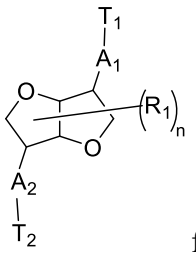
CLAIMS

1. A compound, having a structure represented by formula (I) or a stereoisomer thereof:



formula (I)

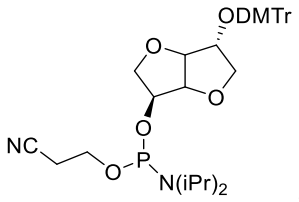
wherein A_1 and A_2 are each independently selected from O, S, SO, SO_2, NR_2, and CR_3R_4; R_2, R_3, and R_4 are each independently selected from hydrogen, halogen, sulfonyl, sulfinyl, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_3-C_6 cycloalkyl, substituted or unsubstituted C_2-C_6 alkenyl, substituted or unsubstituted C_2-C_6 alkynyl, substituted or unsubstituted C_5-C_{12} aryl, substituted or unsubstituted 5- to 12-membered heteroaryl, and substituted or unsubstituted 5- to 12-membered heterocyclyl;

one of T_1 and T_2 is a protecting group, Z, L, or -Z-L, wherein Z represents a targeting group or a lipophilic group, the lipophilic group being optionally linked to one of A_1 or A_2 via a linker, and L represents a carrier spacer or a carrier moiety linked via a spacer; the other of T_1 and T_2 is an active phosphorus group or a protecting group; and T_1 and T_2 are not protecting groups simultaneously;

each R_1 is independently selected from halogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_3-C_6 cycloalkyl, substituted or unsubstituted C_2-C_6 alkenyl, substituted or unsubstituted C_2-C_6 alkynyl, substituted or unsubstituted C_5-C_{12} aryl, substituted or unsubstituted 5- to 12-membered heteroaryl, and substituted or unsubstituted 5- to 12-membered heterocyclyl;

n is an integer of 0-6;

wherein formula (I) does not comprise the following structure:



2. The compound according to claim 1, wherein:

(i) A_1 is O, S, NR_2, wherein R_2 is hydrogen or CH_3; and/or

(ii) A_2 is O, S, NR_2, wherein R_2 is hydrogen or CH_3.

3. The compound according to claim 1, wherein:

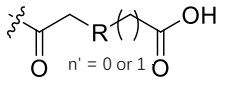
A_1 is O, and A_2 is O;

A_1 is O, and A_2 is S;

A_1 is O, and A_2 is NR_2, wherein R_2 is hydrogen or CH_3; or

A_1 is S, and A_2 is NR_2, wherein R_2 is hydrogen or CH_3.

4. The compound according to claim 1, wherein:

(i) one of T_1 and T_2 is a carrier spacer or a carrier moiety linked via a spacer; the carrier spacer is preferably a dicarboxylic acid-derived group 

; wherein R is absent, ether, polyethylene glycol, oxygen, sulfur, nitrogen, alkylene, alkenyl, alkynyl, aryl, aralkyl, heteroalkyl, or heteroaryl; the carrier spacer is preferably a C_3-C_6 alkyl dicarboxylate group, and more preferably a succinic acid group; the carrier is preferably a polymethacrylate vinyl alcohol copolymer, a silicon chip glass, cellulose, a polystyrene bead, a polypropylene sheet, a non-porous silica bead, polyacrylamide, or polyacrylate, and more preferably long-chain alkylamine-controlled pore glass (LCAA-CPG);

(ii) one of T_1 and T_2 is a protecting group, wherein

the protecting group for one of T_1 and T_2 is a hydroxyl-protecting group; the hydroxyl-protecting groups are each independently selected from acetyl, tert-butyl, tert-butoxymethyl, methoxymethyl, tetrahydropyranyl, 1-ethoxyethyl, 1-(2-chloroethoxy)ethyl, 2-trimethylsilylethyl, p-chlorophenyl,

2,4-dinitrophenyl, benzyl, benzoyl, p-phenylbenzoyl, 2,6-dichlorobenzyl, diphenylmethyl, p-nitrobenzyl, trimethylsilyl, triethylsilyl, tert-butyldimethylsilyl, tert-butyldiphenylsilyl, triphenylsilyl, triisopropylsilyl, benzoylformate, chloroacetyl, trichloroacetyl, trifluoroacetyl, pivaloyl, 9-fluorenylmethoxycarbonyl, mesyl, tosyl, trifyl, trityl, monomethoxytrityl, dimethoxytrityl, trimethoxytrityl, and substituted 9-phenylxanthine-9-yl; the preferred hydroxyl-protecting groups are each independently selected from acetyl, benzyl, tert-butyldimethylsilyl, tert-butyldiphenylsilyl, and 4,4'-dimethoxytrityl;

the protecting group for one of T_1 and T_2 is a sulfhydryl-protecting group; the sulfhydryl-protecting groups are each independently selected from acetyl, tert-butyl, tert-butoxymethyl, methoxymethyl, tetrahydropyranyl, 1-ethoxyethyl, 1-(2-chloroethoxy)ethyl, 2-trimethylsilylethyl, p-chlorophenyl, 2,4-dinitrophenyl, benzyl, benzoyl, p-phenylbenzoyl, 2,6-dichlorobenzyl, diphenylmethyl, p-nitrobenzyl, trimethylsilyl, triethylsilyl, tert-butyldimethylsilyl, tert-butyldiphenylsilyl, triphenylsilyl, triisopropylsilyl, benzoylformate, chloroacetyl, trichloroacetyl, trifluoroacetyl, pivaloyl, 9-fluorenylmethoxycarbonyl, mesyl, tosyl, trifyl, trityl, monomethoxytrityl, dimethoxytrityl, trimethoxytrityl, and substituted 9-phenylxanthine-9-yl; the preferred sulfhydryl-protecting groups are each independently selected from benzyl and 4,4'-dimethoxytrityl; or

the protecting group for one of T_1 and T_2 is an amino-protecting group; the amino-protecting groups are each independently selected from 2-(trimethylsilyl)ethoxycarbonyl (Teoc), 1-methyl-1-(4-biphenyl)ethoxycarbonyl (Bpoc), tert-butoxycarbonyl (BOC), allyloxycarbonyl (Alloc), 9-fluorenylmethoxycarbonyl (Fmoc), benzyloxycarbonyl (Cbz), formyl, acetyl, trihaloacetyl, benzoyl, nitrophenyl, 2-nitrobenzenesulfonyl, phthalimido, and dithiosuccinyl;

(iii) one of T_1 and T_2 is a lipophilic group, wherein the lipophilicity of the lipophilic group is determined by logKow, and the logKow exceeds 0; preferably, the logKow of the lipophilic group exceeds 1, exceeds 1.5, exceeds 2, exceeds 3, exceeds 4, exceeds 5, or exceeds 10; or

(iv) one of T_1 and T_2 is a targeting group.

5. The compound according to claim 4, wherein:

(a) the lipophilic group is selected from the group consisting of a saturated or unsaturated C_4-C_{30} hydrocarbon chain, an aliphatic ring, an aryl group, a fatty acid group or a fatty acid-derived group, a steroid-derived group, and any fat-soluble vitamin group; or

(b) the lipophilic group is a saturated or unsaturated C_{10}-C_{18} hydrocarbon chain, any saturated or unsaturated fatty acid that comprises a hydrocarbon chain having 4 to 28 carbon atoms and may contain one or two carboxyl groups, cholesterol, vitamin E (tocopherol), or bile acid; more preferably, the lipophilic group is saturated linear C_{14}, C_{16}, or C_{18} alkyl, octanoic acid, decanoic acid, dodecanoic acid, tetradecanoic acid, hexadecanoic acid, octadecanoic acid, eicosanoic acid, docosanoic acid, tetracosanoic acid, myristoleic acid, palmitoleic acid, hexadecenoic acid, oleic acid, elaidic acid, vaccenic acid, linoleic acid, linolelaidic acid, α-linolenic acid, arachidonic acid, erucic acid, docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), docosanoic acid (DCA), sterol cholesterol (bile), tocopherol succinate (TS), lithocholic acid (LA), or retinoic acid (vitamin A acid).

6. The compound according to any one of claims 4-5, wherein the lipophilic group may be covalently linked to A_1 or A_2 via a linker.

7. The compound according to claim 6, wherein:

(i) the linker is selected from the group consisting of an amide bond, phosphatidylcholine, a hydrocarbon linker or polyethylene glycol (PEG) linker, amino-alkyl-alcohol, hydroxyproline, hydroxyprolinol, an amino-alkyl-phosphorothioate linker, an amino-PEG-phosphorothioate linker, an α-carboxylate-amino-alkyl

phosphorothioate linker, an α-carboxylate-amino-PEG-phosphorothioate linker, ether, thioether, urea, carbonate, amine, amide, maleimide-thioether, disulfide, phosphodiester, a sulfonamide bond, a product from a click reaction, and carbamate; or

(ii) the linker is a cleavable linker selected from the group consisting of a redox-cleavable linker, an acid-cleavable linker, an esterase-cleavable linker, a phosphatase-cleavable linker, and a peptidase-cleavable linker; or the linker is a biocleavable linker selected from the group consisting of DNA, RNA, disulfide, amide, functionalized monosaccharides or oligosaccharides of galactosamine, glucosamine, glucose, galactose, and mannose, and combinations thereof.

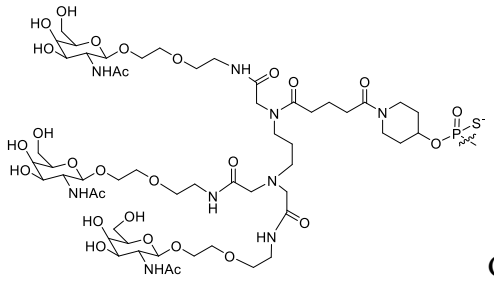
8. The compound according to claim 4, wherein

(i) the targeting group is selected from one or more of ligands comprising the following targeting molecules or derivatives thereof: polymers, saccharides, ligands for receptors expressed on hepatocytes, antibodies, quantum dots, polypeptides, and small molecule ligands;

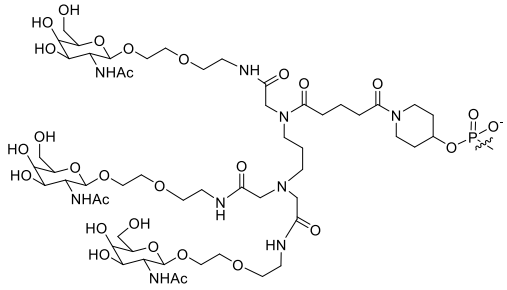
(ii) each of the targeting group is independently a ligand that has an affinity for an asialoglycoprotein receptor (ASGPR) on the surface of a mammalian hepatocyte; preferably, the targeting group is independently selected from ligands comprising one or more of D-mannopyranose, L-mannopyranose, D-arabinose, D-xylofuranose, L-xylofuranose, D-glucose, L-glucose, D-galactose, L-galactose, α-D-mannofuranose, β-D-mannofuranose, α-D-mannopyranose, β-D-mannopyranose, α-D-glucopyranose, β-D-glucopyranose, α-D-glucofuranose, β-D-glucofuranose, α-D-fructofuranose, α-D-fructopyranose, α-D-galactopyranose, β-D-galactopyranose, α-D-galactofuranose, β-D-galactofuranose, glucosamine, sialic acid, galactosamine, N-acetylgalactosamine, N-trifluoroacetylgalactosamine, N-propionylgalactosamine, N-n-butyrylgalactosamine, N-isobutyrylgalactosamine, 2-amino-3-O-[(R)-1-carboxyethyl]-2-deoxy-β-D-glucopyranose, 2-deoxy-2-methylamino-L-glucopyranose, 4,6-dideoxy-4-carboxamido-2,3-di-O-methyl-D-mannopyranose, 2-deoxy-2-sulfoamino-D-glucopyranose, N-glycoloyl-α-neuraminic acid, 5-thio-β-D-glucopyranose, methyl

2,3,4-tri-O-acetyl-1-thio-6-O-trityl-α-D-glucopyranoside, 4-thio-β-D-galactopyranose, ethyl 3,4,6,7-tetra-O-acetyl-2-deoxy-1,5-dithio-α-D-glucoheptopyranoside, 2,5-anhydro-D-allononitrile, ribose, D-ribose, D-4-thioribose, L-ribose, or L-4-thioribose; more preferably, the targeting group is a ligand comprising galactose or N-acetylgalactosamine; or

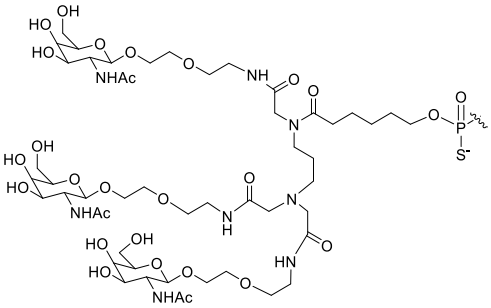
(iii) the targeting group is linked to one of A_1 or A_2 and selected from one of the following compound fragments:



GLS15*,

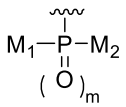


GLO15,



GLS5*.

9. The compound according to any one of claims 1-8, wherein:

(i) the other of T_1 and T_2 is an active phosphorus group having the following structure: ,

wherein M_1 is H, substituted or unsubstituted C_1-C_6 alkyl, OR_5, SR_5, OH, SH, or

NR_6R_7; M_2 is OH, SH, OR_5', or $NR_6'R_7'$; each R_5, R_6, R_7, R_5', R_6', or R_7' is independently hydrogen, substituted or unsubstituted C_1-C_6 alkyl, or sulfonyl; m is 0 or 1;

(ii) the other of T_1 and T_2 is an active phosphorus group selected from diisopropylcyanoethoxy phosphoramidite, diisopropylmethyl phosphoramidite, diisopropylethyl phosphoramidite, and H-phosphonate.

10. The compound according to claim 9, wherein:

(i) M_1 is selected from methyl, ethyl, propyl, isopropyl, OR_5, and methanesulfonamido, and R_5 is selected from substituted or unsubstituted methyl, ethyl, propyl, and isopropyl; and/or

(ii) M_2 is selected from $N(CH(CH_3)_2)_2$.

11. The compound according to any one of claims 9-10, wherein R_5, R_6, or R_7 is independently substituted alkyl, and the substituent is selected from cyano, halogen, hydroxyl, and amino.

12. The compound according to claim 9, wherein M_1 is $O(CH_2)_2CN$; M_2 is $N(CH(CH_3)_2)_2$; m is 0.

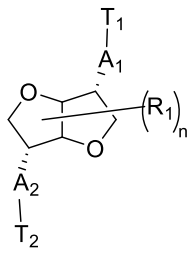
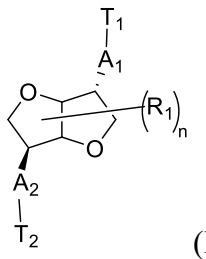
13. The compound according to any one of claims 1-12, wherein one of T_1 and T_2 is diisopropylcyanoethoxy phosphoramidite, and the other is 4,4'-dimethoxytrityl, a targeting group, or a lipophilic group; alternatively, one of T_1 and T_2 is a protecting group, and the other is a carrier spacer, a carrier moiety linked via a spacer, a targeting group, or a lipophilic group.

14. The compound according to any one of claims 1-13, wherein:

(i) each R_1 is independently selected from halogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_2-C_6 alkenyl, and substituted or unsubstituted C_2-C_6 alkynyl; or

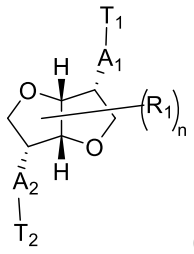
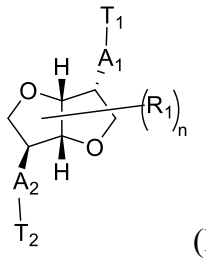
(ii) n is 0.

15. The compound according to any one of claims 1-14, wherein the compound has a configuration of formula (IIa) or formula (IIb):


(IIa) ,

(IIb),

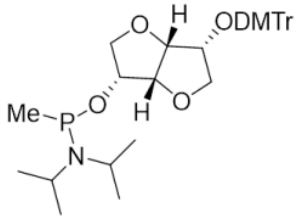
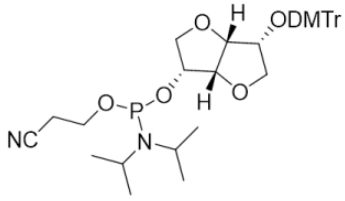
wherein A_1, A_2, T_1, T_2, R_1, and n are as defined in claims 1-14.

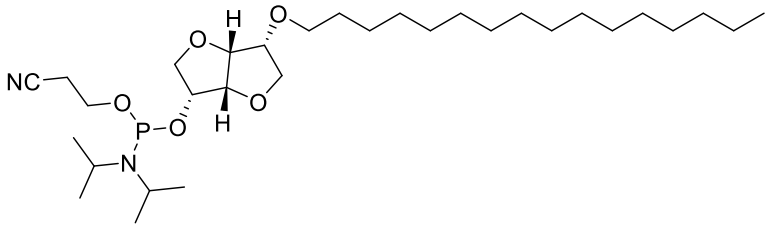
16. The compound according to any one of claims 1-15, wherein the compound provided herein has a configuration of formula (IIa-1) or formula (IIb-1):

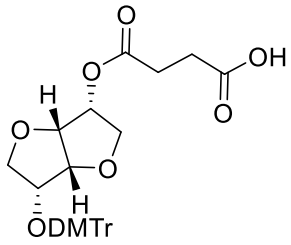

(IIa-1) ,

(IIb-1),

wherein A_1, A_2, T_1, T_2, R_1, and n are as defined in claims 1-14.

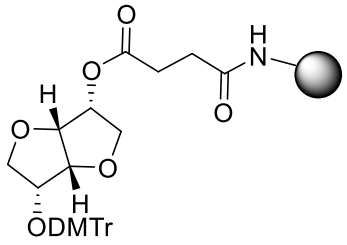
17. The compound according to any one of claims 1-16, wherein the compound has the following specific structures:


compound 1,

compound 2,

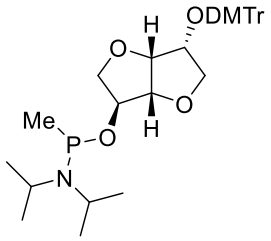

compound 3,



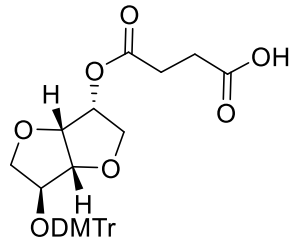
compound 4,



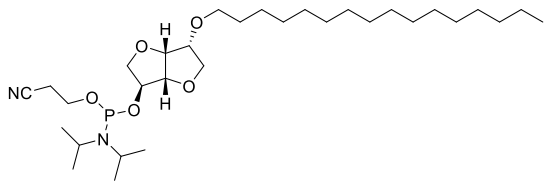
, N- is a solid-phase carrier (LCAA-CPG), compound 5,



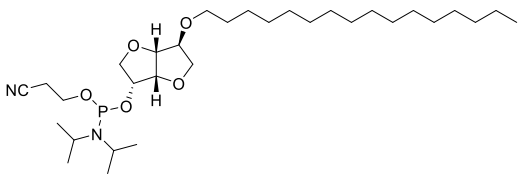
compound 6,



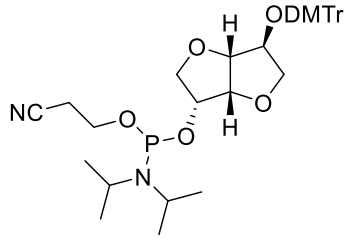
compound 7,



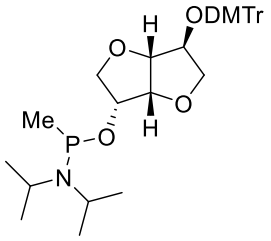
compound 8,



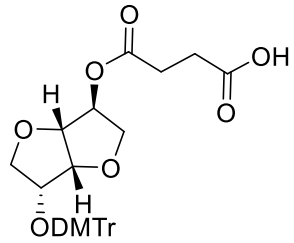
compound 9,



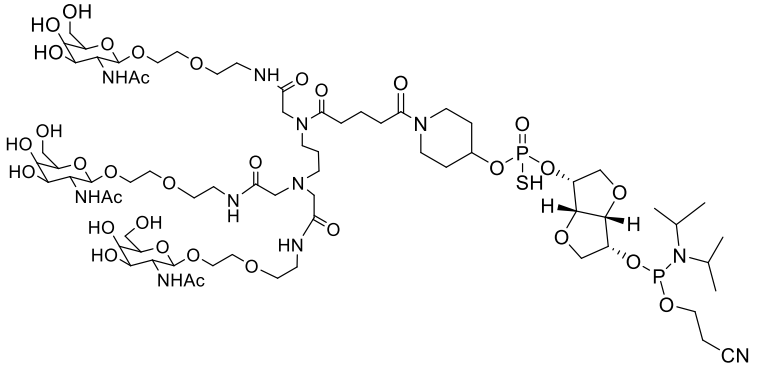
compound 10,



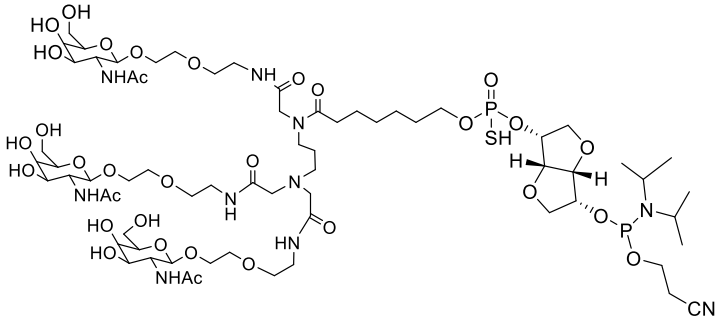
compound 11,



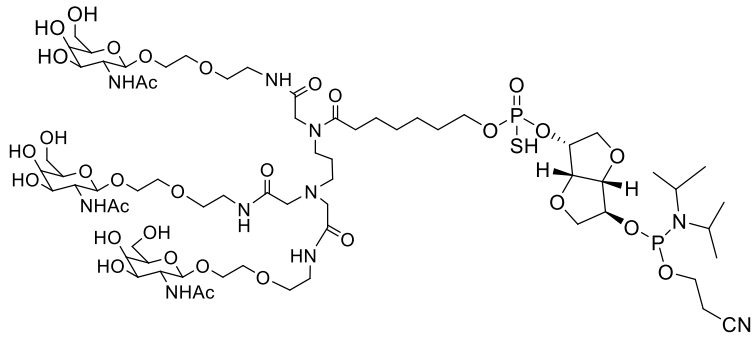
compound 12,



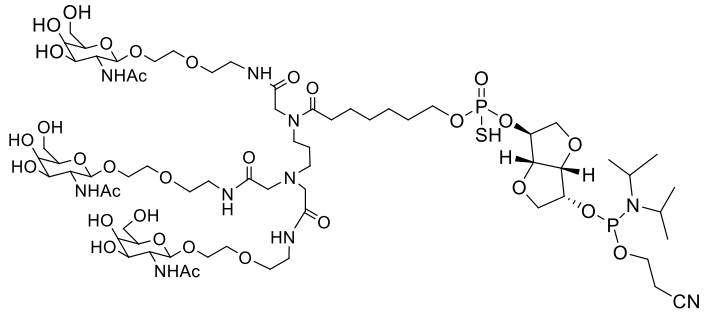
compound 13,



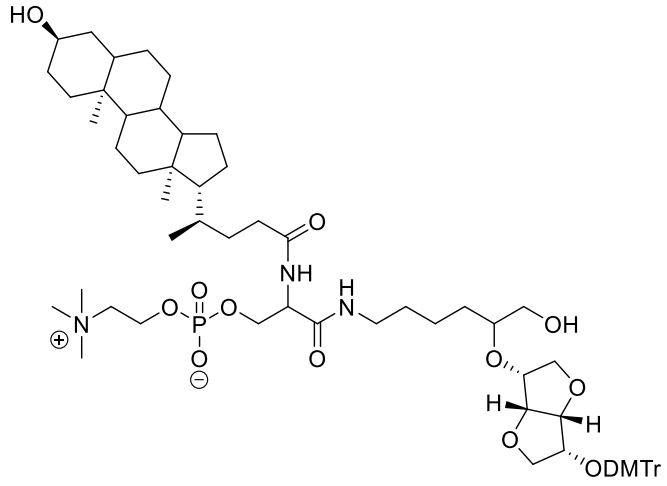
compound 14,



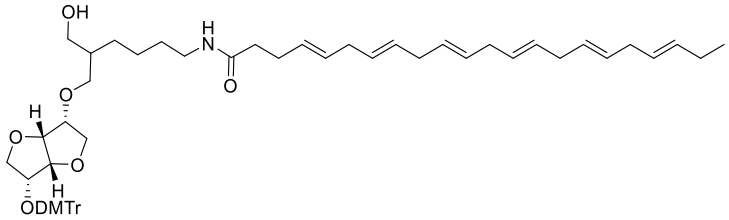
compound 15,



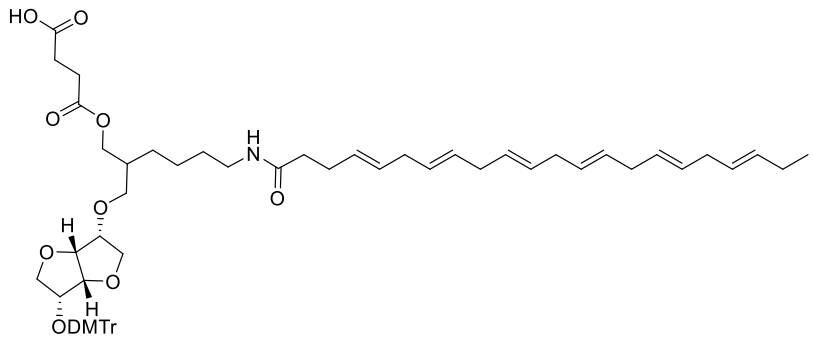
compound 16,



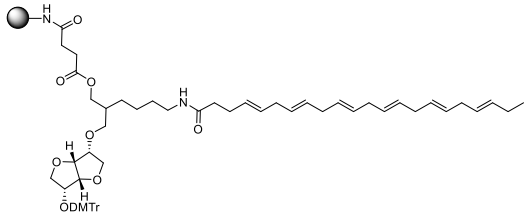
compound 17,



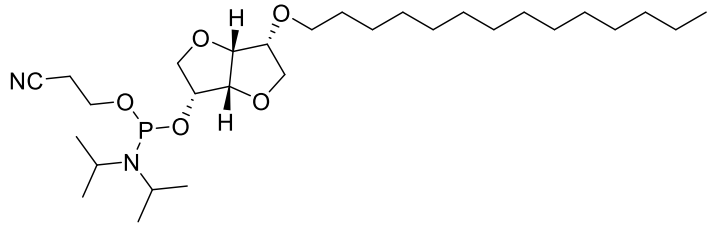
compound 18,



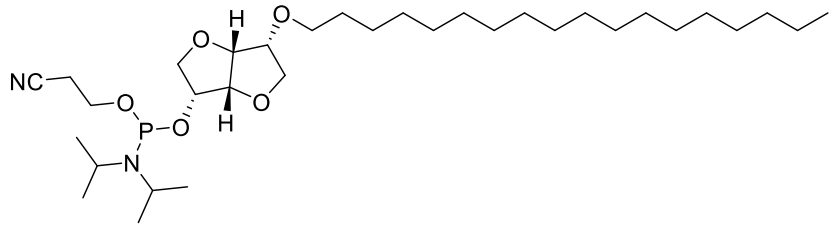
compound 19,



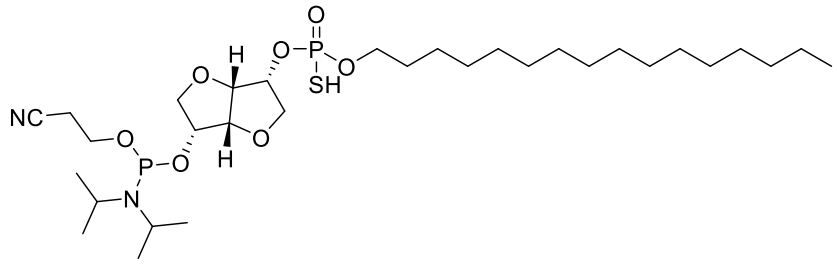
, N-  is a solid-phase carrier (LCAA-CPG), compound 20,



compound 21,

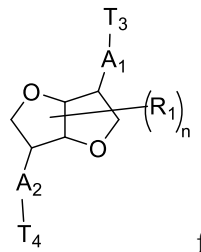


compound 22, and



compound 23.

18. An oligomeric compound, comprising at least one 5'-terminal and/or 3'-terminal monomer represented by formula (III) or a stereoisomer thereof:



formula (III)

wherein A_1 and A_2 are each independently selected from O, S, SO, SO_2, NR_2, and CR_3R_4; R_2, R_3, and R_4 are each independently selected from hydrogen, halogen, sulfonyl, sulfinyl, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_3-C_6 cycloalkyl, substituted or unsubstituted C_2-C_6 alkenyl, substituted or unsubstituted C_2-C_6 alkynyl, substituted or unsubstituted C_5-C_{12} aryl, substituted or unsubstituted 5- to 12-membered heteroaryl, and substituted or unsubstituted 5- to 12-membered heterocyclyl;

one of T_3 and T_4 is H, a protecting group, a lipophilic group, or optionally a covalent bond; the lipophilic group is optionally linked to one of A_1 or A_2 via a linker; and the other of T_3 and T_4 is an internucleoside linking group that links the monomer of formula (III) or the stereoisomer thereof to the oligomeric compound;

each R_1 is independently selected from halogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_3-C_6 cycloalkyl, substituted or unsubstituted C_2-C_6 alkenyl, substituted or unsubstituted C_2-C_6 alkynyl, substituted or unsubstituted C_5-C_{12} aryl, substituted or unsubstituted 5- to 12-membered heteroaryl, and substituted or unsubstituted 5- to 12-membered heterocyclyl;

n is an integer of 0-6;

the oligomeric compound optionally further comprises a targeting group.

19. The oligomeric compound according to claim 18, wherein:

(i) A_1 is O;

(ii) A_2 is O, S, NR_2, wherein R_2 is hydrogen or CH_3.

20. The oligomeric compound according to claim 18, wherein:

A_1 is O, and A_2 is S;

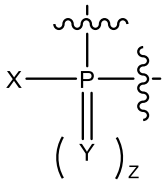
A_1 is O, and A_2 is NR_2, wherein R_2 is hydrogen, methylsulfonyl, or CH_3; or

A_1 is S, and A_2 is NR_2, wherein R_2 is hydrogen, methylsulfonyl, or CH_3.

21. The oligomeric compound according to any one of claims 18-20, wherein:

(i) the other of T_3 and T_4 is an internucleoside linking group that links the monomer to the 5'-end and/or the 3'-end of the oligomeric compound, and the internucleoside linking group is selected from a phosphorus-containing linking group and a phosphorus-free linking group.

22. The oligomeric compound according to claim 21, wherein:

(i) the phosphorus-containing internucleoside linking group has a structural fragment represented by , wherein X represents H, substituted or unsubstituted C_1-C_6 alkyl, OR_8, SR_8', OH, SH, or NR_9R_{10}; Y represents O or S; z may be 0 or 1; R_8, R_8', R_9, or R_{10} is independently hydrogen, substituted or unsubstituted C_1-C_6 alkyl, or sulfonyl; each "∿∿∿" independently represents a moiety linked to one of A_1 or A_2 and a moiety linked to an adjacent nucleotide;

(ii) the phosphorus-containing internucleoside linking group is independently a phosphodiester linking group, a phosphotriester linking group, a phosphorothioate linking group, a phosphorodithioate linking group, an alkylphosphonate linking group, an aminophosphonate linking group, a phosphonate linking group, a phosphinate linking group, a phosphoramidothioate linking group, or a phosphoramidate linking group.

23. The oligomeric compound according to any one of claims 18-22, wherein:

(i) one of T_3 and T_4 is a protecting group, wherein

the protecting group for one of T_3 and T_4 is a hydroxyl-protecting group; the hydroxyl-protecting groups are each independently selected from

acetyl, tert-butyl, tert-butoxymethyl, methoxymethyl, tetrahydropyranyl, 1-ethoxyethyl, 1-(2-chloroethoxy)ethyl, 2-trimethylsilylethyl, p-chlorophenyl, 2,4-dinitrophenyl, benzyl, benzoyl, p-phenylbenzoyl, 2,6-dichlorobenzyl, diphenylmethyl, p-nitrobenzyl, trimethylsilyl, triethylsilyl, tert-butyldimethylsilyl, tert-butyldiphenylsilyl, triphenylsilyl, triisopropylsilyl, benzoylformate, chloroacetyl, trichloroacetyl, trifluoroacetyl, pivaloyl, 9-fluorenylmethoxycarbonyl, mesyl, tosyl, trifyl, trityl, monomethoxytrityl, dimethoxytrityl, trimethoxytrityl, and substituted 9-phenylxanthine-9-yl; the preferred hydroxyl-protecting groups are each independently selected from acetyl, benzyl, tert-butyldimethylsilyl, tert-butyldiphenylsilyl, and 4,4'-dimethoxytrityl;

the protecting group for one of T_3 and T_4 is a sulfhydryl-protecting group; the sulfhydryl-protecting groups are each independently selected from acetyl, tert-butyl, tert-butoxymethyl, methoxymethyl, tetrahydropyranyl, 1-ethoxyethyl, 1-(2-chloroethoxy)ethyl, 2-trimethylsilylethyl, p-chlorophenyl, 2,4-dinitrophenyl, benzyl, benzoyl, p-phenylbenzoyl, 2,6-dichlorobenzyl, diphenylmethyl, p-nitrobenzyl, trimethylsilyl, triethylsilyl, tert-butyldimethylsilyl, tert-butyldiphenylsilyl, triphenylsilyl, triisopropylsilyl, benzoylformate, chloroacetyl, trichloroacetyl, trifluoroacetyl, pivaloyl, 9-fluorenylmethoxycarbonyl, mesyl, tosyl, trifyl, trityl, monomethoxytrityl, dimethoxytrityl, trimethoxytrityl, and substituted 9-phenylxanthine-9-yl; the preferred sulfhydryl-protecting groups are each independently selected from benzyl and 4,4'-dimethoxytrityl; or

the protecting group for one of T_3 and T_4 is an amino-protecting group; the amino-protecting groups are each independently selected from 2-(trimethylsilyl)ethoxycarbonyl (Teoc), 1-methyl-1-(4-biphenyl)ethoxycarbonyl (Bpoc), tert-butoxycarbonyl (BOC), allyloxycarbonyl (Alloc), 9-fluorenylmethoxycarbonyl (Fmoc),

benzyloxycarbonyl (Cbz), formyl, acetyl, trihaloacetyl, benzoyl, nitrophenyl, 2-nitrobenzenesulfonyl, phthalimido, and dithiosuccinyl;

(ii) one of T_3 and T_4 is a lipophilic group, wherein the lipophilicity of the lipophilic group is determined by logKow, and the logKow exceeds 0; preferably, the logKow of the lipophilic group exceeds 1, exceeds 1.5, exceeds 2, exceeds 3, exceeds 4, exceeds 5, or exceeds 10;

(iii) one of T_3 and T_4 is denoted as a covalent bond, and the oligomeric compound is linked to a targeting group via one of T_3 and T_4 in the form of a covalent bond.

24. The oligomeric compound according to any one of claims 18-22, wherein one of T_3 and T_4 is hydrogen, and the other of T_3 and T_4 is an internucleoside linking group that links the monomer of formula (III) or the stereoisomer thereof to the 5'-end and/or the 3'-end of the oligomeric compound.

25. The oligomeric compound according to claim 23, wherein:

(a) the lipophilic group is selected from the group consisting of a saturated or unsaturated C_4-C_{30} hydrocarbon chain, an aliphatic ring, an aryl group, a fatty acid group or a fatty acid-derived group, a steroid-derived group, and any fat-soluble vitamin group; or

(b) the lipophilic group is a saturated or unsaturated C_{10}-C_{18} hydrocarbon chain, any saturated or unsaturated fatty acid that comprises a hydrocarbon chain having 4 to 28 carbon atoms and may contain one or two carboxyl groups, cholesterol, vitamin E (tocopherol), or bile acid; more preferably, the lipophilic group is saturated linear C_{16} alkyl, octanoic acid, decanoic acid, dodecanoic acid, tetradecanoic acid, hexadecanoic acid, octadecanoic acid, eicosanoic acid, docosanoic acid, tetracosanoic acid, myristoleic acid, palmitoleic acid, hexadecenoic acid, oleic acid, elaidic acid, vaccenic acid, linoleic acid, linolelaidic acid, α-linolenic acid, arachidonic acid, erucic acid, docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), docosanoic acid (DCA), sterol cholesterol (bile), tocopherol succinate (TS), lithocholic acid (LA), or retinoic acid (vitamin A acid).

26. The oligomeric compound according to any one of claims 24-25, wherein the lipophilic group may be covalently linked to A_1 or A_2 via a linker.

27. The oligomeric compound according to claim 26, wherein:

(i) the linker is selected from the group consisting of an amide bond, phosphatidylcholine, a hydrocarbon linker or polyethylene glycol (PEG) linker, amino-alkyl-alcohol, hydroxyproline, hydroxyprolinol, an amino-alkyl-phosphorothioate linker, an amino-PEG-phosphorothioate linker, an α-carboxylate-amino-alkyl phosphorothioate linker, an α-carboxylate-amino-PEG-phosphorothioate linker, ether, thioether, urea, carbonate, amine, amide, maleimide-thioether, disulfide, phosphodiester, a sulfonamide bond, a product from a click reaction, and carbamate; or

(ii) the linker is a cleavable linker selected from the group consisting of a redox-cleavable linker, an acid-cleavable linker, an esterase-cleavable linker, a phosphatase-cleavable linker, and a peptidase-cleavable linker; or the linker is a biocleavable linker selected from the group consisting of DNA, RNA, disulfide, amide, functionalized monosaccharides or oligosaccharides of galactosamine, glucosamine, glucose, galactose, and mannose, and combinations thereof.

28. The oligomeric compound according to any one of claims 28-23, wherein the 5'-end and/or the 3'-end of the oligomeric compound further comprise one or more targeting groups.

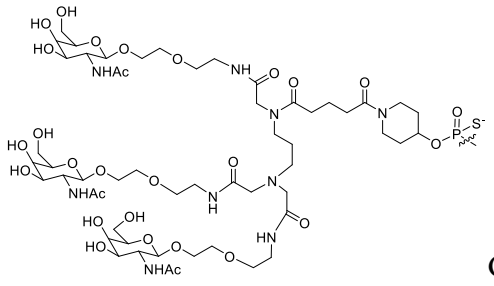
29. The oligomeric compound according to any one of claims 18-28, wherein:

(i) the targeting group is selected from one or more of ligands comprising the following targeting molecules or derivatives thereof: polymers, saccharides, ligands for receptors expressed on hepatocytes, antibodies, quantum dots, polypeptides, and small molecule ligands;

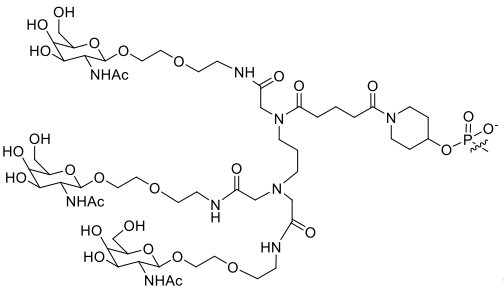
(ii) each of the targeting groups is independently a ligand that has an affinity for an asialoglycoprotein receptor (ASGPR) on the surface of a mammalian hepatocyte; preferably, the targeting group is independently selected from ligands comprising one or more of D-mannopyranose, L-mannopyranose, D-arabinose, D-xylofuranose, L-

xylofuranose, D-glucose, L-glucose, D-galactose, L-galactose, α-D-mannofuranose, β-D-mannofuranose, α-D-mannopyranose, β-D-mannopyranose, α-D-glucopyranose, β-D-glucopyranose, α-D-glucofuranose, β-D-glucofuranose, α-D-fructofuranose, α-D-fructopyranose, α-D-galactopyranose, β-D-galactopyranose, α-D-galactofuranose, β-D-galactofuranose, glucosamine, sialic acid, galactosamine, N-acetylgalactosamine, N-trifluoroacetylgalactosamine, N-propionylgalactosamine, N-n-butyrylgalactosamine, N-isobutyrylgalactosamine, 2-amino-3-O-[(R)-1-carboxyethyl]-2-deoxy-β-D-glucopyranose, 2-deoxy-2-methylamino-L-glucopyranose, 4,6-dideoxy-4-carboxamido-2,3-di-O-methyl-D-mannopyranose, 2-deoxy-2-sulfoamino-D-glucopyranose, N-glycoloyl-α-neuraminic acid, 5-thio-β-D-glucopyranose, methyl 2,3,4-tri-O-acetyl-1-thio-6-O-trityl-α-D-glucopyranoside, 4-thio-β-D-galactopyranose, ethyl 3,4,6,7-tetra-O-acetyl-2-deoxy-1,5-dithio-α-D-glucoheptopyranoside, 2,5-anhydro-D-allononitrile, ribose, D-ribose, D-4-thioribose, L-ribose, or L-4-thioribose; more preferably, the targeting group is a ligand comprising galactose or N-acetylgalactosamine; or

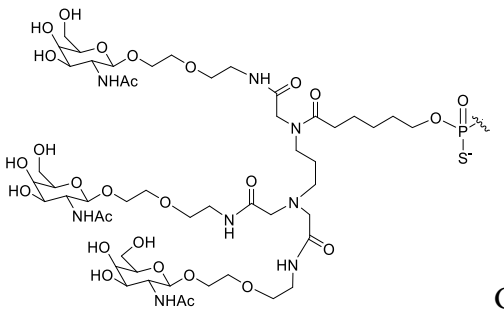
(iii) the targeting group is linked to one of A_1 or A_2 and selected from one of the following compound fragments:



GLS15*,

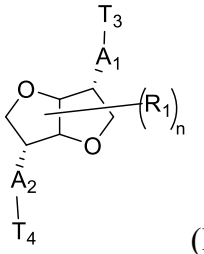


GLO15,

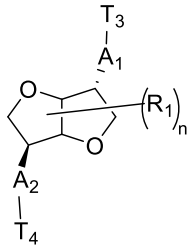


GLS5*.

30. The oligomeric compound according to any one of claims 18-29, comprising at least one 5'-terminal and/or 3'-terminal monomer of a configuration represented by formula (IVa) or formula (IVb):



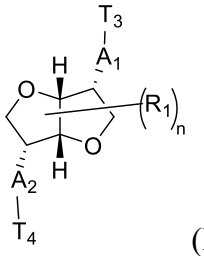
(IVa) ,



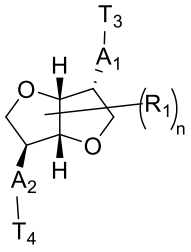
(IVb),

wherein A_1, A_2, T_3, T_4, R_1, and n are as defined in claims 18-29.

31. The oligomeric compound according to any one of claims 18-29, comprising at least one 5'-terminal and/or 3'-terminal monomer of a configuration represented by formula (IVa-1) or formula (IVb-1):



(IVa-1),



(IVb-1),

wherein A_1, A_2, T_3, T_4, R_1, and n are as defined in any one of claims 218-29.

32. The oligomeric compound according to any one of claims 18-31, wherein:

(i) each R_1 is independently selected from halogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_2-C_6 alkenyl, and substituted or unsubstituted C_2-C_6 alkynyl; or

(ii) n is 0 .

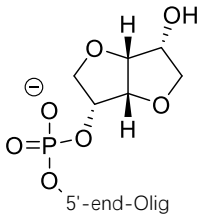
33. The oligomeric compound according to any one of claims 18-32, wherein:

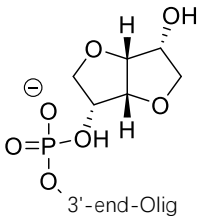
(i) one of T_3 and T_4 is H, a protecting group, a lipophilic group, or optionally a covalent bond; the lipophilic group is optionally linked to one of A_1 or A_2 via a linker; and the other of T_3 and T_4 is an internucleoside linking group that links the monomer according to any one of claims 29-52 to the 5'-end of the oligomeric compound;

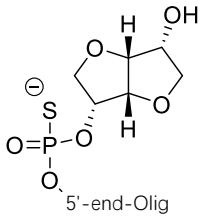
(ii) one of T_3 and T_4 is H, a protecting group, a lipophilic group, or optionally a covalent bond; the lipophilic group is optionally linked to one of A_1 or A_2 via a linker; and the other of T_3 and T_4 is an internucleoside linking group that links the monomer according to any one of claims 29-52 to the 3'-end of the oligomeric compound; or

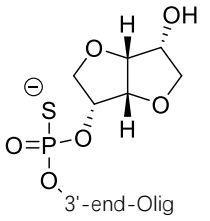
(iii) one of T_3 and T_4 is H, a protecting group, a lipophilic group, or optionally a covalent bond; the lipophilic group is optionally linked to one of A_1 or A_2 via a linker; and the other of T_3 and T_4 is an internucleoside linking group that independently links one identical or different monomer according to any one of claims 29-52 to the 5'-end and the 3'-end of the oligomeric compound.

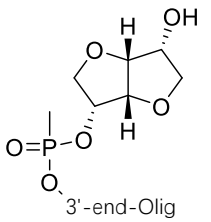
34. The oligomeric compound according to any one of claims 18-33, wherein the oligomeric compound has the following specific structures:

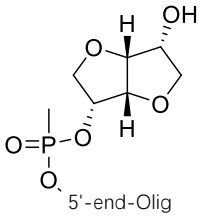


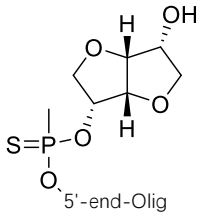
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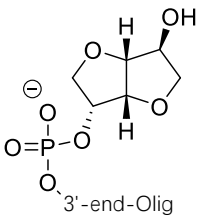
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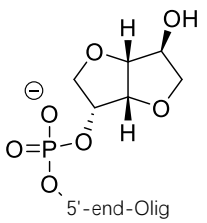
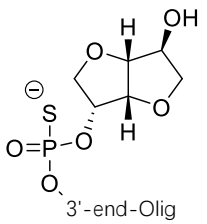
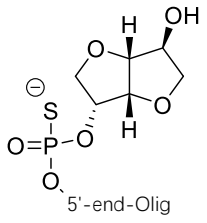
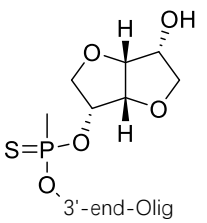
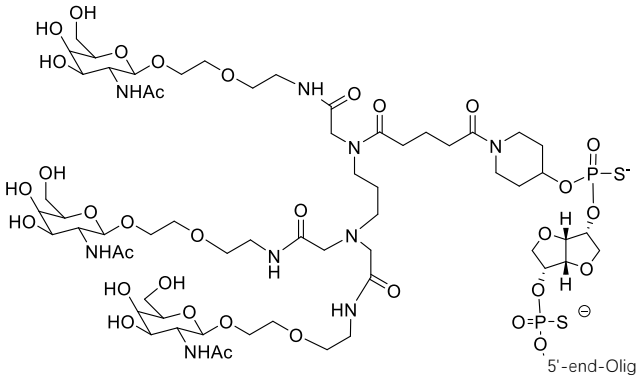
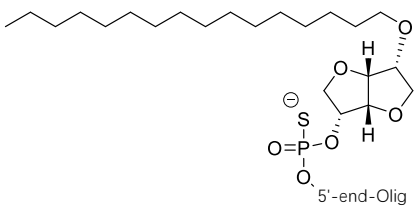
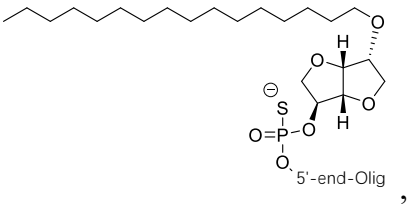
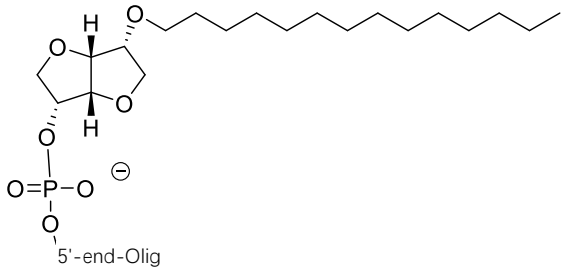
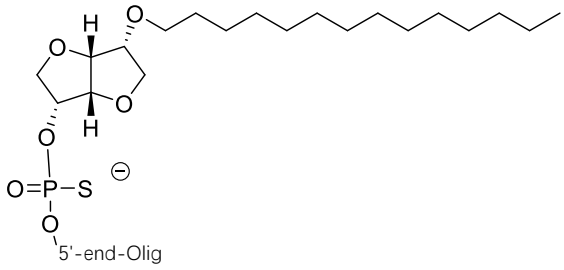
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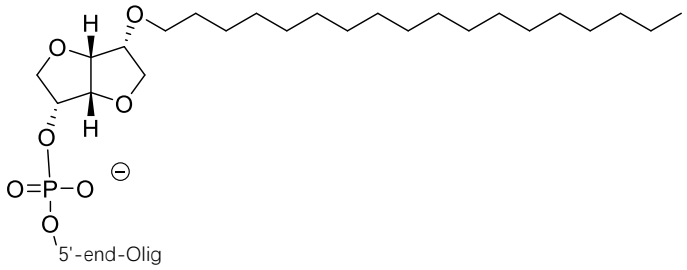
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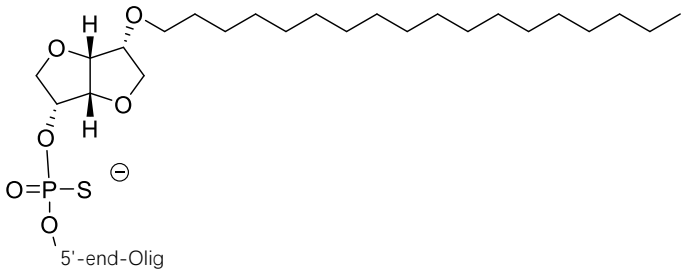
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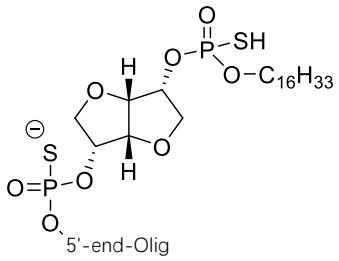

5'-end-Olig
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3'-end-Olig
,

5'-end-Olig
,

3'-end-Olig
,

5'-end-Olig
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5'-end-Olig
,

5'-end-Olig
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5'-end-Olig
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5'-end-Olig
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wherein Olig represents an oligonucleotide moiety that separately links the monomer to the 5'-end and/or 3'-end of the oligomeric compound.

35. The oligomeric compound according to any one of claims 18-34, wherein the oligomeric compound is a single-stranded oligonucleotide comprising an antisense oligonucleotide (also known as ASO), a ribozyme, or an aptamer.

36. A double-stranded ribonucleic acid (dsRNA) agent, comprising a sense strand and an antisense strand, wherein the sense strand and the antisense strand are fully or partially complementary, and the antisense strand is complementary to a nucleic acid target gene; at least one of the sense strand and the antisense strand is the oligomeric compound according to any one of claims 18-34; and the double-stranded ribonucleic acid (dsRNA) agent optionally further comprises an independent targeting group.

37. The double-stranded ribonucleic acid (dsRNA) agent according to claim 36, wherein:

(i) the sense strand is the defined oligomeric compound comprising the 5'-terminal

monomer, the provided oligomeric compound comprising the 3'-terminal monomer, or the provided oligomeric compound comprising the 5'-terminal and 3'-terminal monomers according to any one of claims 18-32 and 34; and/or

(ii) the antisense strand is the provided oligomeric compound comprising the 5'-terminal and/or 3'-terminal monomers according to any one of claims 29-52 and 56; preferably, in the double-stranded ribonucleic acid (dsRNA) agent, the antisense strand is the provided oligomeric compound comprising the 3'-terminal monomer according to claims 29-52 and 56, or the provided oligomeric compound comprising the 5'-terminal monomer according to any one of claims 18-32 and 34.

38. The oligomeric compound or the double-stranded ribonucleic acid (dsRNA) according to any one of claims36-37, wherein each strand of the sense strand or the antisense strand has a length of 8-40 nucleotides.

39. Use of the oligomeric compound or the double-stranded ribonucleic acid (dsRNA) agent according to any one of claims 18-38 in the preparation of a medicament for inhibiting gene expression.

40. The use according to claim 39, wherein:

(i) the medicament is used for intrahepatic administration and extrahepatic administration, and the medicament used for extrahepatic administration comprises central nervous system (CNS) target genes selected from APP, ATXN2, C9orf72, TARDBP, HTT, SNCA, FUS, ATXN3, ATXN1, SCA7, SCA8, ATN1, MeCP2, prion disease-related gene PRNP, DMPK, and TTR, as well as ocular tissue genes: AMD, CFB, MYOC, ROCK2, ADRB2, CA2, CRYGC, and PPP3C; or

(ii) the medicament is applied in CNS diseases comprising Alzheimer’s disease, amyotrophic lateral sclerosis (ALS), frontotemporal dementia, Huntington’s disease, Parkinson’s disease, spinocerebellar disease, prion disease, and Lafora disease, and in ophthalmic diseases comprising age-related macular degeneration (AMD) (dry and wet), birdshot chorioretinopathy, dominant retinitis pigmentosa, Fuch’s dystrophy, hereditary and sporadic glaucoma, stargardt’s disease, targeted glaucoma, cataract, and

dry eye syndrome.