We claim:

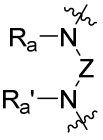
1. Use of a lipidoid nanoparticle in the manufacture of a medicament for treating a lipoprotein metabolism disorder or a cardiovascular disease, wherein the lipidoid nanoparticle comprises a lipid, a CRISPR/Cas9 mRNA, and a single guide RNA (sgRNA), wherein

the sgRNA is single guide Angiopoietin-like 3 (sgANGPTL3) or single guide proprotein convertase subtilisin/kexin type 9 (sgPCSK9);

wherein the lipid is represented by formula I:

$$R^{Head}—R^{Lipid} \quad (I),$$

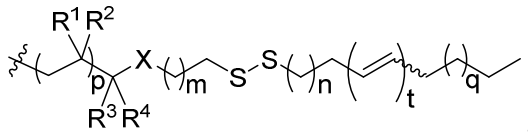
or a pharmaceutically acceptable salt thereof, wherein

R^{Head} is 

R^a and $R^{a'}$ are each R^{Lipid};

Z is a C_1-C_{20} bivalent aliphatic radical, a C_1-C_{20} bivalent heteroaliphatic radical, a bivalent aryl radical, or a bivalent heteroaryl radical; and

R^{Lipid} each independently is



,

wherein:

R^1 and R^2 are H, OH, NHR^{30}, or SH;

R^3 and R^4 are taken together to form an oxo (=O) group;

X is CH_2, O, NR^{30}, or S;

R^{30} is H, C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl;

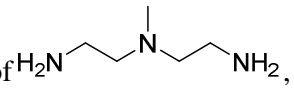
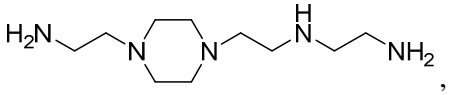
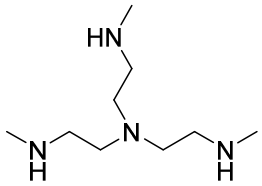
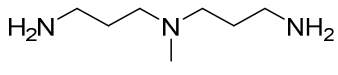
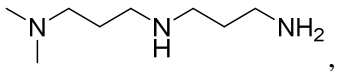
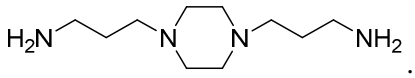
m is an integer selected from 1-3;

n is an integer selected from 1-14;

p is 0 or 1;

q is an integer selected from 1-10; and

t is 0, 1, or 2.

2. The use of claim 1, wherein R^{Head} is derived from a compound selected from the group consisting of , , , , , and .

3. The use of claim 1 or 2, wherein R^1 and R^2 are H.

4. The use of claim 1 or 2, wherein R^1 is H; and R^2 is OH.

5. The use of any one of claims 1-4, wherein Z is CH_2, O, or NR^{30}.

6. The use of any one of claims 1-4, wherein Z is CH_2.

7. The use of any one of claims 1-4, wherein Z is O.

8. The use of any one of claims 1-4, wherein Z is NR^{30}.

9. The use of any one of claims 1-8, wherein m is 1 or 2.

10. The use of any one of claims 1-9, wherein n is an integer selected from 4-12.

11. The use of any one of claims 1-9, wherein n is an integer selected from 6-10.

12. The use of any one of claims 1-11, wherein p is 0.

13. The use of any one of claims 1-11, wherein p is 1.

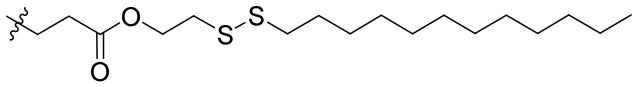
14. The use of any one of claims 1-13, wherein q is an integer selected from 2-8.

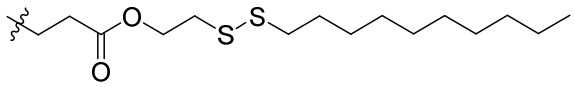
15. The use of any one of claims 1-13, wherein q is an integer selected from 4-8.

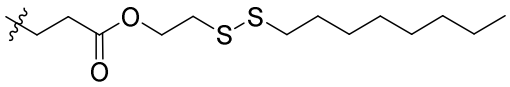
16. The use of any one of claims 1-15, wherein t is 0.

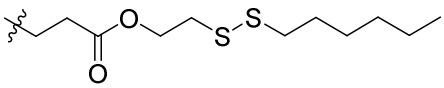
17. The use of any one of claims 1-15, wherein t is 1.

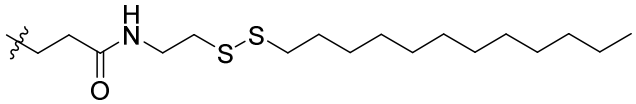
18. The use of any one of claims 1-17, wherein R^{Lipid} each independently is selected from the group consisting of

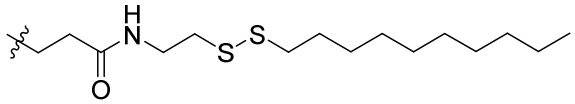

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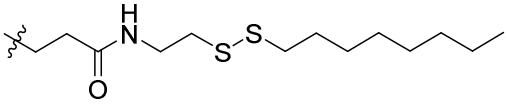

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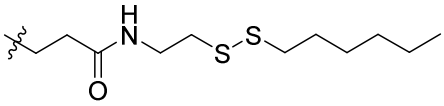

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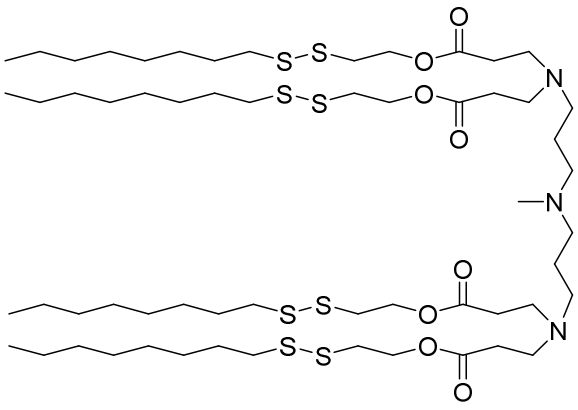

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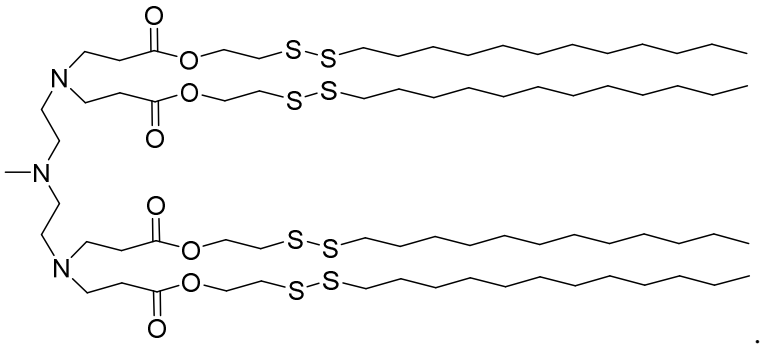

, and


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19. The use of claim 1, wherein the lipid is selected from the group consisting of



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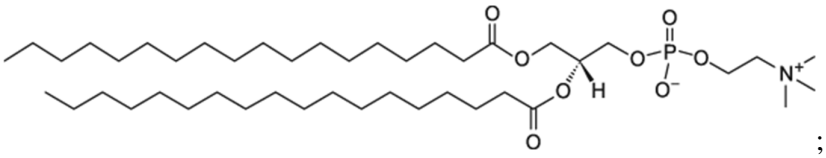
20. The use of any one of claims 1-19, wherein the ratio of the lipid to the CRISPR/Cas9 mRNA is about 3:1 to about 15:1.

21. The use of any one of claims 1-19, wherein the ratio of the lipid to the CRISPR/Cas9 mRNA is about 7.5:1.

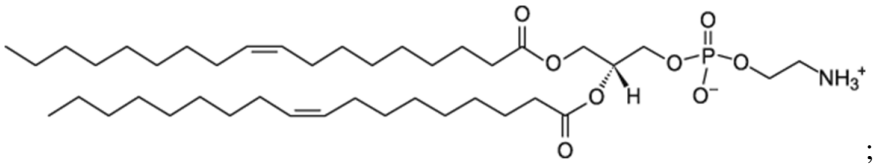
22. The use of any one of claims 1-21, wherein the lipidoid nanoparticle further comprises cholesterol.

23. The use of claim 22, wherein the ratio of the lipid to the cholesterol is about 1:1 to about 2:1.

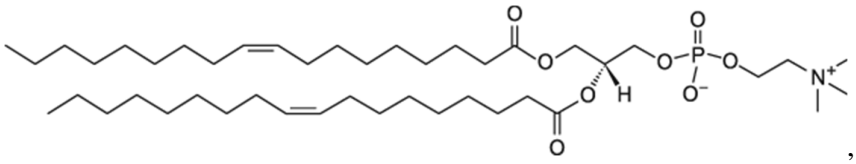
24. The use of any one of claims 1-23, wherein the lipidoid nanoparticle further comprises DOPE, DSPC, or DOPC; and DMG-PEG2K; wherein
DSPC has the structure:


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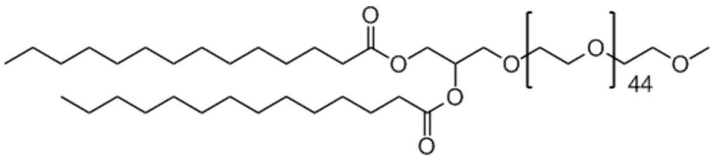
DOPE has the structure:


;

DOPC has the structure:


, and

DMG-PEG2K has the structure:


.

25. The use of claim 24, wherein the lipidoid nanoparticle comprises DOPC and DMG-PEG2K.

26. The use of claim 25, wherein the ratio of the lipid to the DOPC is about 4:1 to about 6:1; and the ratio of the lipid to the DMG-PEG2K is about 4:1 to about 100:1 to about 4:1 to about 20:1.

27. The use of any one of claims 1-26, wherein the lipidoid nanoparticle has a particle size of about 25 nm to about 1000 nm.

28. The use of any one of claims 1-26, wherein the lipidoid nanoparticle has a particle size of about 50 nm to about 500 nm.

29. The use of any one of claims 1-28, wherein the human lipoprotein metabolism disorder is associated with loss-of-function mutations in ANGPTL3 gene.

30. The use of any one of claims 1-28, wherein the cardiovascular disease is

associated with proprotein convertase subtilisin/kexin type 9 gene (PCSK9).

31. The use of any one of claims 1-28, wherein the human lipoprotein metabolism disorder is associated with low levels of plasma high density lipoprotein cholesterol, high levels of serum low density lipoprotein cholesterol, or high levels of triglycerides.

32. The use of any one of claims 1-28, wherein the cardiovascular disease is selected from the group consisting of homozygous familial hypercholesterolemia, and hypercholesterolemia.