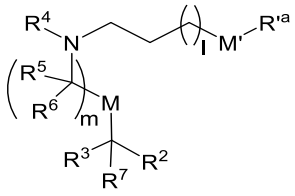
Summary of the Disclosure

[0005] The present disclosure provides novel compounds and compositions and methods involving the same.

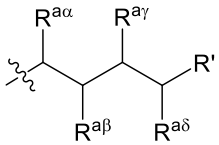
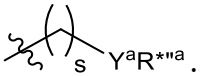
[0005a] In an aspect of the present disclosure, .there is provided a compound of Formula (A):



(A),

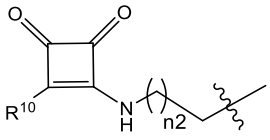
or a salt thereof, wherein

R'^{a} is $R'^{branched}$ or R'^{cyclic};

$R'^{branched}$ is:  ; R'^{cyclic} is:  ; wherein  denotes a point of attachment;

$R^{a\alpha}$ is H, and $R^{a\beta}$, $R^{a\gamma}$, and $R^{a\delta}$ are independently selected from the group consisting of H, $C_{2\text{-}12}$ alkyl, and $C_{2\text{-}12}$ alkenyl, wherein at least one of $R^{a\beta}$, $R^{a\gamma}$, and $R^{a\delta}$ is selected from the group consisting of $C_{2\text{-}12}$ alkyl and $C_{2\text{-}12}$ alkenyl;

R^2 and R^3 are independently $C_{1\text{-}14}$ alkyl;

R^4 is selected from the group consisting of $-(CH_2)_2OH$, $-(CH_2)_3OH$, $-(CH_2)_4OH$, $-(CH_2)_5OH$ and  , wherein R^{10} is $N(R)_2$; each R is independently selected from the group consisting of $C_{1\text{-}6}$ alkyl, $C_{2\text{-}3}$ alkenyl, and H; and n2 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

each R^5 is independently selected from the group consisting of OH, $C_{1\text{-}3}$ alkyl, $C_{2\text{-}3}$ alkenyl, and H;

each R^6 is independently selected from the group consisting of OH, $C_{1\text{-}3}$ alkyl, $C_{2\text{-}3}$ alkenyl, and H;

R^7 is H;

M and M' are independently selected from the group consisting of -C(O)O- and -OC(O)-;

R' is $C_{1\text{-}12}$ alkyl or $C_{2\text{-}12}$ alkenyl;

Y^a is C_{3-6} carbocycle;

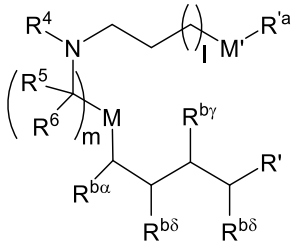
$R^{*"a}$ is selected from the group consisting of C_{1-15} alkyl and C_{2-15} alkenyl;

l is selected from the group consisting of 1, 2, 3, 4, and 5;

s is 2 or 3; and

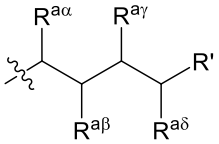
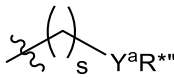
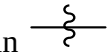
m is selected from the group consisting of 5, 6, 7, 8, 9, 10, 11, 12, and 13.

[0005b] In another aspect of the present disclosure, there is provided a compound of Formula (B):



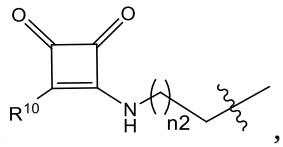
(B) or its N-oxide, or a salt or isomer thereof,

wherein R'^a is $R'^{branched}$ or R'^{cyclic}; wherein

$R'^{branched}$ is:  ; R'^{cyclic} is:  ; wherein  denotes a point of attachment;

wherein $R^{a\alpha}$ and $R^{a\beta}$ are each H, and $R^{a\gamma}$ and $R^{a\delta}$ are each independently selected from the group consisting of H, C_{2-12} alkyl, and C_{2-12} alkenyl, wherein at least one of $R^{a\gamma}$ and $R^{a\delta}$ is selected from the group consisting of C_{2-12} alkyl and C_{2-12} alkenyl;

$R^{b\alpha}$, $R^{b\beta}$, $R^{b\gamma}$, and $R^{b\delta}$ are each independently selected from the group consisting of H, C_{2-30} alkyl, and C_{5-20} alkenyl, wherein at least one of $R^{b\alpha}$, $R^{b\beta}$, $R^{b\gamma}$, and $R^{b\delta}$ is selected from the group consisting of C_{2-30} alkyl and C_{5-20} alkenyl;

R^4 is selected from the group consisting of $-(CH_2)_2OH$, $-(CH_2)_3OH$, $-(CH_2)_4OH$, $-(CH_2)_5OH$ and  ,

wherein  denotes a point of attachment;

R^{10} is $N(R)_2$; each R is independently selected from the group consisting of C_{1-6} alkyl, C_{2-3} alkenyl, and H; and n2 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

each R^5 is independently selected from the group consisting of OH, C_{1-3} alkyl, C_{2-3} alkenyl, and H;

each R^6 is independently selected from the group consisting of OH, C_{1-3} alkyl, C_{2-3} alkenyl, and H;

M and M' are each independently selected from the group consisting of -C(O)O- and -OC(O)-;

R' is a C_{1-12} alkyl or C_{2-12} alkenyl;

Y^a is a C_{3-6} carbocycle;

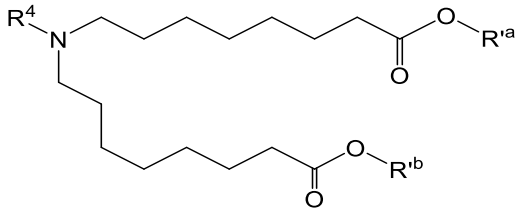
$R^{*"a}$ is selected from the group consisting of C_{1-15} alkyl and C_{2-15} alkenyl;

l is selected from the group consisting of 1, 2, 3, 4, and 5;

s is 2 or 3; and

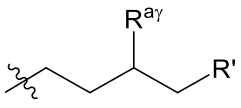
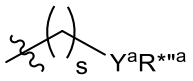
m is selected from the group consisting of 5, 6, 7, 8, 9, 10, 11, 12, and 13.

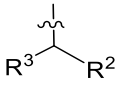
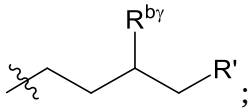
[0005c] In a further aspect of the present disclosure, there is provided a compound of Formula (1-1):



(1-1) or its N-oxide, or a salt or isomer thereof,

wherein R'^a is $R'^{branched}$ or R'^{cyclic}; wherein

$R'^{branched}$ is:  and R'^{cyclic} is:  ; and

R'^b is:  or  ;

wherein  denotes a point of attachment;

wherein $R^{a\gamma}$ and $R^{b\gamma}$ are each independently a C_{2-12} alkyl or C_{2-12} alkenyl;

R^2 and R^3 are each independently selected from the group consisting of C_{1-14} alkyl and C_{2-14} alkenyl;

R^4 is $-(CH_2)_2OH$;

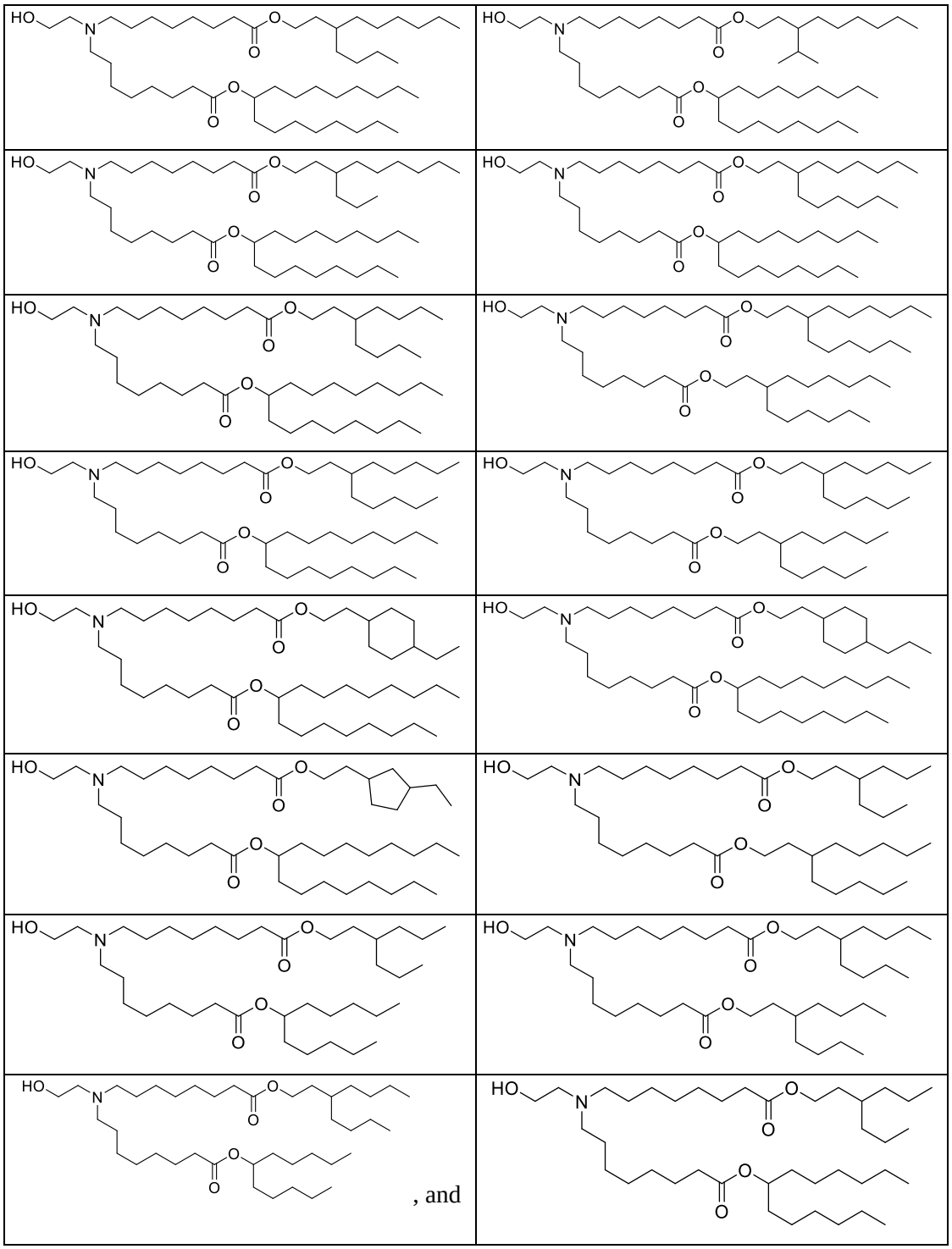
each R' independently is a C_{1-12} alkyl or C_{2-12} alkenyl;

Y^a is a C_{3-6} carbocycle;

$R^{*"a}$ is selected from the group consisting of C_{1-15} alkyl and C_{2-15} alkenyl; and

s is 2 or 3.

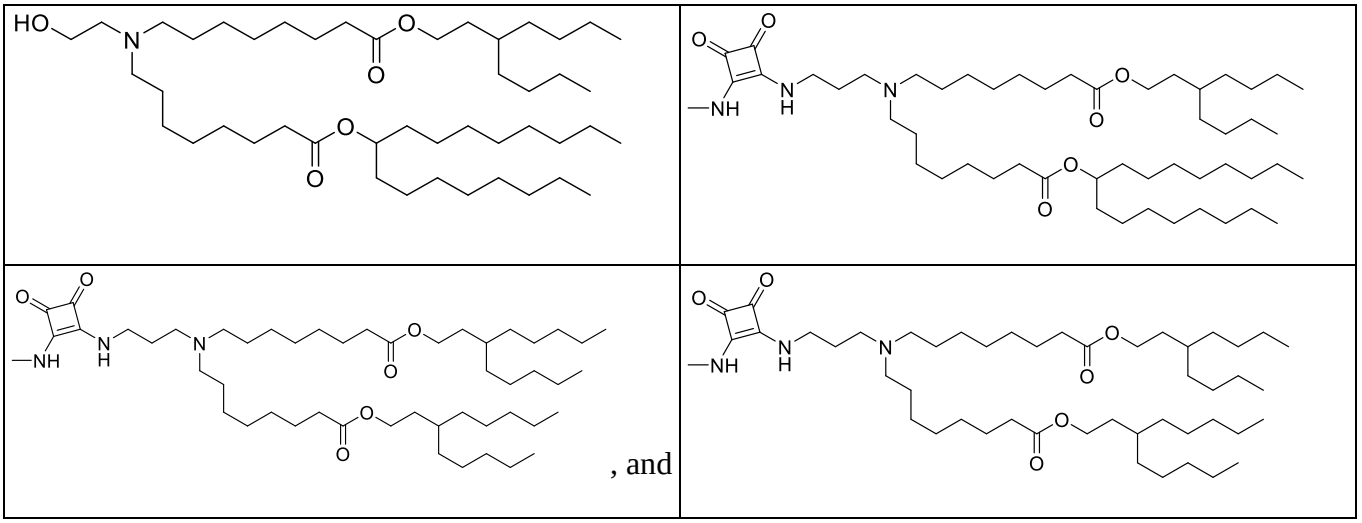
[0005d] In another aspect of the present disclosure, there is provided a compound selected from:



, and

or a pharmaceutically acceptable salt thereof.

[0005e] In a further aspect of the present disclosure, there is provided a compound selected from:



, and

or a pharmaceutically acceptable salt thereof.

[0005f] In another aspect of the present disclosure, there is provided anempty lipid nanoparticle (empty LNP) comprising a compound disclosed herein, a phospholipid, a structural lipid, and a PEG lipid.

[0005g] In a further aspect of the present disclosure, there is provided a loaded lipid nanoparticle (loaded LNP), which comprises the empty LNP disclosed herein and one or more therapeutic and/or prophylactic agents.

[0005h] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising the loaded LNP disclosed herein and a pharmaceutically acceptable carrier.

[0005i] In a further aspect of the present disclosure, there is provided a use of the loaded LNP disclosed herein, or the pharmaceutical composition disclosed herein, in the manufacture of a medicament for delivering a therapeutic and/or prophylactic agent to a cell within a subject.

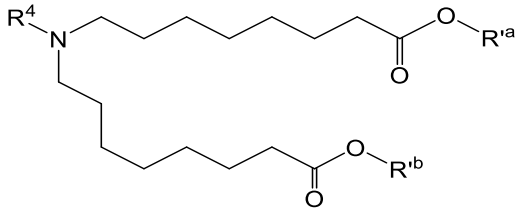
[0005j] In another aspect of the present disclosure, there is provided a use of the loaded LNP disclosed herein, or the pharmaceutical composition disclosed herein, in the manufacture of a medicament for specifically delivering a therapeutic and/or prophylactic agent to an organ of a subject.

[0005k] In a further aspect of the present disclosure, there is provided a use of the loaded LNP disclosed herein, or the pharmaceutical composition disclosed herein, in the manufacture of a medicament for producing a polypeptide of interest in a cell within a subject.

[0005l] In another aspect of the present disclosure, there is provided a use of the loaded LNP disclosed herein, or the pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating a disease or disorder in a subject in need thereof.

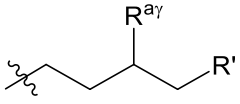
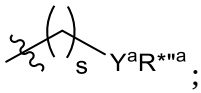
[0005m] In a further aspect of the present disclosure, there is provided a loaded LNP disclosed herein, or the pharmaceutical composition disclosed herein, for use in therapy.

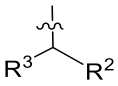
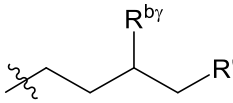
[0006] In some examples, the disclosure relates to a compound of Formula (1-1):



(1-1) or its N-oxide, or a salt or isomer thereof,

wherein R'^{a} is R'^{branched} or R'^{cyclic}; wherein

R'^{branched} is:  and R'^{cyclic} is:  ; and

R'^{b} is:  or  ;

wherein  denotes a point of attachment;

wherein $R^{a\gamma}$ and $R^{b\gamma}$ are each independently a C_{2-12} alkyl or C_{2-12} alkenyl;

R^2 and R^3 are each independently selected from the group consisting of C_{1-14} alkyl and C_{2-14} alkenyl;

R^4 is $-(CH_2)_2OH$;

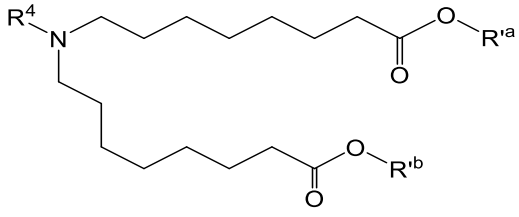
each R' independently is a C_{1-12} alkyl or C_{2-12} alkenyl;

Y^a is a C_{3-6} carbocycle;

R*"^{a} is selected from the group consisting of C_{1-15} alkyl and C_{2-15} alkenyl; and

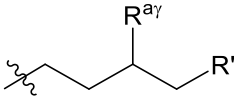
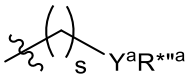
s is 2 or 3.

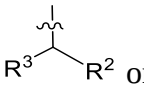
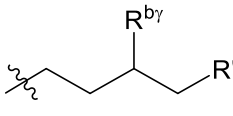
[0007] In some examples, the disclosure relates to a compound of Formula (2-1):



(2-1) or its N-oxide, or a salt or isomer thereof,

wherein R'^{a} is R'^{branched} or R'^{cyclic}; wherein

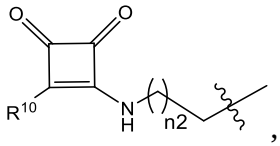
R'^{branched} is:  and R'^{cyclic} is:  ; and

R'^{b} is:  or  ;

wherein  denotes a point of attachment;

wherein $R^{a\gamma}$ and $R^{b\gamma}$ are each independently a $C_{2\text{-}12}$ alkyl or $C_{2\text{-}12}$ alkenyl;

R^2 and R^3 are each independently selected from the group consisting of $C_{1\text{-}14}$ alkyl and $C_{2\text{-}14}$ alkenyl;

R^4 is  , wherein  denotes a point of attachment; R^{10} is $N(R)_2$; each R is independently selected from the group consisting of $C_{1\text{-}6}$ alkyl, $C_{2\text{-}3}$ alkenyl, and H; and n2 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

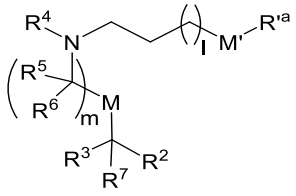
each R' independently is a $C_{1\text{-}12}$ alkyl or $C_{2\text{-}12}$ alkenyl;

Y^a is a $C_{3\text{-}6}$ carbocycle;

R*"^{a} is selected from the group consisting of $C_{1\text{-}15}$ alkyl and $C_{2\text{-}15}$ alkenyl; and

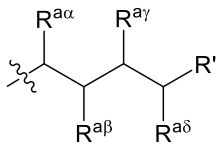
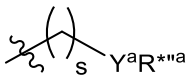
s is 2 or 3.

[0008] In some examples, the disclosure relates to a compound of Formula (A):



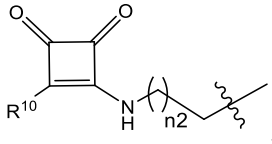
(A) or its N-oxide, or a salt or isomer thereof,

wherein R'^{a} is R'^{branched} or R'^{cyclic}; wherein

R'^{branched} is:  ; R'^{cyclic} is:  ; wherein  denotes a point of attachment;

wherein $R^{a\alpha}$ is H, and $R^{a\beta}$, $R^{a\gamma}$, and $R^{a\delta}$ are each independently selected from the group consisting of H, $C_{2\text{-}12}$ alkyl, and $C_{2\text{-}12}$ alkenyl, wherein at least one of $R^{a\beta}$, $R^{a\gamma}$, and $R^{a\delta}$ is selected from the group consisting of $C_{2\text{-}12}$ alkyl and $C_{2\text{-}12}$ alkenyl;

R^2 and R^3 are each $C_{1\text{-}14}$ alkyl;

R^4 is selected from the group consisting of -$(CH_2)_2OH$, -$(CH_2)_3OH$, -$(CH_2)_4OH$, -$(CH_2)_5OH$ and  ,

wherein  denotes a point of attachment;

R^{10} is $N(R)_2$; each R is independently selected from the group consisting of C_{1-6} alkyl, C_{2-3} alkenyl, and H; and n2 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

each R^5 is independently selected from the group consisting of OH, C_{1-3} alkyl, C_{2-3} alkenyl, and H;

each R^6 is independently selected from the group consisting of OH, C_{1-3} alkyl, C_{2-3} alkenyl, and H;

R^7 is H;

M and M' are each independently selected from the group consisting of -C(O)O- and -OC(O)-;

R' is a C_{1-12} alkyl or C_{2-12} alkenyl;

Y^a is a C_{3-6} carbocycle;

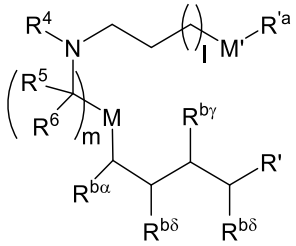
$R^{*"a}$ is selected from the group consisting of C_{1-15} alkyl and C_{2-15} alkenyl;

l is selected from the group consisting of 1, 2, 3, 4, and 5;

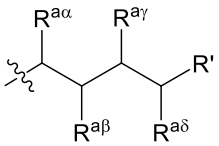
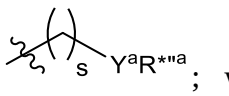
s is 2 or 3; and

m is selected from the group consisting of 5, 6, 7, 8, 9, 10, 11, 12, and 13.

[0009] In some examples, the disclosure relates to a compound of Formula (B):

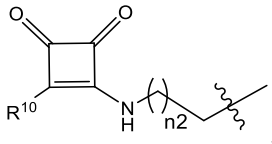
 (B) or its N-oxide, or a salt or isomer thereof,

wherein R'^a is $R'^{branched}$ or R'^{cyclic}; wherein

$R'^{branched}$ is:  ; R'^{cyclic} is:  ; wherein  denotes a point of attachment;

wherein $R^{a\alpha}$ and $R^{a\beta}$ are each H, and $R^{a\gamma}$ and $R^{a\delta}$ are each independently selected from the group consisting of H, $C_{2\text{-}12}$ alkyl, and $C_{2\text{-}12}$ alkenyl, wherein at least one of $R^{a\gamma}$ and $R^{a\delta}$ is selected from the group consisting of $C_{2\text{-}12}$ alkyl and $C_{2\text{-}12}$ alkenyl;

$R^{b\alpha}$, $R^{b\beta}$, $R^{b\gamma}$, and $R^{b\delta}$ are each independently selected from the group consisting of H, $C_{2\text{-}30}$ alkyl, and $C_{5\text{-}20}$ alkenyl, wherein at least one of $R^{b\alpha}$, $R^{b\beta}$, $R^{b\gamma}$, and $R^{b\delta}$ is selected from the group consisting of $C_{2\text{-}30}$ alkyl and $C_{5\text{-}20}$ alkenyl;

R^4 is selected from the group consisting of $-(CH_2)_2OH$, $-(CH_2)_3OH$, $-(CH_2)_4OH$, $-(CH_2)_5OH$ and  ,

wherein  denotes a point of attachment;

R^{10} is $N(R)_2$; each R is independently selected from the group consisting of $C_{1\text{-}6}$ alkyl, $C_{2\text{-}3}$ alkenyl, and H; and n2 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

each R^5 is independently selected from the group consisting of OH, $C_{1\text{-}3}$ alkyl, $C_{2\text{-}3}$ alkenyl, and H;

each R^6 is independently selected from the group consisting of OH, $C_{1\text{-}3}$ alkyl, $C_{2\text{-}3}$ alkenyl, and H;

M and M' are each independently selected from the group consisting of -C(O)O- and -OC(O)-;

R' is a $C_{1\text{-}12}$ alkyl or $C_{2\text{-}12}$ alkenyl;

Y^a is a $C_{3\text{-}6}$ carbocycle;

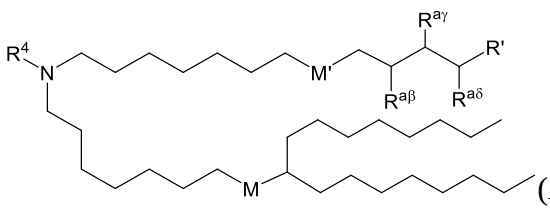
$R^{*"a}$ is selected from the group consisting of $C_{1\text{-}15}$ alkyl and $C_{2\text{-}15}$ alkenyl;

l is selected from the group consisting of 1, 2, 3, 4, and 5;

s is 2 or 3; and

m is selected from the group consisting of 5, 6, 7, 8, 9, 10, 11, 12, and 13.

[0010] In some examples, the disclosure relates to a compound of Formula (A-a):



(A-a) or its N-oxide, or a salt or isomer thereof,

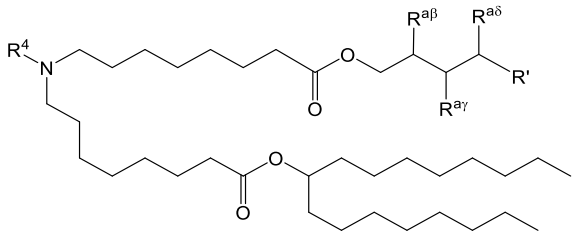
wherein $R^{a\beta}$, $R^{a\gamma}$ and $R^{a\delta}$ are each independently selected from the group consisting of H, C_{2-12} alkyl, and C_{2-12} alkenyl, wherein at least one of $R^{a\beta}$, $R^{a\gamma}$, and $R^{a\delta}$ is selected from the group consisting of C_{2-12} alkyl and C_{2-12} alkenyl;

R^4 is selected from the group consisting of $-(CH_2)_2OH$, $-(CH_2)_3OH$, $-(CH_2)_4OH$, and $-(CH_2)_5OH$;

M and M' are each independently selected from the group consisting of -C(O)O- and -OC(O)-; and

R' is a C_{1-12} alkyl or C_{2-12} alkenyl.

[0011] In some examples, the disclosure relates to a compound of Formula (A-b):



(A-b) or its N-oxide, or a salt or isomer thereof,

wherein $R^{a\beta}$, $R^{a\gamma}$ and $R^{a\delta}$ are each independently selected from the group consisting of H, C_{2-12} alkyl, and C_{2-12} alkenyl, wherein at least one of $R^{a\beta}$, $R^{a\gamma}$, and $R^{a\delta}$ is selected from the group consisting of C_{2-12} alkyl and C_{2-12} alkenyl;

R^4 is selected from the group consisting of $-(CH_2)_2OH$, $-(CH_2)_3OH$, $-(CH_2)_4OH$ and $-(CH_2)_5OH$; and

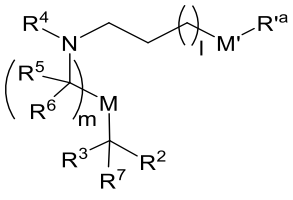
R' is a C_{1-12} alkyl or C_{2-12} alkenyl.

Detailed Description

[0012] The disclosure relates to novel lipids and lipid lipid nanoparticles (e.g., empty LNPs or loaded LNPs) including a novel lipid. The disclosure also provides methods of delivering a therapeutic and/or prophylactic to a mammalian cell, specifically delivering a therapeutic and/or prophylactic to a mammalian organ, producing a polypeptide of interest in a mammalian cell, improving levels of protein produced in a mammalian cell as compared to LNPs comprising other lipids, and treating a disease or disorder in a mammal in need thereof. For example, a method of producing a polypeptide of interest in a cell involves contacting a nanoparticle comprising an mRNA with a mammalian cell, whereby the mRNA may be translated to produce the polypeptide of interest. A method of delivering a therapeutic and/or prophylactic to a mammalian cell or organ may involve administration of a nanoparticle

CLAIMS

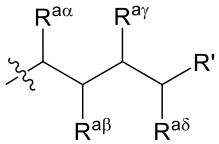
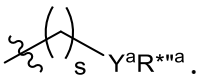
1. A compound of Formula (A):



(A),

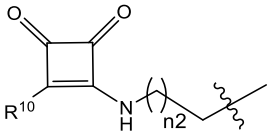
or a salt thereof, wherein

R'^{a} is $R'^{branched}$ or R'^{cyclic};

$R'^{branched}$ is:  ; R'^{cyclic} is:  ; wherein  denotes a point of attachment;

$R^{a\alpha}$ is H, and $R^{a\beta}$, $R^{a\gamma}$, and $R^{a\delta}$ are independently selected from the group consisting of H, C_{2-12} alkyl, and C_{2-12} alkenyl, wherein at least one of $R^{a\beta}$, $R^{a\gamma}$, and $R^{a\delta}$ is selected from the group consisting of C_{2-12} alkyl and C_{2-12} alkenyl;

R^2 and R^3 are independently C_{1-14} alkyl;

R^4 is selected from the group consisting of $-(CH_2)_2OH$, $-(CH_2)_3OH$, $-(CH_2)_4OH$, $-(CH_2)_5OH$ and  , wherein R^{10} is $N(R)_2$; each R is independently selected from the group consisting of C_{1-6} alkyl, C_{2-3} alkenyl, and H; and n2 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

each R^5 is independently selected from the group consisting of OH, C_{1-3} alkyl, C_{2-3} alkenyl, and H;

each R^6 is independently selected from the group consisting of OH, C_{1-3} alkyl, C_{2-3} alkenyl, and H;

R^7 is H;

M and M' are independently selected from the group consisting of -C(O)O- and -OC(O)-;

R' is C_{1-12} alkyl or C_{2-12} alkenyl;

Y^a is C_{3-6} carbocycle;

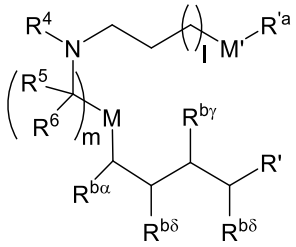
$R^{*"a}$ is selected from the group consisting of C_{1-15} alkyl and C_{2-15} alkenyl;

l is selected from the group consisting of 1, 2, 3, 4, and 5;

s is 2 or 3; and

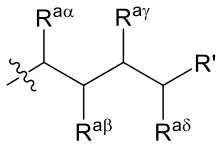
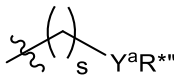
m is selected from the group consisting of 5, 6, 7, 8, 9, 10, 11, 12, and 13.

2. A compound of Formula (B):



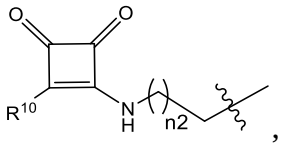
(B) or its N-oxide, or a salt or isomer thereof,

wherein R'^a is $R'^{branched}$ or R'^{cyclic}; wherein

$R'^{branched}$ is:  ; R'^{cyclic} is:  ; wherein  denotes a point of attachment;

wherein $R^{a\alpha}$ and $R^{a\beta}$ are each H, and $R^{a\gamma}$ and $R^{a\delta}$ are each independently selected from the group consisting of H, C_{2-12} alkyl, and C_{2-12} alkenyl, wherein at least one of $R^{a\gamma}$ and $R^{a\delta}$ is selected from the group consisting of C_{2-12} alkyl and C_{2-12} alkenyl;

$R^{b\alpha}$, $R^{b\beta}$, $R^{b\gamma}$, and $R^{b\delta}$ are each independently selected from the group consisting of H, C_{2-30} alkyl, and C_{5-20} alkenyl, wherein at least one of $R^{b\alpha}$, $R^{b\beta}$, $R^{b\gamma}$, and $R^{b\delta}$ is selected from the group consisting of C_{2-30} alkyl and C_{5-20} alkenyl;

R^4 is selected from the group consisting of $-(CH_2)_2OH$, $-(CH_2)_3OH$, $-(CH_2)_4OH$, $-(CH_2)_5OH$ and  ,

wherein  denotes a point of attachment;

R^{10} is $N(R)_2$; each R is independently selected from the group consisting of C_{1-6} alkyl, C_{2-3} alkenyl, and H; and n2 is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

each R^5 is independently selected from the group consisting of OH, C_{1-3} alkyl, C_{2-3} alkenyl, and H;

each R^6 is independently selected from the group consisting of OH, C_{1-3} alkyl, C_{2-3} alkenyl, and H;

M and M' are each independently selected from the group consisting of -C(O)O- and -OC(O)-;

R' is a C_{1-12} alkyl or C_{2-12} alkenyl;

Y^a is a C_{3-6} carbocycle;

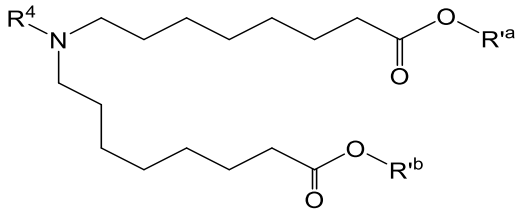
$R^{*"a}$ is selected from the group consisting of C_{1-15} alkyl and C_{2-15} alkenyl;

l is selected from the group consisting of 1, 2, 3, 4, and 5;

s is 2 or 3; and

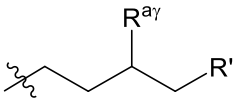
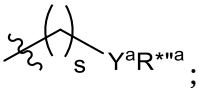
m is selected from the group consisting of 5, 6, 7, 8, 9, 10, 11, 12, and 13.

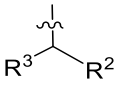
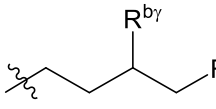
3. A compound of Formula (1-1):



(1-1) or its N-oxide, or a salt or isomer thereof,

wherein R'^a is $R'^{branched}$ or R'^{cyclic}; wherein

$R'^{branched}$ is:  and R'^{cyclic} is:  ; and

R'^b is:  or  ;

wherein  denotes a point of attachment;

wherein $R^{a\gamma}$ and $R^{b\gamma}$ are each independently a C_{2-12} alkyl or C_{2-12} alkenyl;

R^2 and R^3 are each independently selected from the group consisting of C_{1-14} alkyl and C_{2-14} alkenyl;

R^4 is $-(CH_2)_2OH$;

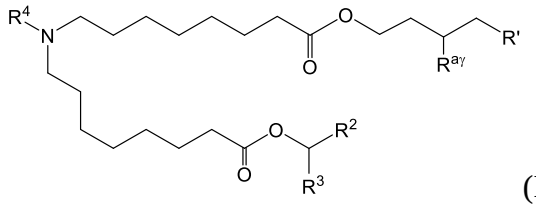
each R' independently is a C_{1-12} alkyl or C_{2-12} alkenyl;

Y^a is a C_{3-6} carbocycle;

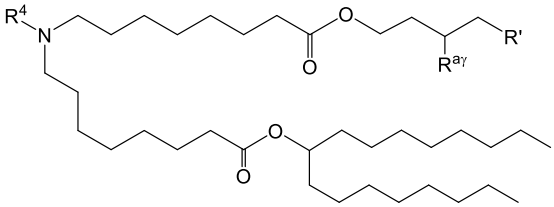
$R^{*"a}$ is selected from the group consisting of C_{1-15} alkyl and C_{2-15} alkenyl; and

s is 2 or 3.

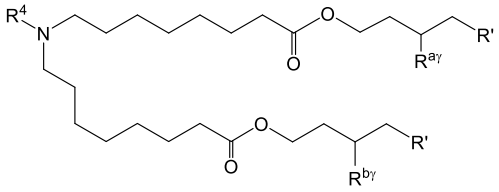
4. The compound of any one of the preceding claims, having one of the following structures:



(I-a),



(A-c),



(B-c).

5. The compound of any one of the preceding claims, wherein $R^{a\gamma}$ is a $C_{2\text{-}6}$ alkyl.

6. The compound of any one of the preceding claims, wherein $R^{b\gamma}$ is a $C_{2\text{-}6}$ alkyl.

7. The compound of any one of the preceding claims, wherein $R^{a\gamma}$ and $R^{b\gamma}$ are each independently a $C_{2\text{-}6}$ alkyl.

8. The compound of any one of the preceding claims, wherein $R^{b\gamma}$ is a $C_{4\text{-}6}$ alkyl.

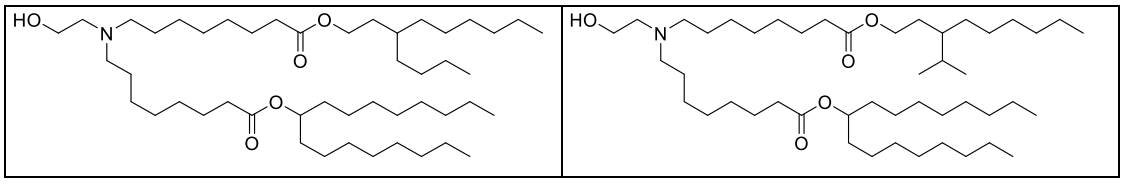
9. The compound of any one of the preceding claims, wherein R^2 and R^3 are each C_8 alkyl.

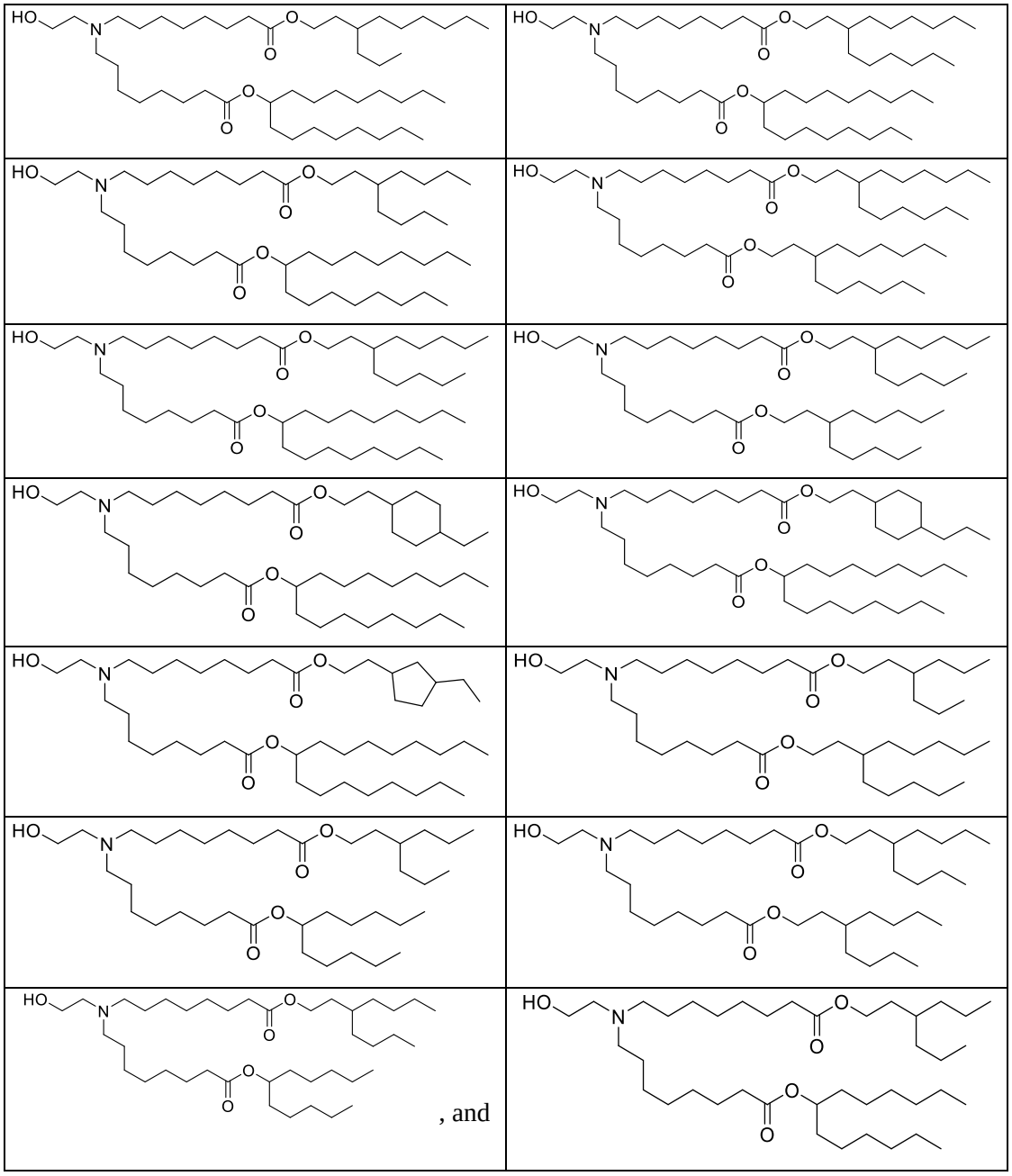
10. The compound of any one of the preceding claims, wherein Y^a is cyclohexyl or cyclopentyl.

11. The compound of any one of the preceding claims, wherein $R^{*"a}$ is a C_2-alkyl or C_3-alkyl.

12. The compound of any one of the preceding claims, wherein each R' independently is a $C_{2\text{-}5}$ alkyl.

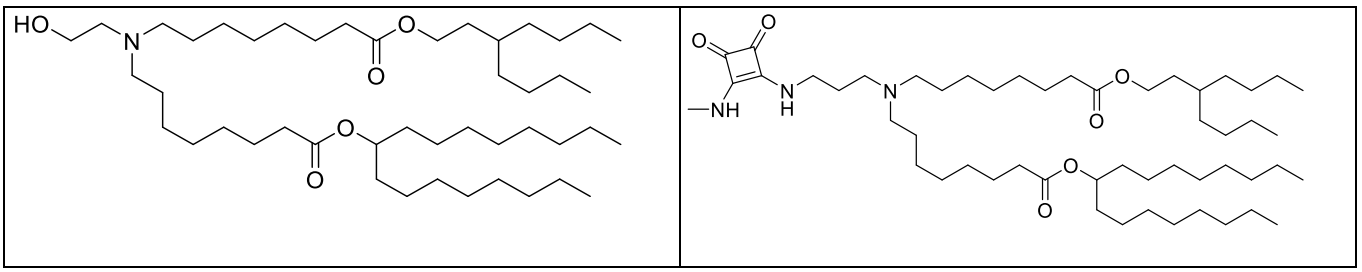
13. A compound selected from:

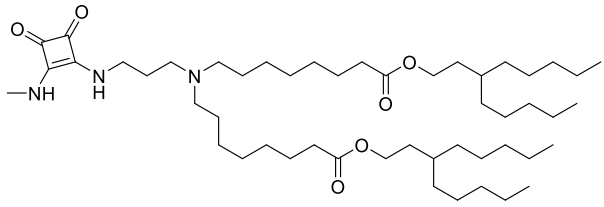




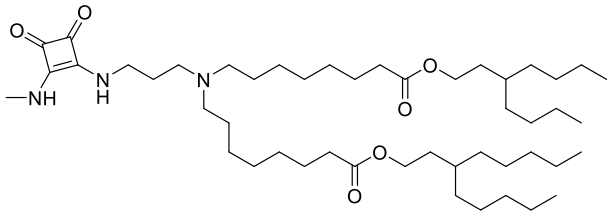
or a pharmaceutically acceptable salt thereof.

14. A compound selected from:





, and



or a pharmaceutically acceptable salt thereof.

15. An empty lipid nanoparticle (empty LNP) comprising a compound of any one of the preceding claims, a phospholipid, a structural lipid, and a PEG lipid.

16. The empty LNP of claim 15:

(a) comprising about 40 mol % to about 60 mol % said compound, about 0 mol % to about 20 mol % phospholipid, about 30 mol % to about 50 mol % structural lipid, and about 0 mol % to about 5 mol % PEG lipid;

(b) wherein the phospholipid is selected from the group consisting of:

1,2-dilinoleoyl-sn-glycero-3-phosphocholine (DLPC),

1,2-dimyristoyl-sn-glycero-phosphocholine (DMPC),

1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC),

1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC),

1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC),

1,2-diundecanoyl-sn-glycero-phosphocholine (DUPC),

1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC),

1,2-di-O-octadecenyl-*sn*-glycero-3-phosphocholine (18:0 Diether PC),

1-oleoyl-2-cholesterylhemisuccinoyl-*sn*-glycero-3-phosphocholine (OChemsPC),

1-hexadecyl-sn-glycero-3-phosphocholine (C16 Lyso PC),

1,2-dilinolenoyl-sn-glycero-3-phosphocholine,

1,2-diarachidonoyl-sn-glycero-3-phosphocholine,

1,2-didocosahexaenoyl-sn-glycero-3-phosphocholine,

1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE),

1,2-diphytanoyl-sn-glycero-3-phosphoethanolamine (ME 16.0 PE),

1,2-distearoyl-sn-glycero-3-phosphoethanolamine,

1,2-dilinoleoyl-sn-glycero-3-phosphoethanolamine,

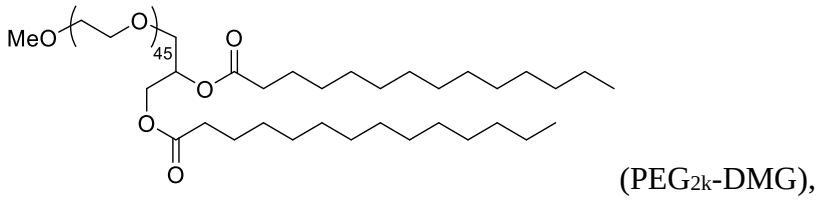
1,2-dilinolenoyl-sn-glycero-3-phosphoethanolamine,

1,2-diarachidonoyl-sn-glycero-3-phosphoethanolamine,
1,2-didocosahexaenoyl-sn-glycero-3-phosphoethanolamine,
1,2-dioleoyl-sn-glycero-3-phospho-rac-(1-glycerol) sodium salt (DOPG), sphingomyelin, and mixtures thereof;

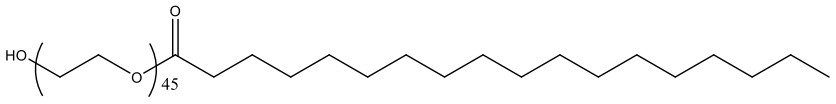
(c) wherein the structural lipid is selected from the group consisting of cholesterol, fecosterol, sitosterol, ergosterol, campesterol, stigmasterol, brassicasterol, and mixtures thereof;

(d) wherein the PEG lipid is selected from the group consisting of a PEG-modified phosphatidylethanolamine, a PEG-modified phosphatidic acid, a PEG-modified ceramide, a PEG-modified dialkylamine, a PEG-modified diacylglycerol, a PEG-modified dialkylglycerol, and mixtures thereof; and/or

(e) wherein the PEG lipid is selected from PEG_{2k}-DMG and PEG-1:



(PEG_{2k}-DMG),



(PEG-1),

and mixtures thereof.

17. A loaded lipid nanoparticle (loaded LNP), which comprises the empty LNP of any one of claims 15-16 and one or more therapeutic and/or prophylactic agents.

18. The loaded LNP of claim 17, wherein the one or more therapeutic and/or prophylactic agents is a nucleic acid.

19. The loaded LNP of any one of claims 17-18, wherein the nucleic acid is an RNA, and wherein the RNA is selected from the group consisting of a short interfering RNA (siRNA), an asymmetrical interfering RNA (aiRNA), a RNA interference (RNAi) molecule, a microRNA (miRNA), an antagomir, an antisense RNA, a ribozyme, a Dicer-substrate RNA (dsRNA), a small hairpin RNA (shRNA), a messenger RNA (mRNA), and mixtures thereof.

20. The loaded LNP of any one of claims 17-19, wherein the RNA is an mRNA.

21. A pharmaceutical composition comprising the loaded LNP of any one of claims 17-20 and a pharmaceutically acceptable carrier.

22. Use of the loaded LNP of claims 17-20, or the pharmaceutical composition of claim 21, in the manufacture of a medicament for delivering a therapeutic and/or prophylactic agent to a cell within a subject.

23. Use of the loaded LNP of claims 17-20, or the pharmaceutical composition of claim 21, in the manufacture of a medicament for specifically delivering a therapeutic and/or prophylactic agent to an organ of a subject.

24. Use of the loaded LNP of claims 17-20, or the pharmaceutical composition of claim 21, in the manufacture of a medicament for producing a polypeptide of interest in a cell within a subject.

25. Use of the loaded LNP of claims 17-20, or the pharmaceutical composition of claim 21, in the manufacture of a medicament for treating a disease or disorder in a subject in need thereof.

26. The use of claim 23, wherein the organ is selected from the group consisting of liver, kidney, lung, and spleen.

27. The use of any one of claims 22-26, wherein the medicament is to be administered to the subject parenterally, intramuscularly, intradermally, subcutaneously, and/or intravenously.

28. The loaded LNP of claims 17-20, or the pharmaceutical composition of claim 21, for use in therapy.