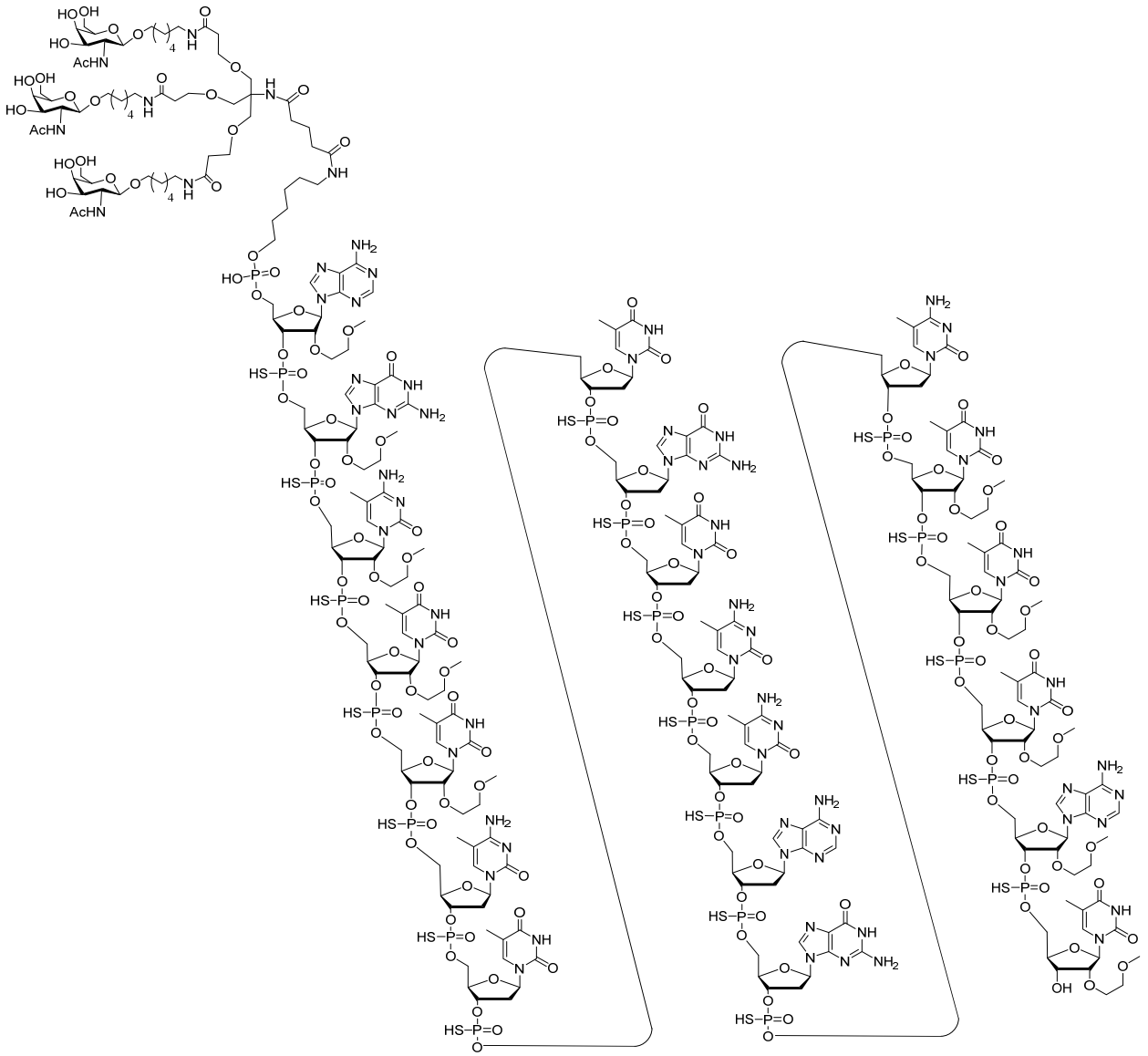
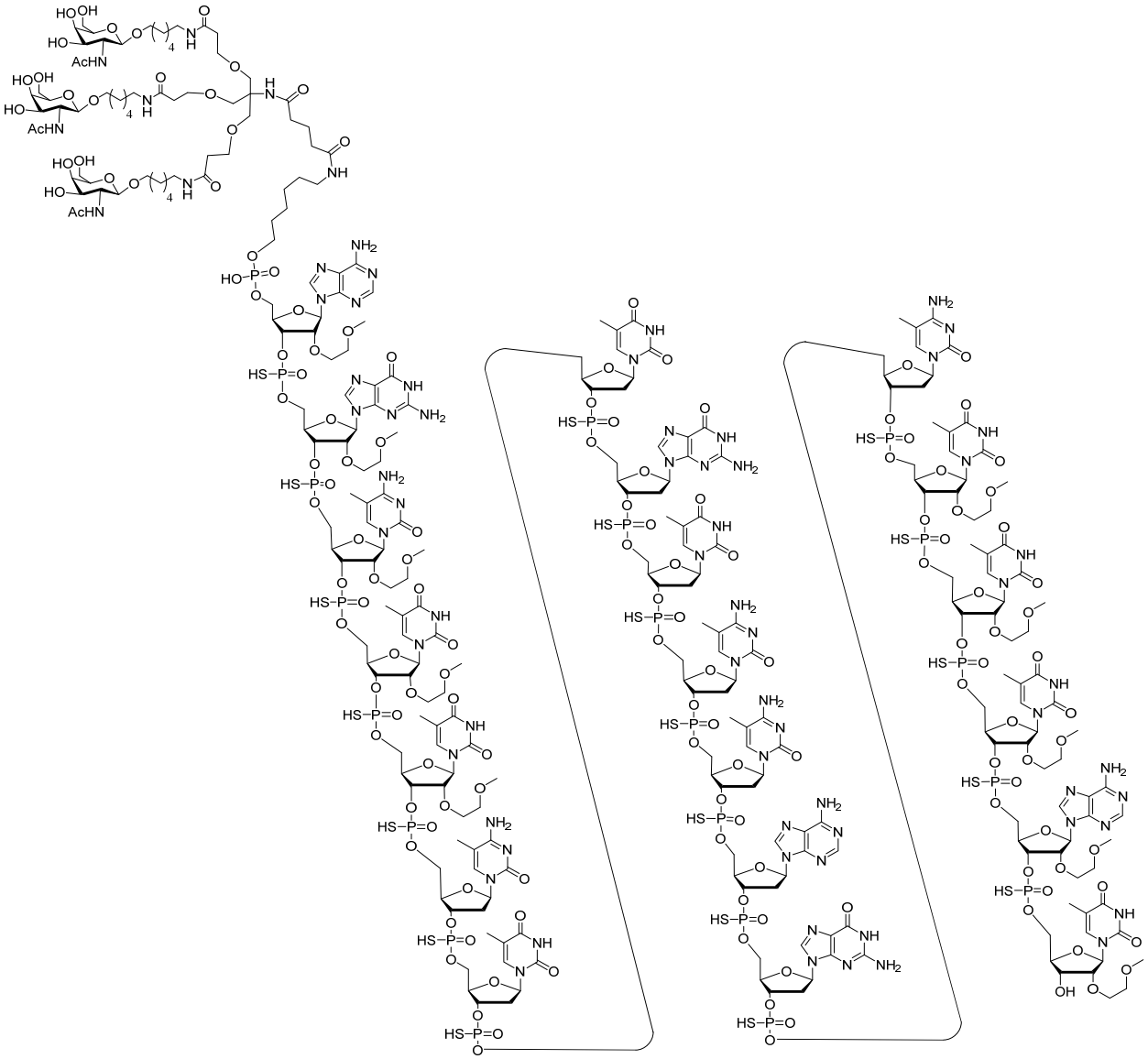
CLAIMS:

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.

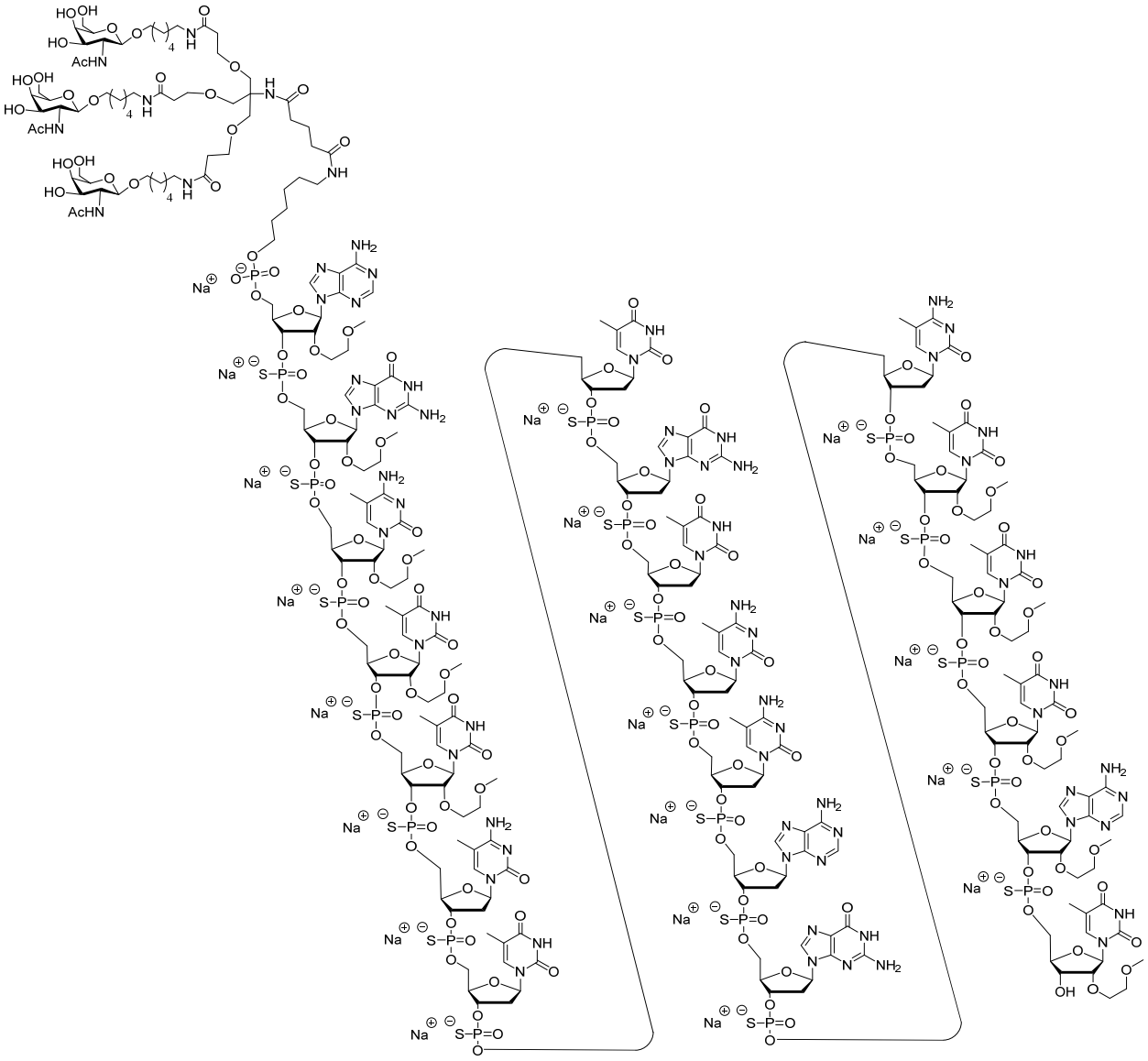
2. Use of a compound according to the following chemical structure:



(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.

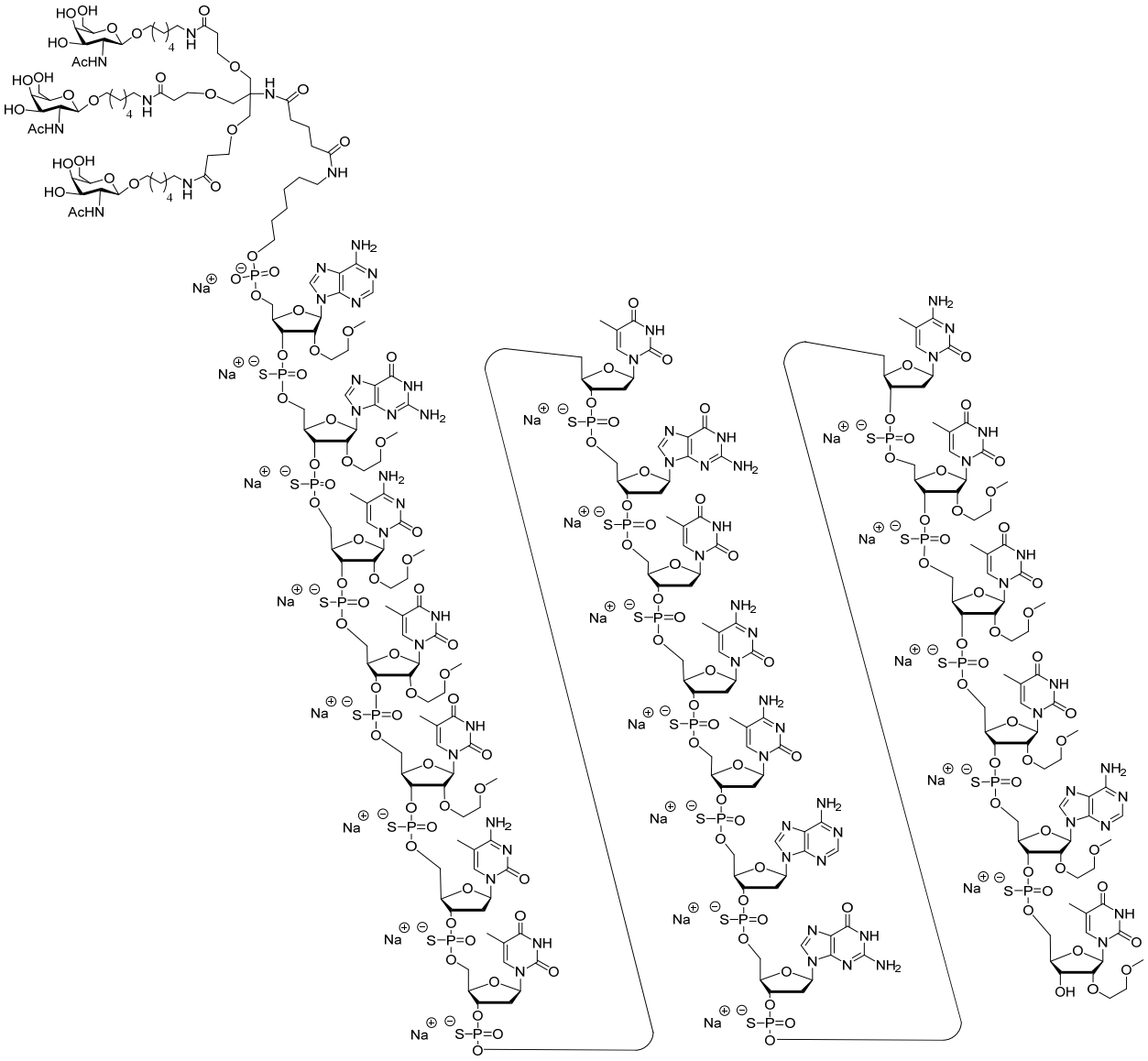
3. The use of claim 1 or claim 2, wherein the compound is the sodium salt or the potassium salt.

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,

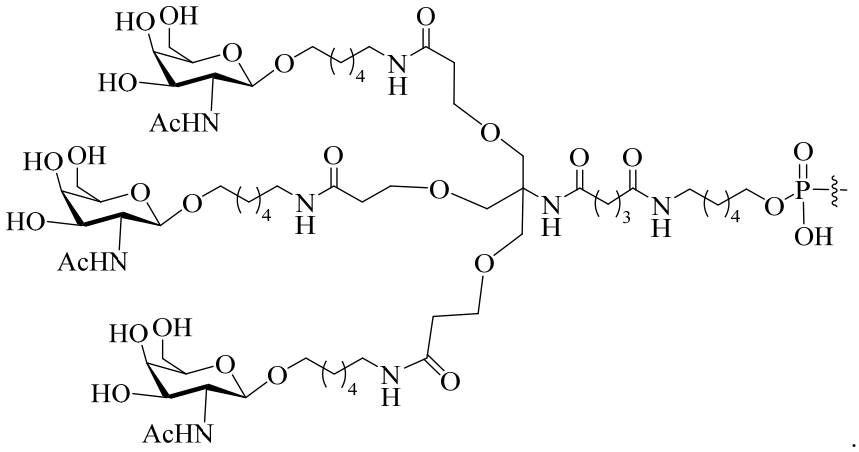
T = a thymine nucleobase,

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:



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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,

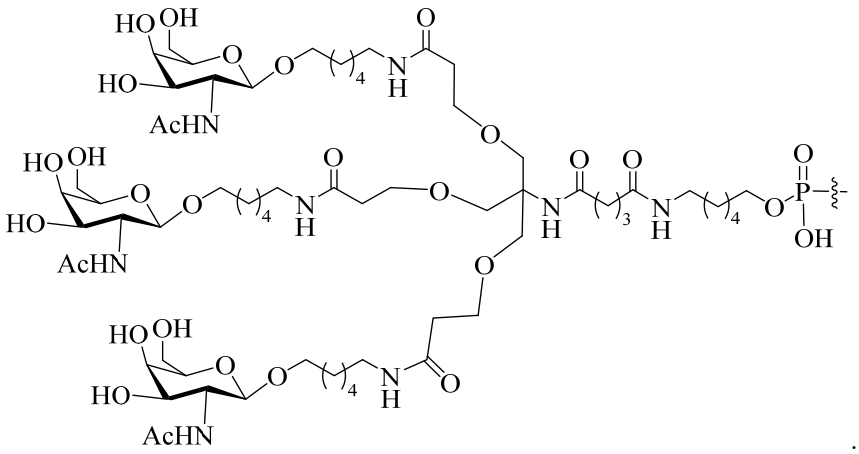
T = a thymine nucleobase,

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.