

CLAIMS

What is claimed:

1. Use of an LPA RNAi construct in the preparation of a medicament for treating, reducing, or preventing atherosclerosis in a patient in need thereof, wherein the medicament is to be administered or formulated for administration at a dose from 9 mg to 675 mg at a dosing interval of at least 8 weeks, wherein the LPA RNAi construct comprises a sense strand comprising the sequence of SEQ ID NO: 1, an antisense strand comprising the sequence of SEQ ID NO: 2, and a targeting moiety comprising an asialoglycoprotein receptor ligand, wherein the targeting moiety is covalently attached to the 5' end of the sense strand.
2. Use of an LPA RNAi construct in the preparation of a medicament for reducing serum or plasma Lp(a) levels in a patient in need thereof, wherein the medicament is to be administered or formulated for administration at a dose from 9 mg to 675 mg at a dosing interval of at least 8 weeks, wherein the LPA RNAi construct comprises a sense strand comprising the sequence of SEQ ID NO: 1, an antisense strand comprising the sequence of SEQ ID NO: 2, and a targeting moiety comprising an asialoglycoprotein receptor ligand, wherein the targeting moiety is covalently attached to the 5' end of the sense strand.
3. The use of claim 2, wherein the patient is diagnosed with or at risk of a cardiovascular disease.
4. The use of claim 3, wherein the cardiovascular disease is coronary artery disease, carotid artery disease, peripheral artery disease, myocardial infarction, cerebrovascular disease, stroke, aortic valve stenosis, stable or unstable angina, atrial fibrillation, heart failure, hyperlipidemia, heterozygous familial hypercholesterolemia, or homozygous familial hypercholesterolemia.
5. The use of claim 2, wherein the patient is diagnosed with chronic kidney disease.
6. The use of claim 2, wherein the patient has a history of myocardial infarction.

7. The use of claim 2, wherein the patient is diagnosed with acute coronary syndrome.
8. Use of an LPA RNAi construct in the preparation of a medicament for treating, reducing, or preventing a cardiovascular disease in a patient in need thereof, wherein the medicament is to be administered or formulated for administration at a dose from 9 mg to 675 mg at a dosing interval of at least 8 weeks, wherein the LPA RNAi construct comprises a sense strand comprising the sequence of SEQ ID NO: 1, an antisense strand comprising the sequence of SEQ ID NO: 2, and a targeting moiety comprising an asialoglycoprotein receptor ligand, wherein the targeting moiety is covalently attached to the 5' end of the sense strand.
9. The use of claim 8, wherein the cardiovascular disease is coronary artery disease, carotid artery disease, peripheral artery disease, myocardial infarction, cerebrovascular disease, stroke, aortic valve stenosis, stable or unstable angina, atrial fibrillation, heart failure, hyperlipidemia, heterozygous familial hypercholesterolemia, or homozygous familial hypercholesterolemia.
10. Use of an LPA RNAi construct in the preparation of a medicament for reducing the risk of a cardiovascular event in a patient with atherosclerotic cardiovascular disease, wherein the medicament is to be administered or formulated for administration at a dose from 9 mg to 675 mg at a dosing interval of at least 8 weeks, wherein the LPA RNAi construct comprises a sense strand comprising the sequence of SEQ ID NO: 1, an antisense strand comprising the sequence of SEQ ID NO: 2, and a targeting moiety comprising an asialoglycoprotein receptor ligand, wherein the targeting moiety is covalently attached to the 5' end of the sense strand.
11. The use of claim 10, wherein the cardiovascular event is cardiovascular death, myocardial infarction, stroke, and/or coronary revascularization.
12. The use of claim 10 or 11, wherein the patient has a history of coronary revascularization, a history of coronary artery bypass grafting, a diagnosis of coronary artery disease, a diagnosis of atherosclerotic cerebrovascular disease, a diagnosis of peripheral artery disease, and/or a history of myocardial infarction.

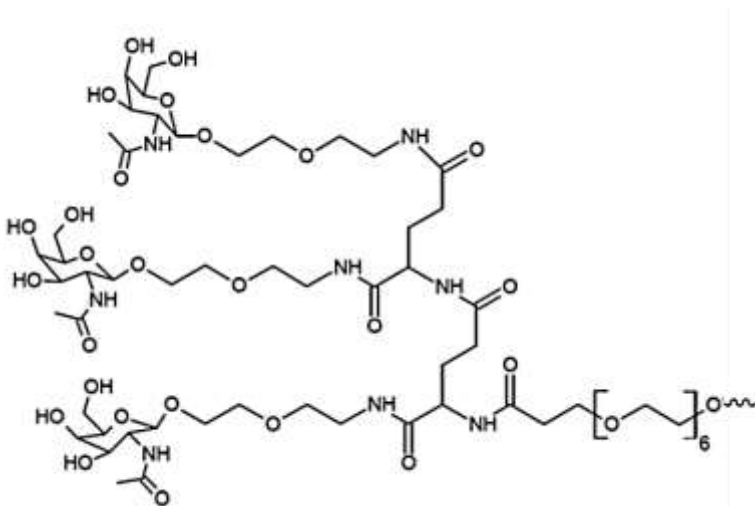
13. The use of any one of claims 10 to 12, wherein the patient has experienced a myocardial infarction within 1 year prior to the first administration of the medicament.
14. The use of any one of claims 10 to 12, wherein the patient is hospitalized for acute coronary syndrome or unstable angina.
15. The use of any one of claims 1 to 14, wherein the patient has a serum or plasma Lp(a) level of about 125 nmol/L or greater prior to the first administration of the medicament.
16. The use of any one of claims 1 to 14, wherein the patient has a serum or plasma Lp(a) level of about 150 nmol/L or greater prior to the first administration of the medicament.
17. The use of any one of claims 1 to 14, wherein the patient has a serum or plasma Lp(a) level of about 175 nmol/L or greater prior to the first administration of the medicament.
18. The use of any one of claims 1 to 14, wherein the patient has a serum or plasma Lp(a) level of about 200 nmol/L or greater prior to the first administration of the medicament.
19. The use of any one of claims 1 to 14, wherein the patient has a serum or plasma Lp(a) level of about 225 nmol/L or greater prior to the first administration of the medicament.
20. The use of any one of claims 1 to 19, wherein the dosing interval is about 12 weeks.
21. The use of any one of claims 1 to 19, wherein the dosing interval is about 24 weeks.
22. The use of any one of claims 1 to 19, wherein the medicament is to be administered or formulated for administration to the patient at a dose from 10 mg to 225 mg once every 12 weeks.
23. The use of claim 22, wherein the medicament is to be administered or formulated for administration to the patient at a dose from 50 mg to 100 mg once every 12 weeks.

24. The use of claim 22, wherein the medicament is to be administered or formulated for administration to the patient at a dose from 150 mg to 225 mg once every 12 weeks.
25. The use of claim 22, wherein the medicament is to be administered or formulated for administration to the patient at a dose of about 75 mg once every 12 weeks.
26. The use of claim 22, wherein the medicament is to be administered or formulated for administration to the patient at a dose of about 150 mg once every 12 weeks.
27. The use of claim 22, wherein the medicament is to be administered or formulated for administration to the patient at a dose of about 225 mg once every 12 weeks.
28. The use of any one of claims 1 to 19, wherein the medicament is to be administered or formulated for administration to the patient at a dose from 225 mg to 675 mg once every 24 weeks.
29. The use of claim 28, wherein the medicament is to be administered or formulated for administration to the patient at a dose of about 225 mg once every 24 weeks.
30. The use of any one of claims 1 to 29, wherein the patient is receiving a lipid-lowering therapy.
31. The use of claim 30, wherein the lipid-lowering therapy is a statin, ezetimibe, a PCSK9 inhibitor, bempedoic acid, or combinations thereof.
32. The use of any one of claims 1 to 31, wherein the patient has a serum low-density lipoprotein cholesterol (LDL-C) level of about 100 mg/dL or less prior to the first administration of the medicament.

33. The use of any one of claims 1 to 32, wherein the sense strand of the LPA RNAi construct comprises or consists of the sequence of SEQ ID NO: 3 and the antisense strand of the LPA RNAi construct comprises or consists of the sequence of SEQ ID NO: 4.

34. The use of any one of claims 1 to 33, wherein the sense strand of the LPA RNAi construct comprises or consists of the sequence of modified nucleotides according to SEQ ID NO: 5 and the antisense strand of the LPA RNAi construct comprises or consists of the sequence of modified nucleotides according to SEQ ID NO: 6.

35. The use of any one of claims 1 to 34, wherein the targeting moiety of the LPA RNAi construct has the structure of:



36. The use of any one of claims 1 to 35, wherein the LPA RNAi construct is olpasiran.

37. The use of any one of claims 1 to 36, wherein the medicament is to be administered or formulated for administration to the patient in a pharmaceutical composition comprising potassium phosphate and sodium chloride.

38. The use of any one of claims 1 to 37, wherein the medicament is to be administered or formulated for administration to the patient by subcutaneous injection.

39. The use of claim 38, wherein the injection volume is about 1 mL or less.