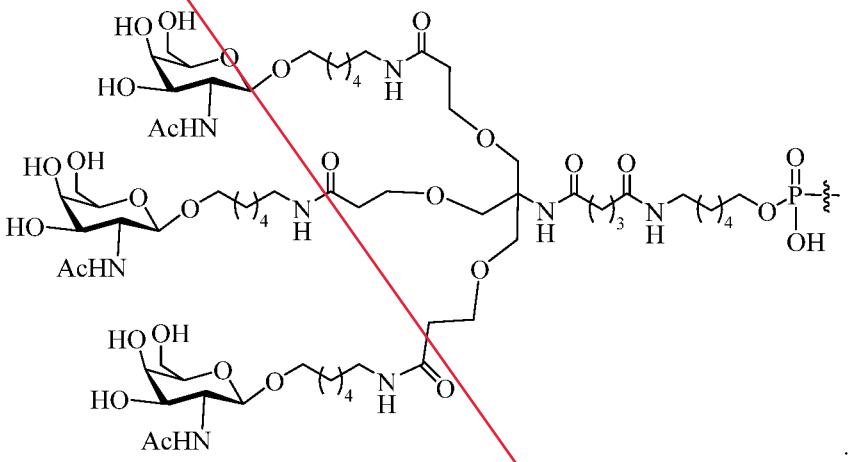
T = a thymine nucleobase,

e = a 2'- $OCH_2CH_2OCH_3$ modified ribosyl sugar moiety,

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

s = a phosphorothioate internucleoside linkage,

and wherein the modified oligonucleotide has a 5'-trishexylamino-(THA)-C_6GalNAc$_3$ endcap, represented by the structure below, wherein the phosphate group is attached to the 5'-oxygen atom of the 5'-nucleoside:



42. A method of ameliorating FCS, reducing APOCIII RNA, or reducing APOCIII protein in a human subject in need thereof, the method comprising subcutaneously administering to the human subject a therapeutically effective amount of 80 mg or about 80 mg of a compound, wherein the compound comprises a modified oligonucleotide having the following chemical notation (5' to 3'):
$A_{es}G_{es}{}^{m}C_{es}T_{es}T_{es}{}^{m}C_{ds}T_{ds}T_{ds}G_{ds}T_{ds}{}^{m}C_{ds}{}^{m}C_{ds}A_{ds}G_{ds}{}^{m}C_{ds}T_{es}T_{es}T_{es}A_{es}T_{e}$ (SEQ ID NO: 3); wherein,

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

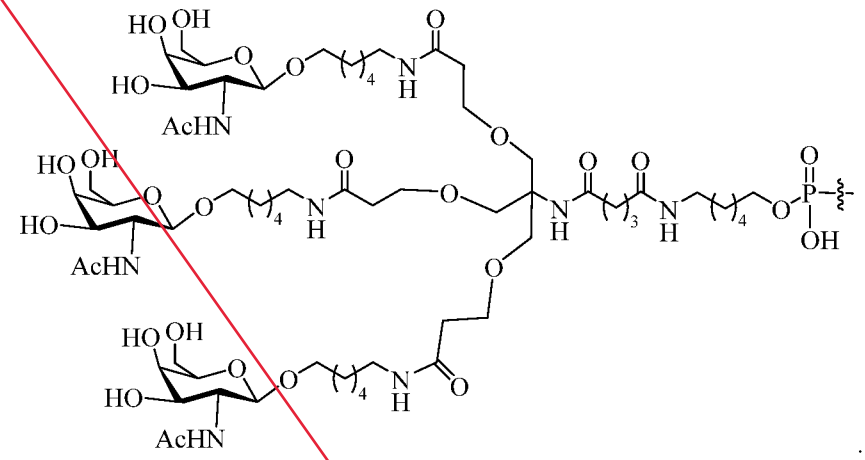
T = a thymine nucleobase,

e = a 2'- $OCH_2CH_2OCH_3$ modified ribosyl sugar moiety,

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

s = a phosphorothioate internucleoside linkage,

and wherein the modified oligonucleotide has a 5'-trishexylamino-(THA)-C_6GalNAc$_3$ endcap, represented by the structure below, wherein the phosphate group is attached to the 5'-oxygen atom of the 5'-nucleoside:



43. The method of any one of claims 36-42, comprising administering the modified oligonucleotide about once every 4 weeks.

44. The method of any one of claims 36-42, comprising administering the modified oligonucleotide about once every 8 weeks.

45. The method of any one of claims 36-42, comprising administering the modified oligonucleotide about once every 16 weeks.

46. The method of any one of claims 36-45, wherein at least one symptom of FCS is ameliorated.

47. The method of claim 46, wherein the at least one symptom comprises comprises severe elevations in chylomicrons and extremely elevated TG levels (always reaching well above 1000 mg/dL and not infrequently rising as high as 10,000 mg/dL or more) with episodes of abdominal pain, physical fatigue, difficulty thinking, diarrhea, recurrent acute pancreatitis, eruptive cutaneous xanthomata, and hepatosplenomegaly, or a combination thereof.

48. The method of any of claims 1-47, wherein APOCIII RNA is reduced.

49. The method of any of claims 1-47, wherein APOCIII protein is reduced.

50. The method of any one of claims 1-49, comprising detecting fasting triglyceride levels in a biological sample from the human subject.

51: The method of any one of claims 1-49, comprising detecting fasting apoB-48 levels in a biological sample from the human subject.

52. The method of any of claims 50 and 51, wherein the biological sample is plasma.

53: The method of any one of claims 1-49, comprising recording the adjudicated acute pancreatits event rate of the human subject.

54. The method of any of claims 50-52, wherein the detecting occurs before the administering.

55. The method of any of claims 50-52, wherein the detecting occurs after the administering.

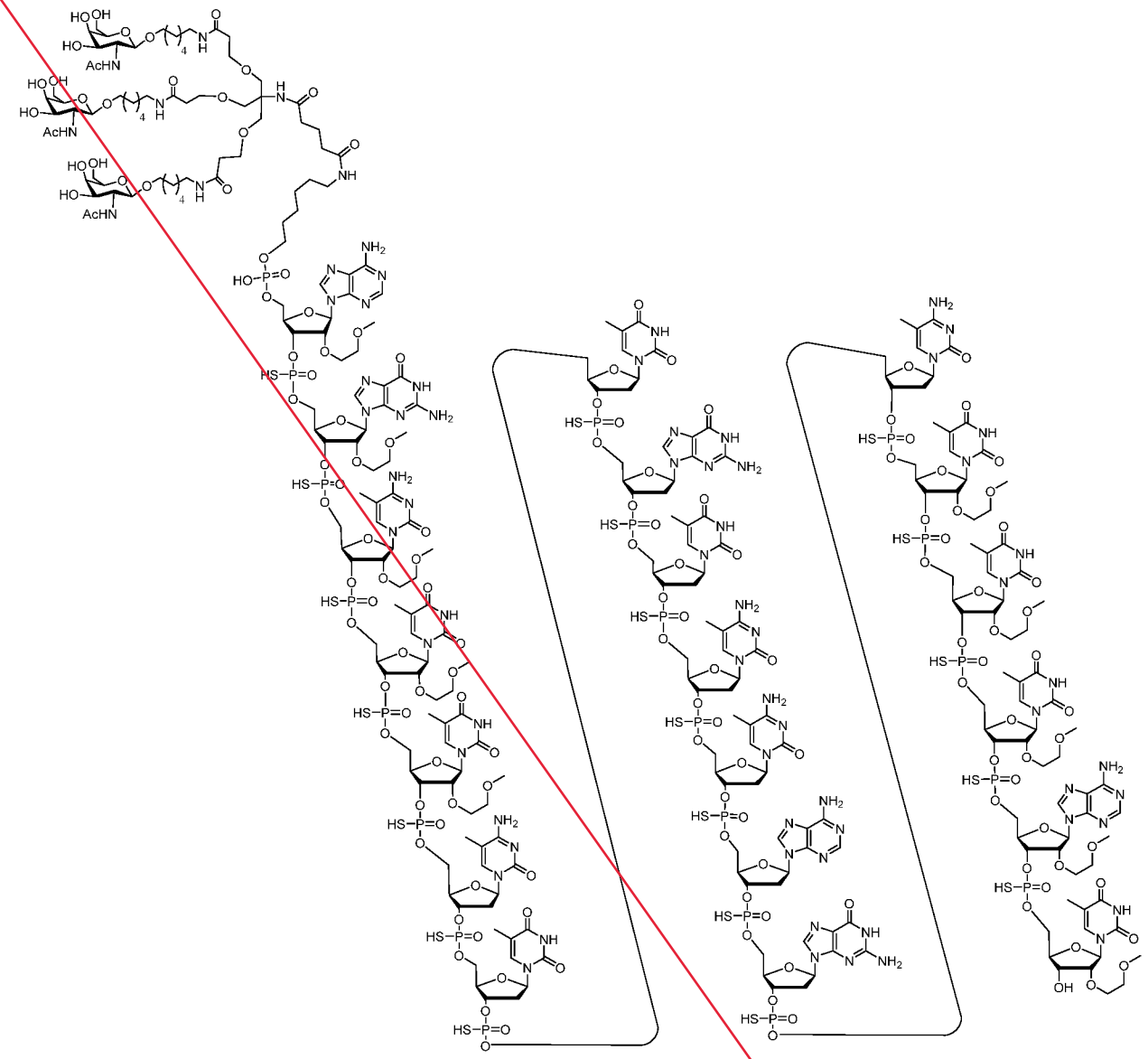
56. The method of any of claims 50-52, wherein the detecting occurs before and after the administering.

57. The method of any one of claims 50-56, comprising adjusting the initial therapeutically effective amount administered after detecting the amount of APOCIII RNA, or APOCIII protein, or combination thereof.

58. The method of claims 57, wherein the dose is at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 90%, or at least about 100% greater than the therapeutically effective amount.

59. The method of any one of claims 50-58, wherein the therapeutically effective amount is about 50 mg or 80 mg.

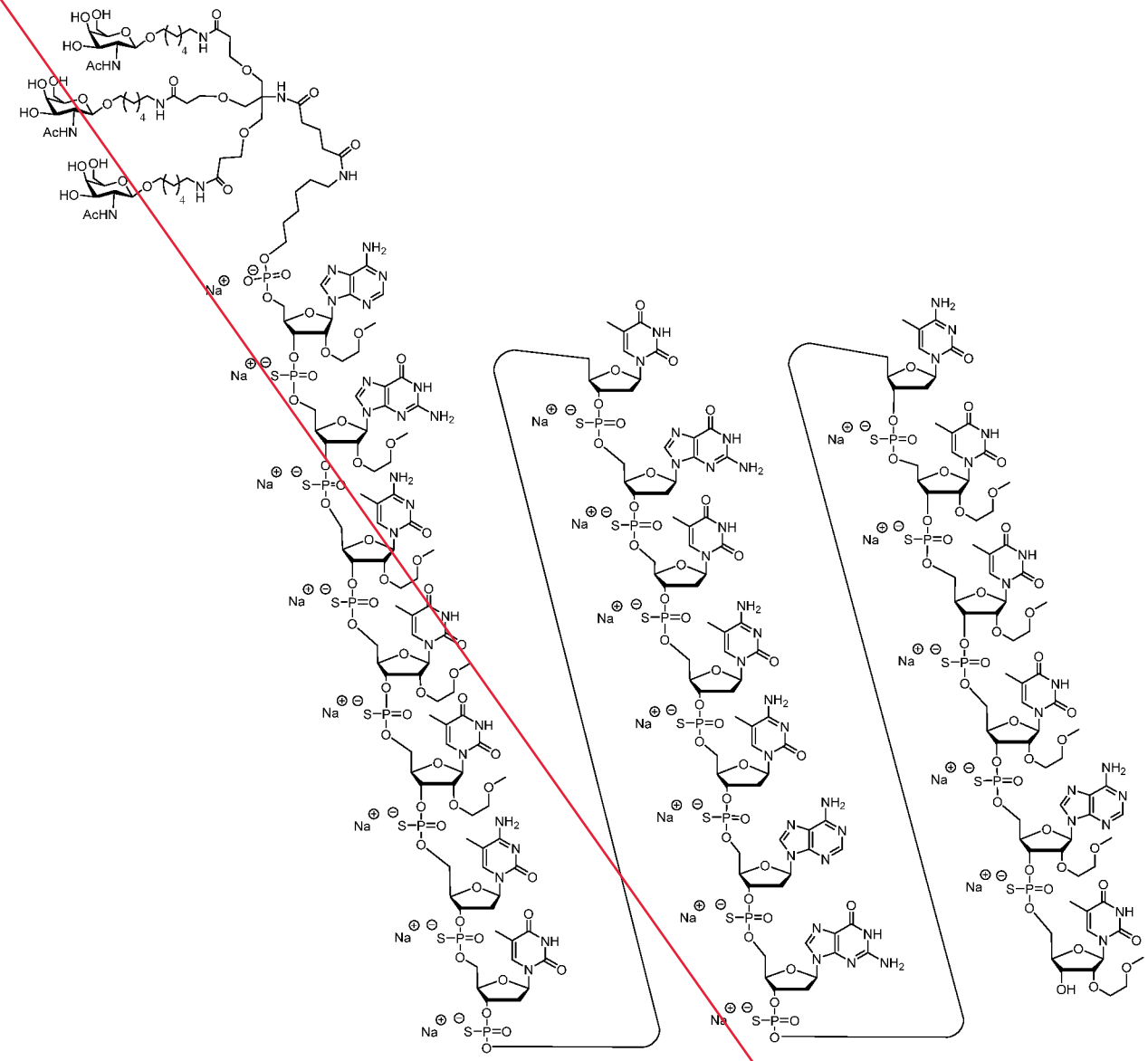
60. A method of ameliorating Familial Chylomicronemia Syndrome (FCS), severe hypertriglyceridemia (SHTG), or Familial Partial Lipodystrophy (FPL) in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of a compound according to the following chemical structure:



(SEQ ID NO: 3), or a salt thereof.

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

62. A method of ameliorating Familial Chylomicronemia Syndrome (FCS), severe hypertriglyceridemia (SHTG), or Familial Partial Lipodystrophy (FPL) in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of a compound according to the following chemical structure:



(SEQ ID NO: 3).

63. A method of ameliorating Familial Chylomicronemia Syndrome (FCS), severe hypertriglyceridemia (SHTG), or Familial Partial Lipodystrophy (FPL) in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of a compound comprising a modified oligonucleotide having the following chemical notation (5' to 3'): $A_{es}G_{es}{}^{m}C_{es}T_{es}T_{es}{}^{m}C_{ds}T_{ds}T_{ds}G_{ds}T_{ds}{}^{m}C_{ds}{}^{m}C_{ds}A_{ds}G_{ds}{}^{m}C_{ds}T_{es}T_{es}T_{es}A_{es}T_{e}$ (SEQ ID NO: 3); wherein,

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

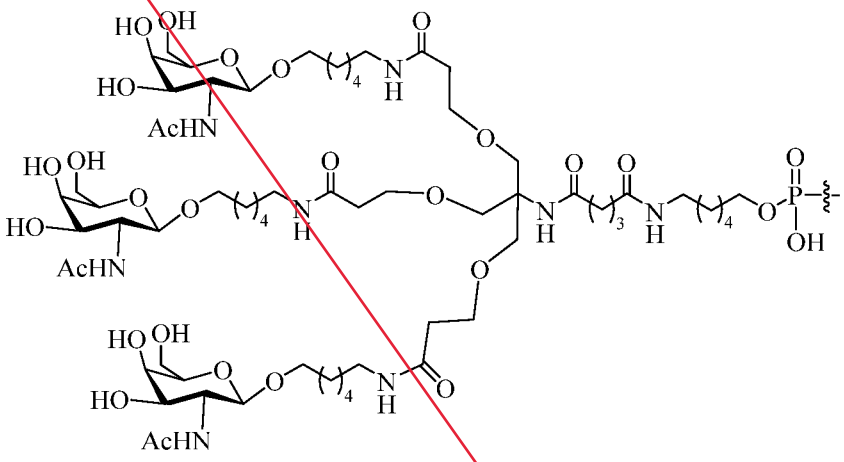
T = a thymine nucleobase,

e = a 2'- $OCH_2CH_2OCH_3$ modified ribosyl sugar moiety,

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

s = a phosphorothioate internucleoside linkage,

and wherein the modified oligonucleotide has a 5'-trishexylamino-(THA)-C_6GalNAc$_3$ endcap, represented by the structure below, wherein the phosphate group is attached to the 5'-oxygen atom of the 5'-nucleoside:



64. The method of any one of claims 60-63, wherein at least one symptom of Familial Chylomicronemia Syndrome (FCS), severe hypertriglyceridemia (SHTG), or Familial Partial Lipodystrophy (FPL) is ameliorated.

65. The method of claim 64, wherein the at least one symptom of FCS comprises chylomicronemia, hypertriglyceridemia of at least 1000 mg/dL triglycerides, abdominal pain, colicky pain, physical fatigue, difficulty thinking, diarrhea, acute pancreatitis, eruptive xanthomas, lipemia retinalis, and hepatosplenomegaly, or a combination thereof.

66. The method of claim 64, wherein the at least one symptom of SHTG comprises chylomicronemia, abdominal pain, colicky pain, physical fatigue, difficulty thinking, diarrhea, acute pancreatitis, eruptive xanthomas, lipemia retinalis, and hepatosplenomegaly, or a combination thereof.

67. The method of claim 64, wherein the at least one symptom of FPL comprises chylomicronemia, abdominal pain, colicky pain, physical fatigue, difficulty thinking, diarrhea, acute pancreatitis, eruptive xanthomas, lipemia retinalis, and hepatosplenomegaly, or a combination thereof.

68. The method of any one of claims 60-67, wherein the therapeutically effective amount is 50 mg.

69. The method of any one of claims 60-67, wherein the therapeutically effective amount is 60 mg.

70. The method of any one of claims 60-67, wherein the therapeutically effective amount is 70 mg.

71. The method of any one of claims 60-67, wherein the therapeutically effective amount is 80 mg.

72. The method of any one of claims 60-67, wherein the therapeutically effective amount is any of 40 mg, 45 mg, 50 mg, 55 mg, 60 mg, 65 mg, 70 mg, 75 mg, 80 mg, 85 mg, 90 mg, 95 mg, and 100 mg.

73. The method of any one of claims 60-67, wherein the therapeutically effective amount is any of about 40 mg, about 45 mg, about 50 mg, about 55 mg, about 60 mg, about 65 mg, about 70 mg, about 75 mg, about 80 mg, about 85 mg, about 90 mg, about 95 mg, and about 100 mg.

74. The method of any one of claims 60-67, wherein the therapeutically effective amount is any of 40.0 mg, 40.1 mg, 40.2 mg, 40.3 mg, 40.4 mg, 40.5 mg, 40.6 mg, 40.7 mg, 40.8 mg, 40.9 mg, 41.0 mg, 41.1 mg, 41.2 mg, 41.3 mg, 41.4 mg, 41.5 mg, 41.6 mg, 41.7 mg, 41.8 mg, 41.9 mg, 42.0 mg, 42.1 mg, 42.2 mg, 42.3 mg, 42.4 mg, 42.5 mg, 42.6 mg, 42.7 mg, 42.8 mg, 42.9 mg, 43.0 mg, 43.1 mg, 43.2 mg, 43.3 mg, 43.4 mg, 43.5 mg, 43.6 mg, 43.7 mg, 43.8 mg, 43.9 mg, 44.0 mg, 44.1 mg, 44.2 mg, 44.3 mg, 44.4 mg, 44.5 mg, 44.6 mg, 44.7 mg, 44.8 mg, 44.9 mg, 45.0 mg, 45.1 mg, 45.2 mg, 45.3 mg, 45.4 mg, 45.5 mg, 45.6 mg, 45.7 mg, 45.8 mg, 45.9 mg, 46.0 mg, 46.1 mg, 46.2 mg, 46.3 mg, 46.4 mg, 46.5 mg, 46.6 mg, 46.7 mg, 46.8 mg, 46.9 mg, 47.0 mg, 47.1 mg, 47.2 mg, 47.3 mg, 47.4 mg, 47.5 mg, 47.6 mg, 47.7 mg, 47.8 mg, 47.9 mg, 48.0 mg, 48.1 mg, 48.2 mg, 48.3 mg, 48.4 mg, 48.5 mg, 48.6 mg, 48.7 mg, 48.8 mg, 48.9 mg, 49.0 mg, 49.1 mg, 49.2 mg, 49.3 mg, 49.4 mg, 49.5 mg, 49.6 mg, 49.7 mg, 49.8 mg, 49.9 mg, 50.0 mg, 50.1 mg, 50.2 mg, 50.3 mg, 50.4 mg, 50.5 mg, 50.6 mg, 50.7 mg, 50.8 mg, 50.9 mg, 51.0 mg, 51.1 mg, 51.2 mg, 51.3 mg, 51.4 mg, 51.5 mg, 51.6 mg, 51.7 mg, 51.8 mg, 51.9 mg, 52.0 mg, 52.1 mg, 52.2 mg, 52.3 mg, 52.4 mg, 52.5 mg, 52.6 mg, 52.7 mg, 52.8 mg, 52.9 mg, 53.0 mg, 53.1 mg, 53.2 mg, 53.3 mg. 53.4 mg, 53.5 mg, 53.6 mg, 53.7 mg, 53.8 mg, 53.9 mg, 54.0 mg, 54.1 mg, 54.2 mg, 54.3 mg, 54.4 mg, 54.5 mg, 54.6 mg, 54.7 mg, 54.8 mg, 54.9 mg, 55.0 mg, 50.0 mg, 50.1 mg, 50.2 mg, 50.3 mg, 50.4 mg, 50.5 mg, 50.6 mg, 50.7 mg, 50.8 mg, 50.9 mg, 51.0 mg, 51.1 mg, 51.2 mg, 51.3 mg, 51.4 mg, 51.5 mg, 51.6 mg, 51.7 mg, 51.8 mg, 51.9 mg, 52.0 mg, 52.1 mg, 52.2 mg, 52.3 mg, 52.4 mg, 52.5 mg, 52.6 mg, 52.7 mg, 52.8 mg, 52.9 mg, 53.0 mg, 53.1 mg, 53.2 mg, 53.3 mg. 53.4 mg, 53.5 mg, 53.6 mg, 53.7 mg, 53.8 mg, 53.9 mg, 54.0 mg, 54.1 mg, 54.2 mg, 54.3 mg, 54.4 mg, 54.5 mg, 54.6 mg, 54.7 mg, 54.8 mg, 54.9 mg, 55.0 mg, 55.1 mg, 55.2 mg, 55.3 mg. 55.4 mg, 55.5 mg, 55.6 mg, 55.7 mg, 55.8 mg, 55.9 mg, 55.0 mg, 55.1 mg, 55.2 mg, 55.3 mg, 55.4 mg, 55.5 mg, 55.6 mg, 55.7 mg, 55.8 mg, 55.9 mg, 56.0 mg, 56.1 mg, 56.2 mg, 56.3 mg. 56.4 mg, 56.5 mg, 56.6 mg, 56.7 mg, 56.8 mg, 56.9 mg, 57.0 mg, 57.1 mg, 57.2 mg, 57.3 mg, 57.4 mg, 57.5 mg, 57.6 mg, 57.7 mg, 57.8 mg, 57.9 mg, 58.0 mg, 58.1 mg, 58.2 mg, 58.3 mg. 58.4 mg, 58.5 mg, 58.6 mg, 58.7 mg, 58.8 mg, 58.9 mg, 59.0 mg, 59.1 mg, 59.2 mg, 59.3 mg, 59.4 mg, 59.5 mg, 59.6 mg, 59.7 mg, 59.8 mg, 59.9 mg, 60.0 mg, 60.1 mg, 60.2 mg, 60.3 mg, 60.4 mg, 60.5 mg, 60.6 mg, 60.7 mg, 60.8 mg, 60.9 mg, 61.0 mg, 61.1 mg, 61.2 mg, 61.3 mg, 61.4 mg, 61.5 mg, 61.6 mg, 61.7 mg, 61.8 mg, 61.9 mg, 62.0 mg, 62.1 mg, 62.2 mg, 62.3 mg, 62.4 mg, 62.5 mg, 62.6 mg, 62.7 mg, 62.8 mg, 62.9 mg, 63.0 mg, 63.1 mg, 63.2 mg, 63.3 mg, 63.4 mg, 63.5 mg, 63.6 mg, 63.7 mg, 63.8 mg, 63.9 mg, 64.0 mg, 64.1 mg, 64.2 mg, 64.3 mg, 64.4 mg, 64.5 mg, 64.6 mg, 64.7 mg, 64.8 mg, 64.9 mg, 65.0 mg, 65.1 mg, 65.2 mg, 65.3 mg, 65.4 mg, 65.5 mg, 65.6 mg, 65.7 mg, 65.8 mg, 65.9 mg, 66.0 mg, 66.1 mg, 66.2 mg, 66.3 mg, 66.4 mg, 66.5 mg, 66.6 mg, 66.7 mg, 66.8 mg, 66.9 mg, 67.0 mg, 67.1 mg, 67.2 mg, 67.3 mg, 67.4 mg, 67.5 mg, 67.6 mg, 67.7 mg, 67.8 mg, 67.9 mg, 68.0 mg, 68.1 mg, 68.2 mg, 68.3 mg, 68.4 mg, 68.5 mg, 68.6 mg, 68.7 mg, 68.8 mg, 68.9 mg, 69.0 mg, 69.1 mg, 69.2 mg, 69.3 mg, 69.4 mg, 69.5 mg, 69.6 mg, 69.7 mg, 69.8 mg, 69.9 mg, 70.0 mg, 70.1 mg, 70.2 mg, 70.3 mg, 70.4 mg, 70.5 mg, 70.6 mg, 70.7 mg, 70.8 mg, 70.9 mg, 71.0 mg, 71.1 mg, 71.2 mg, 71.3 mg, 71.4 mg, 71.5 mg, 71.6 mg, 71.7 mg, 71.8 mg, 71.9 mg, 72.0 mg, 72.1 mg, 72.2 mg, 72.3 mg, 72.4 mg, 72.5 mg, 72.6 mg, 72.7 mg, 72.8 mg, 72.9 mg, 73.0 mg, 73.1 mg, 73.2 mg, 73.3 mg, 73.4 mg, 73.5 mg, 73.6 mg, 73.7 mg, 73.8 mg, 73.9 mg, 74.0 mg, 74.1

mg, 74.2 mg, 74.3 mg, 74.4 mg, 74.5 mg, 74.6 mg, 74.7 mg, 74.8 mg, 74.9 mg, 75.0 mg, 75.1 mg, 75.2 mg, 75.3 mg, 75.4 mg, 75.5 mg, 75.6 mg, 75.7 mg, 75.8 mg, 75.9 mg, 76.0 mg, 76.1 mg, 76.2 mg, 76.3 mg, 76.4 mg, 76.5 mg, 76.6 mg, 76.7 mg, 76.8 mg, 76.9 mg, 77.0 mg, 77.1 mg, 77.2 mg, 77.3 mg, 77.4 mg, 77.5 mg, 77.6 mg, 77.7 mg, 77.8 mg, 77.9 mg, 78.0 mg, 78.1 mg, 78.2 mg, 78.3 mg, 78.4 mg, 78.5 mg, 78.6 mg, 78.7 mg, 78.8 mg, 78.9 mg, 79.0 mg, 79.1 mg, 79.2 mg, 79.3 mg, 79.4 mg, 79.5 mg, 79.6 mg, 79.7 mg, 79.8 mg, 79.9 mg, 80.0 mg, 80.1 mg, 80.2 mg, 80.3 mg, 80.4 mg, 80.5 mg, 80.6 mg, 80.7 mg, 80.8 mg, 80.9 mg, 81.0 mg, 81.1 mg, 81.2 mg, 81.3 mg, 81.4 mg, 81.5 mg, 81.6 mg, 81.7 mg, 81.8 mg, 81.9 mg, 82.0 mg, 82.0 mg, 82.1 mg, 82.2 mg, 82.3 mg, 82.4 mg, 82.5 mg, 82.6 mg, 82.7 mg, 82.8 mg, 82.9 mg, 83.0 mg, 83.1 mg, 83.2 mg, 83.3 mg, 83.4 mg, 83.5 mg, 83.6 mg, 83.7 mg, 83.8 mg, 83.9 mg, 84.0 mg, 84.1 mg, 84.2 mg, 84.3 mg, 84.4 mg, 84.5 mg, 84.6 mg, 84.7 mg, 84.8 mg, 84.9 mg, 85.0 mg, 85.0 mg, 85.1 mg, 85.2 mg, 85.3 mg, 85.4 mg, 85.5 mg, 85.6 mg, 85.7 mg, 85.8 mg, 85.9 mg, 86.0 mg, 86.1 mg, 86.2 mg, 86.3 mg, 86.4 mg, 86.5 mg, 86.6 mg, 86.7 mg, 86.8 mg, 86.9 mg, 87.0 mg, 87.1 mg, 87.2 mg, 87.3 mg, 87.4 mg, 87.5 mg, 87.6 mg, 87.7 mg, 87.8 mg, 87.9 mg, 88.0 mg, 88.1 mg, 88.2 mg, 88.3 mg, 88.4 mg, 88.5 mg, 88.6 mg, 88.7 mg, 88.8 mg, 88.9 mg, 89.0 mg, 89.0 mg, 89.1 mg, 89.2 mg, 89.3 mg, 89.4 mg, 89.5 mg, 89.6 mg, 89.7 mg, 89.8 mg, 89.9 mg, 90.0 mg, 90.1 mg, 90.2 mg, 90.3 mg, 90.4 mg, 90.5 mg, 90.6 mg, 90.7 mg, 90.8 mg, 90.9 mg, 91.0 mg, 91.1 mg, 91.2 mg, 91.3 mg, 91.4 mg, 91.5 mg, 91.6 mg, 91.7 mg, 91.8 mg, 91.9 mg, 92.0 mg, 92.0 mg, 92.1 mg, 92.2 mg, 92.3 mg, 92.4 mg, 92.5 mg, 92.6 mg, 92.7 mg, 92.8 mg, 92.9 mg, 93.0 mg, 93.1 mg, 93.2 mg, 93.3 mg, 93.4 mg, 93.5 mg, 93.6 mg, 93.7 mg, 93.8 mg, 93.9 mg, 94.0 mg, 94.1 mg, 94.2 mg, 94.3 mg, 94.4 mg, 94.5 mg, 94.6 mg, 94.7 mg, 94.8 mg, 94.9 mg, 95.0 mg, 95.1 mg, 95.2 mg, 95.3 mg, 95.4 mg, 95.5 mg, 95.6 mg, 95.7 mg, 95.8 mg, 95.9 mg, 96.0 mg, 96.1 mg, 96.2 mg, 96.3 mg, 96.4 mg, 96.5 mg, 96.6 mg, 96.7 mg, 96.8 mg, 96.9 mg, 97.0 mg, 97.1 mg, 97.2 mg, 97.3 mg, 97.4 mg, 97.5 mg, 97.6 mg, 97.7 mg, 97.8 mg, 97.9 mg, 98.0 mg, 98.1 mg, 98.2 mg, 98.3 mg, 98.4 mg, 98.5 mg, 98.6 mg, 98.7 mg, 98.8 mg, 98.9 mg, 99.0 mg, 99.1 mg, 99.2 mg, 99.3 mg, 99.4 mg, 99.5 mg, 99.6 mg, 99.7 mg, 99.8 mg, 99.9 mg, and 100.0 mg.

75. The method of any one of claims 60-67, wherein the therapeutically effective amount is any of about 40.0 mg, about 40.1 mg, about 40.2 mg, about 40.3 mg, about 40.4 mg, about 40.5 mg, about 40.6 mg, about 40.7 mg, about 40.8 mg, about 40.9 mg, about 41.0 mg, about 41.1 mg, about 41.2 mg, about 41.3 mg, about 41.4 mg, about 41.5 mg, about 41.6 mg, about 41.7 mg, about 41.8 mg, about 41.9 mg, about 42.0 mg, about 42.1 mg, about 42.2 mg, about 42.3 mg, about 42.4 mg, about 42.5 mg, about 42.6 mg, about 42.7 mg, about 42.8 mg, about 42.9 mg, about 43.0 mg, about 43.1 mg, about 43.2 mg, about 43.3 mg, about 43.4 mg, about 43.5 mg, about 43.6 mg, about 43.7 mg, about 43.8 mg, about 43.9 mg, about 44.0 mg, about 44.1 mg, about 44.2 mg, about 44.3 mg, about 44.4 mg, about 44.5 mg, about 44.6 mg, about 44.7 mg, about 44.8 mg, about 44.9 mg, about 45.0 mg, about 45.1 mg, about 45.2 mg, about 45.3 mg, about 45.4 mg, about 45.5 mg, about 45.6 mg, about 45.7 mg, about 45.8 mg, about 45.9 mg, about 46.0 mg, about 46.1 mg, about 46.2 mg, about 46.3 mg, about 46.4 mg, about 46.5 mg, about 46.6 mg, about 46.7 mg, about 46.8 mg, about 46.9 mg, about 47.0 mg, about 47.1 mg, about 47.2 mg, about 47.3 mg, about 47.4 mg, about 47.5 mg, about 47.6 mg, about 47.7 mg, about 47.8 mg, about 47.9 mg, about 48.0 mg, about 48.1 mg, about 48.2 mg, about 48.3 mg,

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about 97.7 mg, about 97.8 mg, about 97.9 mg, about 98.0 mg, about 98.1 mg, about 98.2 mg, about 98.3 mg, about 98.4 mg, about 98.5 mg, about 98.6 mg, about 98.7 mg, about 98.8 mg, about 98.9 mg, about 99.0 mg, about 99.1 mg, about 99.2 mg, about 99.3 mg, about 99.4 mg, about 99.5 mg, about 99.6 mg, about 99.7 mg, about 99.8 mg, about 99.9 mg, and about 100.0 mg.

76. The method of any one of claims 60-67, wherein the therapeutically effective amount is within the range of any of 40 mg to 100 mg, 40 mg to 80 mg, 40 mg to 70 mg, 40 mg to 60 mg, 40 mg to 50 mg, 50 mg to 100 mg, 50 mg to 80 mg, 50 mg to 70 mg, 50 mg to 60 mg, 60 mg to 100 mg, 60 mg to 80 mg, 60 mg to 70 mg, 70 mg to 100 mg, 70 mg to 80 mg, 80 mg to 100 mg, 80 mg to 90 mg, and 90 mg to 100 mg.

77. The method of any one of claims 60-67, wherein the therapeutically effective amount is any of less than 100 mg, less than 95 mg, less than 90 mg, less than 85 mg, less than 80 mg, less than 75 mg, less than 70 mg, less than 65 mg, less than 60 mg, less than 55 mg, less than 50 mg, less than 45 mg, and less than 40 mg.

78. The method of any one of claims 60-67, wherein the therapeutically effective amount is any of less than about less than about 100 mg, less than about 95 mg, less than about 90 mg, less than about 85 mg, less than about 80 mg, less than about 75 mg, less than about 70 mg, less than about 65 mg, less than about 60 mg, less than about 55 mg, less than about 50 mg, less than about 45 mg, and less than about 40 mg.

79. The method of any one of claims 60-67, wherein the therapeutically effective amount is any of at least 40 mg, at least 45 mg, at least 50 mg, at least 55 mg, at least 60 mg, at least 65 mg, at least 70 mg, at least 75 mg, at least 80 mg, at least 85 mg, at least 90 mg, at least 95 mg, and at least about 100 mg.

80. The method of any one of claims 60-67, wherein the therapeutically effective amount is any of at least about 40 mg, at least about 45 mg, at least about 50 mg, at least about 55 mg, at least about 60 mg, at least about 65 mg, at least about 70 mg, at least about 75 mg, at least about 80 mg, at least about 85 mg, at least about 90 mg, at least about 95 mg, and at least about 100 mg.

81. The method of any one of claims 60-80, comprising administering the modified oligonucleotide once every 4 weeks.

82. The method of any one of claims 60-80, comprising administering the modified oligonucleotide once every 8 weeks.

83. The method of any one of claims 60-80, comprising administering the modified oligonucleotide once every 12 weeks.

84. The method of any one of claims 60-80, comprising administering the modified oligonucleotide once every 16 weeks.

85. The method of any one of claims 60-80, comprising administering the modified oligonucleotide once every 20 weeks.

86. The method of any one of claims 60-80, comprising administering the modified oligonucleotide about once every 4 weeks.

87. The method of any one of claims 60-80, comprising administering the modified oligonucleotide about once every 8 weeks.

88. The method of any one of claims 60-80, comprising administering the modified oligonucleotide about once every 12 weeks.

89. The method of any one of claims 60-80, comprising administering the modified oligonucleotide about once every 16 weeks.

90. The method of any one of claims 60-80, comprising administering the modified oligonucleotide about once every 20 weeks.

91. The method of any one of claims 60-80, comprising administering the modified oligonucleotide any of once every 1 week, once every 2 weeks, once every 3 weeks, once every 4 weeks, once every 5 weeks, once every 6 weeks, once every 7 weeks, once every 8 weeks, once every 9 weeks, once every 10 weeks, once every 11 weeks, once every 12 weeks, once every 13 weeks, once every 14 weeks, once every 15 weeks, once every 16 weeks, once every 17 weeks, once every 18 weeks, once every 19 weeks, and once every 20 weeks.

92. The method of any one of claims 60-80, comprising administering the modified oligonucleotide any of once about every 1 week, once about every 2 weeks, once about every 3 weeks, once about every 4 weeks, once about every 5 weeks, once about every 6 weeks, once about every 7 weeks, once about every 8 weeks, once about every 9 weeks, once about every 10 weeks, once about every 11 weeks, once about every 12 weeks, once about every 13 weeks, once about every 14 weeks, once about every 15 weeks, once about every 16 weeks, once about every 17 weeks, once about every 18 weeks, once about every 19 weeks, and once about every 20 weeks.

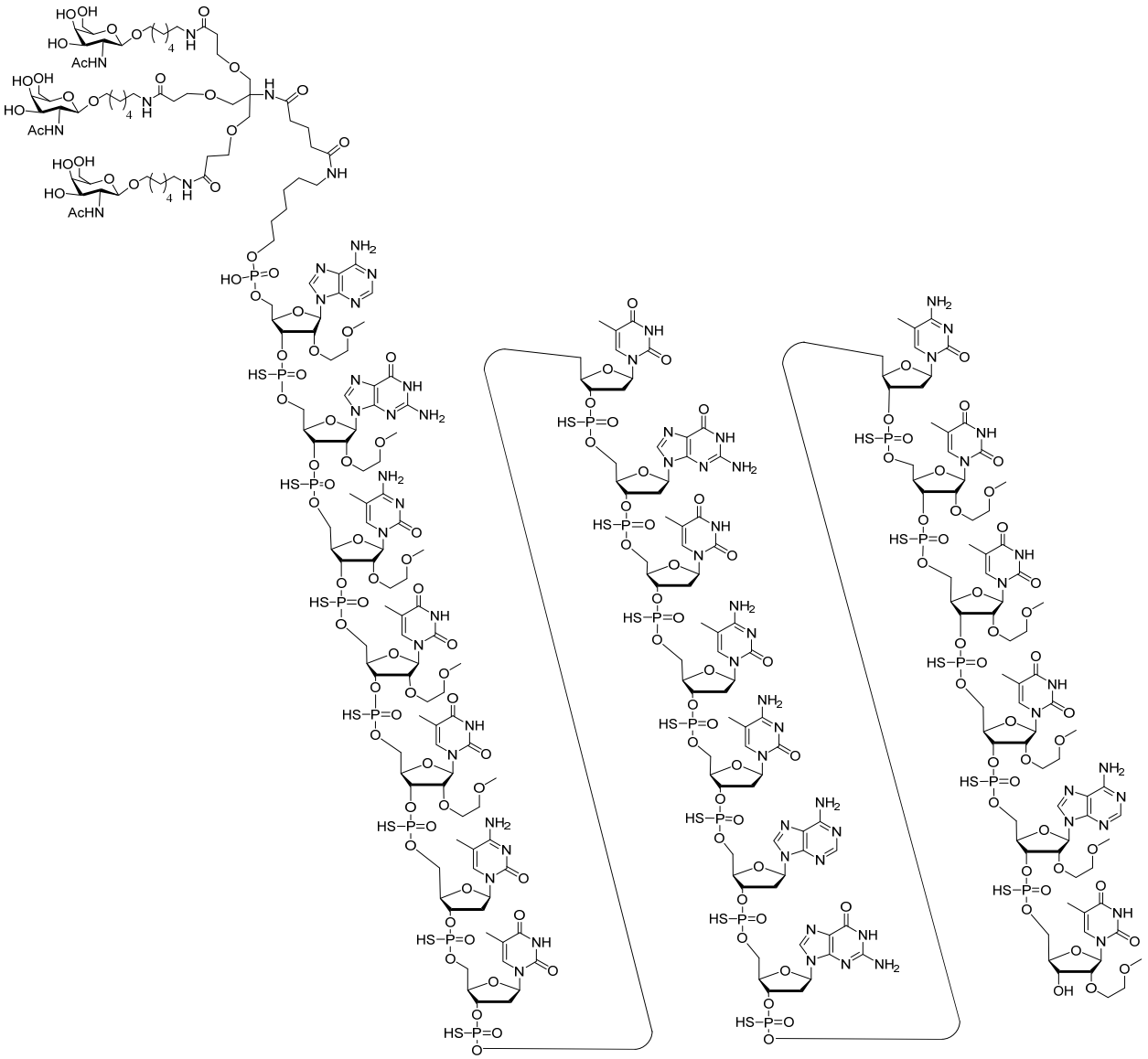
93. The method of any one of claims 60-92, wherein the subject has FCS.

94. The method of any one of claims 60-92, wherein the subject has FPL.

95. The method of any one of claims 60-94, wherein the subject has STHG.

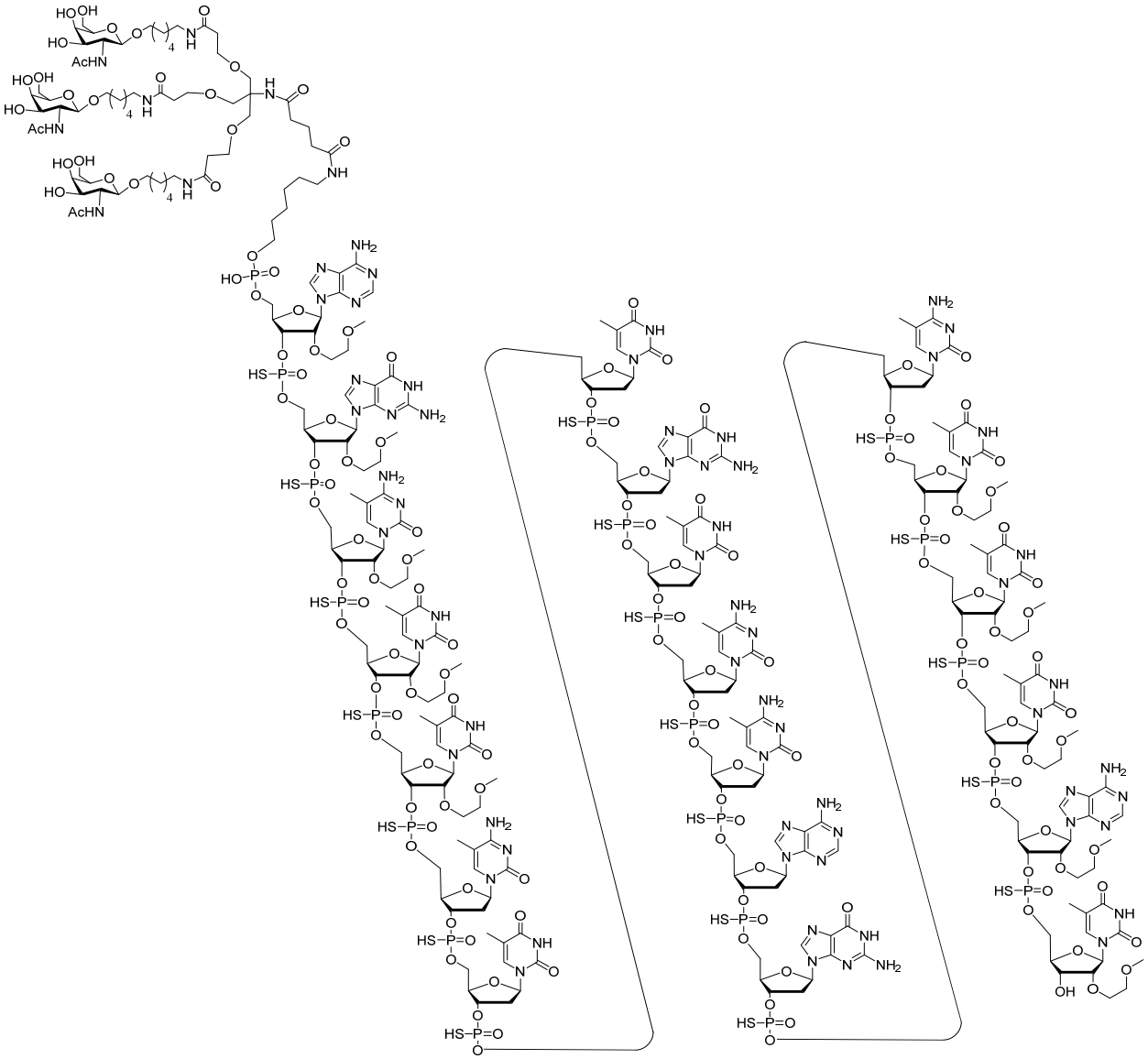
CLAIMS:

1. Use of a compound according to the following chemical structure:



(SEQ ID NO: 3), or a salt thereof, in the manufacture of a medicament for ameliorating at least one symptom of FCS, reducing APOCIII RNA, or reducing APOCIII protein in a human subject in need thereof, wherein a therapeutically effective amount of 50 mg or about 50 mg of the compound or the salt thereof, is to be subcutaneously administered to the human subject, about once every 4 weeks.

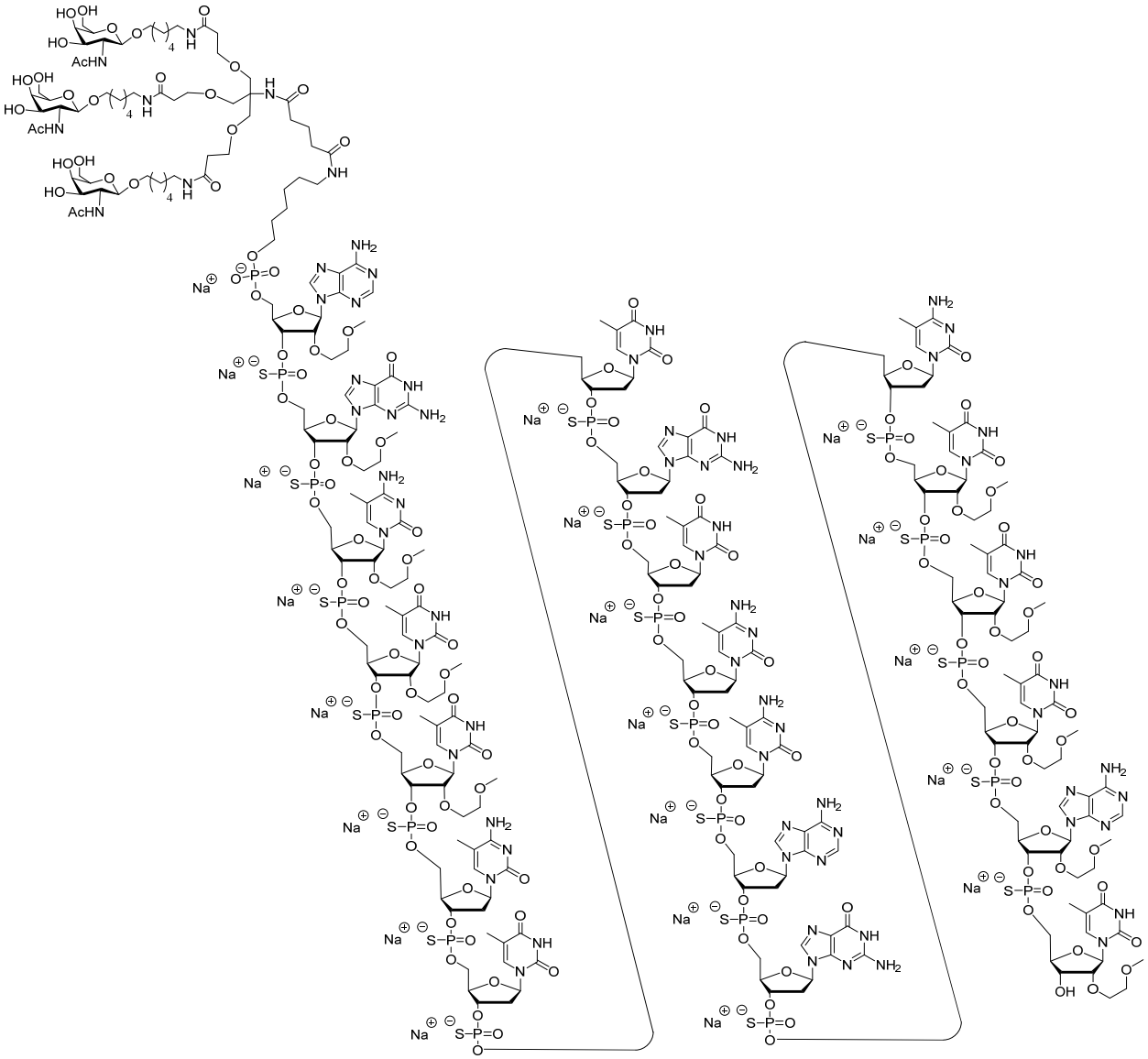
2. Use of a compound according to the following chemical structure:



(SEQ ID NO: 3), or a salt thereof, in the manufacture of a medicament for ameliorating at least one symptom of FCS, reducing APOCIII RNA, or reducing APOCIII protein in a human subject in need thereof, wherein a therapeutically effective amount of 80 mg or about 80 mg of the compound or the salt thereof, is to be subcutaneously administered to the human subject, about once every 4 weeks.

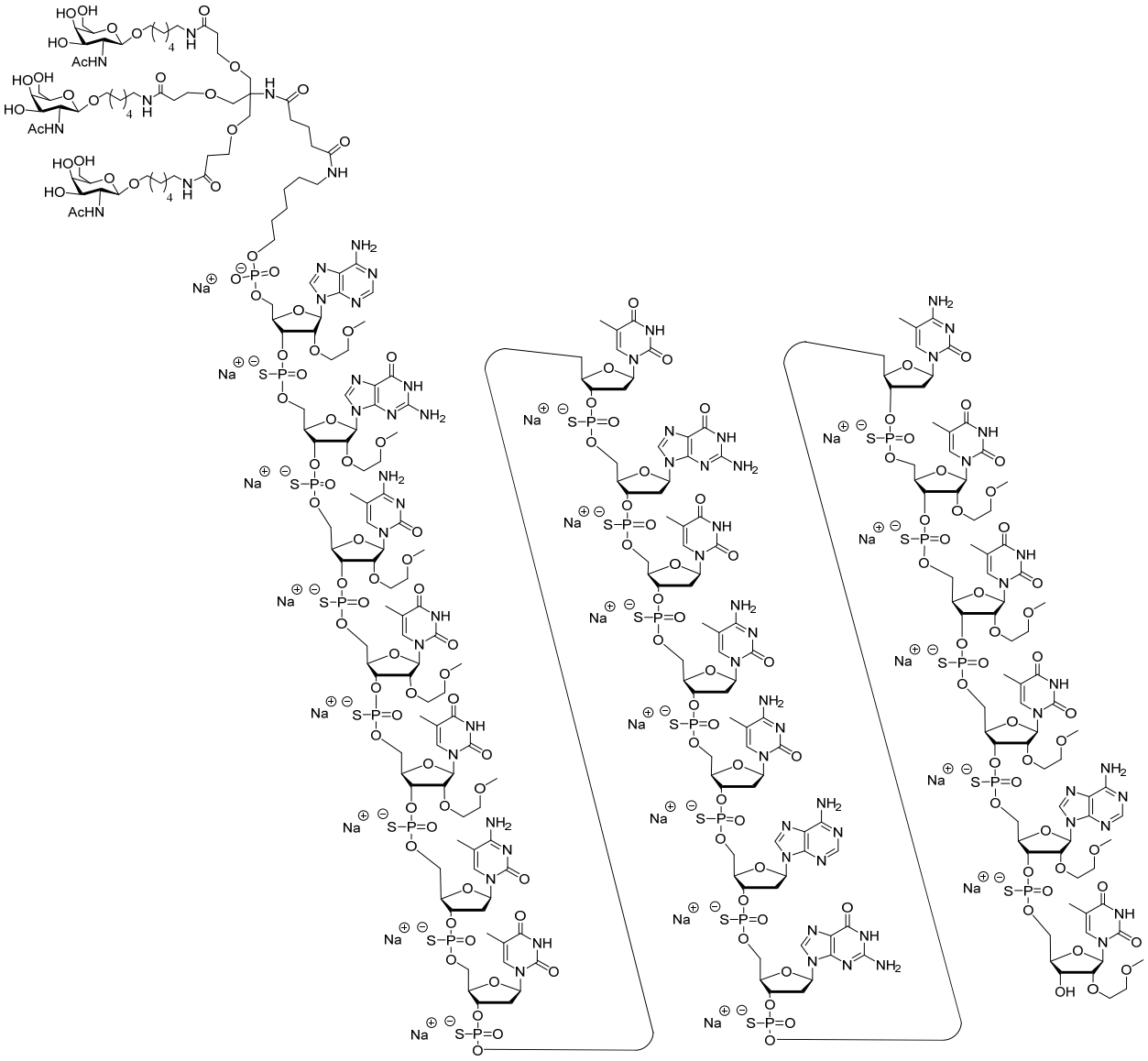
3. The use of claim 1 or claim 2, wherein the compound is the sodium salt or the potassium salt.

4. Use of a compound according to the following chemical structure:



(SEQ ID NO: 3), in the manufacture of a medicament for ameliorating at least one symptom of FCS, reducing APOCIII RNA, or reducing APOCIII protein in a human subject in need thereof, wherein a therapeutically effective amount of 50 mg or about 50 mg of the compound or the salt thereof, is to be subcutaneously administered to the human subject, about once every 4 weeks.

5. Use of a compound according to the following chemical structure:



(SEQ ID NO: 3), in the manufacture of a medicament for ameliorating at least one symptom of FCS, reducing APOCIII RNA, or reducing APOCIII protein in a human subject in need thereof, wherein a therapeutically effective amount of 80 mg or about 80 mg of the compound or the salt thereof, is to be subcutaneously administered to the human subject, about once every 4 weeks.

6. Use of a compound comprising a modified oligonucleotide in the manufacture of a medicament for ameliorating at least one symptom of FCS, reducing APOCIII RNA, or reducing APOCIII protein in a human subject in need thereof, wherein a therapeutically effective amount of 50 mg or about 50 mg of the compound or the salt thereof, is to be subcutaneously administered to the human subject, about once every 4 weeks,

wherein the modified oligonucleotide has the following chemical notation (5’ to 3’): $A_{es}G_{es}{}^{m}C_{es}T_{es}T_{es}{}^{m}C_{ds}T_{ds}T_{ds}G_{ds}T_{ds}{}^{m}C_{ds}{}^{m}C_{ds}A_{ds}G_{ds}{}^{m}C_{ds}T_{es}T_{es}T_{es}A_{es}T_{e}$ (SEQ ID NO: 3); wherein,

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

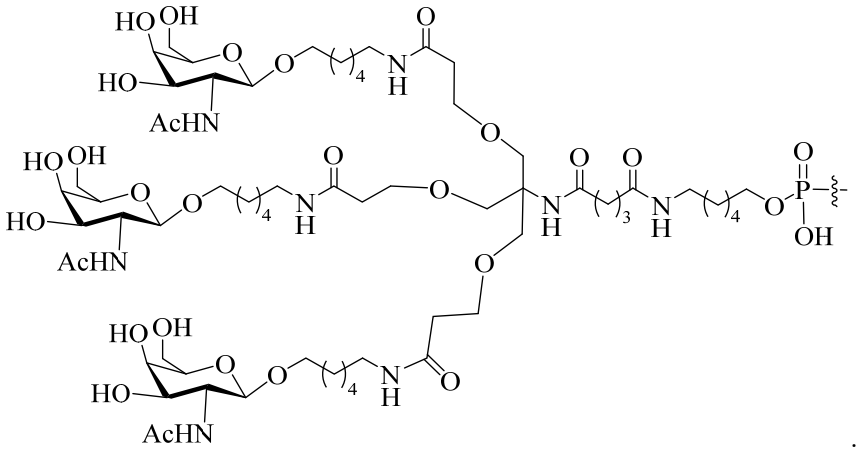
T = a thymine nucleobase,

e = a 2’- $OCH_2CH_2OCH_3$ modified ribosyl sugar moiety,

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

s = a phosphorothioate internucleoside linkage,

and wherein the modified oligonucleotide has a 5’-trishexylamino-(THA)-C_6GalNAc$_3$ endcap, represented by the structure below, wherein the phosphate group is attached to the 5'-oxygen atom of the 5'-nucleoside:



7. Use of a compound comprising a modified oligonucleotide in the manufacture of a medicament for ameliorating at least one symptom of FCS, reducing APOCIII RNA, or reducing APOCIII protein in a human subject in need thereof, wherein a therapeutically effective amount of 80 mg or about 80 mg of the compound or the salt thereof, is to be subcutaneously administered to the human subject, about once every 4 weeks,

wherein the modified oligonucleotide has the following chemical notation (5’ to 3’): $A_{es}G_{es}{}^{m}C_{es}T_{es}T_{es}{}^{m}C_{ds}T_{ds}T_{ds}G_{ds}T_{ds}{}^{m}C_{ds}{}^{m}C_{ds}A_{ds}G_{ds}{}^{m}C_{ds}T_{es}T_{es}T_{es}A_{es}T_{e}$ (SEQ ID NO: 3); wherein,

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

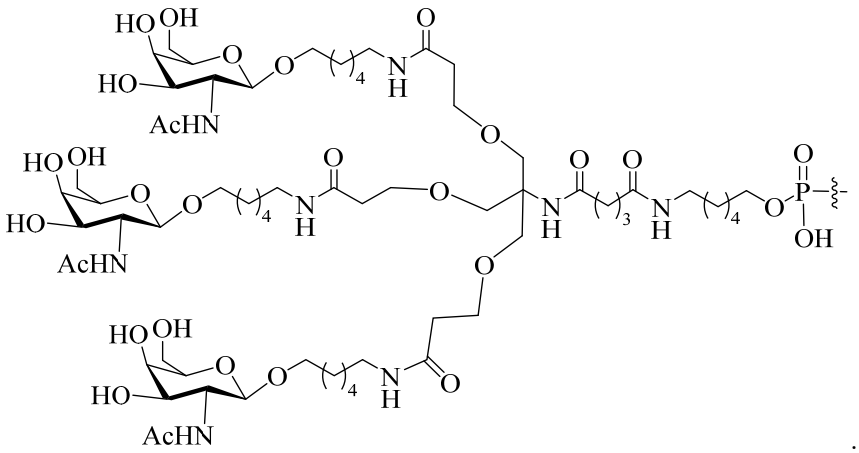
T = a thymine nucleobase,

e = a 2’- $OCH_2CH_2OCH_3$ modified ribosyl sugar moiety,

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

s = a phosphorothioate internucleoside linkage,

and wherein the modified oligonucleotide has a 5'-trishexylamino-(THA)-C_6GalNAc$_3$ endcap, represented by the structure below, wherein the phosphate group is attached to the 5'-oxygen atom of the 5'-nucleoside:



8. The use of any one of claims 1-7, wherein the at least one symptom comprises severe elevations in chylomicrons and extremely elevated TG levels (always reaching well above 1000 mg/dL and not infrequently rising as high as 10,000 mg/dL or more) with episodes of abdominal pain, physical fatigue, difficulty thinking, diarrhea, recurrent acute pancreatitis, eruptive cutaneous xanthomata, and hepatosplenomegaly, or a combination thereof.

9. The use of any one of claims 1-8, wherein the subject has FCS.

10. The use of any one of claims 1-8, wherein the subject has FPL.

11. The use of any one of claims 1-8, wherein the subject has STHG.