WHAT IS CLAIMED IS:

1. A lipid having a structural Formula (I):

X-A-Y-Z;

(I)

or salts thereof, wherein:

X is alkylamino;

A is C_1 to C_6 optionally substituted alkyl, wherein said C_1 to C_6 optionally substituted alkyl can be saturated or unsaturated, and wherein A may or may not be present;

Y is selected from the group consisting of ketal, ester, optionally substituted carbamate, ether, and optionally substituted amide; and

Z is a hydrophobic moiety consisting of three alkyl chains wherein each of the alkyl chains has a length of from C_8 to C_{11}, wherein each of the three alkyl chains can independently be saturated or unsaturated, and wherein each of the three alkyl chains is optionally substituted.

2. The lipid of claim 1, wherein each of the alkyl chains has a length of from C_9 to C_{10}.

3. The lipid of claim 1, wherein at least one of the alkyl chains has a double bond.

4. The lipid of claim 1, wherein at least one of the alkyl chains has a cis double bond.

5. The lipid of claim 1, wherein at least one of the alkyl chains comprises a cycloalkyl moiety.

6. The lipid of claim 1, wherein X is selected from the group consisting of dimethylamino, diethylamino and ethylmethylamino.

7. The lipid of claim 1, wherein A is present.

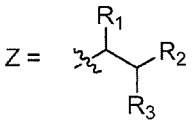
8. The lipid of claim 1, wherein Y is an ester or ketal.

9. The lipid of claim 1, wherein Y is an optionally substituted carbamate.

10. The lipid of claim 1, wherein Y is an ether.

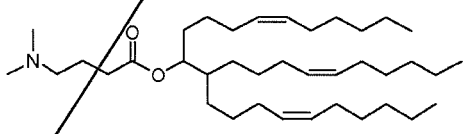
11. The lipid of claim 1, wherein Y is an optionally substituted amide.

12. The lipid of claim 1, wherein Z has the formula:



wherein, R_1, R_2, and R_3 are each independently selected from the group consisting of C_8 to C_{11} alkyl, wherein each of R_1, R_2, and R_3 can independently be saturated or unsaturated, and wherein each of R_1, R_2, and R_3 is optionally substituted.

13. The lipid of claim 1, wherein the lipid is selected from the group consisting of:



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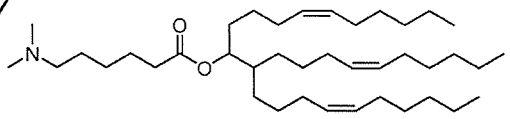

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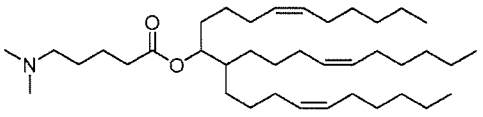

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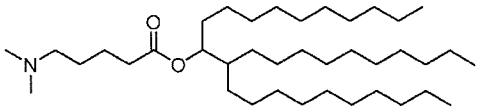

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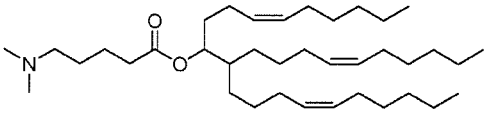

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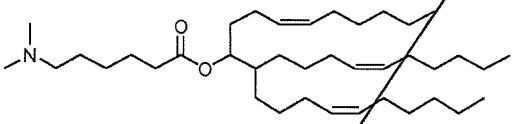

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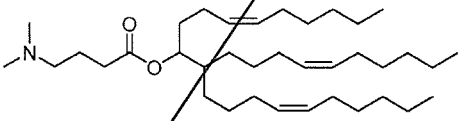

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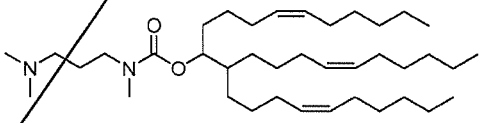

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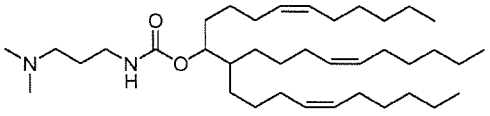

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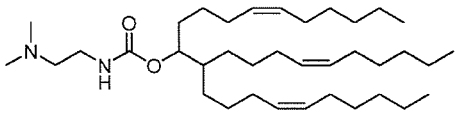

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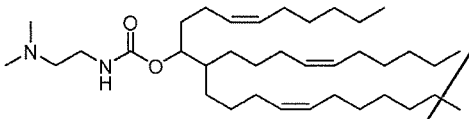

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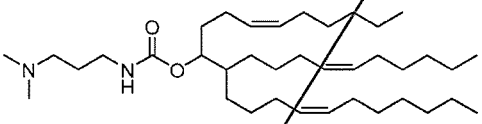

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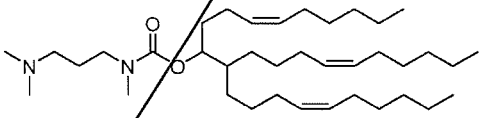

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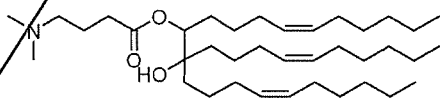

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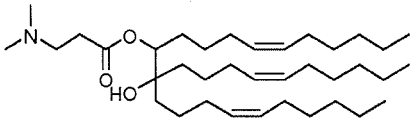

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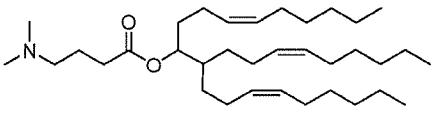

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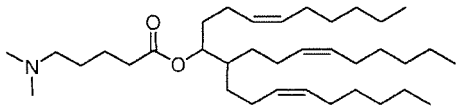

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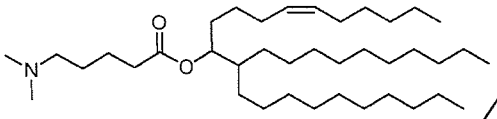

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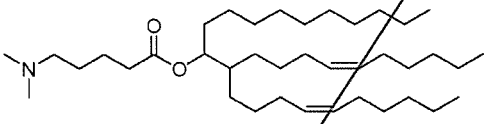

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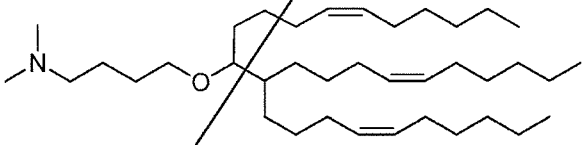

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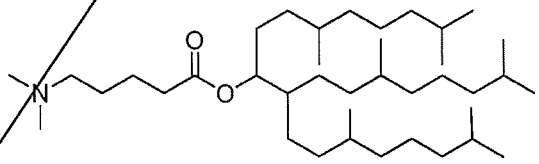

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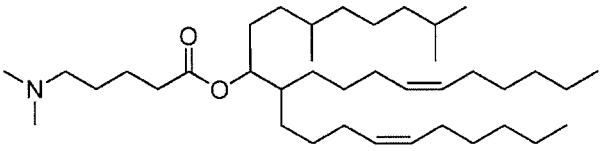

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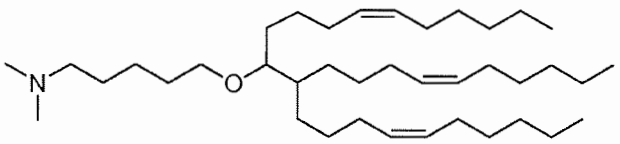

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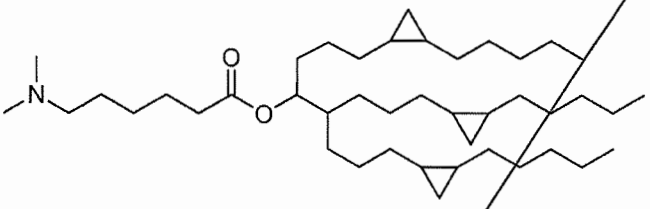

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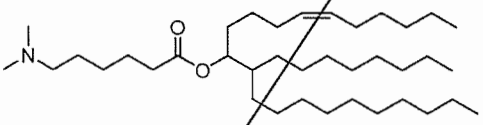

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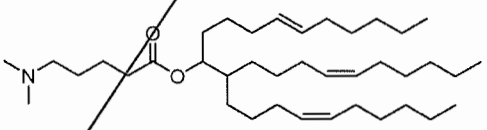

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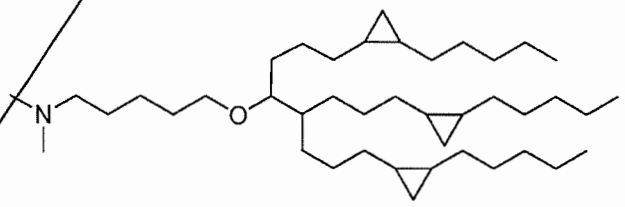


Compound 90.

14. A lipid particle comprising a lipid of any of the preceding claims.

15. The lipid particle of claim 14, wherein the particle further comprises a non-cationic lipid.

16. The lipid particle of claim 15, wherein the non-cationic lipid is selected from the group consisting of a phospholipid, cholesterol, or a mixture of a phospholipid and cholesterol.

17. The lipid particle of claim 16, wherein the phospholipid comprises dipalmitoylphosphatidylcholine (DPPC), distearoylphosphatidylcholine (DSPC), or a mixture thereof.

18. The lipid particle of claim 16, wherein the cholesterol is a cholesterol derivative.

19. The lipid particle of any of claims 14 to 18, wherein the particle further comprises a conjugated lipid that inhibits aggregation of particles.

20. The lipid particle of claim 19, wherein the conjugated lipid that inhibits aggregation of particles comprises a polyethyleneglycol (PEG)-lipid conjugate.

21. The lipid particle of claim 20, wherein the PEG-lipid conjugate comprises a PEG-diacylglycerol (PEG-DAG) conjugate, a PEG-dialkyloxypropyl (PEG-DAA) conjugate, or a mixture thereof.

22. The lipid particle of any of claims 14 to 21 wherein the particle further comprises a therapeutic agent.

23. The lipid particle of claim 22, wherein the therapeutic agent is a nucleic acid.

24. The lipid particle of claim 23, wherein the nucleic acid is an interfering RNA.

25. The lipid particle of claim 24, wherein the interfering RNA is selected from the group consisting of a small interfering RNA (siRNA), an asymmetrical interfering RNA (aiRNA), a microRNA (miRNA), a Dicer-substrate dsRNA, a small hairpin RNA (shRNA), and mixtures thereof.

26. The lipid particle of claim 25, wherein the interfering RNA is an siRNA.

27. The lipid particle of claim 22, wherein the therapeutic agent is not substantially degraded after incubation of the particle in serum at 37°C for 30 minutes.

28. The lipid particle of claim 22, wherein the therapeutic agent is fully encapsulated in the particle.

29. The lipid particle of claim 22, wherein the particle has a lipid:therapeutic agent mass ratio of from about 5:1 to about 15:1.

30. The lipid particle of any of claims 14 to 29, wherein the particle has a median diameter of from about 30 nm to about 150 nm.

31. A pharmaceutical composition comprising a lipid particle of any of claims 14 to 30 and a pharmaceutically acceptable carrier.

32. A method for introducing a therapeutic agent into a cell, the method comprising:

contacting the cell with a lipid particle of claim 14.

33. The method of claim 32, wherein the cell is in a mammal.

34. A method for the *in vivo* delivery of a therapeutic agent, the method comprising:

administering to a mammal a lipid particle of claim 14.

35. The method of claim 34, wherein the administration is selected from the group consisting of oral, intranasal, intravenous, intraperitoneal, intramuscular, intra-articular, intralesional, intratracheal, subcutaneous, and intradermal.

36. The method of claim 34, wherein the mammal is a human.

37. A method for treating a disease or disorder in a mammal in need thereof, the method comprising:

administering to the mammal a therapeutically effective amount of a lipid particle of claim 14.

38. The method of claim 37, wherein the disease or disorder is selected from the group consisting of a viral infection, a liver disease or disorder, and cancer.

39. The method of claim 37, wherein the mammal is a human.

CLAIMS

1. A lipid having a structural Formula (I):

X-A-Y-Z;

(I)

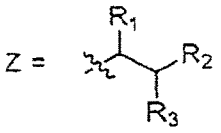
or salts thereof, wherein;

X is alkylamino;

A is C_1 to C_6 alkyl or cycloalkyl or substituted C_1 to C_6 alkyl or substituted cycloalkyl, wherein said alkyl or cycloalkyl can be saturated or unsaturated, and wherein A may or may not be present;

Y is selected from the group consisting of ketal, ester, carbamate, substituted carbamate, ether, amide and substituted amide; and

Z has the formula:

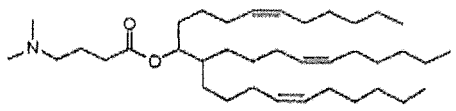


wherein R_1, R_2 and R_3 are each independently selected from the group consisting of C_8 to C_{11} alkyl and substituted C_8 to C_{11} alkyl, wherein each of R_1, R_2 and R_3 can independently be saturated or unsaturated.

2. The lipid of claim 1, wherein at least one of R_1, R_2 and R_3 alkyl has a double bond, preferably a cis double bond.

3. The lipid of claim 1, wherein X is selected from the group consisting of dimethylamino, diethylamino and ethylmethylamino.

4. A lipid, selected from the group consisting of:



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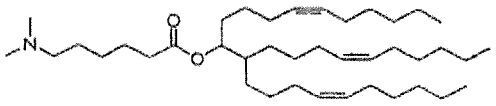

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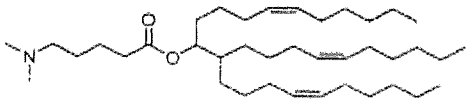

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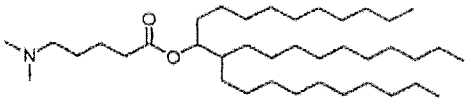

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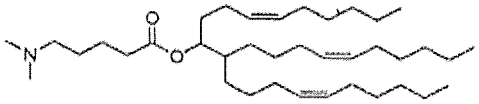

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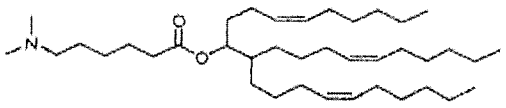

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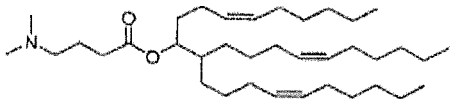

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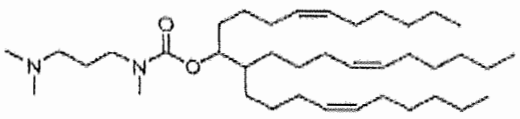

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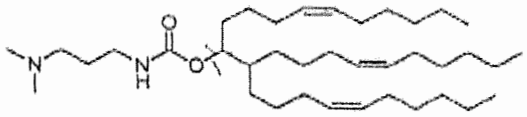

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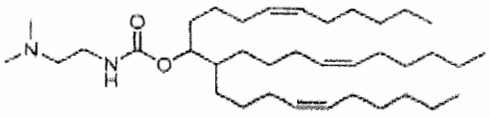

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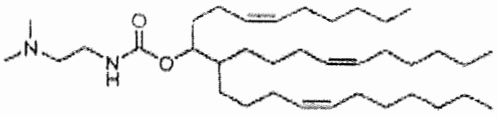

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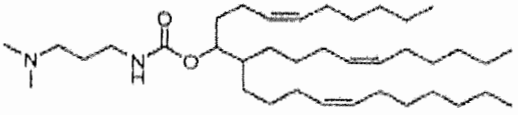

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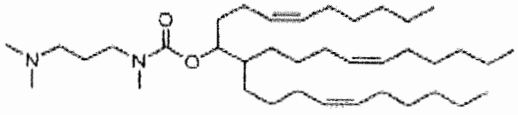

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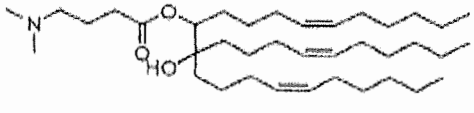

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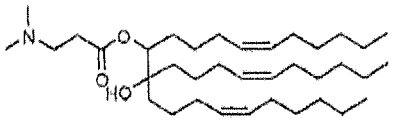

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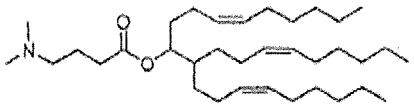

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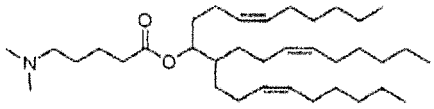

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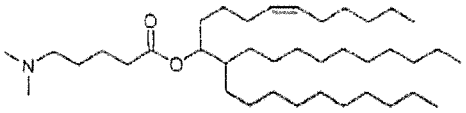

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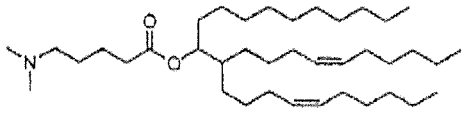
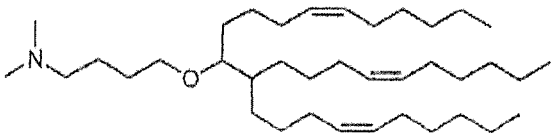


Compound 53,



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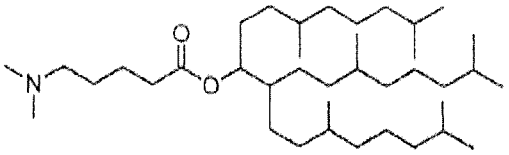

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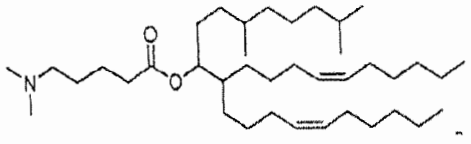

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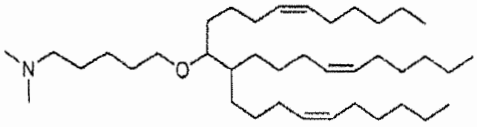
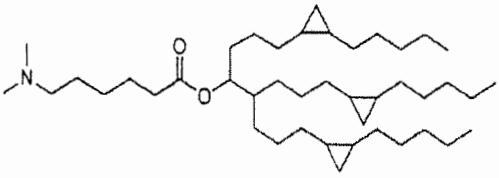


Compound 76,



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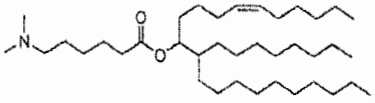
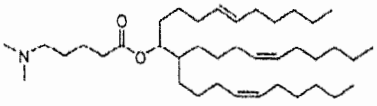
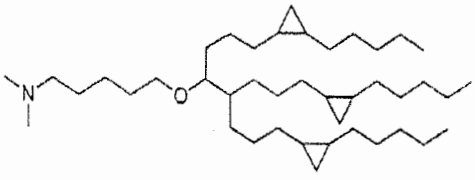


Compound 83,



Compound 89, and



Compound 90.

5. A lipid particle comprising a lipid of any of the preceding claims.

6. The lipid particle of claim 5, wherein the particle further comprises a non-cationic lipid, preferably selected from the group consisting of a phospholipid, cholesterol or cholesterol derivative, or a mixture of a phospholipid and cholesterol or cholesterol derivative, wherein the phospholipid preferably comprises dipalmitoylphosphatidylcholine (DPPC), distearoylphosphatidylcholine (DSPC), or a mixture thereof.

7. The lipid particle of claim 5 or 6, wherein the particle further comprises a conjugated lipid that inhibits aggregation of particles, preferably comprising a polyethyleneglycol (PEG)-lipid conjugate, wherein the PEG-lipid conjugate preferably comprises a PEG diacylglycerol (PEG-DAG) conjugate, a PEG-dialkyloxypropyl (PEG-DAA) conjugate, or a mixture thereof.

8. The lipid particle of any of claims 5 to 7 wherein the particle further comprises a therapeutic agent, wherein the therapeutic agent is preferably a nucleic acid, wherein the nucleic acid is preferably, an interfering RNA, wherein the interfering RNA is preferably selected from the group consisting of a small interfering RNA (siRNA), an asymmetrical interfering RNA (aiRNA), a microRNA (miRNA), a Dicer-substrate (dsRNA), a small hairpin RNA (shRNA), and mixtures thereof.

9. The lipid particle of claim 8, wherein the therapeutic agent is fully encapsulated in the particle.

10. The lipid particle of claim 8, wherein the particle has a lipid : therapeutic agent mass ratio from about 5 : 1 to about 15 : 1.

11. The lipid particle of any of claims 5 to 10, wherein the particle has a median diameter from about 30 nm to about 150 nm.

12. A pharmaceutical composition comprising a lipid particle of any of claims 5 to 11 and a pharmaceutically acceptable carrier.

13. A lipid particle of claim 5 for use in a method for the *in vivo* delivery of a therapeutic agent to a mammal.

14. The lipid particle for use of claim 13, wherein the mammal is a human.

15. The lipid particle for use of claim 13, wherein the administration is selected from the group consisting of oral, intranasal, intravenous, intraperitoneal, intramuscular, intra-articular, intralesional, intratracheal, subcutaneous, and intradermal.

16. A lipid particle of claim 5 for use in the treatment of a disease or disorder, selected from the group consisting of a viral infection, a liver disease or disorder, and cancer in a mammal in need thereof.

17. The lipid particle for use of claim 16 wherein the mammal is a human.