

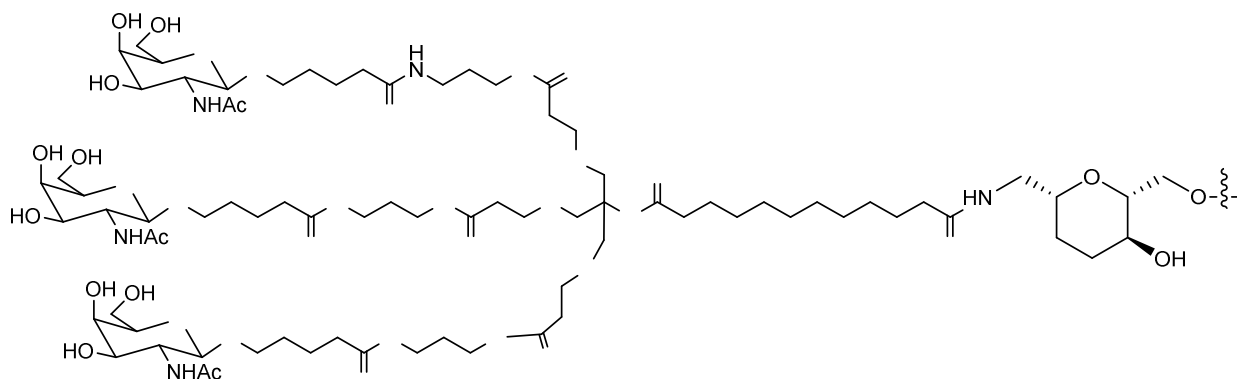
Claims

What is claimed is:

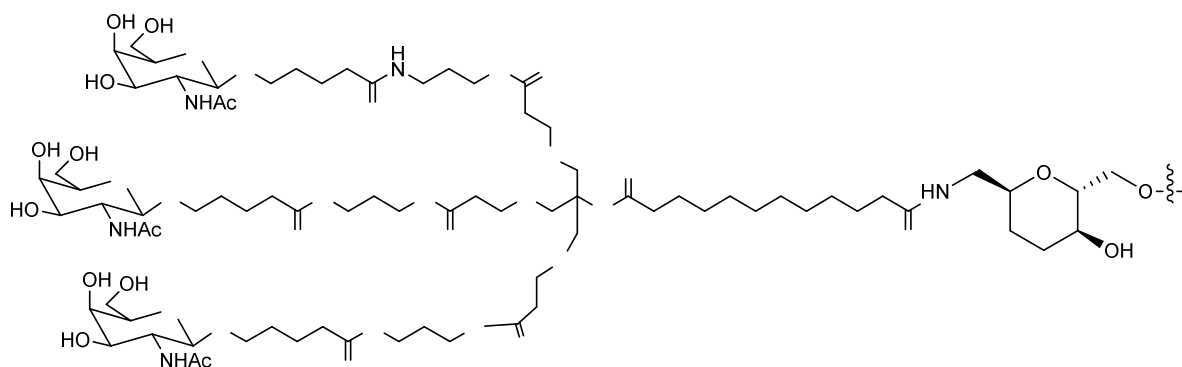
1. An LPA RNA interference agent, wherein the antisense strand comprises any AS strand in the following table, or the sense strand comprises any SS strand in the following table:

ID of AS strand	AS strand 5'-3'	Original SEQ ID	ID of SS strand	SS strand 5'-3'	Original SEQ ID
359A S	AmsUfsAmAmCfUm CmUmGm UmCmCm AmUfUm AfCmCm AmUmGms GmsUm	10	370S S	CmsAmsUm GmGmUm AmAmUf GfGfAm CmAmGm AmGmUm UmAmUms	101
384A S	VP(U)sUfsAmAmCf UmCmUmGm UmCmCm AmUfUm AfCmCm AmUmGms GmsUm	10	370S S	CmsAmsUm GmGmUm AmAmUf GfGfAm CmAmGm AmGmUm UmAmUms	101
385A S	AmsUfsAm AmCfUmCmUmGm UmCmCm AmUfUm AfCmCf AmUmGms GmsUm	10	370S S	CmsAmsUm GmGmUm AmAmUf GfGfAm CmAmGm AmGmUm UmAmUms	101
387A S	AmsUfsAm AmCfUfCmUmGm UmCmCm AmUfUm AfCmCm AmUmGms GmsUm	10	370S S	CmsAmsUm GmGmUm AmAmUf GfGfAm CmAmGm AmGmUm UmAmUms	101
359A S	AmsUfsAm AmCfUmCmUmGm UmCmCm AmUfUm AfCmCm AmUmGms GmsUm	10	397S S	CmsAmsUm GmGmUm AfAmUf GfGfAf CmAmGm AmGmUm UmAmUms	101

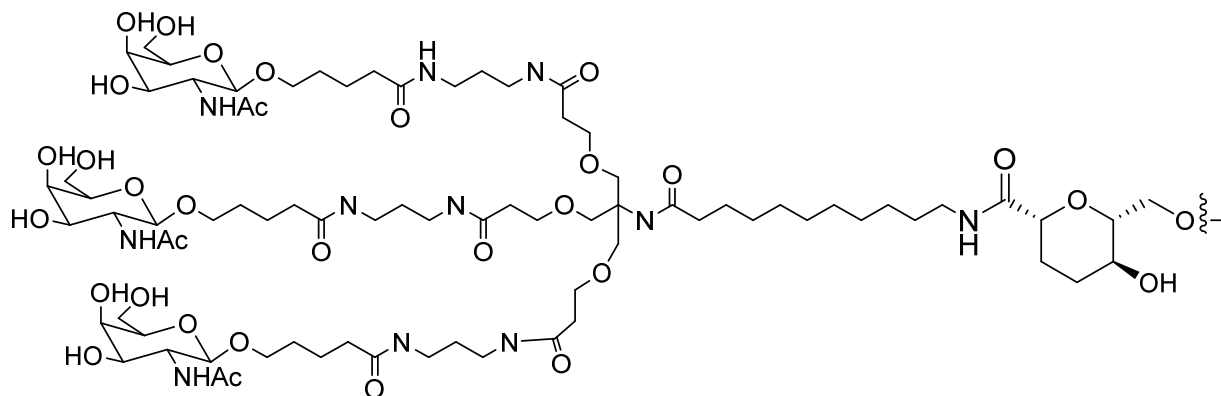
2. The LPA RNA interference agent of claim 1, wherein the RNA interfering agent also comprises a ligand, and the ligand comprises at least one of chemical formulas I-1 to I-16:



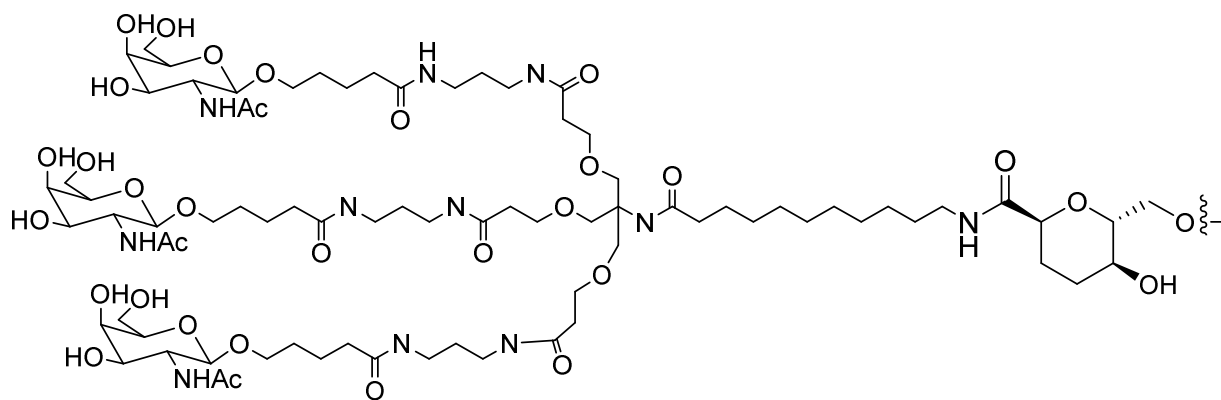
(I-1),



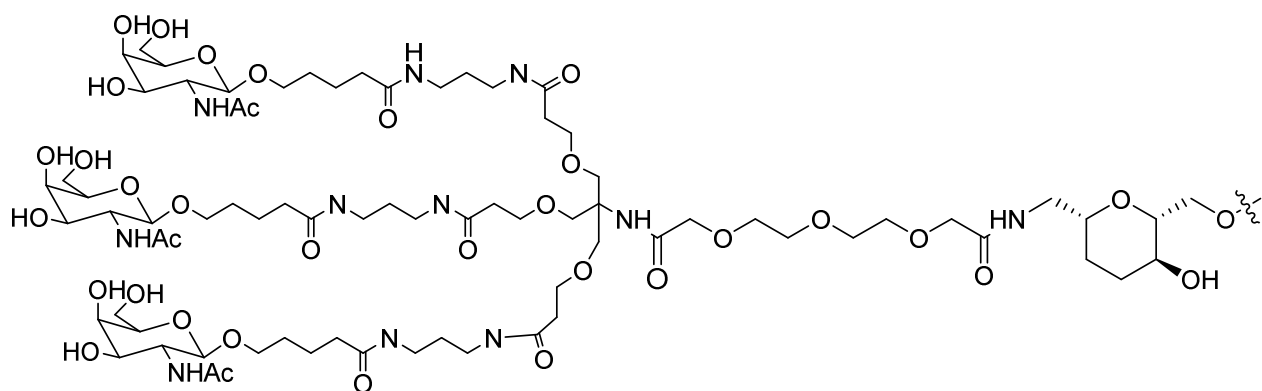
(I-2),



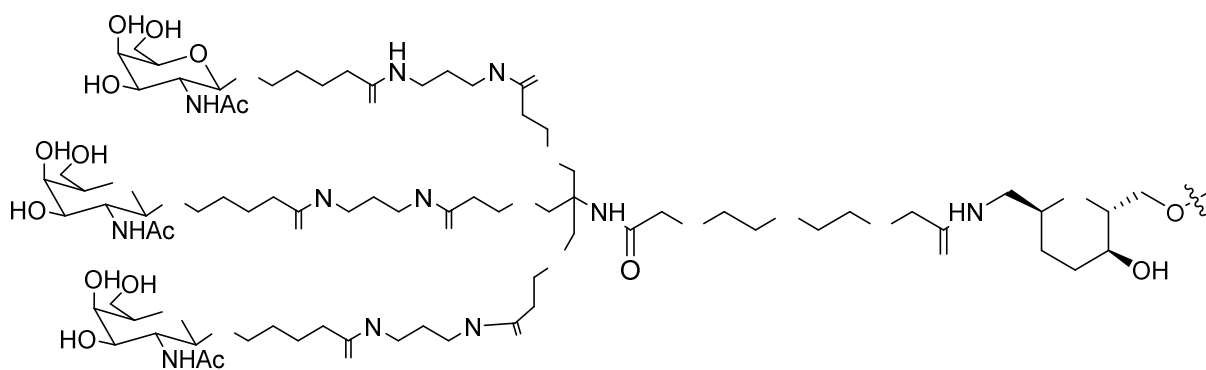
(I-3),



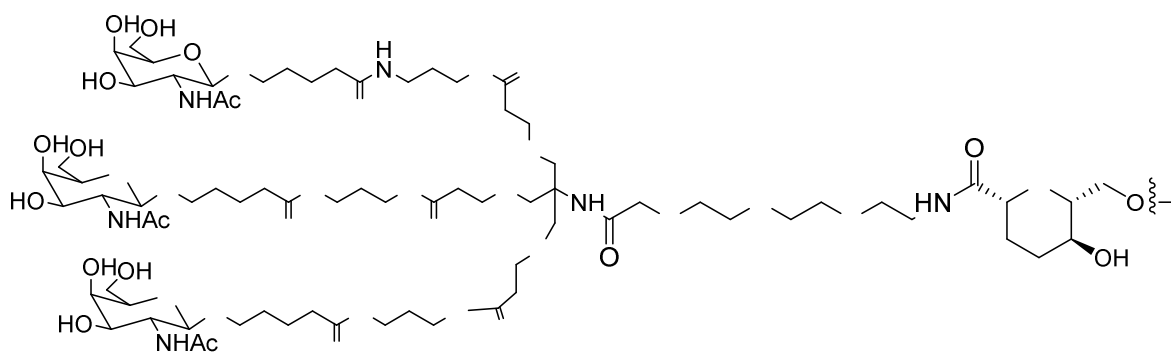
(I-4),



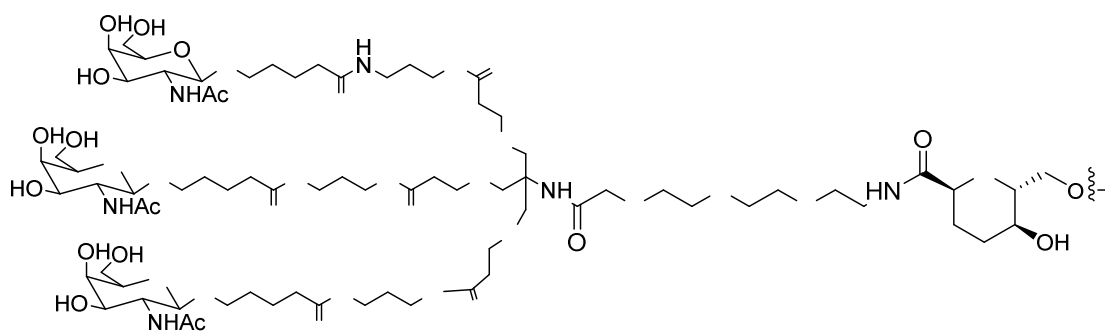
(I-5),



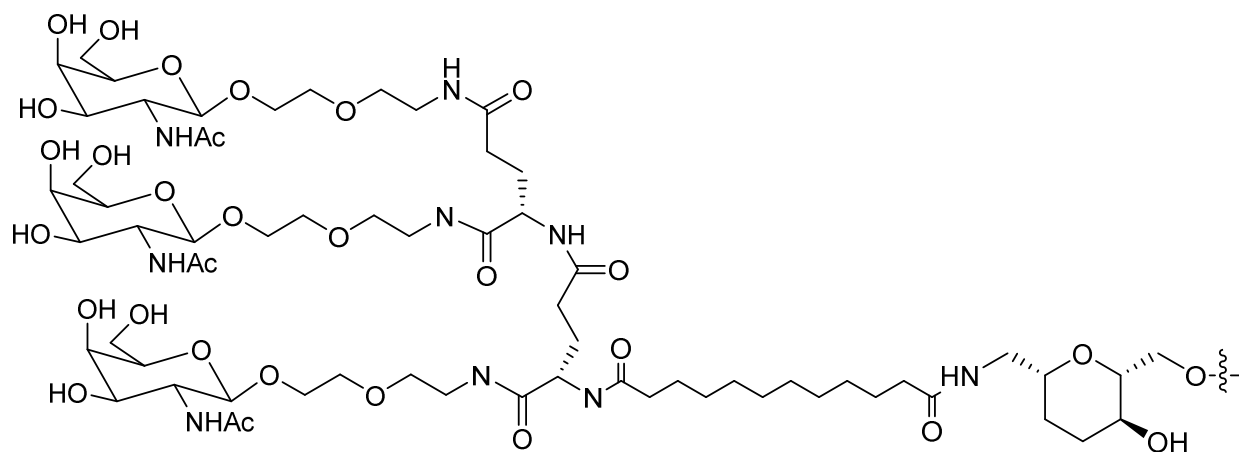
(I-6),



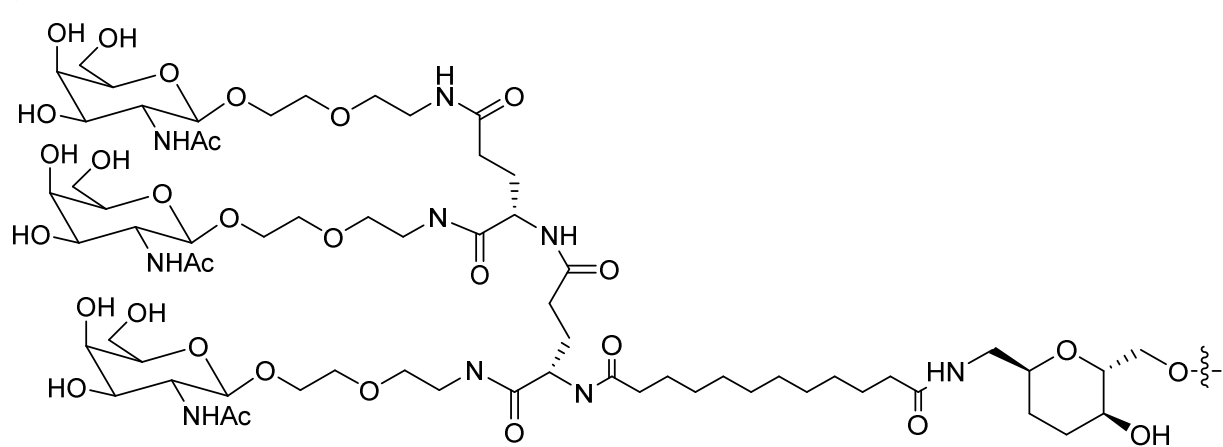
(I-7),



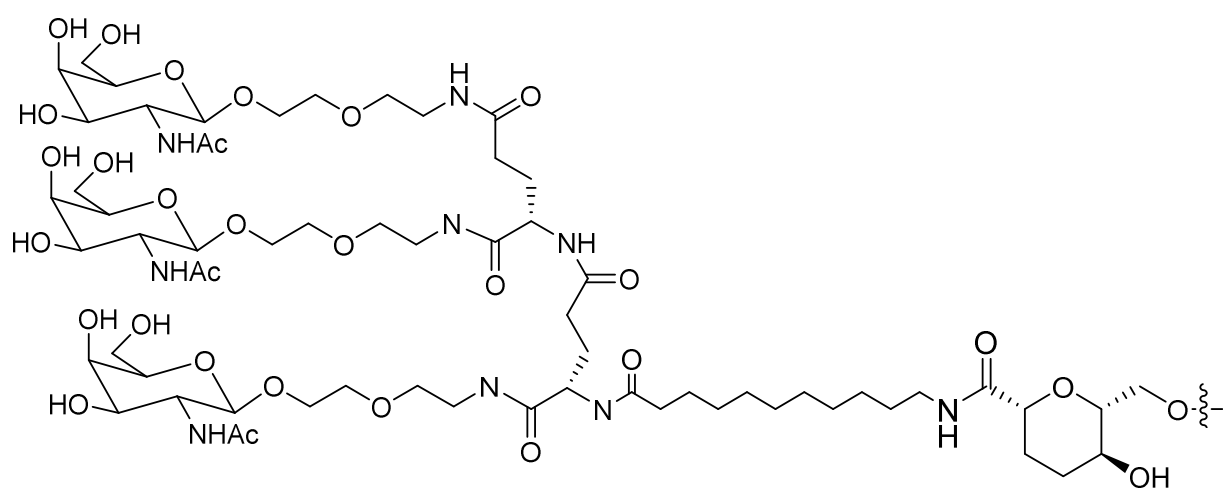
(I-8),

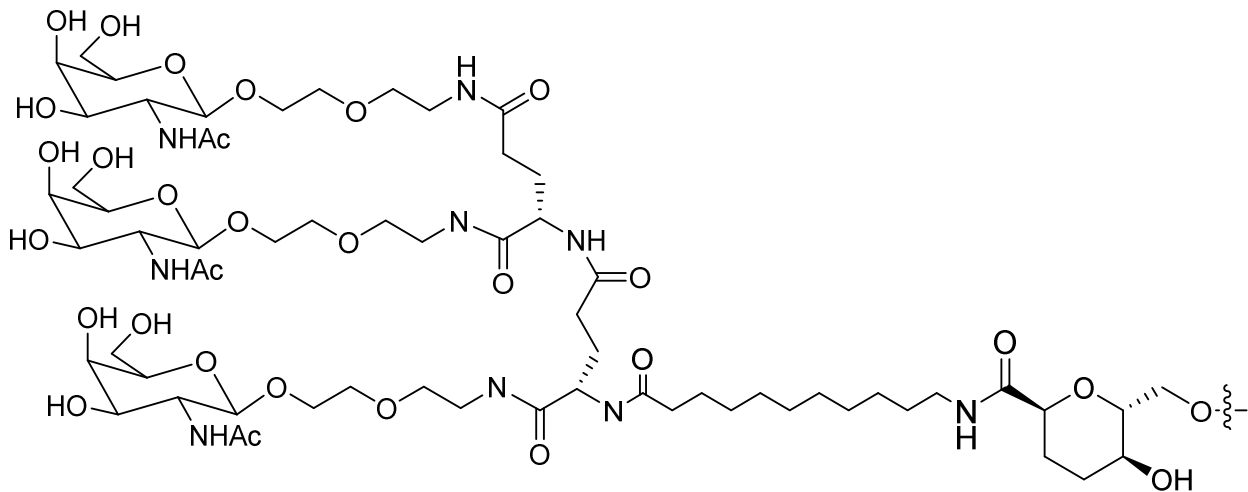


(I-9),

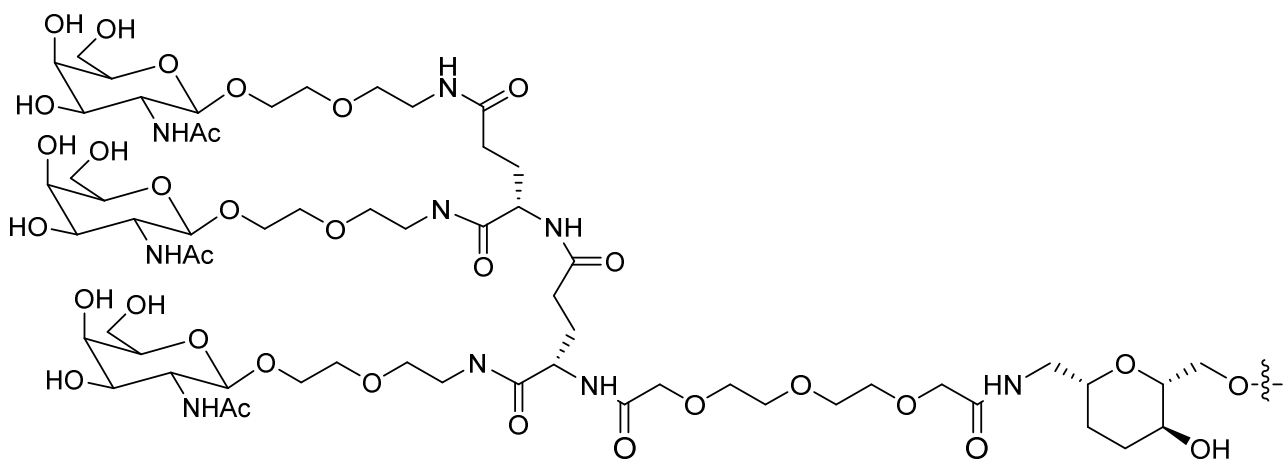


(I-10),

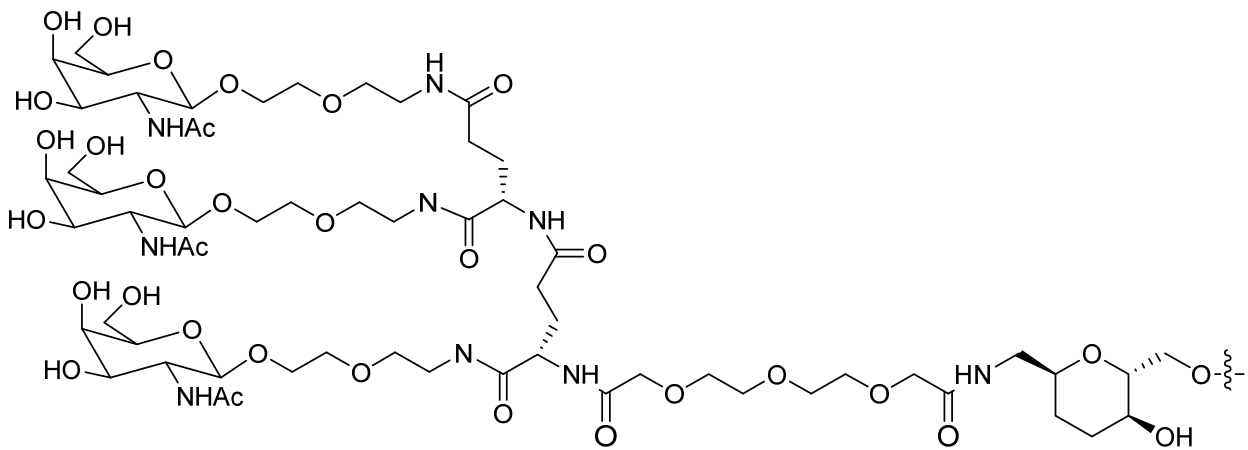


$$(I-11),$$


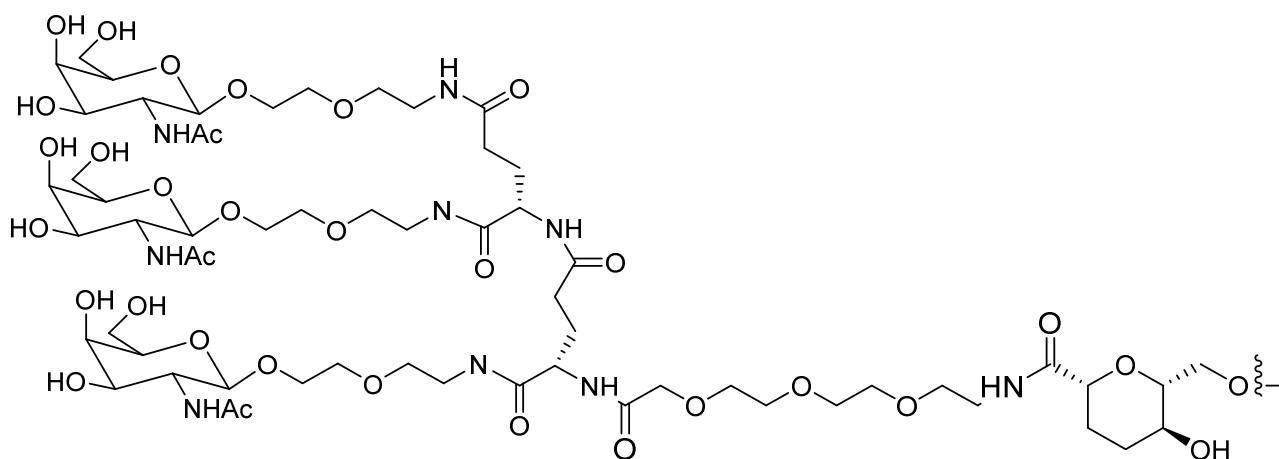
(I-12),



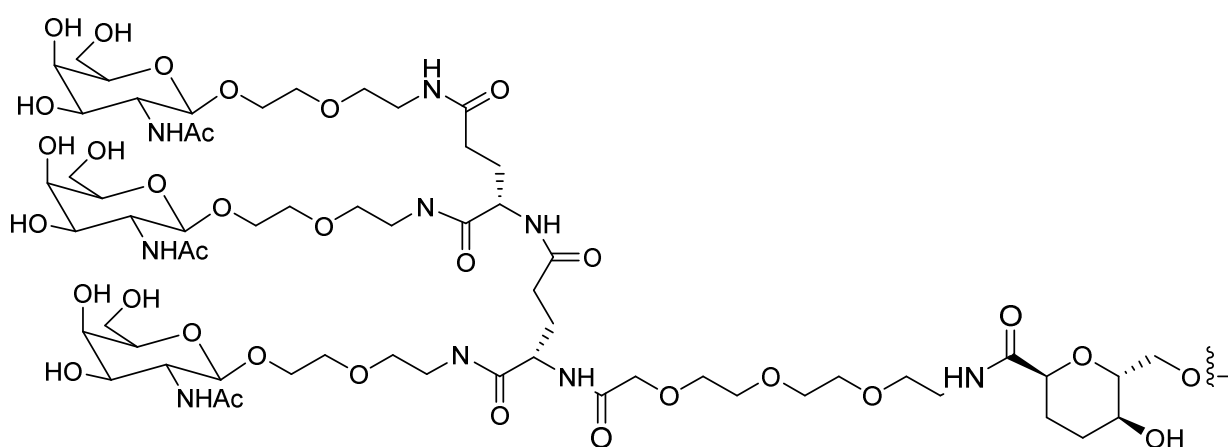
(I-13),



(I-14),

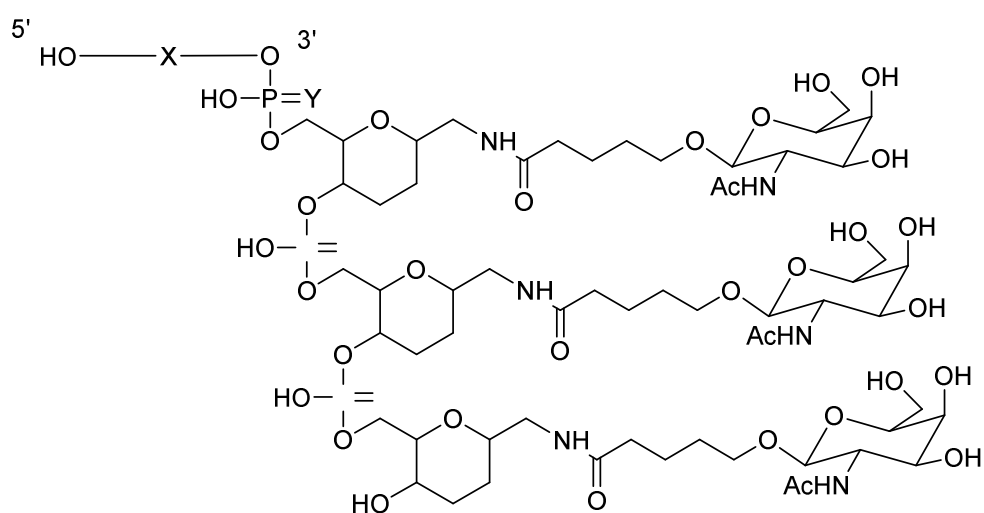


(I-15), or

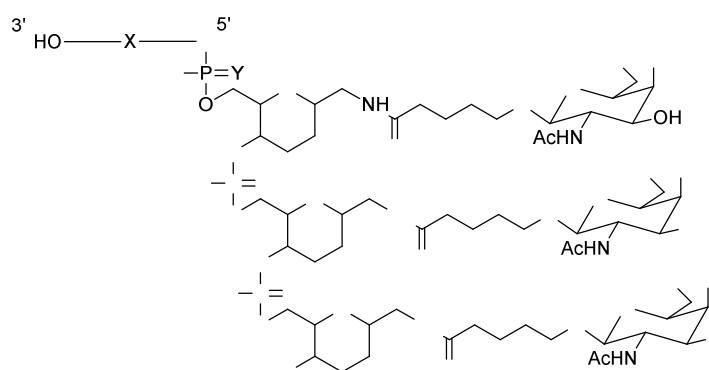


(I-16);

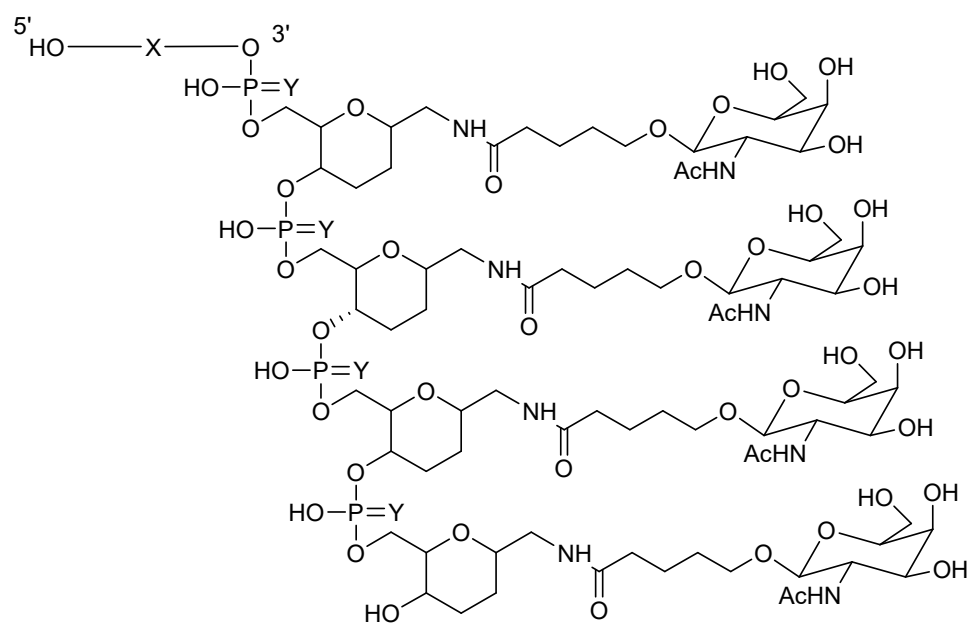
or at least one of chemical formulas II-1 to II-28:



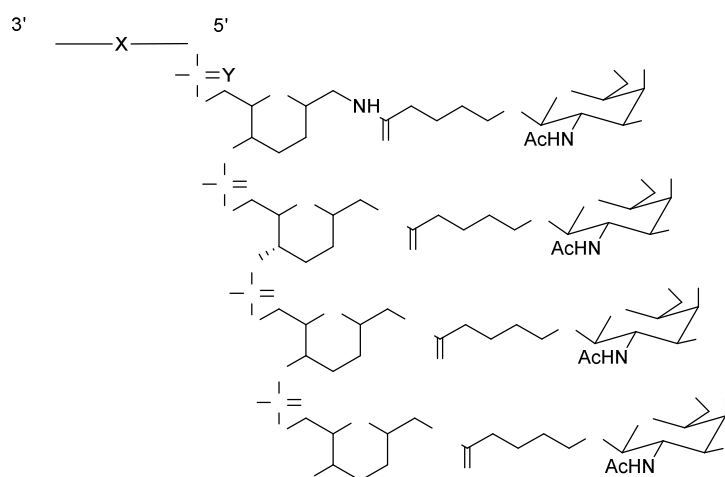
(II-1),



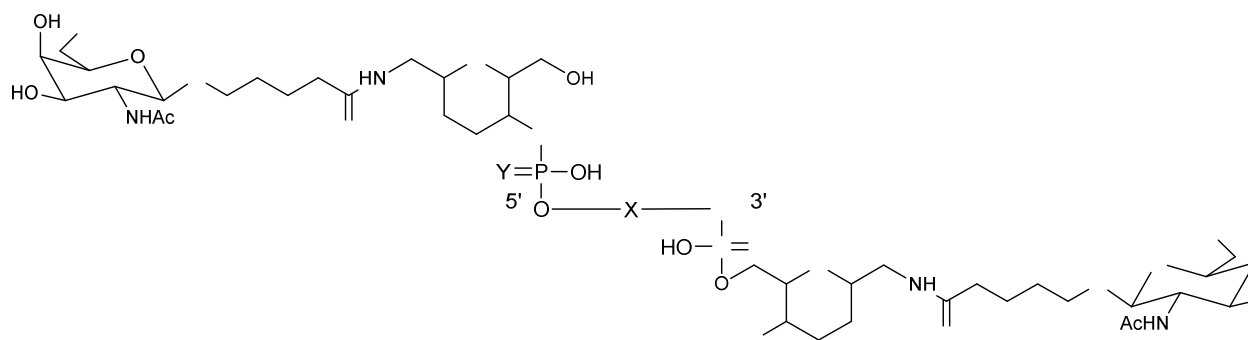
(II-2),



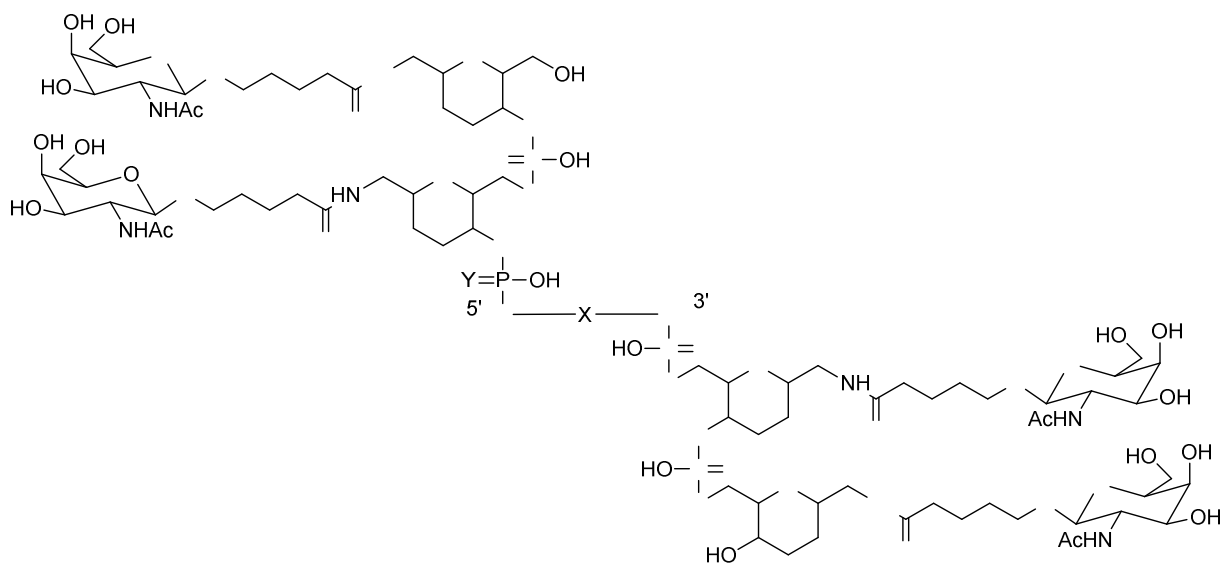
(II-3),



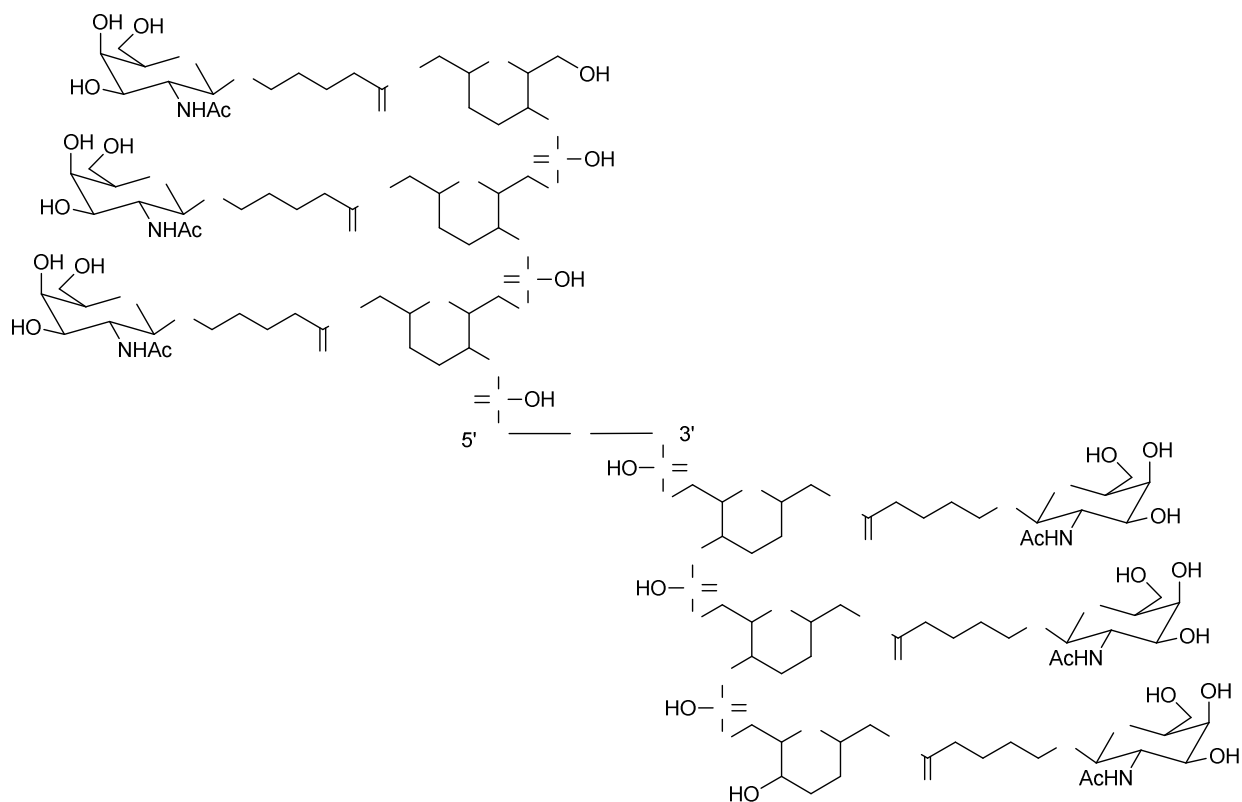
(II-4),



(II-5),



(II-6),



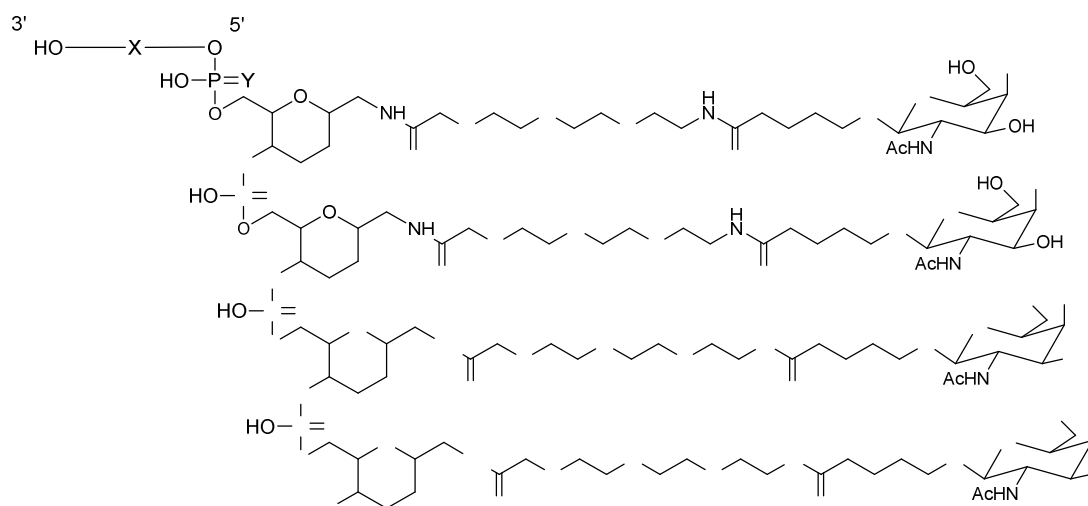
Chemical structure of a branched dendritic polymer with three arms. Each arm consists of a 6-membered cyclic acetal, a carbamate, a poly(ethylene glycol) chain, and a terminal 2-acetamido-2-deoxy-D-glucopyranose unit. The arms are connected via phosphate groups to a central core. The 3' end of the top arm is labeled with 'HO-X-O-3''.

The image displays three chemical structures of lipid analogs, likely representing different lipid species or modifications. Each structure consists of a head group, a sugar moiety, and a long hydrophobic chain.

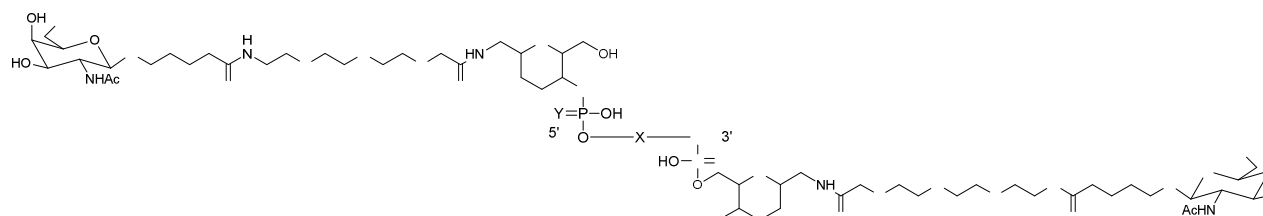
- Top Structure:** Features a 3' phosphate group (HO-X-O^{5'}), a 2' sugar moiety, and a long chain with two amide linkages and a terminal sugar moiety (AcHN).
- Middle Structure:** Features a 3' phosphate group (HO-I=O), a 2' sugar moiety, and a long chain with two amide linkages and a terminal sugar moiety (AcHN).
- Bottom Structure:** Features a 3' phosphate group (HO-I=O), a 2' sugar moiety, and a long chain with two amide linkages and a terminal sugar moiety (AcHN).

Chemical structures of four lipid analogs (1-4) showing their attachment to a nucleic acid backbone. Structure 1 is a phospholipid with a phosphate group linked to a sugar moiety. Structures 2 and 3 are phospholipids with a phosphate group linked to a sugar moiety. Structure 4 is a phospholipid with a phosphate group linked to a sugar moiety. All structures feature a long hydrophobic tail and a head group containing a sugar moiety.

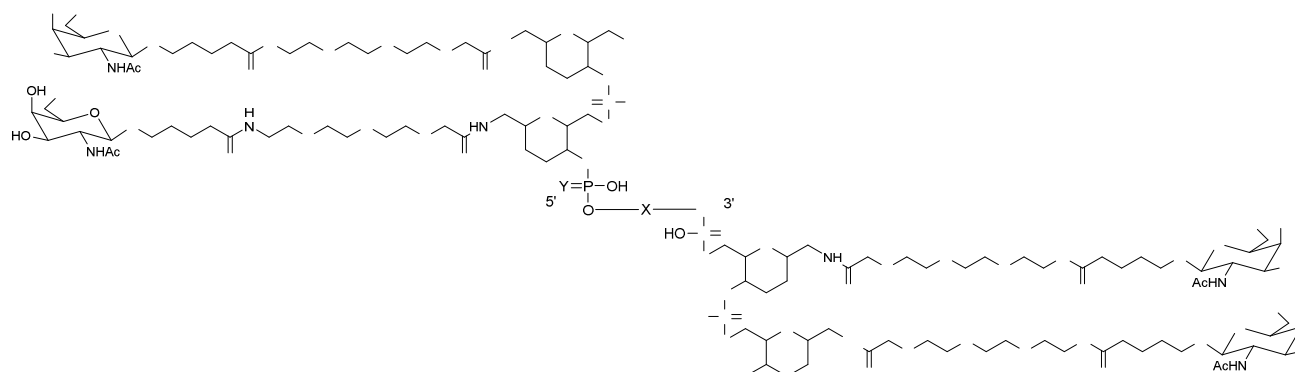
127



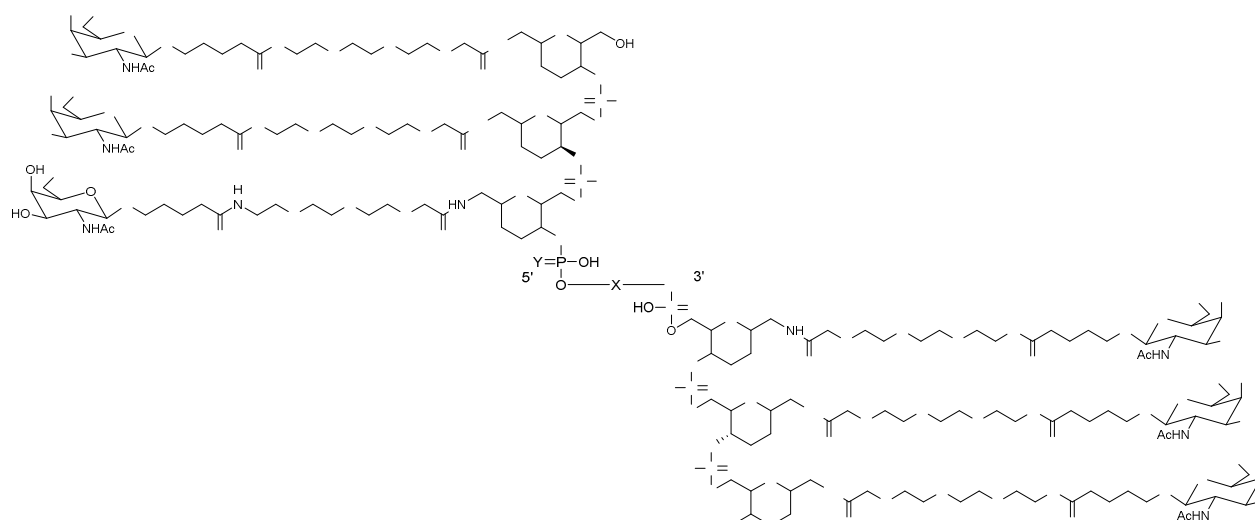
(II-11),



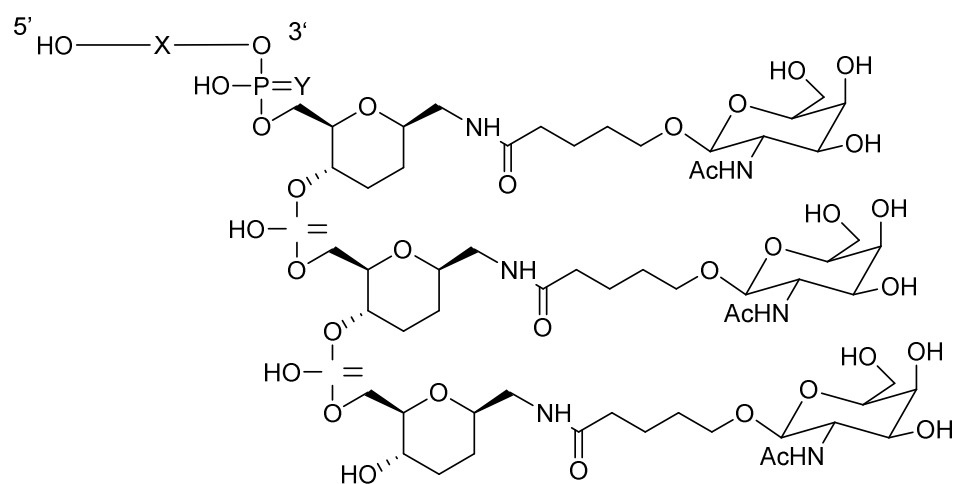
(II-12),



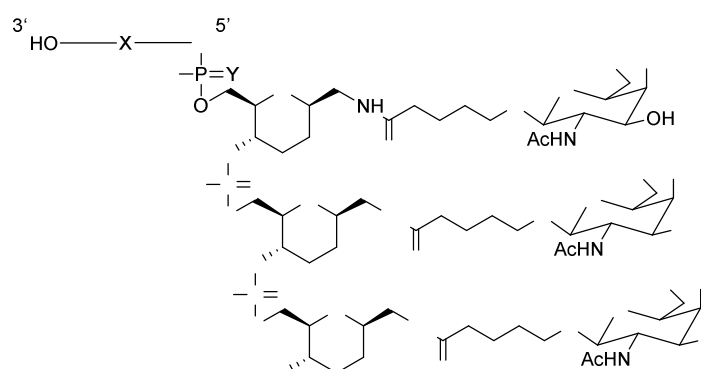
(II-13),



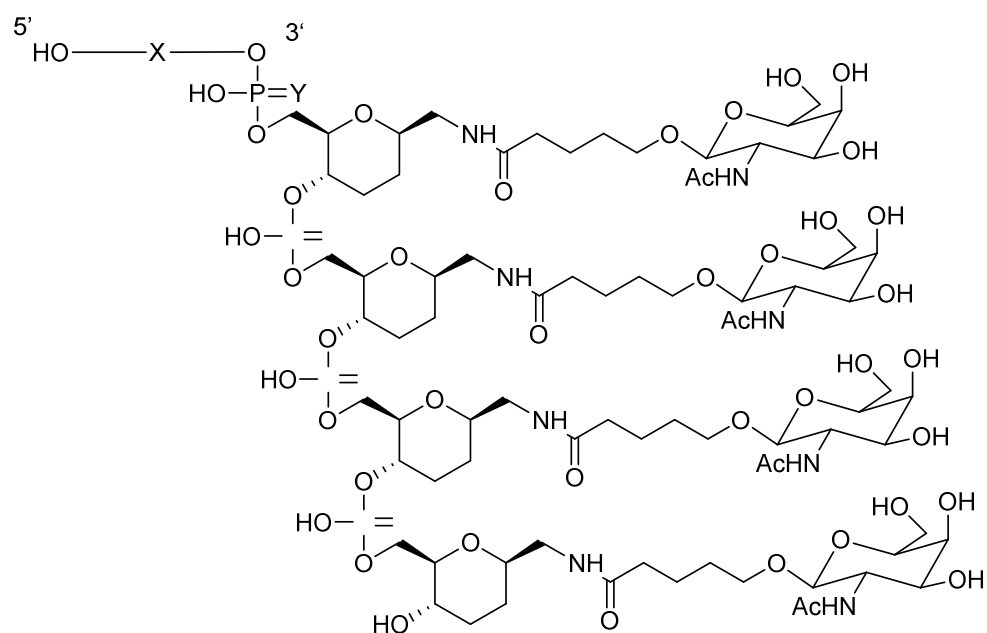
(II-14),



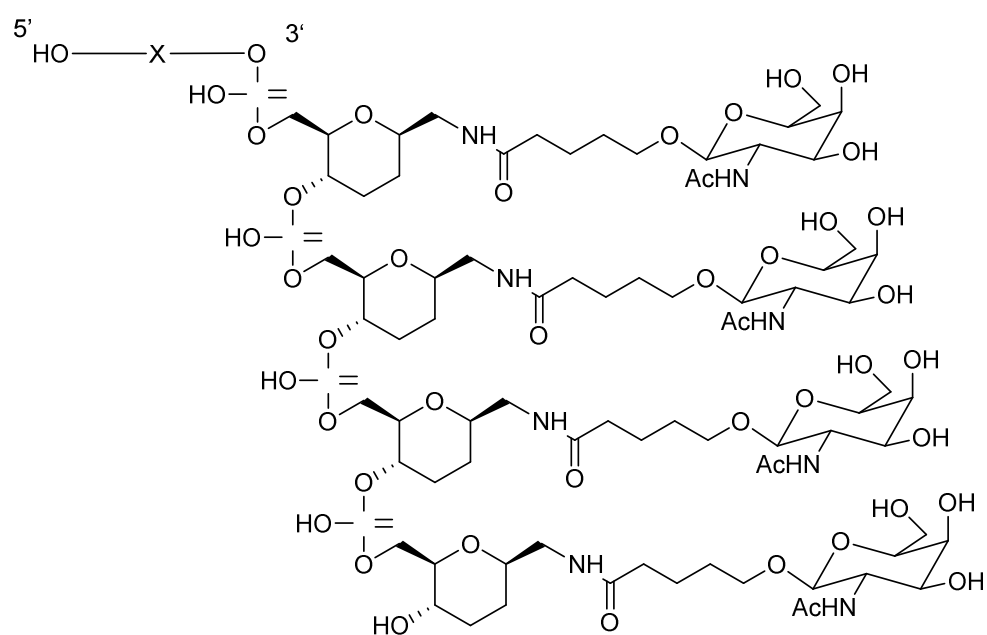
(II-15),



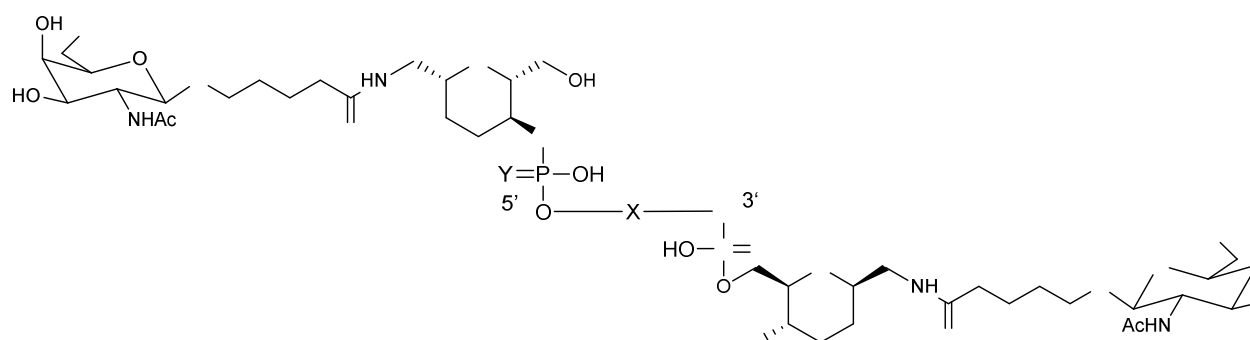
(II-16),



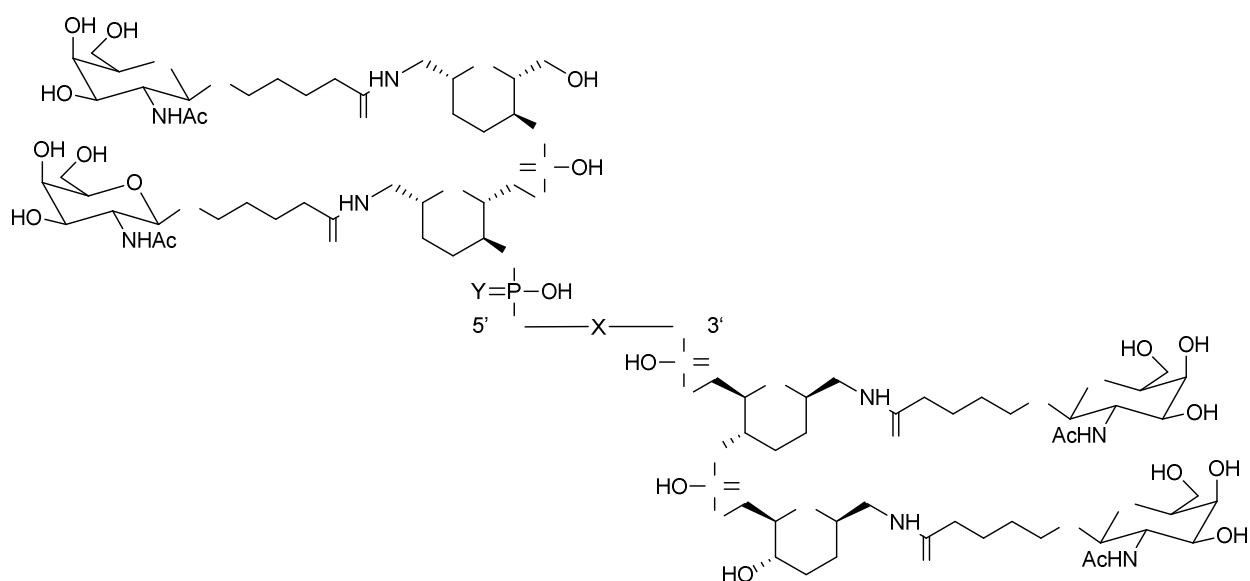
(II-17),



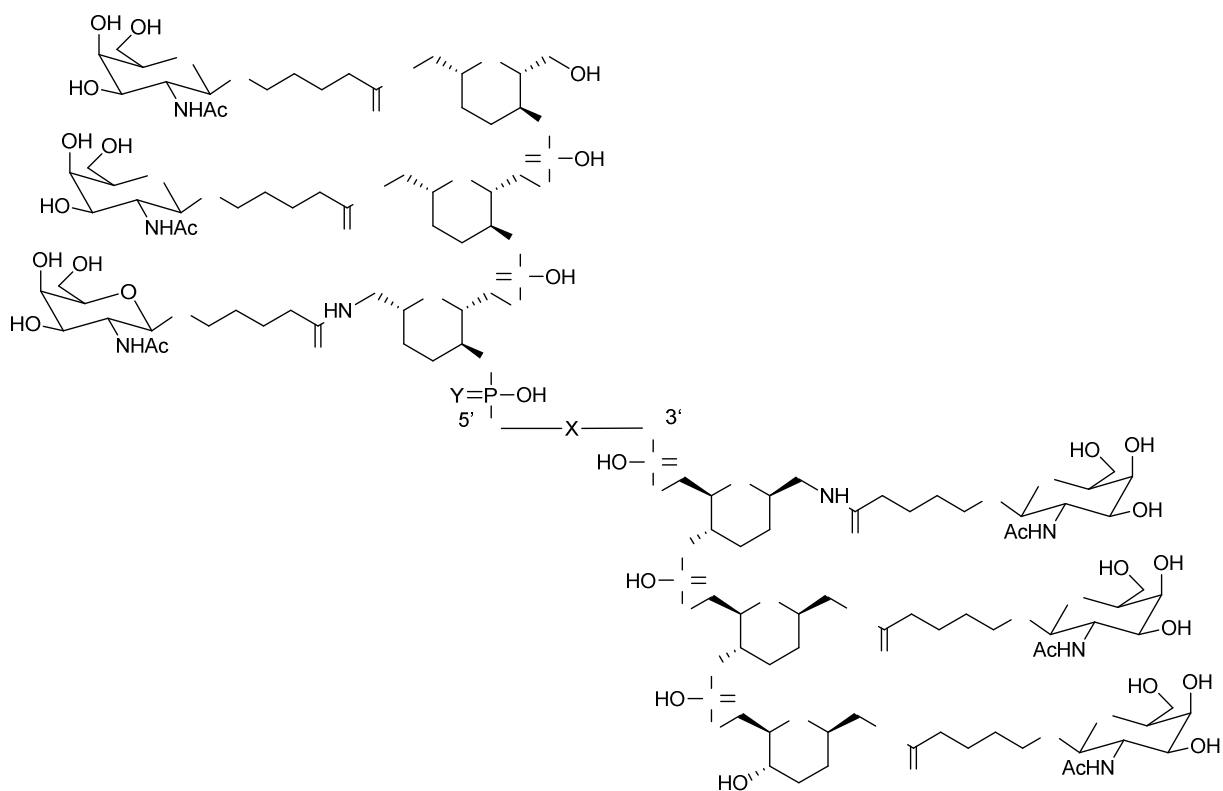
(II-18),



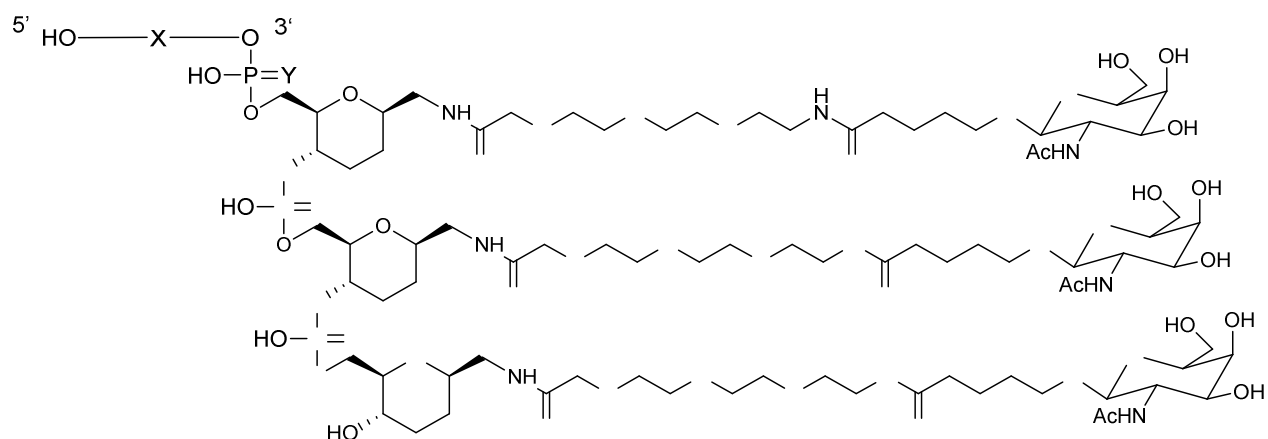
(II-19),



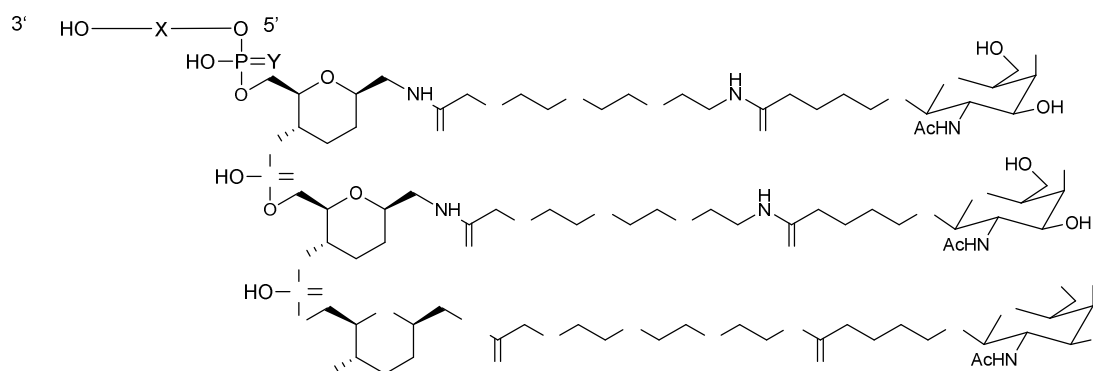
(II-20),



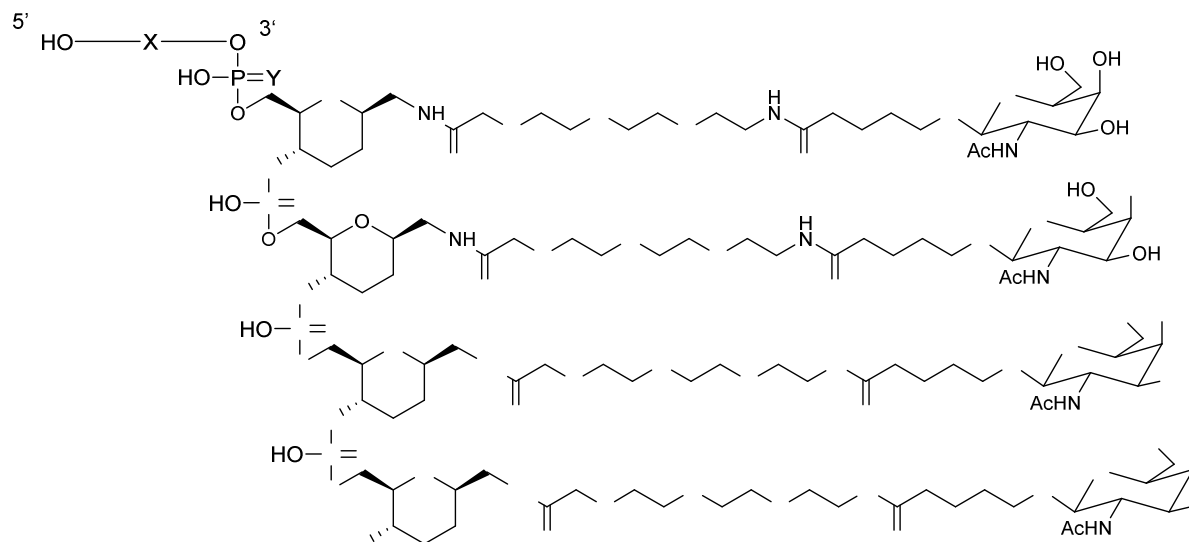
(II-21),



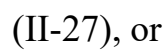
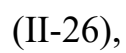
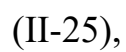
(II-22),



(II-23),



(II-24),

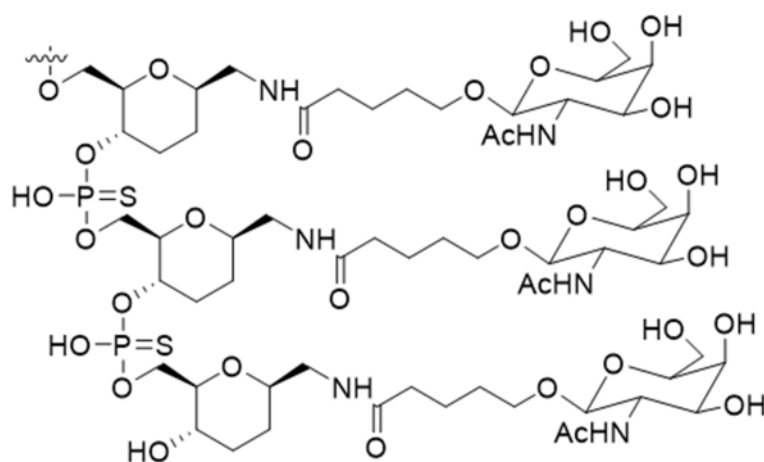


(II-28), wherein Y is O or S.

3. The LPA RNA interference agent of claim 2, wherein the ligand is conjugated to the 5' end and/or 3' end of the sense strand.

4. The LPA RNA interference agent of claim 3, wherein a) the antisense strand comprises: 359AS: AmsUfsAmAmCfUmCmUmGm UmCmCm AmUfUm AfCmCm AmUmGms GmsUm, and/or the sense strand comprises: CmsAmsUm GmGmUm AmAmUf GfGfAm CmAmGm AmGmUm UmAmUms[Gal-6]s[Gal-6]s[Gal-6];

wherein the [Gal-6] s [Gal-6] s [Gal-6] structure is given as follows:



5. A use of the LPA RNA interference agent of any of claims 1 to 4 in the preparation of a drug, wherein the drug is used to treat diseases or conditions related to elevated LPA expressions.

6. The use of claim 5, wherein the apo(a) protein has an expression level of 34.100 nmol/L or more before the LPA RNA interference agent is administered.

7. The use of claim 5, wherein the diseases or conditions comprise cardiovascular and cerebrovascular diseases, wherein the cardiovascular and cerebrovascular diseases comprise hyperlipidemia, stroke, atherosclerosis,

thrombosis, coronary heart disease, cardiac apoplexy, cerebral apoplexy or aortic stenosis.

8. The use of claim 5, wherein the drug is a composition which further comprises at least one selected from the group consisting of LDL-C, cholesterol, and triglyceride lowering agent.

9. The use of claim 5, wherein the drug is a composition which further comprises a PCSK9 RNAi inhibitor, a PCSK9 antibody inhibitor, and a PCSK9 small molecule inhibitor.