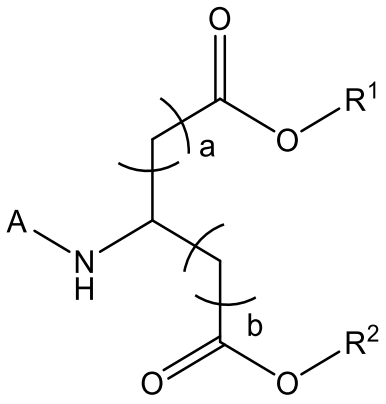
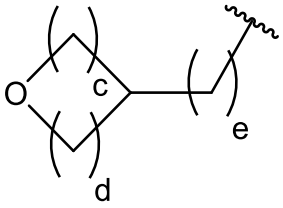
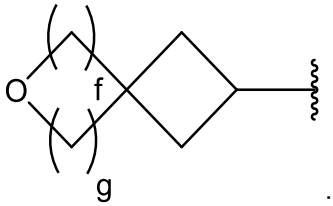
Claims

1. A compound of Formula (I):



Formula (I)

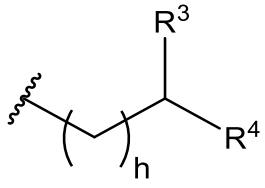
or a pharmaceutically acceptable salt thereof, wherein

A is  or ;

a and b are each independently 6, 7 or 8;

c, d, f and g are each independently 1 or 2;

e is 0, 1 or 2;

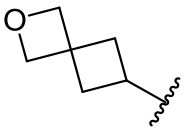
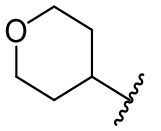
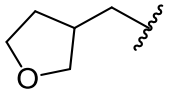
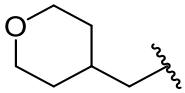
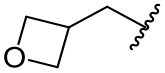
R^1 and R^2 are each independently ;

h is 0, 1, 2 or 3;

R^3 and R^4 are each independently $-(CH_2)_iCH_3$; and

i is 3, 4, 5, 6 or 7.

2. The compound of claim 1, wherein e is 0 or 1.

3. The compound of claim 1, wherein A is selected from , , ,  and .

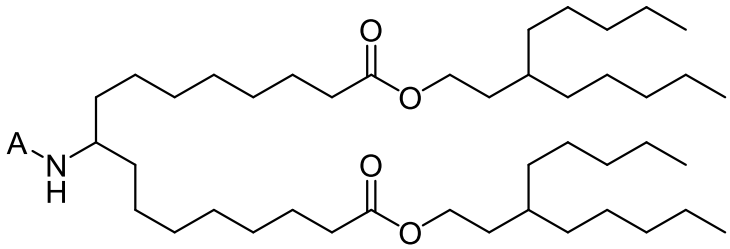
4. The compound of any one of the preceding claims, wherein a is 7.

5. The compound of any one of the preceding claims, wherein b is 7.

6. The compound of any one of the preceding claims, wherein h is 2.

7. The compound of any one of the preceding claims, wherein R^3 and R^4 are each $–(CH_2)_4CH_3$.

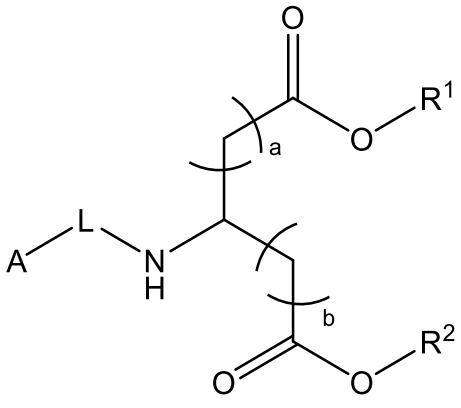
8. The compound of any one of claims 1-3, wherein the compound is of Formula (II):



Formula (II),

or a pharmaceutically acceptable salt thereof.

9. A compound of Formula (III):



Formula (III),

or a pharmaceutically acceptable salt thereof; wherein

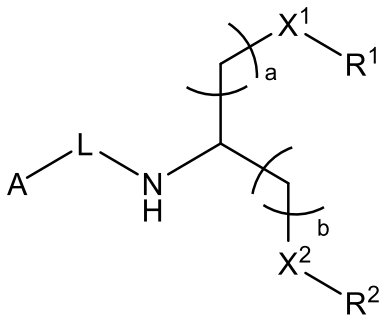
A is 4- to 6-membered monocyclic oxacyclyl or 6- to 10-membered bicyclic oxacyclyl;

L is a covalent bond or C_1-C_3 alkylene;

a and b are each independently 5, 6, 7 or 8; and

R^1 and R^2 are each independently C_7-C_{11} straight chain alkyl or C_9-C_{19} branched alkyl; provided that R^1 and R^2 is are not both C_7-C_{11} straight chain alkyl.

10. A compound of Formula (IIIa):

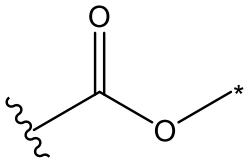
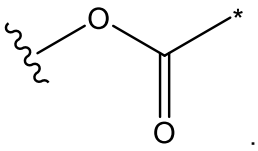


Formula (IIIa),

or a pharmaceutically acceptable salt thereof; wherein

A is 4- to 6-membered monocyclic oxacyclyl or 6- to 10-membered bicyclic oxacyclyl;

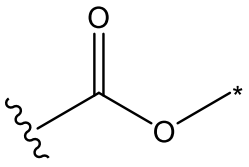
L is a covalent bond or C_1-C_3 alkylene;

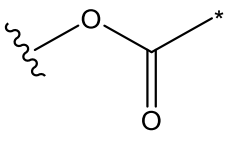
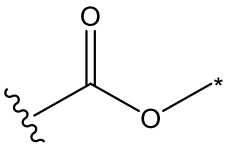
X^1 and X^2 are each independently  or ;

* indicates the attachment point to R^1;

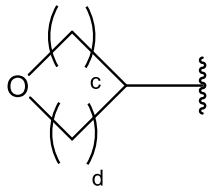
a and b are each independently 4, 5, 6, 7, 8 or 9; provided that when one of a and b is 4 or 5, then the other is 6, 7, 8 or 9;

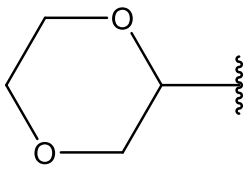
R^1 and R^2 are each independently C_7-C_{11} straight chain alkyl, C_7-C_{19} branched alkyl, or C_7-C_{19} alkylene-cyclopropylene-alkyl; provided that R^1 and R^2 are not both C_7-C_{11} straight chain alkyl or both C_7-C_{19} alkylene-cyclopropylene-alkyl.

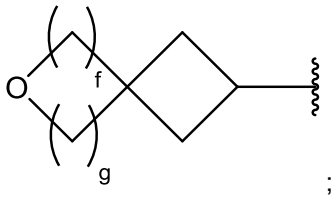
11. The compound of claim 10, wherein X^1 and X^2 are both .

12. The compound of claim 10, wherein X^1 is ; and X^2 is .

13. The compound of any one of claims 9-12, wherein

A is 

, 

, or 

;

c is 0, 1 or 2;

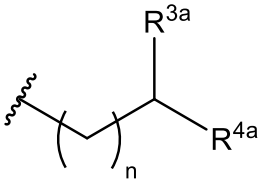
d is 1, 2 or 3; provided that the sum of c and d is from 2 to 4;

f is 0, 1 or 2; and

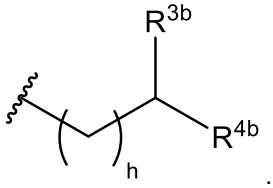
g is 1, 2 or 3; provided that the sum of f and g is from 2 to 4.

14. The compound of any one of claims 9-13, wherein L is a covalent bond, $-CH_2-$, or $-CH_2CH_2-$.

15. The compound of any one of claims 9-14, wherein

R^1 is $–(CH_2)_m-CH_3$ or 

;

R^2 is 

.

m is 7, 8, or 9;

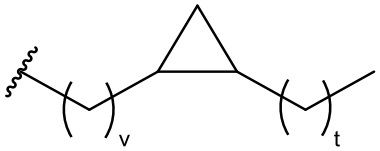
n and h are each independently 0, 1, 2, or 3;

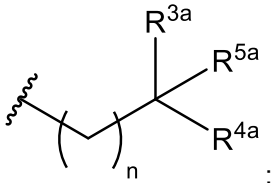
R^{3a} and R^{4a} are each independently $-(CH_2)_pCH_3$;

R^{3b} and R^{4b} are each independently $-(CH_2)_qCH_3$;

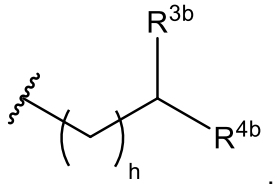
p and q are each independently 0, 1, 2, 3, 4, 5, 6, 7, 8, or 9; and provided that R^{3a} and R^{4a}, together with the carbon atom to which they are attached, contain at least 9 carbon atoms and R^{3b} and R^{4b}, together with the carbon atom to which they are attached, contain at least 9 carbon atoms.

16. The compound of any one of claims 10 to 14, wherein

R^1 is $–(CH_2)_m-CH_3$, 

, or 

;

R^2 is 

.

m is 6, 7, 8, or 9;

v is 1, 2 or 3;

t is 3, 4, 5, 6, 7, or 8;

n and h are each independently 0, 1, 2, or 3;

R^{3a} and R^{4a} are each independently $-(CH_2)_pCH_3$;

R^{3b} and R^{4b} are each independently $-(CH_2)_qCH_3$;

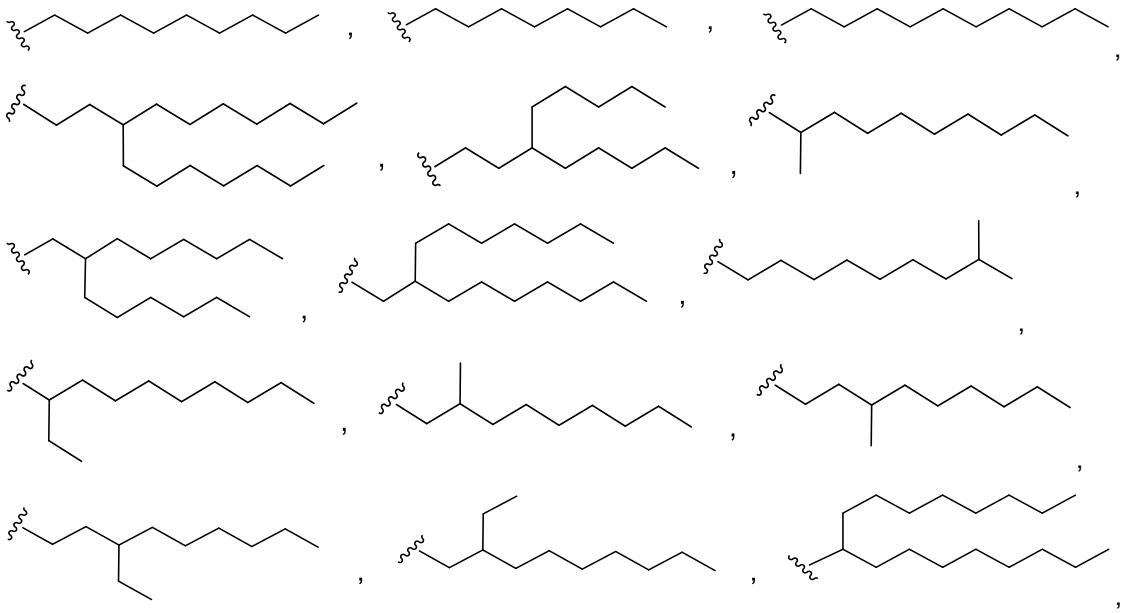
R^{5a} is hydrogen or methyl;

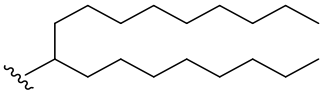
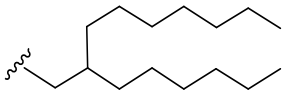
p and q are each independently 0, 1, 2, 3, 4, 5, 6, 7, 8, or 9; and provided that R^{3a}, R^{4a} and R^{5a}, together with the carbon atom to which they are attached, contain at least 7 carbon atoms and R^{3b} and R^{4b}, together with the carbon atom to which they are attached, contain at least 9 carbon atoms.

17. The compound of claim 16, wherein R^{3a} is $-(CH_2)_pCH_3$, wherein p is 0, 1, 2 or 3; and R^{4a} is $-(CH_2)_qCH_3$, wherein p is 4, 5, 6, 7, 8 or 9.

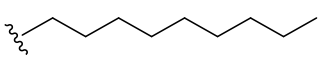
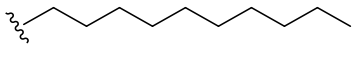
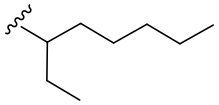
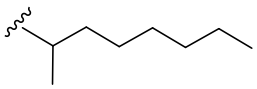
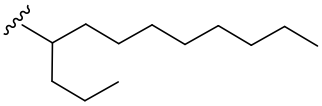
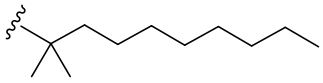
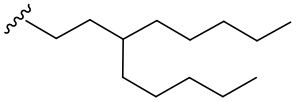
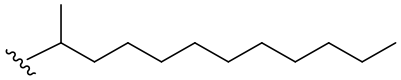
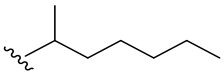
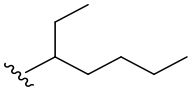
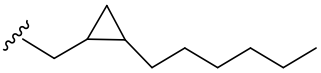
18. The compound of claim 16, wherein R^{3b} and R^{4b} are both $-(CH_2)_qCH_3$, wherein q is 5, 6, 7 or 8.

19. The compound of any one of claims 9 and 13-15, wherein R^1 is selected from

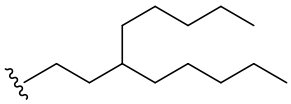
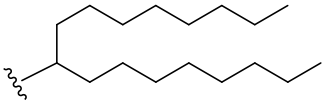
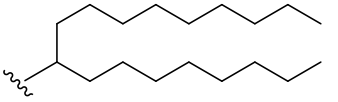
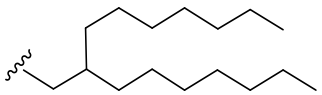
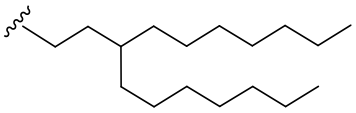
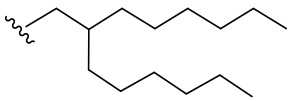
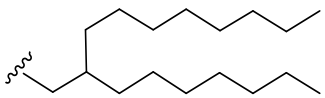
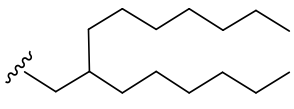
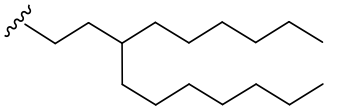
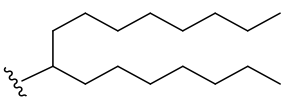
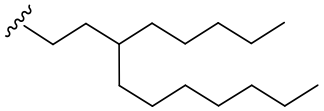


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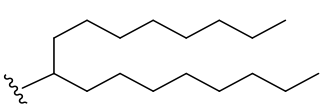
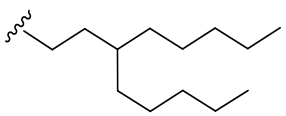
20. The compound of any one of claims 10-14 and 16, wherein R^1 is selected from

, ,
, , ,
, , ,
, , and .

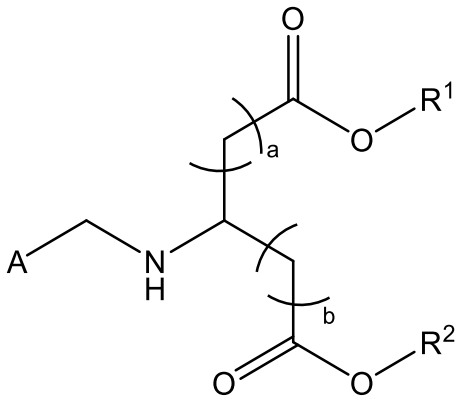
21. The compound of any one of claims 9, 13-15 and 19, wherein R^2 is selected from

, , ,
, , ,
, , ,
, and .

22. The compound of any one of claims 10-14, 16 and 20, wherein R^2 is selected from

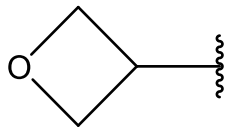
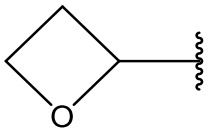
, and .

23. The compound of any one of claims 9, 13-15, 19 and 21, which is represented by Formula (IV):



Formula (IV),

or a pharmaceutically acceptable salt thereof; wherein

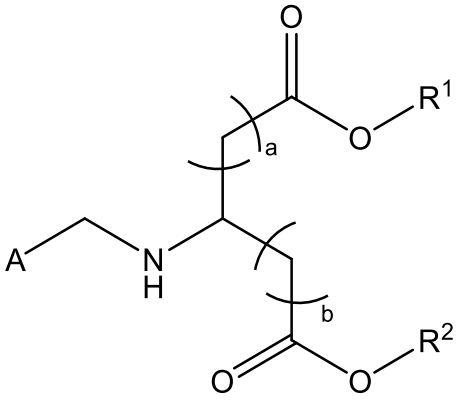
A is  or  ;

a and b are each independently 5, 6, 7 or 8;

R^1 is C_7-C_{11} straight chain alkyl or C_9-C_{19} branched alkyl; and

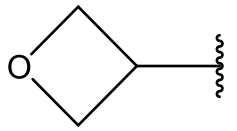
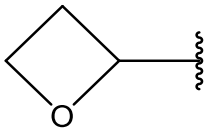
R^2 is C_9-C_{19} branched alkyl.

24. The compound of any one of claims 10-14, 16, 20 and 22, which is represented by Formula (IVa):



Formula (IVa),

or a pharmaceutically acceptable salt thereof; wherein

A is  or  ;

a and b are each independently 5, 6, 7 or 8;

R^1 is C_7-C_{11} straight chain alkyl, C_7-C_{15} branched alkyl or C_7-C_{15} alkylene-cyclopropylene-alkyl; and

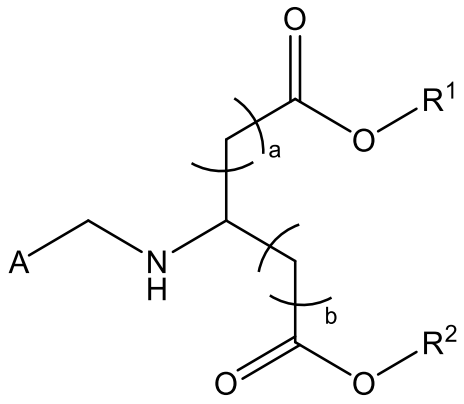
R^2 is C_{15}-C_{19} branched alkyl.

25. The compound of claim 23, wherein R^1 and R^2 are both C_{10}-C_{17} branched alkyl and contain the same number of carbon atoms.

26. The compound of claim 23, wherein R^1 is C_7-C_{11} straight chain alkyl or C_9-C_{13} branched alkyl; R^2 is C_{13}-C_{19} branched alkyl; and provided that R^1 and R^2 are not both C_{13} branched alkyl.

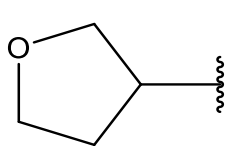
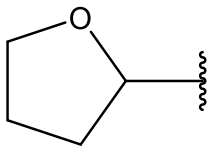
27. The compound of any one of claims 23, 25 and 26, wherein a and b are both 5, 6, 7 or 8.

28. The compound of any one of claims 9, 13-15, 19 and 21, which is represented by Formula (V):



Formula (V),

or a pharmaceutically acceptable salt thereof; wherein

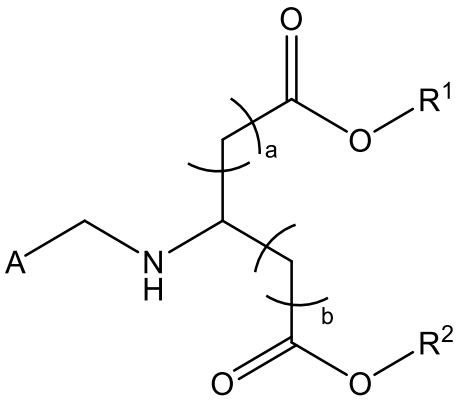
A is  or ;

a and b are each independently 5, 6, 7 or 8;

R^1 is C_7-C_{11} straight chain alkyl or C_9-C_{19} branched alkyl; and

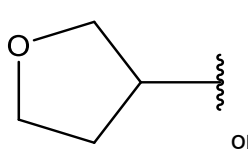
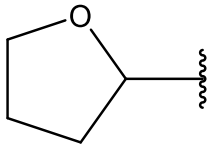
R^2 is C_9-C_{19} branched alkyl.

29. The compound of any one of claims 10-14, 16, 20 and 22, which is represented by Formula (Va):



Formula (Va),

or a pharmaceutically acceptable salt thereof; wherein

A is  or ;

a and b are each independently 5, 6, 7 or 8;

R^1 is C_7-C_{15} branched alkyl or C_7-C_{15} alkylene-cyclopropylene-alkyl; and

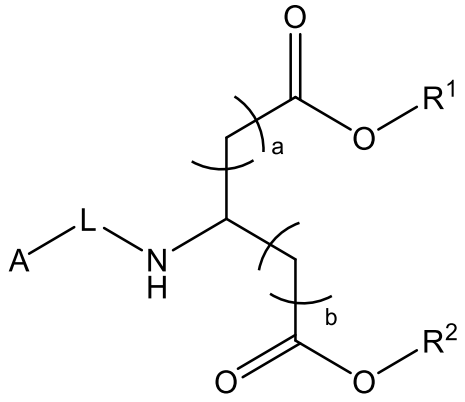
R^2 is C_{15}-C_{19} branched alkyl.

30. The compound of claim 28, wherein R^1 and R^2 are both C_{10}-C_{17} branched alkyl and contain the same number of carbon atoms.

31. The compound of claim 28, wherein R^1 is C_7-C_{11} straight chain alkyl or C_9-C_{13} branched alkyl; R^2 is C_{13}-C_{19} branched alkyl; and provided that R^1 and R^2 are not both C_{13} branched alkyl.

32. The compound of any one of claims 28, 30 and 31, wherein a and b are both 5, 6, 7 or 8.

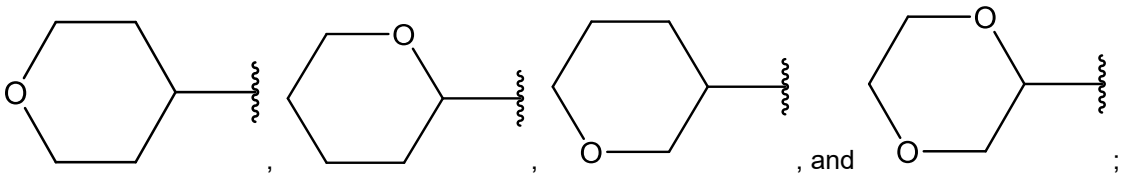
33. The compound of any one of claims 9, 13-15, 19 and 21, which is represented by Formula (VI):



Formula (VI),

or a pharmaceutically acceptable salt thereof; wherein

A is selected from:



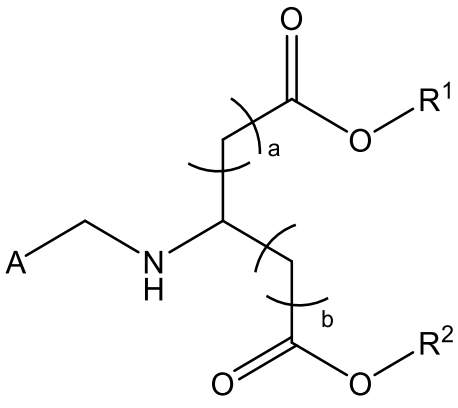
L is a covalent bond, $-CH_2-$, or $-CH_2CH_2-$;

a and b are each independently 5, 6, 7 or 8;

R^1 is C_7-C_{11} straight chain alkyl or C_9-C_{19} branched alkyl; and

R^2 is C_9-C_{19} branched alkyl.

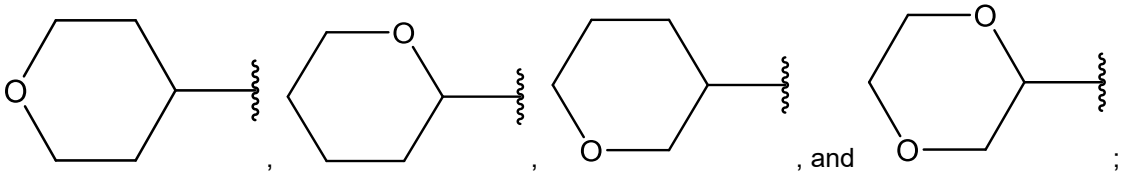
34. The compound of any one of claims 10-14, 16, 20 and 22, which is represented by Formula (VIa):



Formula (VIa),

or a pharmaceutically acceptable salt thereof; wherein

A is selected from:



a and b are each independently 5, 6, 7 or 8;

R^1 is C_7-C_{15} branched alkyl or C_7-C_{15} alkylene-cyclopropylene-alkyl; and

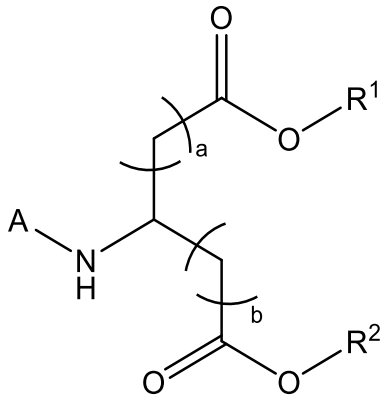
R^2 is C_{15}-C_{19} branched alkyl.

35. The compound of claim 33, wherein R^1 and R^2 are both C_{10}-C_{17} branched alkyl and contain the same number of carbon atoms.

36. The compound of claim 33, wherein R^1 is C_7-C_{11} straight chain alkyl or C_9-C_{13} branched alkyl; R^2 is C_{13}-C_{19} branched alkyl; and provided that R^1 and R^2 are not both C_{13} branched alkyl.

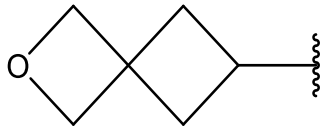
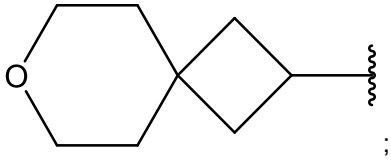
37. The compound of any one of claims 33, 35 and 36, wherein a and b are both 5, 6, 7 or 8.

38. The compound of any one of claims 9, 13-15, 19 and 21, which is represented by Formula (VII):



Formula (VII),

or a pharmaceutically acceptable salt thereof; wherein

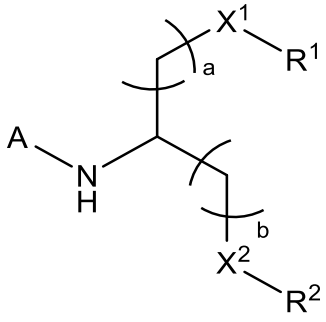
A is  or ;

a and b are each independently 5, 6, 7 or 8;

R^1 is C_7-C_{11} straight chain alkyl or C_9-C_{19} branched alkyl; and

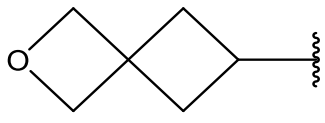
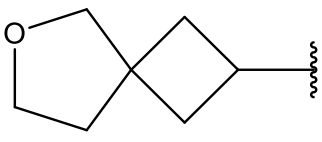
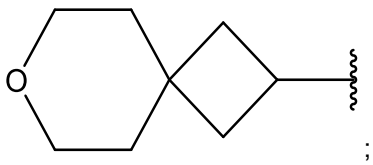
R^2 is C_9-C_{19} branched alkyl.

39. The compound of any one of claims 10-14, 16, 20 and 22, which is represented by Formula (VIIa):

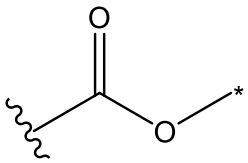
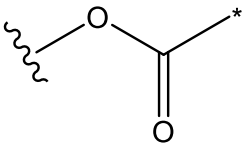


Formula (VIIa),

or a pharmaceutically acceptable salt thereof; wherein

A is ,  or ;

a and b are each independently 4, 5, 6, 7 or 8; provided that when one of a and b is 4 or 5, then the other is 6, 7, 8 or 9;

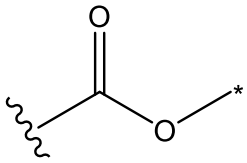
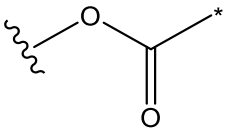
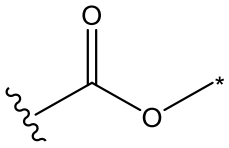
X^1 and X^2 are each independently  or ;

* indicates the attachment point to R^1;

R^1 is C_7-C_{11} straight chain alkyl or C_7-C_{15} branched alkyl; and

R^2 is C_{15}-C_{19} branched alkyl.

40. The compound of 39, wherein a and b are both 6, 7, or 8; or alternatively, a and b are each independently 4 to 9; provided that (a) when one of a and b is 4 or 5, then the other is 6, 7, 8 or 9; and (b) the sum of a and b is 12 to 16.

41. The compound of 39 or 40, wherein X^1 and X^2 are both ; or alternatively, X^1 is , and X^2 is .

42. The compound of claim 38, wherein R^1 and R^2 are both C_{10}-C_{17} branched alkyl and contain the same number of carbon atoms.

43. The compound of claim 38, wherein R^1 is C_7-C_{11} straight chain alkyl or C_9-C_{13} branched alkyl; R^2 is C_{13}-C_{19} branched alkyl; and provided that R^1 and R^2 are not both C_{13} branched alkyl.

44. The compound of any one of claims 38, 42 and 43, wherein a and b are both 5, 6, 7 or 8.

45. The compound of claim 1, or a pharmaceutically acceptable salt thereof; wherein the compound is selected from:

bis(3-pentyloctyl) 9-((2-oxaspiro[3.3]heptan-6-yl)amino)heptadecanedioate;

bis(3-pentyloctyl) 9-((tetrahydro-2H-pyran-4-yl)amino)heptadecanedioate;

bis(3-pentyloctyl) 9-(((tetrahydrofuran-3-yl)methyl)amino)heptadecanedioate;

bis(3-pentyloctyl) 9-(((tetrahydro-2H-pyran-4-yl)methyl)amino)heptadecanedioate; and

bis(3-pentyloctyl) 9-((oxetan-3-ylmethyl)amino)heptadecanedioate.

46. The compound of claim 9 or 10, or a pharmaceutically acceptable salt thereof; wherein the compound is selected from Compounds 6 to 57 as described in the specification.

47. The compound of claim 1, wherein the compound is bis(3-pentyloctyl) 9-((2-oxaspiro[3.3]heptan-6-yl)amino)heptadecanedioate, or a pharmaceutically acceptable salt thereof.

48. A lipid nanoparticle comprising the compound of any one of claims 1-47 or a pharmaceutically acceptable salt thereof, at least one neutral lipid, at least one sterol and at least one polymer-conjugated lipid.

49. The lipid nanoparticle of claim 48, further comprising a nucleic acid segment.

50. A pharmaceutical composition comprising a plurality of the lipid nanoparticles of claim 49.