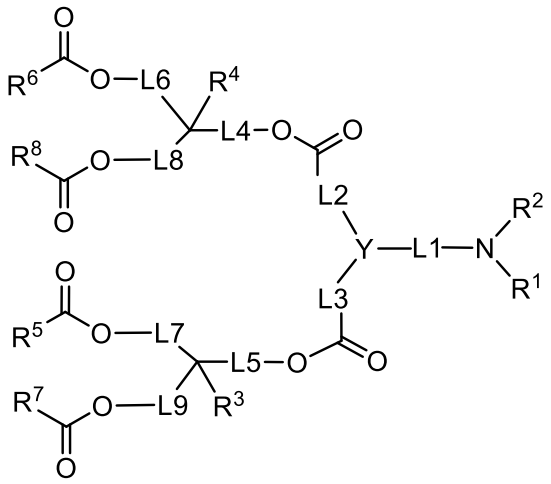
WHAT IS CLAIMED IS:

1. A compound of Formula I, or a pharmaceutically acceptable salt thereof:



(I)

wherein:

R^1 and R^2 are each independently H or $C_{1\text{-}6}$ alkyl; or

R^1 and R^2 are joined to form a saturated heterocyclic ring, wherein:

R^1 is a linear $C_{1\text{-}4}$ alkylene; and

R^2 is $-(CH_2)_m(X)_n-$, wherein

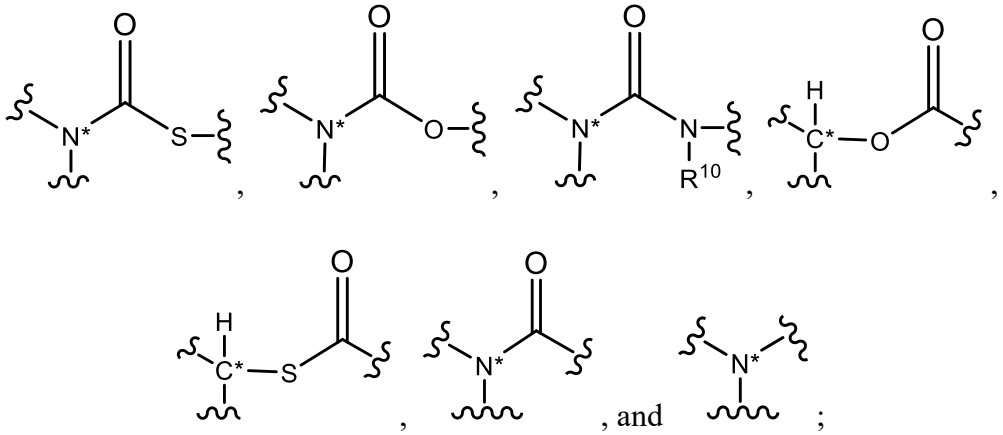
X is O, S, or NR^9, wherein R^9 is H or $C_{1\text{-}6}$ alkyl;

m is 1, 2, 3 or 4, and

n is 0 or 1;

L1 is a linear $C_{1\text{-}6}$ alkylene optionally substituted with one to three methyl groups;

Y is selected from the group consisting of:



wherein:

each asterisk (*) indicates the atom attached to L2 and L3; and

R^{10} is H or C_{1-6} alkyl;

L2 and L3 are each independently a linear C_{1-8} alkylene;

L4, L5, L6, L7, L8 and L9 are each independently absent or $-CH_2-$, provided that:

at least two of L4, L6 and L8 are $-CH_2-$; and

at least two of L5, L7 and L9 are $-CH_2-$;

R^3 and R^4 are each independently H, methyl or ethyl; and

R^5, R^6, R^7 and R^8 are each independently selected from the group consisting of:

linear C_{1-20} alkyl, wherein each said linear C_{1-20} alkyl is optionally substituted with one or more substituents selected from the group consisting of:

C_{6-10} aryl, wherein each said C_{6-10} aryl is a monocyclic or bicyclic aromatic hydrocarbon optionally substituted with one or more C_{6-10} aryl that is optionally substituted with one or more C_{1-6} alkyl;

6-10 membered heteroaryl, wherein each said 6-10 membered heteroaryl is a monocyclic or bicyclic aromatic system optionally substituted with one or more C_{1-6} alkyl;

C_{6-10} aryl, wherein each said C_{6-10} aryl is a monocyclic or bicyclic aromatic hydrocarbon optionally substituted with one or more C_{6-10} aryl that is optionally substituted with one or more C_{1-6} alkyl; and

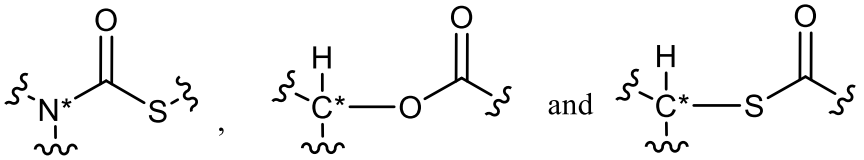
6-10 membered heteroaryl, wherein each said 6-10 membered heteroaryl is a monocyclic or bicyclic aromatic system optionally substituted with one or more C_{1-6} alkyl.

2. The compound of claim 1, wherein:

R^1 is H or C_{1-6} alkyl, and R^2 is C_{1-6} alkyl; or

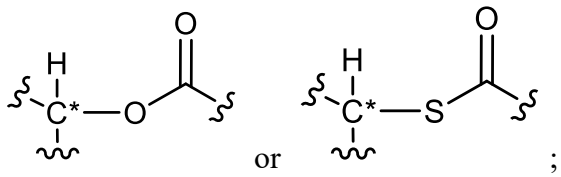
R^1 and R^2 are joined to form said saturated heterocyclic ring.

3. The compound of claim 1 or 2, wherein Y is selected from the group consisting of:



.

4. The compound of claim 1 or 2, wherein Y is:

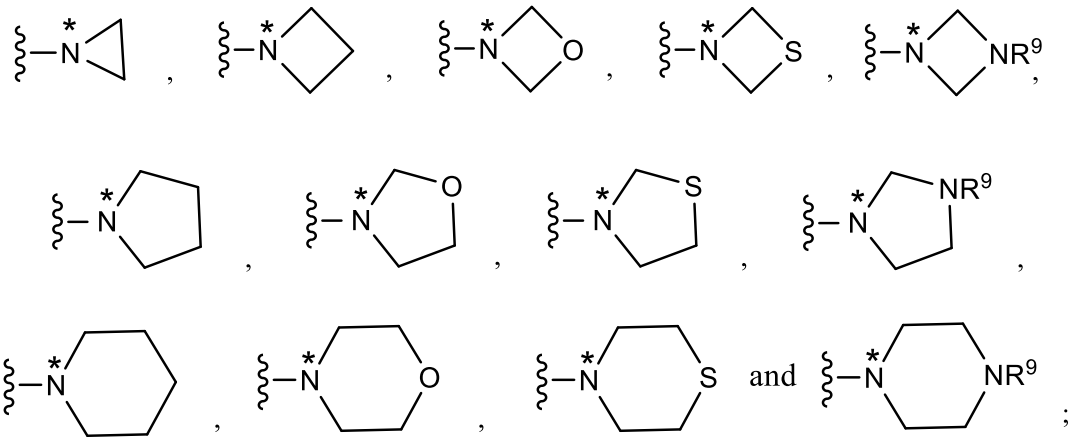


at least one of R^1 and R^2 is H; and

L1 is -CH_2- or -CH_2CH_2-.

5. The compound of any one of claims 1 to 3, wherein R^1 and R^2 are each independently C_{1-6} alkyl or C_{1-3} alkyl or R^1 and R^2 are each methyl.

6. The compound of any one of claims 1 to 3, wherein R^1 and R^2 are joined to form said heterocyclic ring, wherein the heterocyclic ring is selected from the group consisting of:



wherein each asterisk (*) indicates the atom attached to L1.

7. The compound of any one of the preceding claims, wherein R^5, R^6, R^7 and R^8 are each independently linear C_{1-8} alkyl, wherein each said linear C_{1-8} alkyl is optionally substituted with one or more substituents selected from:

C_{6-10} aryl, wherein each said C_{6-10} aryl is a monocyclic or bicyclic aromatic hydrocarbon optionally substituted with one or more C_{6-10} aryl that is optionally substituted with one or more C_{1-6} alkyl; and

6-10 membered heteroaryl, wherein each said 6-10 membered heteroaryl is a monocyclic or bicyclic aromatic system optionally substituted with one or more C_{1-6} alkyl.

8. The compound any one of claims 1-6, wherein R^5, R^6, R^7 and R^8 are:

each independently C_{6-10} aryl, wherein each said C_{6-10} aryl is a monocyclic or bicyclic aromatic hydrocarbon optionally substituted with one or more C_{6-10} aryl that is optionally substituted with one or more C_{1-6} alkyl; or

each independently a 6-10 membered heteroaryl, wherein each said 6-10 membered heteroaryl is a monocyclic or bicyclic aromatic system optionally substituted with one or more C_{1-6} alkyl.

9. The compound of any of the preceding claims, wherein:

R^5 and R^6 are the same; or

R^7 and R^8 are the same; or

L1 is linear unsubstituted alkylene or propylene; or

L2 and L3 are each independently linear C_{1-5} alkylene or L2 and L3 are the same; or

L4 and L5 are the same; or

L6 and L7 are the same; or

L8 and L9 are the same; or

L4, L5, L6, L7, L8 and L9 are each $-CH_2-$; or

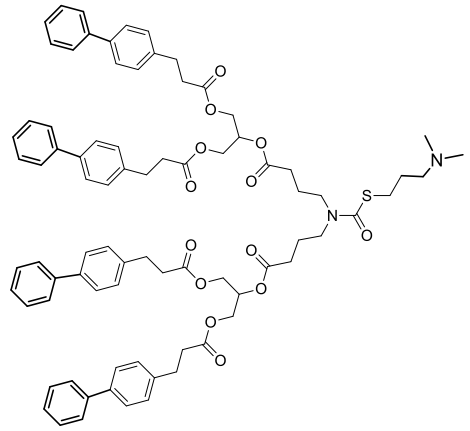
L6, L7, L8 and L9 are each $-CH_2-$; and L4 and L5 are absent; or

L4, L5, L8 and L9 are each $-CH_2-$; and L6 and L7 are absent; or

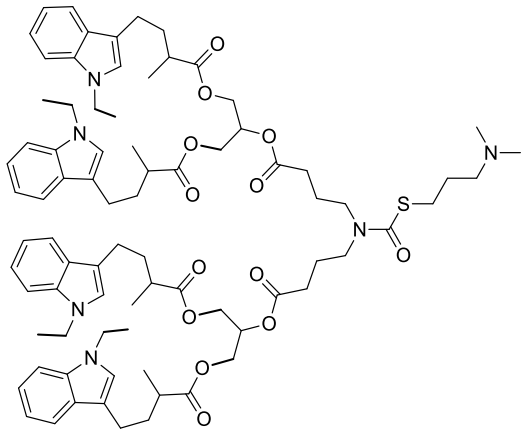
L4, L5, L6 and L7 are each $-CH_2-$; and L8 and L9 are absent; or

R^3 and R^4 are each independently H or methyl or R^3 and R^4 are each H or R^3 and R^4 are each methyl.

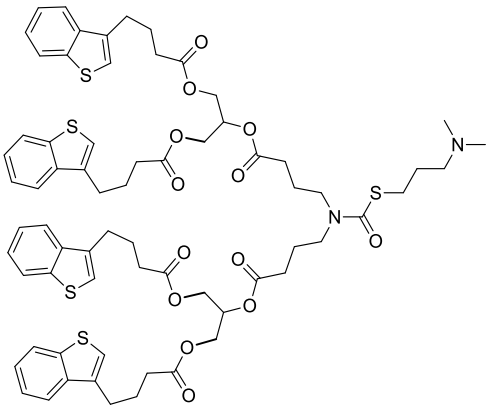
10. The compound of claim 1, selected from the group consisting of:



Lipid 42



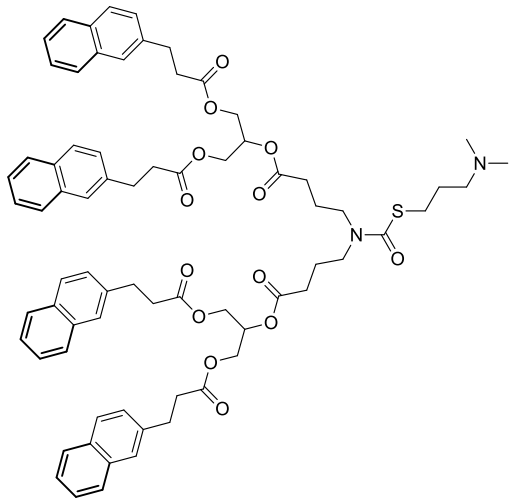
Lipid 43, and



Lipid 45,

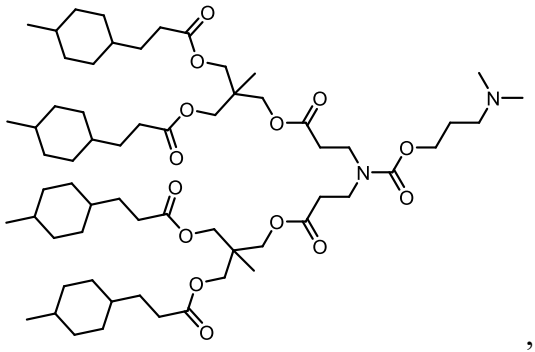
or pharmaceutically acceptable salts thereof.

11. A compound selected from the group consisting of:

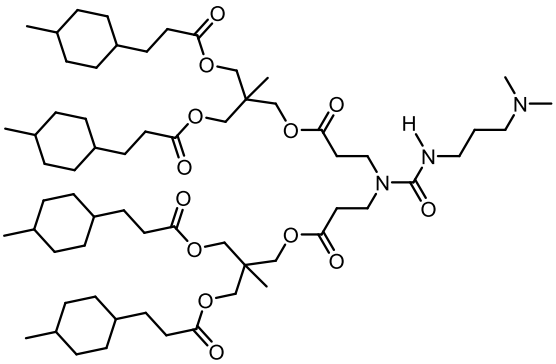


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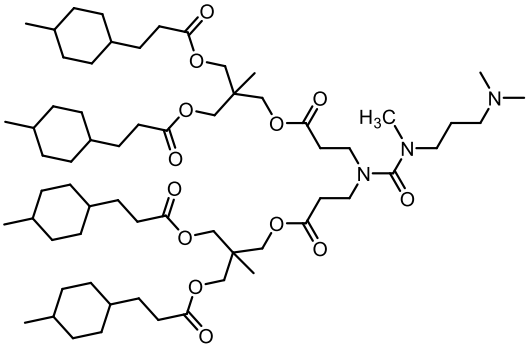
Lipid 44



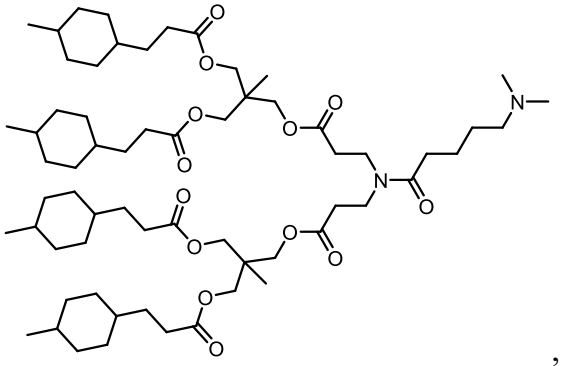
Lipid 46



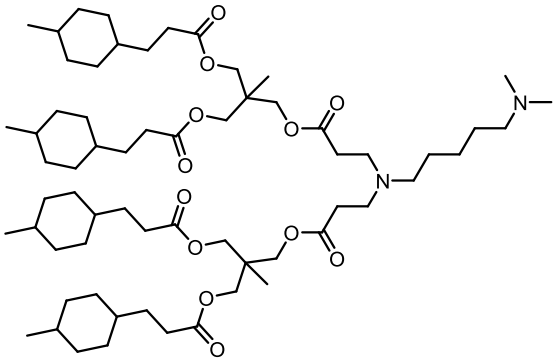
Lipid 47



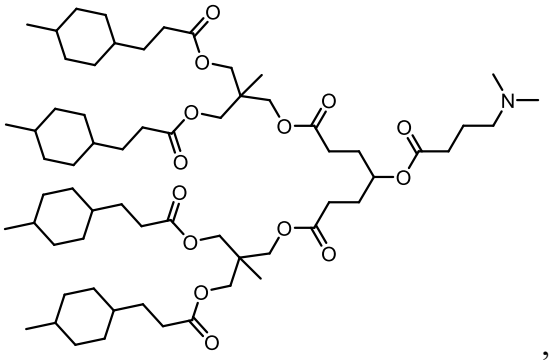
Lipid 48



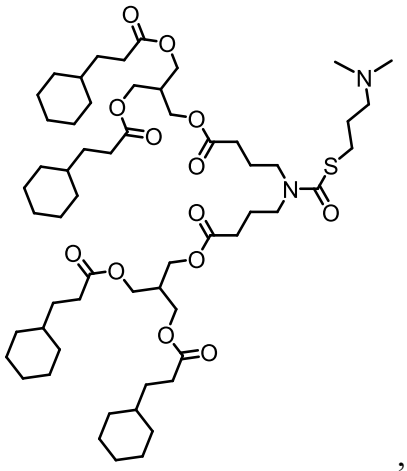
Lipid 49



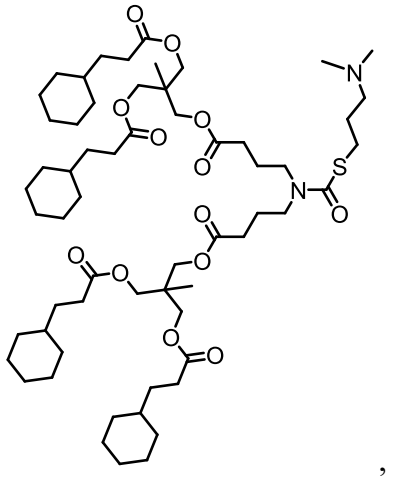
Lipid 50



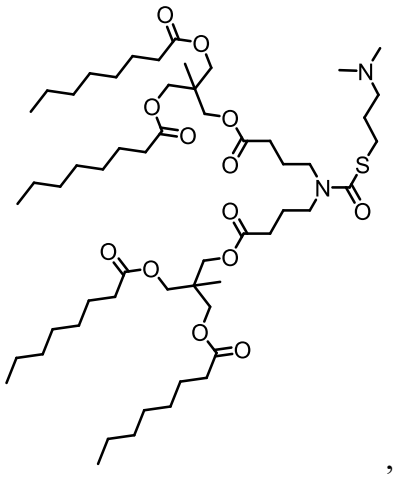
Lipid 51



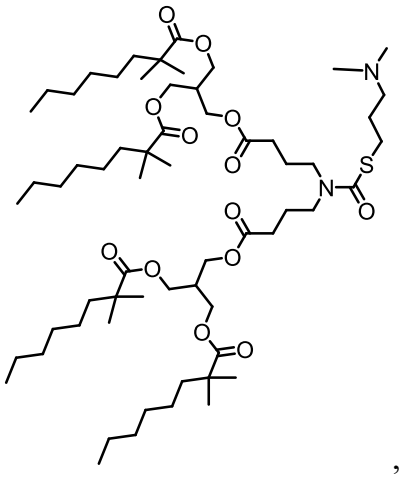
Lipid 52



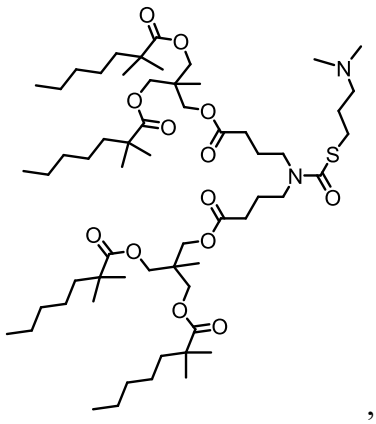
Lipid 53



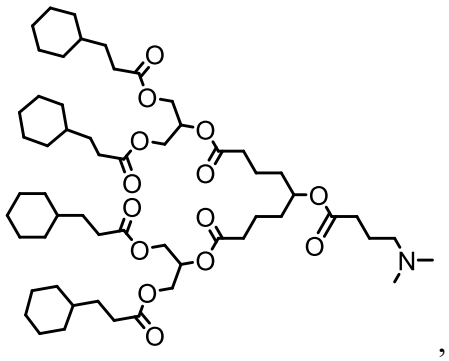
Lipid 54



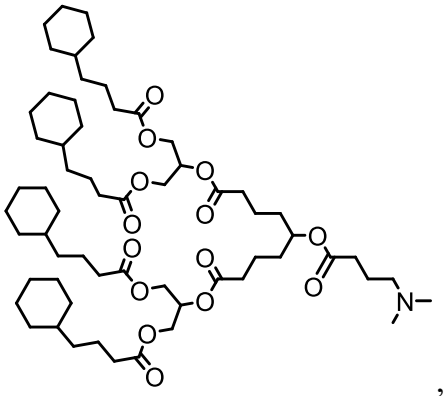
Lipid 55



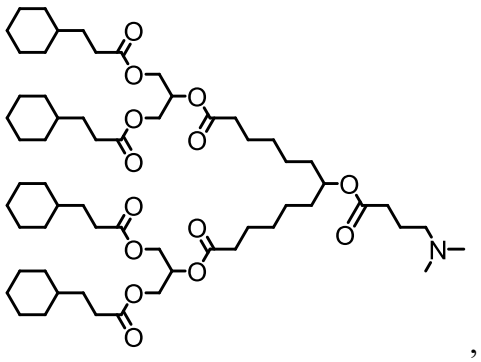
Lipid 56



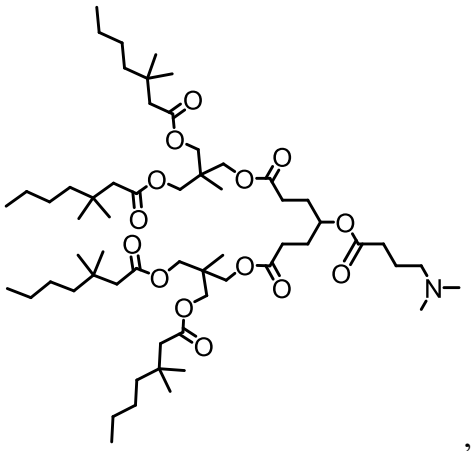
Lipid 57



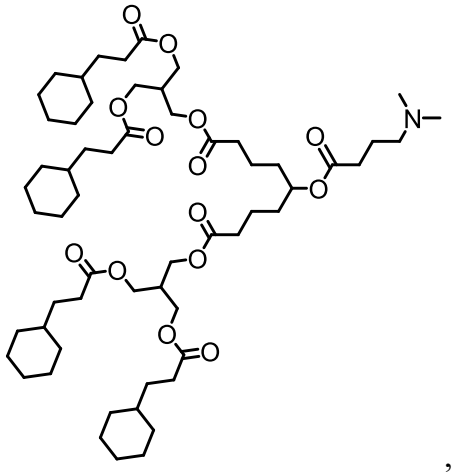
Lipid 58



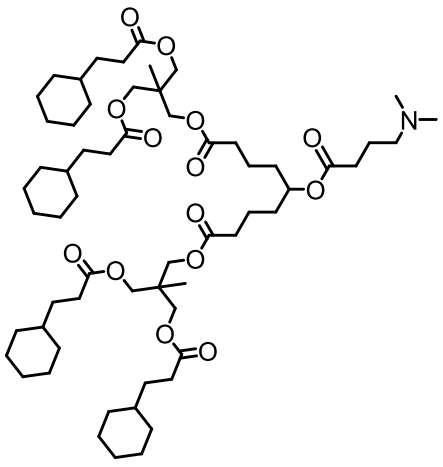
Lipid 59



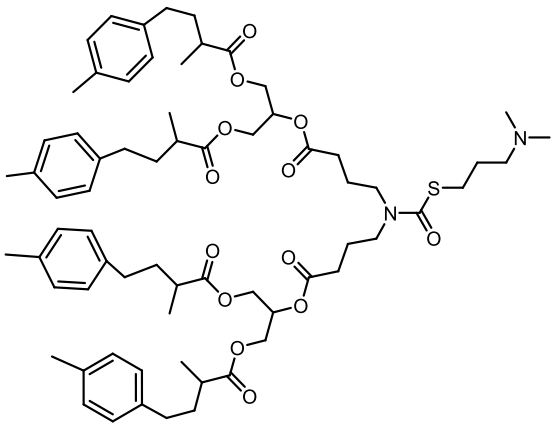
Lipid 60



Lipid 61



Lipid 62, and



Lipid 63;

or pharmaceutically acceptable salts thereof.

12. A lipid composition comprising a nucleic acid and a compound of any one of the preceding claims.

13. The lipid composition of claim 12, wherein the nucleic acid is selected from an siRNA, an mRNA, a self-replicating RNA, a DNA plasmid, and an antisense oligonucleotide.

14. The lipid composition of claim 12 or 13, wherein the nucleic acid is a mRNA or a self-replicating RNA comprising a coding region that encodes a therapeutic protein of interest selected from an enzyme, and antibody, an antigen, a receptor, a transporter or a gene-editing enzyme, optionally wherein the gene-editing enzyme is selected from a TALEN, a CRISPR, a meganuclease, or a zinc finger nuclease.

15. The lipid composition of any one of claims 12-14, wherein the lipid composition comprises liposomes, lipoplexes, or lipid nanoparticles.

16. A lipid nanoparticle, comprising a plurality of lipids, wherein each lipid is independently a compound of any one of claims 1 to 11.

17. The lipid nanoparticle of claim 16, wherein the plurality of lipids self-assembles to form the lipid nanoparticle comprising an interior and exterior.

18. The lipid nanoparticle of claim 16 or 17, wherein the average particle size of the lipid nanoparticle is less than 100 nm or 55 nm to 85 nm.

19. The lipid nanoparticle of any one of claims 16-18, wherein the lipid nanoparticle further comprises a nucleic acid encapsulated in the interior, wherein the nucleic acid is selected from an siRNA, an mRNA, a self-replicating RNA, a DNA plasmid, and an antisense oligonucleotide.

20. The lipid nanoparticle of claim 16-19, wherein the nucleic acid is a mRNA or a self-replicating RNA comprising a coding region that encodes a therapeutic protein of interest selected from an enzyme, and antibody, an antigen, a receptor, a transporter or a gene-editing enzyme is selected from a TALEN, a CRISPR, a meganuclease, or a zinc finger nuclease.

21. The lipid nanoparticle of any one of claims 16 to 20, wherein the lipid nanoparticle further comprises one or more of:

a helper lipid selected from: dioleoylphosphatidyl ethanolamine (DOPE), dimyristoylphosphatidyl choline (DMPC), distearoylphosphatidylcholine (DSPC), dimyristoylphosphatidyl glycerol (DMPG), dipalmitoyl phosphatidylcholine (DPPC),

and phosphatidylcholine (PC), optionally wherein the helper lipid is distearoylphosphatidylcholine (DSPC);

or cholesterol or a cholesterol derivative;

a polyethylene glycol(PEG)-lipid conjugate, optionally wherein PEG-lipid conjugate is PEG-DMG, optionally wherein the PEG-DMG is PEG2000-DMG.

22. The lipid nanoparticle of any one of claims 16-21, wherein the lipid nanoparticle comprises:

45 mol% to 65 mol% of the compound of any one of claims 1 to 11, 2 mol% to 15 mol% of a helper lipid, 20 mol% to 42 mol% of cholesterol or a cholesterol derivative, and 0.5 mol% to 3 mol% of a PEG-lipid conjugate; or

50 mol% to 61 mol% of the compound of any one of claims 1 to 11, 5 mol% to 9 mol% of the helper lipid, 29 mol% to 38 mol% of cholesterol or a cholesterol derivative, and 1 mol% to 2 mol% of the PEG-lipid conjugate; or .

56 mol% to 58 mol% of the compound of any one of claims 1 to 11, 6 mol% to 8 mol% of DSPC, 31 mol% to 34 mol% of cholesterol or a cholesterol derivative, and 1.25 mol% to 1.75 mol% of the PEG-lipid conjugate.

23. The lipid nanoparticle of any one of claims 16-22, wherein the lipid nanoparticle has a total lipid:nucleic acid weight ratio of:

50:1 to 10:1;

40:1 to 20:1;

35:1 to 25:1;

32:1 to 28:1; or

31:1 to 29:1.

24. A pharmaceutical composition comprising the compound of any one of claims 1 to 11, or the lipid nanoparticle of any one of claims 16-23, and a pharmaceutically acceptable excipient optionally wherein the pharmaceutical composition is a lyophilized composition.

25. The pharmaceutical composition of claim 24, wherein the pharmaceutical composition comprises one or more of:

a HEPES buffer at a pH of about 7.4;

2.0 mg/mL to 4.0 mg/mL of NaCl; or

one or more cryoprotectants are selected from sucrose, glycerol, or a combination of sucrose and glycerol.

26. The pharmaceutical composition of claim 25, wherein:

(i) the HEPES buffer is at a concentration of 7 mg/mL to 15 mg/mL; or

(ii) the pharmaceutical composition comprises a combination of sucrose at a concentration of 70 mg/mL to 110 mg/mL and glycerol at a concentration of 50 mg/mL to 70 mg/mL.

27. The lipid nanoparticle of any one of claims 16-23, or the pharmaceutical composition of any one of claims 24-26 for use in treating a disease in a subject in need thereof, optionally wherein the lipid nanoparticle or pharmaceutical composition is formulated to be administered intravenously or intramuscularly.

28. The lipid nanoparticle of any one of claims 16-23, or the pharmaceutical composition of any one of claims 24-26 for use in therapy to express a protein or a polypeptide in a target cell; optionally wherein the protein or polypeptide is an antigen, and expression of the antigen elicits an *in vivo* immunogenic response.

29. The lipid nanoparticle of any one of claims 16-23, wherein a therapeutically effective amount of the nucleic acid is to be encapsulated in the lipid nanoparticle, wherein the lipid nanoparticle is formulated for delivery of the nucleic acid to a subject in need thereof.