some embodiments, the selected useful pH value or range corresponds to the pH condition in an environment of the intended uses of the lipids, such as the physiological pH. As non-limiting examples, neutral lipids that can be used in connection with the present disclosure include, but are not limited to, phosphotidylcholines such as 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC), 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC), 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC), 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC), phophatidylethanolamines such as 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE), 2-((2,3-bis(oleoyloxy)propyl)dimethylammonio)ethyl hydrogen phosphate (DOCP), sphingomyelins (SM), ceramides, steroids such as sterols and their derivatives. Neutral lipids as provided herein may be synthetic or derived (isolated or modified) from a natural source or compound.

**[0018]** The term "charged lipid" encompasses any lipid molecules that exist in either positively charged or negatively charged forms at a selected pH or within a selected pH range. In some embodiments, the selected pH value or range corresponds to the pH condition in an environment of the intended uses of the lipids, such as the physiological pH. As non-limiting examples, charged lipids that can be used in connection with the present disclosure include, but are not limited to, phosphatidylserines, phosphatidic acids, phosphatidylglycerols, phosphatidylinositols, sterol hemisuccinates, dialkyl trimethylarnmonium-propanes, (*e.g.*, DOTAP, DOTMA), dialkyl dimethylaminopropanes, ethyl phosphocholines, dimethylaminoethane carbamoyl sterols (*e.g.*, DC-Chol), 1,2-dioleoyl-sn-glycero-3-phospho-L-serine sodium salt (DOPS-Na), 1,2-dioleoyl-sn-glycero-3-phospho-(1'-rac-glycerol) sodium salt (DOPG-Na), and 1,2-dioleoyl-sn-glycero-3-phosphate sodium salt (DOPA-Na). Charged lipids as provided herein may be synthetic or derived (isolated or modified) from a natural source or compound.

**[0019]** As used herein, and unless otherwise specified, the term "alkyl" refers to a straight or branched hydrocarbon chain radical consisting solely of carbon and hydrogen atoms, which is saturated. In one embodiment, the alkyl group has, for example, from one to twenty-four carbon atoms ($C_1$-$C_{24}$ alkyl), four to twenty carbon atoms ($C_4$-$C_{20}$ alkyl), six to sixteen carbon atoms ($C_6$-$C_{16}$ alkyl), six to nine carbon atoms ($C_6$-$C_9$ alkyl), one to fifteen carbon atoms ($C_1$-$C_{15}$ alkyl), one to twelve carbon atoms ($C_1$-$C_{12}$ alkyl), one to eight carbon atoms ($C_1$-$C_8$ alkyl) or one to six carbon atoms ($C_1$-$C_6$ alkyl) and which is attached to the rest of the molecule by a single bond.

amines (*e.g.*, DODAG N',N'-dioctadecyl-N-4,8-diaza-10-aminodecanoylglycine amide) and guanidinium head groups (*e.g.*, bis-guanidinium-spermidine-cholesterol (BGSC), bis-guanidiniumtren-cholesterol (BGTC), PONA, and (R)-5-guanidinopentane-1,2-diyl dioleate hydrochloride (DOPen-G)). Yet another suitable cationic lipid is (R)-5-(dimethylamino)pentane-1,2-diyl dioleate hydrochloride (DODAPen-Cl). In certain embodiments, the cationic lipid is a particular enantiomer or the racemic form, and includes the various salt forms of a cationic lipid as above (*e.g.*, chloride or sulfate). For example, in some embodiments, the cationic lipid is N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTAP-Cl) or N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium sulfate (DOTAP-Sulfate). In some embodiments, the cationic lipid is an ionizable cationic lipid such as, *e.g.*, dioctadecyldimethylammonium bromide (DDAB); 1,2-dilinoleyloxy-3-dimethylaminopropane (DLinDMA); 2,2-dilinoleyl-4-(2dimethylaminoethyl)-[1,3]-dioxolane (DLin-KC2-DMA); heptatriaconta-6,9,28,31-tetraen-19-yl 4-(dimethylamino)butanoate (DLin-MC3-DMA); 1,2-dioleoyloxy-3-dimethylaminopropane (DODAP); 1,2-dioleyloxy-3-dimethylaminopropane (DODMA); and morpholinocholesterol (Mo-CHOL). In certain embodiments, a lipid nanoparticle includes a combination or two or more cationic lipids (*e.g.*, two or more cationic lipids as above).

**[00234]** Additionally, in some embodiments, the charged or ionizable lipid that can form part of the present nanoparticle composition is a lipid including a cyclic amine group. Additional cationic lipids that are suitable for the formulations and methods disclosed herein include those described in WO2015199952, WO2016176330, and WO2015011633, the entire contents of each of which are hereby incorporated by reference in their entireties.

#### 5.4.2 *Polymer Conjugated Lipids*

**[00235]** In some embodiments, the lipid component of a nanoparticle composition can include one or more polymer conjugated lipids, such as PEGylated lipids (PEG lipids). Without being bound by the theory, it is contemplated that a polymer conjugated lipid component in a nanoparticle composition can improve of colloidal stability and/or reduce protein absorption of the nanoparticles. Exemplary polymer conjugated lipids that can be used in connection with the present disclosure include but are not limited to PEG-modified phosphatidylethanolamines, PEG-modified phosphatidic acids, PEG-modified ceramides, PEG-modified dialkylamines, PEG-

measure the amount of free therapeutic and/or prophylactic agent (*e.g.,* RNA) in a solution. For the nanoparticle compositions described herein, the encapsulation efficiency of a therapeutic and/or prophylactic agent can be at least 50%, for example 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%. In some embodiments, the encapsulation efficiency can be at least 80%. In certain embodiments, the encapsulation efficiency can be at least 90%.

**[00357]** A nanoparticle composition can optionally comprise one or more coatings. For example, a nanoparticle composition can be formulated in a capsule, film, or tablet having a coating. A capsule, film, or tablet including a composition described herein can have any useful size, tensile strength, hardness, or density.

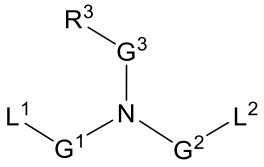
### 5.6 *Pharmaceutical* Compositions

**[00358]** According to the present disclosure, nanoparticle compositions can be formulated in whole or in part as pharmaceutical compositions. Pharmaceutical compositions can include one or more nanoparticle compositions. For example, a pharmaceutical composition can include one or more nanoparticle compositions including one or more different therapeutic and/or prophylactic agents. Pharmaceutical compositions can further include one or more pharmaceutically acceptable excipients or accessory ingredients such as those described herein. General guidelines for the formulation and manufacture of pharmaceutical compositions and agents are available, for example, in Remington's The Science and Practice of Pharmacy, 21st Edition, A. R. Gennaro; Lippincott, Williams & Wilkins, Baltimore, Md., 2006. Conventional excipients and accessory ingredients can be used in any pharmaceutical composition, except insofar as any conventional excipient or accessory ingredient can be incompatible with one or more components of a nanoparticle composition. An excipient or accessory ingredient can be incompatible with a component of a nanoparticle composition if its combination with the component can result in any undesirable biological effect or otherwise deleterious effect.

**[00359]** In some embodiments, one or more excipients or accessory ingredients can make up greater than 50% of the total mass or volume of a pharmaceutical composition including a nanoparticle composition. For example, the one or more excipients or accessory ingredients can make up 50%, 60%, 70%, 80%, 90%, or more of a pharmaceutical composition. In some embodiments, a pharmaceutically acceptable excipient is at least 95%, at least 96%, at least 97%,

WHAT IS CLAIMED IS:

1. A compound of Formula (I):



(I),

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof, wherein:

$G^1$ and $G^2$ are each independently a bond, $C_2$-$C_{12}$ alkylene, or $C_2$-$C_{12}$ alkenylene, wherein one or more -$CH_2$- in the alkylene or alkenylene is optionally replaced by -O-;

$L^1$ is –OC(=O)$R^1$, -C(=O)O$R^1$, -OC(=O)O$R^1$, -C(=O)$R^1$, -O$R^1$, -S(O)$_x$$R^1$, -S-S$R^1$, -C(=O)S$R^1$, -SC(=O)$R^1$, -N$R^a$C(=O)$R^1$, -C(=O)N$R^b$$R^c$, -N$R^a$C(=O)N$R^b$$R^c$, -OC(=O)N$R^b$$R^c$, -N$R^a$C(=O)O$R^1$, -SC(=S)$R^1$, -C(=S)S$R^1$, -C(=S)$R^1$, -CH(OH)$R^1$, -P(=O)(O$R^b$)(O$R^c$), -($C_6$-$C_{10}$ arylene)-$R^1$, -(6- to 10-membered heteroarylene)-$R^1$, or $R^1$;

$L^2$ is –OC(=O)$R^2$, -C(=O)O$R^2$, -OC(=O)O$R^2$, -C(=O)$R^2$, -O$R^2$, -S(O)$_x$$R^2$, -S-S$R^2$, -C(=O)S$R^2$, -SC(=O)$R^2$, -N$R^d$C(=O)$R^2$, -C(=O)N$R^e$$R^f$, -N$R^d$C(=O)N$R^e$$R^f$, -OC(=O)N$R^e$$R^f$, -N$R^d$C(=O)O$R^2$, -SC(=S)$R^2$, -C(=S)S$R^2$, -C(=S)$R^2$, -CH(OH)$R^2$, -P(=O)(O$R^e$)(O$R^f$), -($C_6$-$C_{10}$ arylene)-$R^2$, -(6- to 10-membered heteroarylene)-$R^2$, or $R^2$;

$R^1$ and $R^2$ are each independently $C_6$-$C_{32}$ alkyl or $C_6$-$C_{32}$ alkenyl;

$R^a$, $R^b$, $R^d$, and $R^e$ are each independently H, $C_1$-$C_{24}$ alkyl, or $C_2$-$C_{24}$ alkenyl;

$R^c$ and $R^f$ are each independently $C_1$-$C_{32}$ alkyl or $C_2$-$C_{32}$ alkenyl;

$G^3$ is $C_2$-$C_{24}$ alkylene, $C_2$-$C_{24}$ alkenylene, $C_3$-$C_8$ cycloalkylene, or $C_3$-$C_8$ cycloalkenylene;

$R^3$ is -N($R^4$)$R^5$;

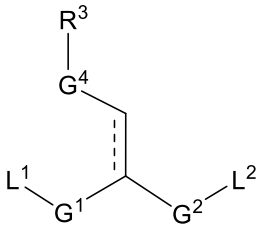
$R^4$ is $C_3$-$C_8$ cycloalkyl, $C_3$-$C_8$ cycloalkenyl, 4- to 8-membered heterocyclyl, or $C_6$-$C_{10}$ aryl; or $R^4$, $G^3$ or part of $G^3$, together with the nitrogen to which they are attached form a cyclic moiety;

$R^5$ is $C_1$-$C_{12}$ alkyl or $C_3$-$C_8$ cycloalkyl; or $R^4$, $R^5$, together with the nitrogen to which they are attached form a cyclic moiety;

x is 0, 1 or 2; and

wherein each alkyl, alkenyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, alkylene, alkenylene, cycloalkylene, cycloalkenylene, arylene, heteroarylene, and cyclic moiety is independently optionally substituted.

2. A compound of Formula (II):




(II),

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof, wherein:

$\overline{\text{------}}$ is a single bond or a double bond;

$G^1$ and $G^2$ are each independently a bond, $C_2$-$C_{12}$ alkylene, or $C_2$-$C_{12}$ alkenylene, wherein one or more -$CH_2$- in the alkylene or alkenylene is optionally replaced by -O-;

$L^1$ is –OC(=O)$R^1$, -C(=O)O$R^1$, -OC(=O)O$R^1$, -C(=O)$R^1$, -O$R^1$, -S(O)$_x$$R^1$, -S-S$R^1$, -C(=O)S$R^1$, -SC(=O)$R^1$, -N$R^a$C(=O)$R^1$, -C(=O)N$R^b$$R^c$, -N$R^a$C(=O)N$R^b$$R^c$, -OC(=O)N$R^b$$R^c$, -N$R^a$C(=O)O$R^1$, -SC(=S)$R^1$, -C(=S)S$R^1$, -C(=S)$R^1$, -CH(OH)$R^1$, -P(=O)(O$R^b$)(O$R^c$), -($C_6$-$C_{10}$ arylene)-$R^1$, -(6- to 10-membered heteroarylene)-$R^1$, or $R^1$;

$L^2$ is –OC(=O)$R^2$, -C(=O)O$R^2$, -OC(=O)O$R^2$, -C(=O)$R^2$, -O$R^2$, -S(O)$_x$$R^2$, -S-S$R^2$, -C(=O)S$R^2$, -SC(=O)$R^2$, -N$R^d$C(=O)$R^2$, -C(=O)N$R^e$$R^f$, -N$R^d$C(=O)N$R^e$$R^f$, -OC(=O)N$R^e$$R^f$, -N$R^d$C(=O)O$R^2$, -SC(=S)$R^2$, -C(=S)S$R^2$, -C(=S)$R^2$, -CH(OH)$R^2$, -P(=O)(O$R^e$)(O$R^f$), -($C_6$-$C_{10}$ arylene)-$R^2$, -(6- to 10-membered heteroarylene)-$R^2$, or $R^2$;

$R^1$ and $R^2$ are each independently $C_6$-$C_{32}$ alkyl or $C_6$-$C_{32}$ alkenyl;

$R^a$, $R^b$, $R^d$, and $R^e$ are each independently H, $C_1$-$C_{24}$ alkyl, or $C_2$-$C_{24}$ alkenyl;

$R^c$ and $R^f$ are each independently $C_1$-$C_{32}$ alkyl or $C_2$-$C_{32}$ alkenyl;

$G^4$ is a bond, $C_1$-$C_{23}$ alkylene, $C_2$-$C_{23}$ alkenylene, $C_3$-$C_8$ cycloalkylene, or $C_3$-$C_8$ cycloalkenylene;

$R^3$ is -N($R^4$)$R^5$;

$R^4$ is $C_1$-$C_{12}$ alkyl, $C_3$-$C_8$ cycloalkyl, $C_3$-$C_8$ cycloalkenyl, 4- to 8-membered heterocyclyl, or $C_6$-$C_{10}$ aryl; or $R^4$, $G^3$ or part of $G^3$, together with the nitrogen to which they are attached form a cyclic moiety;

$R^5$ is $C_1$-$C_{12}$ alkyl or $C_3$-$C_8$ cycloalkyl; or $R^4$, $R^5$, together with the nitrogen to which they are attached form a cyclic moiety;

x is 0, 1 or 2; and

wherein each alkyl, alkenyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, alkylene, alkenylene, cycloalkylene, cycloalkenylene, arylene, heteroarylene, and cyclic moiety is independently optionally substituted.

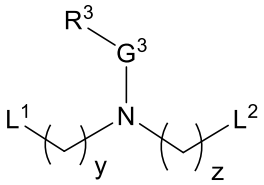
3. The compound of claim 2, wherein ------ is a single bond.

4. The compound of claim 2, wherein ------ is a double bond.

5. The compound of any one of claims 1 to 4, wherein $G^1$ and $G^2$ are each independently $C_2$-$C_{12}$ alkylene.

6. The compound of claim 5, wherein $G^1$ and $G^2$ are each independently $C_5$ alkylene.

7. The compound of claim 5, which is a compound of Formula (I-A):

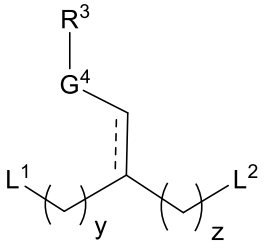



(I-A),

wherein y and z are each independently an integer from 2 to 12,

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof.

8. The compound of claim 5, which is a compound of Formula (II-A):



(II-A),

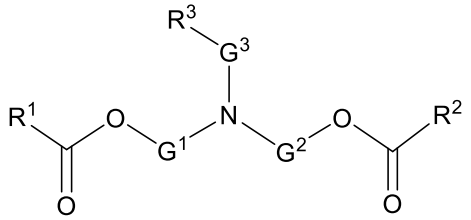
wherein y and z are each independently an integer from 2 to 12,

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof.

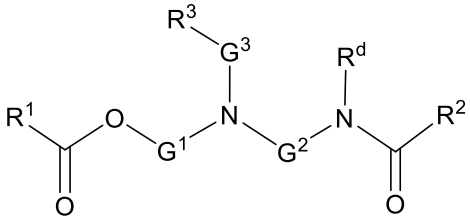
9. The compound of claim 7 or 8, wherein y is 5 and z is 5.

10. The compound of any one of claims 1 to 9, wherein $L^1$ is $–OC(=O)R^1$, $-C(=O)OR^1$, or $-C(=O)NR^bR^c$; and $L^2$ is $–OC(=O)R^2$, $-C(=O)OR^2$, or $-C(=O)NR^eR^f$.

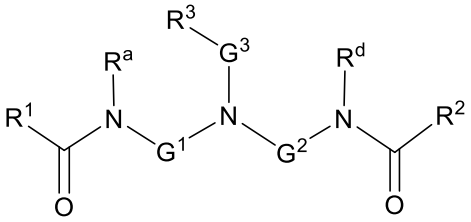
11. The compound of claim 1, which is a compound of Formula (I-B), (I-B'), (I-B"), (I-C), (I-D), or (I-E):



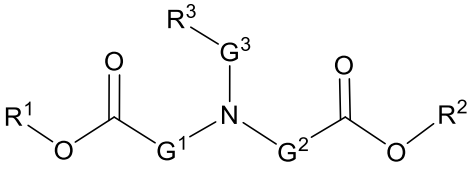
(I-B),



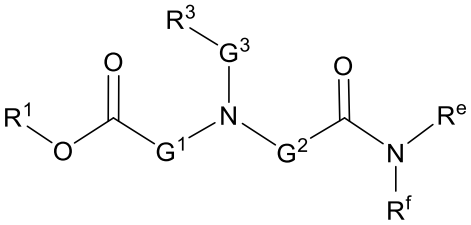
(I-B'),



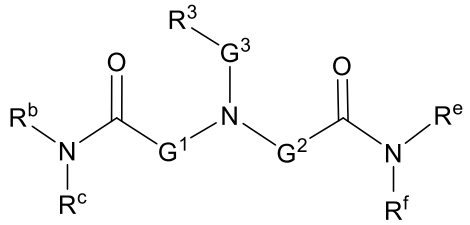
(I-B"),



(I-C),



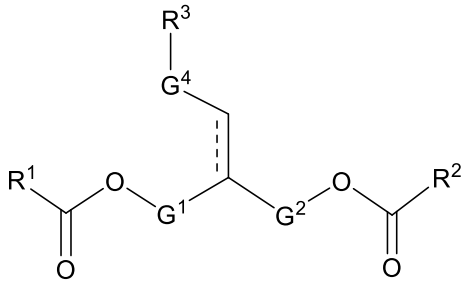
(I-D), or



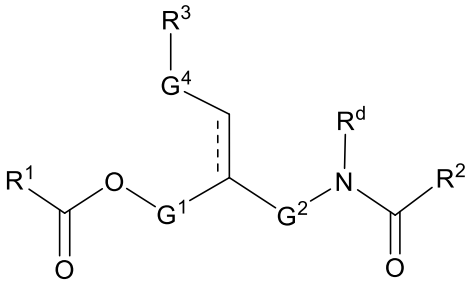
(I-E),

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof.

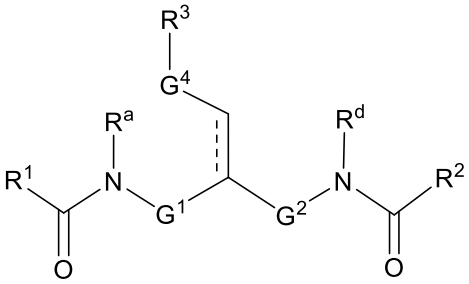
12. The compound of claim 2, which is a compound of Formula (II-B), (II-B'), (II-B"), (II-C), (II-D), or (II-E):



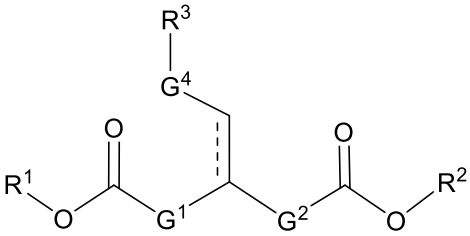
(II-B),



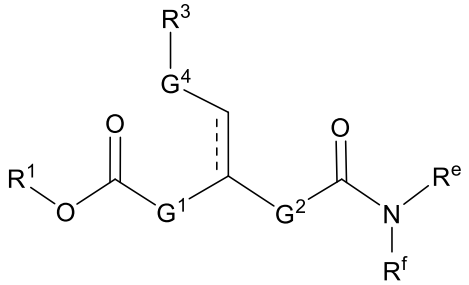
(II-B'),



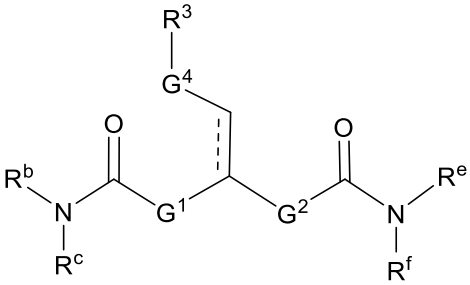
(II-B"),



(II-C),



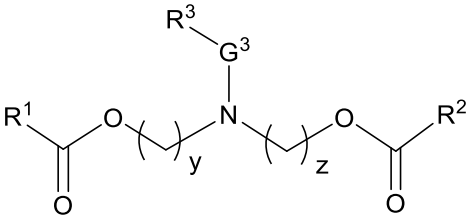
(II-D), or



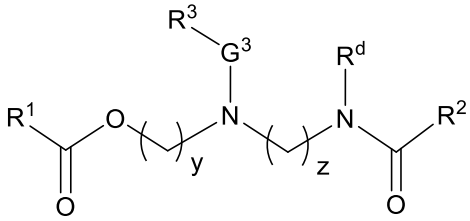
(II-E),

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof.

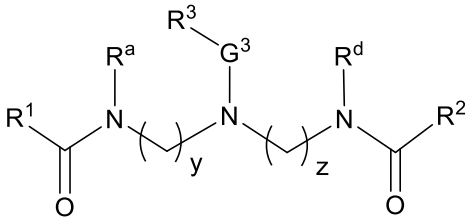
13. The compound of claim 11, which is a compound of Formula (I-F), (I-F'), (I-F"), (I-G), (I-H), or (I-I):



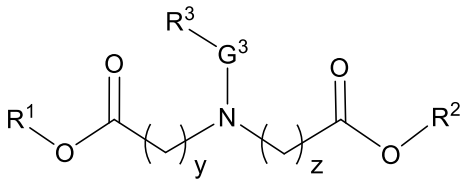
(I-F),



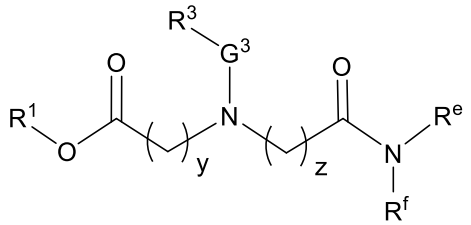
(I-F'),



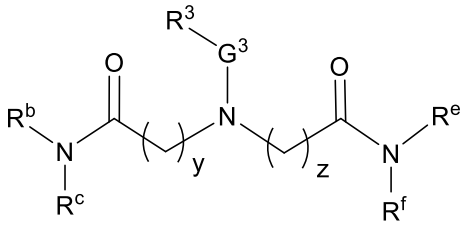
(I-F"),



(I-G),



(I-H), or

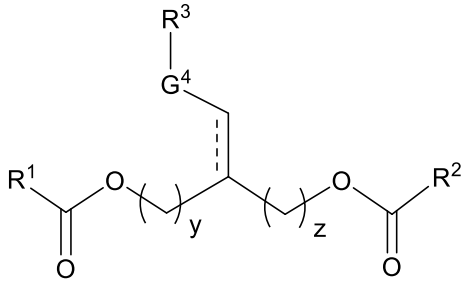


(I-I),

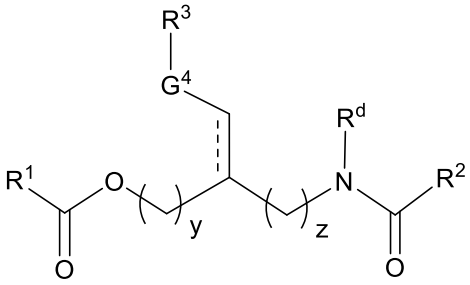
wherein y and z are each independently an integer from 2 to 12,

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof.

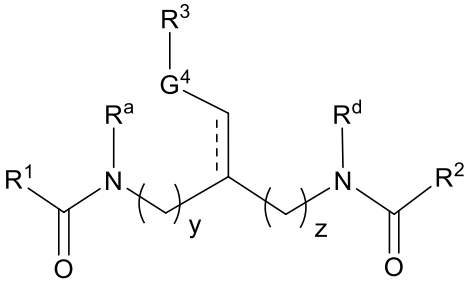
14. The compound of claim 12, which is a compound of Formula (II-F), (II-F'), (II-F"), (II-G), (II-H), or (II-I):



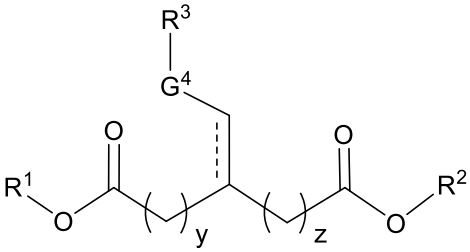
(II-F),



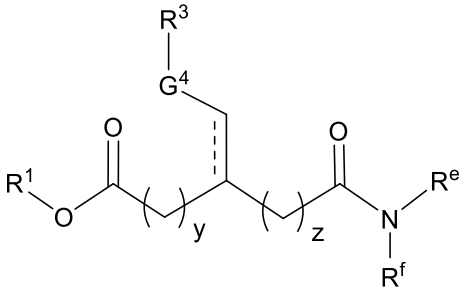
(II-F'),



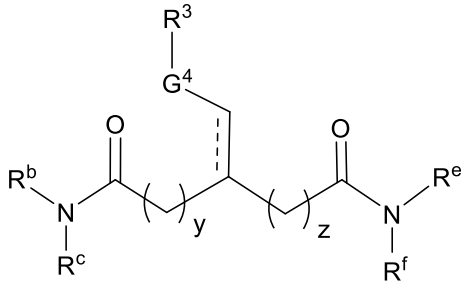
(II-F"),



(II-G),



(II-H), or



(II-I),

wherein y and z are each independently an integer from 2 to 12,

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof.

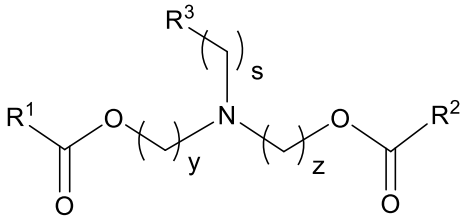
15. The compound of claim 13 or 14, wherein y is 5 and z is 5.

16. The compound of any one of claims 1 to 15, wherein $G^3$ is $C_2$-$C_{24}$ alkylene.

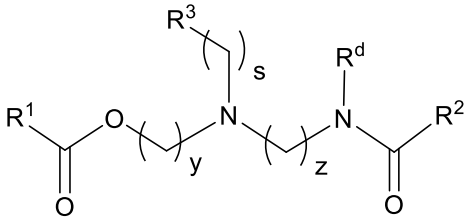
17. The compound of claim 16, wherein $G^3$ is $C_2$-$C_4$ alkylene.

18. The compound of claim 16 or 17, wherein $G^3$ is substituted with one or more oxo.

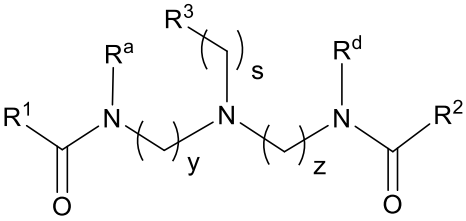
19. The compound of claim 1, which is a compound of Formula (I-J), (I-J'), (I-J"), (I-K), (I-L), or (I-M):



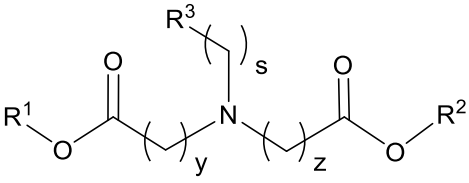
(I-J),



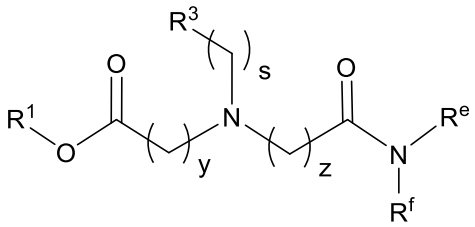
(I-J'),



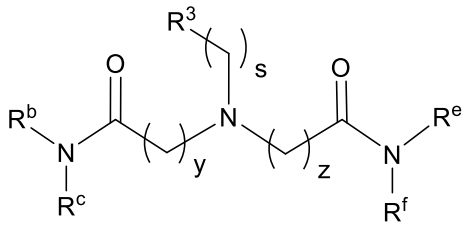
(I-J"),



(I-K),



(I-L), or



(I-M),

wherein y and z are each independently an integer from 2 to 12, and

s is an integer from 2 to 24,

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof.

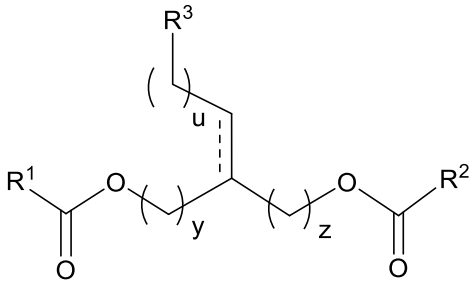
20. The compound of claim 19, wherein y is 5, z is 5, and s is 2.

21. The compound of claim 19, wherein y is 5, z is 5, and s is 4.

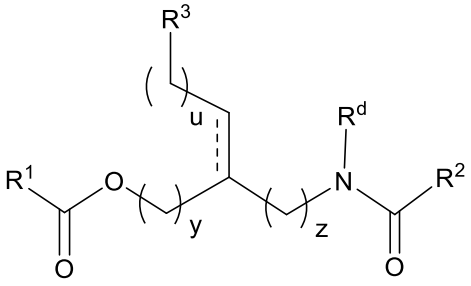
22. The compound of any one of claims 1 to 15, wherein $G^4$ is a bond.

23. The compound of any one of claims 1 to 15, wherein $G^4$ is $C_1$-$C_{23}$ alkylene.

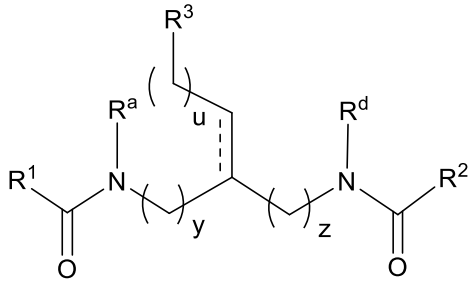
24. The compound of claim 2, which is a compound of Formula (II-J), (II-J'), (II-J"), (II-K), (II-L), or (II-M):



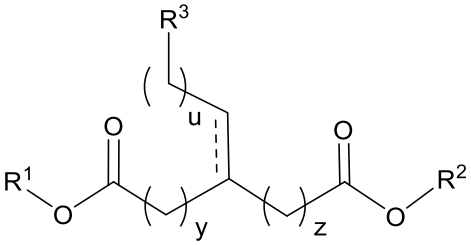
(II-J),



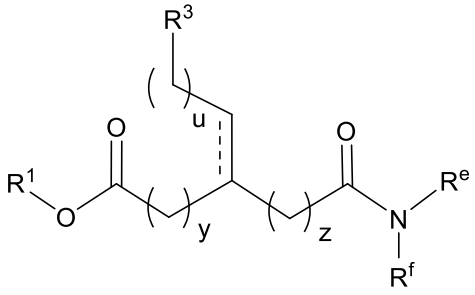
(II-J'),



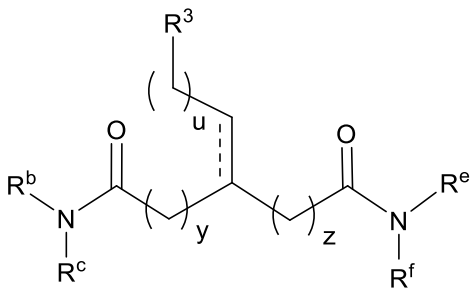
(II-J"),



(II-K),



(II-L), or



(II-M),

wherein y and z are each independently an integer from 2 to 12, and

u is an integer from 0 to 23,

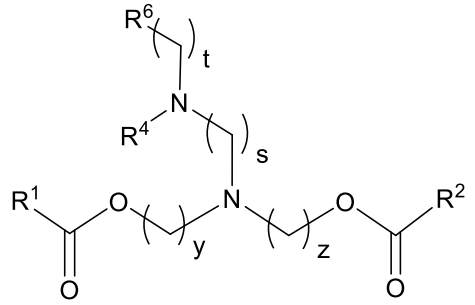
or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof.

25. The compound of claim 24, wherein y is 5, z is 5, and u is 0.

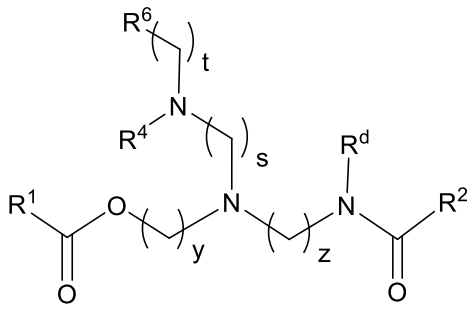
26. The compound of any one of claims 1 to 25, wherein $R^5$ is unsubstituted.

27. The compound of any one of claims 1 to 25, wherein $R^5$ is substituted with one or more hydroxyl.

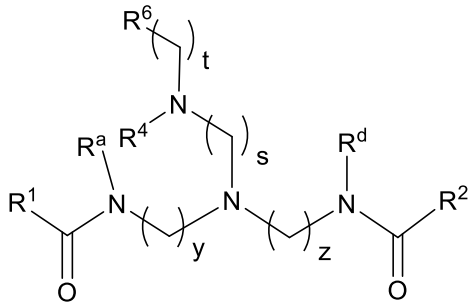
28. The compound of claim 1, which is a compound of Formula (I-N), (I-N'), (I-N"), (I-O), (I-P), or (I-Q):



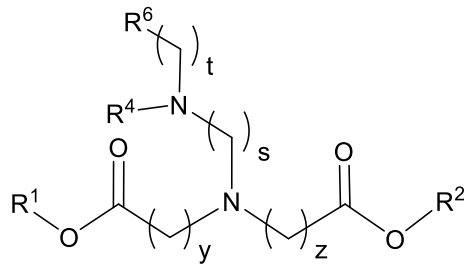
(I-N),



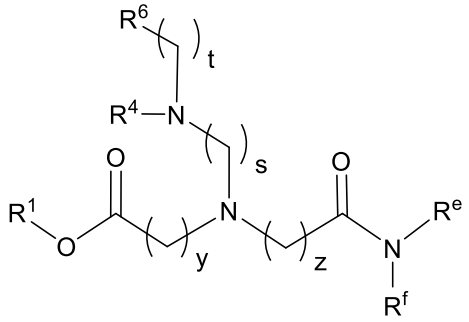
(I-N'),



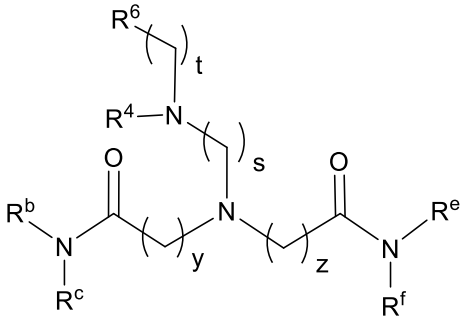
(I-N"),



(I-O),



(I-P), or



(I-Q),

wherein y and z are each independently an integer from 2 to 12,

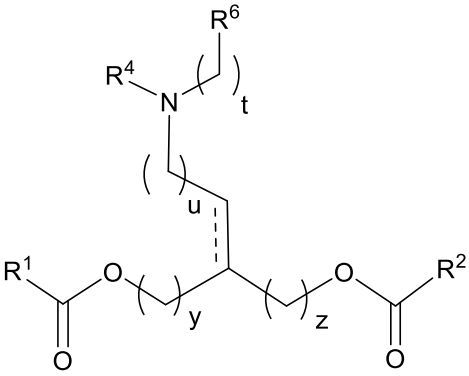
s is an integer from 2 to 24,

t is an integer from 1 to 12, and

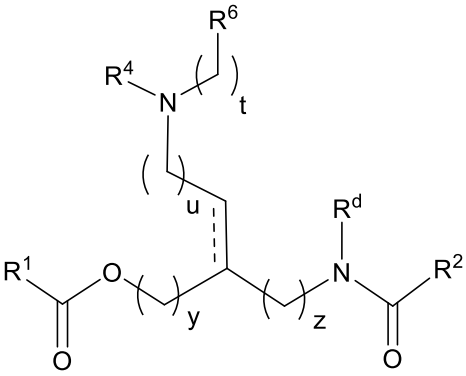
$R^6$ is hydrogen or hydroxyl,

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof.

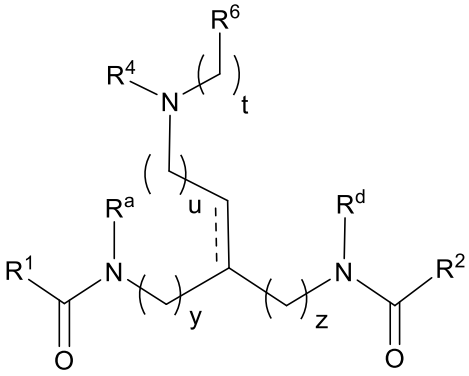
29. The compound of claim 2, which is a compound of Formula (II-N), (II-N'), (II-N"), (II-O), (II-P), or (II-Q):



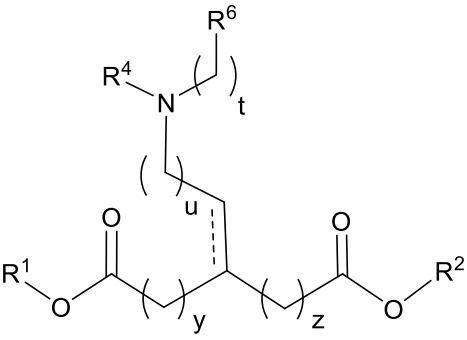
(II-N),



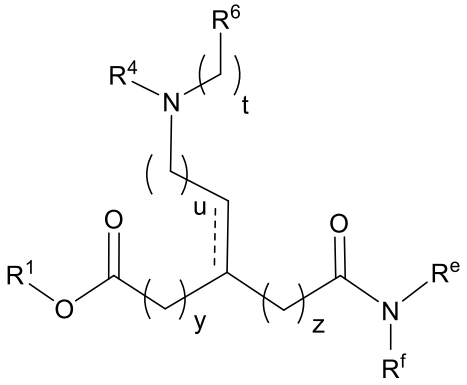
(II-N'),



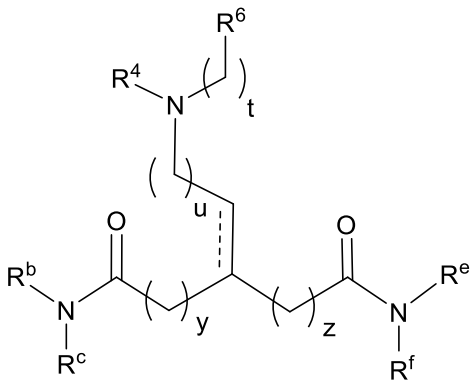
(II-N"),



(II-O),



(II-P), or



(II-Q),

wherein y and z are each independently an integer from 2 to 12,

u is an integer from 0 to 23,

t is an integer from 1 to 12, and

$R^6$ is hydrogen or hydroxyl,

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof.

30. The compound of any one of claims 1 to 25, wherein $R^5$ is substituted with one or more hydroxyl and one or more oxo.

31. The compound of claim 30, wherein $R^5$ is $–CH_2CH_2OH$.

32. The compound of any one of claims 1 to 25, wherein $R^5$ is $-(CH_2)_pQ$, $-(CH_2)_pCHQR$, $-CHQR$, or $-CQ(R)_2$, wherein Q is $C_3$-$C_8$ cycloalkyl, $C_3$-$C_8$ cycloalkenyl, $C_3$-$C_8$ cycloalkynyl, 4- to 8-membered heterocyclyl, $C_6$-$C_{10}$ aryl, 5- to 10-membered heteroaryl, $-OR$, $-O(CH_2)_pN(R)_2$, $-C(O)OR$, $-OC(O)R$, $-CX_3$, $-CX_2H$, $-CXH_2$, $-CN$, $-N(R)_2$, $-C(O)N(R)_2$, $-N(R)C(O)R$, $-N(R)S(O)_2R$, $-N(R)C(O)N(R)_2$, $-N(R)C(S)N(R)_2$, $-N(R)R^{22}$, $-O(CH_2)_pOR$, $-N(R)C(=NR^{23})N(R)_2$, $-N(R)C(=CHR^{23})N(R)_2$, $-OC(O)N(R)_2$, $-N(R)C(O)OR$, $-N(OR)C(O)R$, $-N(OR)S(O)_2R$, $-N(OR)C(O)OR$, $-N(OR)C(O)N(R)_2$, $-N(OR)C(S)N(R)_2$, $-N(OR)C(=NR^{23})N(R)_2$, $-N(OR)C(=CHR^{23})N(R)_2$, $-C(=NR^{23})N(R)_2$, $-C(=NR^{23})R$, $-C(O)N(R)OR$, or $-C(R)N(R)_2C(O)OR$, and each p is independently 1, 2, 3, 4, or 5;

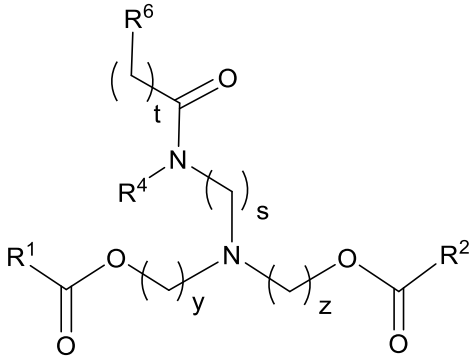
$R^{22}$ is $C_3$-$C_8$ cycloalkyl, $C_3$-$C_8$ cycloalkenyl, $C_3$-$C_8$ cycloalkynyl, 4- to 8-membered heterocyclyl, $C_6$-$C_{10}$ aryl, or 5- to 10-membered heteroaryl;

$R^{23}$ is H, $-CN$, $-NO_2$, $C_1$-$C_6$ alkyl, $-OR$, $-S(O)_2R$, $-S(O)_2N(R)_2$, $C_2$-$C_6$ alkenyl, $C_3$-$C_8$ cycloalkyl, $C_3$-$C_8$ cycloalkenyl, $C_3$-$C_8$ cycloalkynyl, 4- to 8-membered heterocyclyl, $C_6$-$C_{10}$ aryl, or 5- to 10-membered heteroaryl;

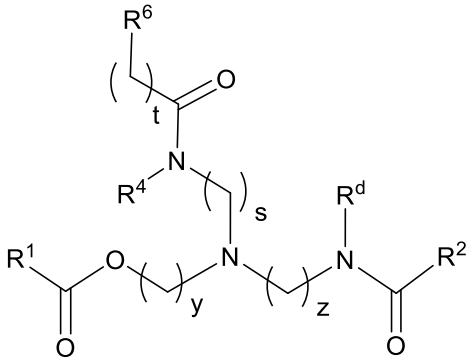
each R is independently H, $C_1$-$C_3$ alkyl, or $C_2$-$C_3$ alkenyl; or two R in a $N(R)_2$ moiety together with the nitrogen to which they are attached form a cyclic moiety; and

each X is independently F, CI, Br, or I.

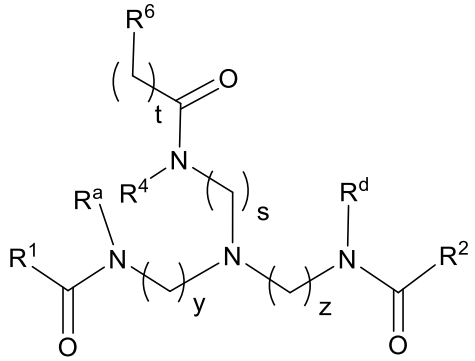
33. The compound of claim 1, which is a compound of Formula (I-R), (I-R'), (I-R"), (I-S), (I-T), or (I-U):



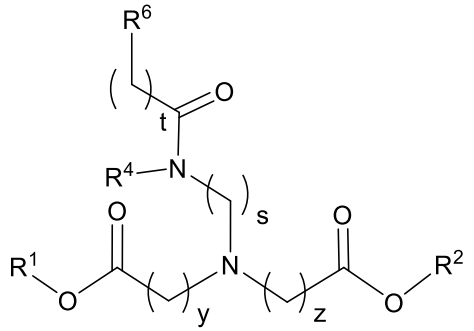
(I-R),



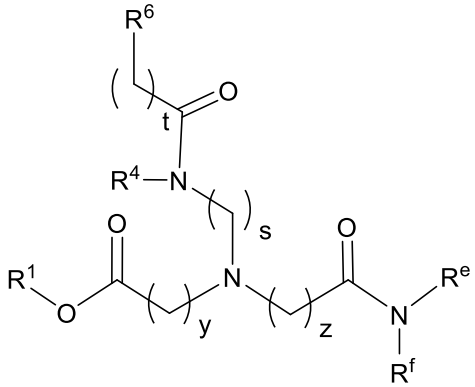
(I-R'),



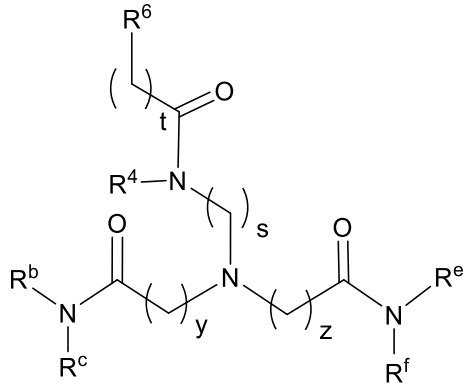
(I-R"),



(I-S),



(I-T), or



(I-U),

wherein y and z are each independently an integer from 2 to 12,

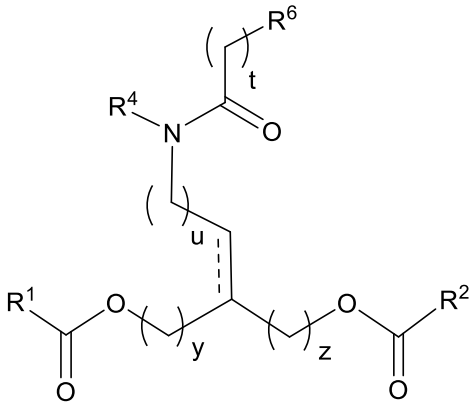
s is an integer from 2 to 24,

t is an integer from 1 to 12, and

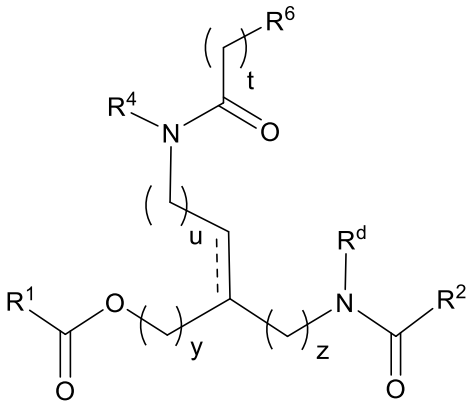
$R^6$ is hydrogen or hydroxyl,

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof.

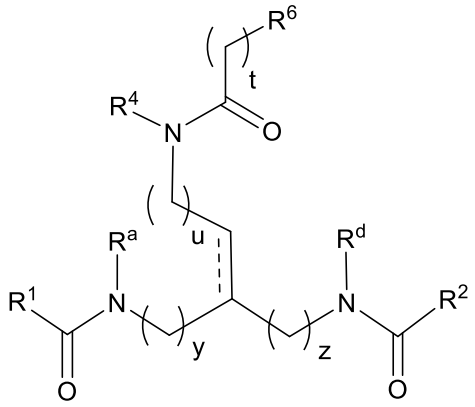
34. The compound of claim 2, which is a compound of Formula (II-R), (II-R'), (II-R"), (II-S), (II-T), or (II-U):



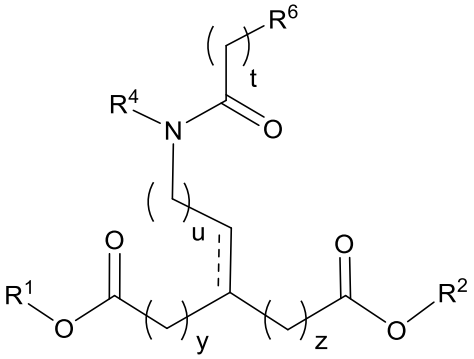
(II-R),



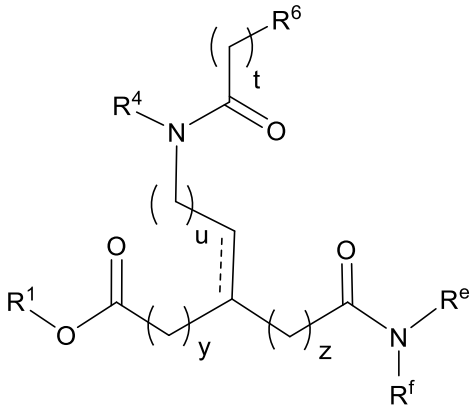
(II-R'),



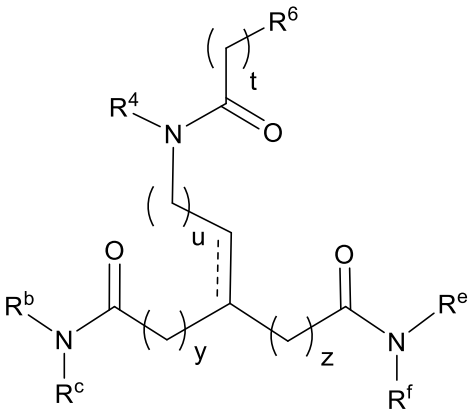
(II-R"),



(II-S),



(II-T), or



(II-U),

wherein y and z are each independently an integer from 2 to 12,

u is an integer from 0 to 23,

t is an integer from 1 to 12, and

$R^6$ is hydrogen or hydroxyl,

or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof.

35. The compound of any one of claims 2 to 34, wherein $R^4$ is $C_1$-$C_{12}$ alkyl.

36. The compound of any one of claims 1 to 34, wherein $R^4$ is $C_3$-$C_8$ cycloalkyl.

37. The compound of any one of claims 1 to 36, wherein $R^4$ is unsubstituted.

38. The compound of any one of claims 1 to 37, wherein $R^1$ and $R^2$ are each independently branched $C_6$-$C_{24}$ alkyl or branched $C_6$-$C_{24}$ alkenyl.

39. The compound of claim 38, wherein $R^1$ and $R^2$ are each independently -$R^7$-$CH(R^8)(R^9)$, wherein $R^7$ is $C_1$-$C_5$ alkylene, and $R^8$ and $R^9$ are independently $C_2$-$C_{10}$ alkyl or $C_2$-$C_{10}$ alkenyl.

40. The compound of any one of claims 1 to 39, wherein $R^a$, $R^b$, $R^d$, and $R^e$ are each independently H.

41. The compound of any one of claims 1 to 40, wherein $R^c$ and $R^f$ are each independently branched $C_6$-$C_{24}$ alkyl or branched $C_6$-$C_{24}$ alkenyl.

42. The compound of claim 41, wherein $R^c$ and $R^f$ are each independently -$R^7$-$CH(R^8)(R^9)$, wherein $R^7$ is $C_1$-$C_5$ alkylene, and $R^8$ and $R^9$ are independently $C_2$-$C_{10}$ alkyl or $C_2$-$C_{10}$ alkenyl.

43. A compound in Table 1, or a pharmaceutically acceptable salt, prodrug or stereoisomer thereof.

44. A composition comprising the compound of any one of claims 1 to 43, and a therapeutic or prophylactic agent.

45. The composition of claim 44, further comprising one or more structural lipids.

46. The composition of claim 45, wherein the one or more structural lipids is DSPC.

47. The composition of claim 45 or 46, wherein the molar ratio of the compound to the structural lipids ranges from about 2:1 to about 8:1.

48. The composition of any one of claims 44 to 47, further comprising a steroid.

49. The composition of claim 48, wherein the steroid is cholesterol.

50. The composition of claim 48 or 49, wherein the molar ratio of the compound to the steroid ranges from about 5:1 to about 1:1.

51. The composition of any one of claims 44 to 50, wherein the composition further comprises one or more polymer conjugated lipids.

52. The composition of claim 51, wherein the polymer conjugated lipids is DMG-PEG2000 or DMPE-PEG2000.

53. The composition of claim 51 or 52, wherein the molar ratio of the compound to the polymer conjugated lipids ranges from about 100:1 to about 20:1.

54. The composition of any one of claims 44 to 53, wherein the therapeutic or prophylactic agent comprises at least one mRNA encoding an antigen or a fragment or epitope thereof.

55. The composition of claim 54, wherein the mRNA is monocistronic mRNA.

56. The composition of claim 54, wherein the mRNA is multicistronic mRNA.

57. The composition of any one of claims 54 to 56, wherein the antigen is a pathogenic antigen.

58. The composition of any one of claims 54to 56, wherein the antigen is a tumor associated antigen.

59. The composition of any one of claims 54 to 58, wherein the mRNA comprises one or more functional nucleotide analog.

60. The composition of claim 59, wherein the functional nucleotide analog is one or more selected from pseudouridine, 1-methyl-pseudouridine and 5-methylcytosine.

61. The composition of any one of claims 44 to 60, wherein the composition is a nanoparticle.

62. A lipid nanoparticle comprising the compound of any one of claims 1 to 43, or the composition of any one of claims 44 to 60.

63. A pharmaceutical composition comprising the compound of any one of claims 1 to 43, the composition of any one of claims 44 to 60, or the lipid nanoparticle of claim 62, and a pharmaceutically acceptable excipient or diluent.