Claims

1. A nucleic acid for inhibiting expression of *LPA* in a cell, comprising at least one duplex region that comprises at least a portion of a first strand and at least a portion of a second strand that is at least partially complementary to the first strand, wherein said first strand is at least partially complementary to at least a portion of RNA transcribed from the *LPA* gene, wherein said first strand comprises a nucleotide sequence of
5’ mA (ps) fU (ps) mA fA mC fU mC fU mG fU mC fC mA fU mU fA mC (ps) fC (ps) mG 3‘ (SEQ ID NO: 165),
and wherein said second strand comprises a nucleotide sequence of
5‘ mC mG mG mU mA mA fU fG fG mA mC mA mG mA mG mU mU (ps) mA (ps) mU 3‘ (SEQ ID NO: 163);
wherein fA, fC, fG and fU denote 2’-deoxy-2’-fluoro ribonucleotides;
mA, mC, mG and mU denote 2‘-O-methyl ribonucleotides; and
(ps) denotes a phosphorothioate linkage.

2. The nucleic acid of claim 1, wherein the first strand consists of a nucleotide sequence of
5’ mA (ps) fU (ps) mA fA mC fU mC fU mG fU mC fC mA fU mU fA mC (ps) fC (ps) mG 3‘ (SEQ ID NO: 165);
wherein fA, fC, fG and fU denote 2’-deoxy-2’-fluoro ribonucleotides;
mA, mC, mG and mU denote 2‘-O-methyl ribonucleotides; and
(ps) denotes a phosphorothioate linkage.

3. The nucleic acid of claim 1 or claim 2, wherein the second strand consists of a nucleotide sequence of
5‘ mC mG mG mU mA mA fU fG fG mA mC mA mG mA mG mU mU (ps) mA (ps) mU 3‘ (SEQ ID NO: 163);
wherein fA, fC, fG and fU denote 2’-deoxy-2’-fluoro ribonucleotides;
mA, mC, mG and mU denote 2‘-O-methyl ribonucleotides; and
(ps) denotes a phosphorothioate linkage.

4. The nucleic acid of any of the preceding claims, wherein the nucleic acid is conjugated to a ligand.

5. The nucleic acid of claim 4, wherein the ligand comprises (i) one or more N-acetyl galactosamine (GalNAc) moieties or derivatives thereof, and (ii) a linker, wherein the linker conjugates the at least one GalNAc moiety or derivative thereof to the nucleic acid.

6. The nucleic acid of any preceding claim, wherein the nucleic acid is conjugated to a ligand comprising a compound of formula (I):

$$[S\text{-}X^1\text{-}P\text{-}X^2]_3\text{-}A\text{-}X^3\text{-} \qquad (I)$$

wherein:

S represents a saccharide, preferably wherein the saccharide is N-acetyl galactosamine;

X^1 represents C_3-C_6 alkylene or $(\text{-}CH_2\text{-}CH_2\text{-}O)_m(\text{-}CH_2)_2\text{-}$ wherein m is 1, 2, or 3;

P is a phosphate or modified phosphate, preferably a thiophosphate;

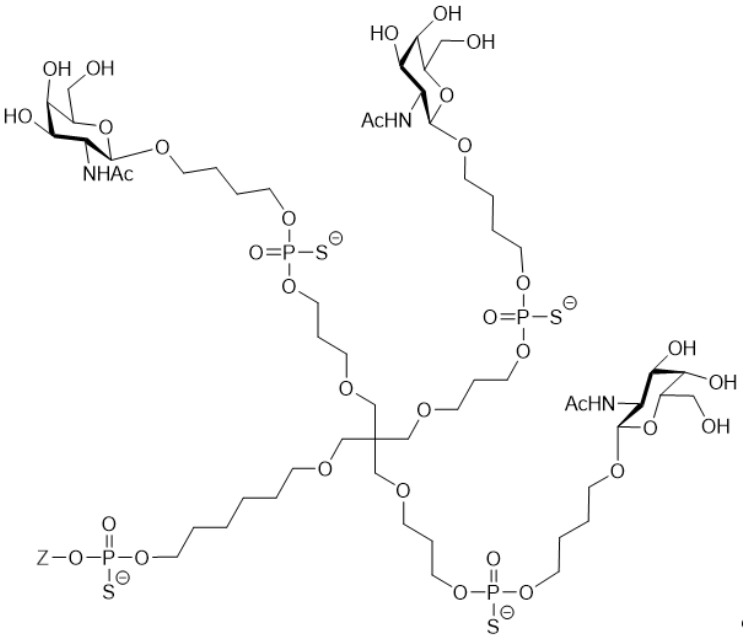
X^2 is alkylene or an alkylene ether of the formula $(\text{-}CH_2)_n\text{-}O\text{-}CH_2\text{-}$ where n = 1- 6;

A is a branching unit;

X^3 represents a bridging unit;

wherein a nucleic acid as defined in any of claims 1 to 5 is conjugated to X^3 via a phosphate or modified phosphate, preferably a thiophosphate, and the nucleic acid is preferably conjugated to X^3 via the 5' end of the second strand.

7. The nucleic acid of any preceding claim, wherein the nucleic acid is conjugated to a ligand and has the following structure



wherein Z is a nucleic acid according any preceding claim and the ligand is preferably conjugated to the 5’ end of the second strand.

8. The nucleic acid of any of claims 4-7, wherein the second strand comprises a nucleotide sequence of

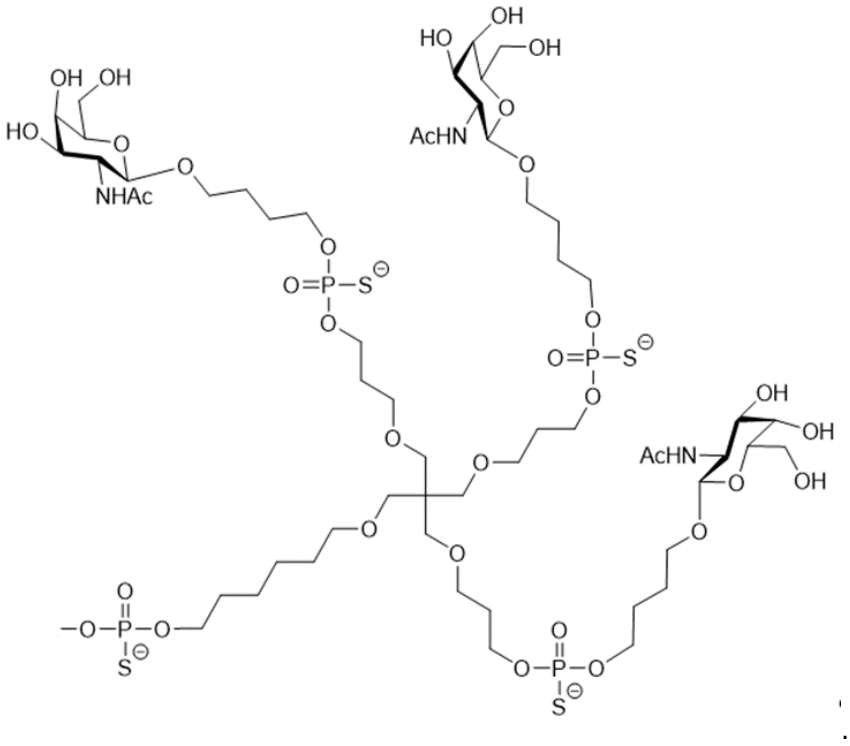
5´ [ST23 (ps)]3 C6XLT (ps) mC mG mG mU mA mA fU fG fG mA mC mA mG mA mG mU mU (ps) mA (ps) mU 3´ (SEQ ID NO: 164);

wherein fA, fC, fG and fU denote 2’-deoxy-2’-fluoro ribonucleotides;

mA, mC, mG and mU denote 2‘-O-methyl ribonucleotides;

(ps) denotes a phosphorothioate linkage; and

[ST23 (ps)]3 C6XLT (ps) denotes



9. The nucleic acid of claim 8, wherein the second strand consists of a nucleotide sequence of

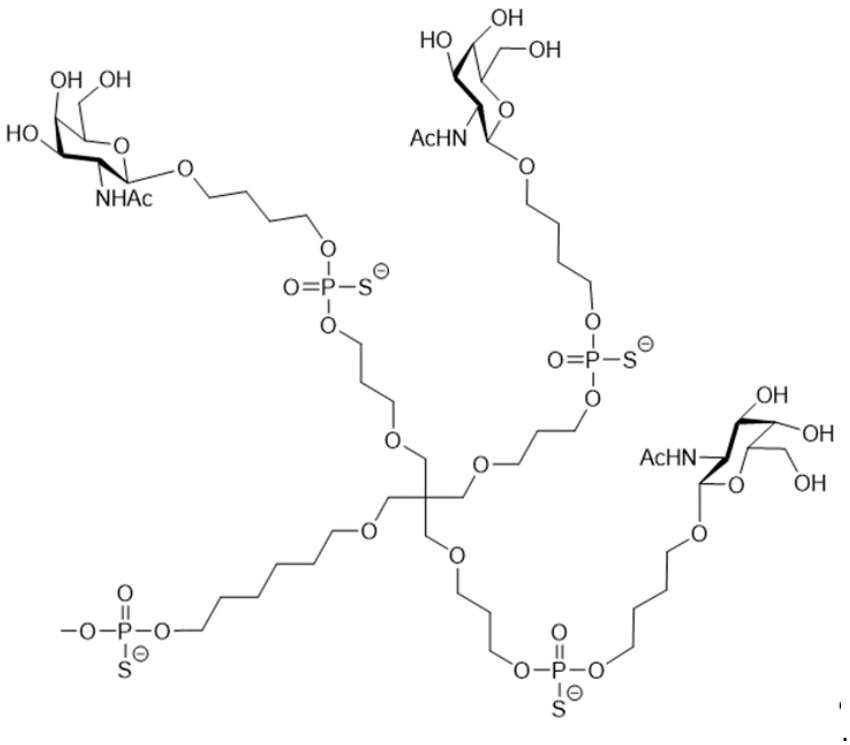
5´ [ST23 (ps)]3 C6XLT (ps) mC mG mG mU mA mA fU fG fG mA mC mA mG mA mG mU mU (ps) mA (ps) mU 3‘ (SEQ ID NO: 164);

wherein fA, fC, fG and fU denote 2’-deoxy-2’-fluoro ribonucleotides;

mA, mC, mG and mU denote 2‘-O-methyl ribonucleotides;

(ps) denotes a phosphorothioate linkage; and

[ST23 (ps)]3 C6XLT (ps) denotes



10. A composition comprising a nucleic acid of any of claims 1-9 and optionally a delivery vehicle and/or a physiologically acceptable excipient and/or a carrier and/or a diluent and/or a buffer and/or a preservative, for use as a medicament.

11. The composition for use according to claim 10, wherein said composition is for use in the prevention or treatment or risk reduction of a disease or pathology, wherein the disease or pathology is a cardiovascular disease.

12. The composition for use according to claim 11, wherein the cardiovascular disease is stroke, atherosclerosis, thrombosis, coronary heart disease or aortic stenosis and/or any other disease or pathology associated to elevated levels of Lp(a) particles.

13. A pharmaceutical composition comprising a nucleic acid of any of claims 1-9 and further comprising a delivery vehicle and/or a physiologically acceptable excipient and/or a carrier and/or a diluent.

14. Use of a nucleic acid of any of claims 1-9, in the manufacture of a medicament for treating cardiovascular disease.

15. The use according to claim 14, wherein the cardiovascular disease is stroke, atherosclerosis, thrombosis, coronary heart disease or aortic stenosis and/or any other disease or pathology associated to elevated levels of Lp(a) particles.