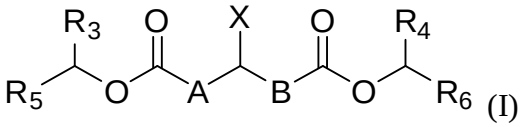
CLAIMS

1. A compound of Formula (I):



(I)

or a pharmaceutically acceptable salt thereof,

wherein

A is absent or -CH_2-;

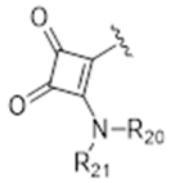
B is -CH_2- or -CH_2CH_2-,;

wherein when A is absent then B is -CH_2CH_2- and when A is -CH_2- then B is -CH_2-;

X is -NR_1R_2 or -O-(C=O)$R_{1'}$;

R_1 is H or an optionally substituted linear C1-C4 alkyl group;

R_2 is H, an optionally substituted linear C1-C8 alkyl group, -C(=O)R_7, -S(=O)$_2$-R_7, or



;

$R_{1'}$ is an optionally substituted linear C1-C8 alkyl group;

R_{20} is H or an optionally substituted linear C1-C8 alkyl group;

R_{21} is an optionally substituted linear C1-C8 alkyl group or –(C=O)-R_{22}, wherein R_{22} is an optionally substituted C1-C8 alkyl group;

R_3 and R_4 are independently H, a linear or branched C4-C60 alkyl, a linear or branched C4-C60 alkenyl, or a linear or branched C4-C60 alkynyl group, wherein at least one of R_3 or R_4 is different from H;

R_5 and R_6 are independently a linear or branched C4-C60 alkyl, a linear or branched C4-C60 alkenyl, or a linear or branched C4-C60 alkynyl group;

R_7 is an optionally substituted linear C1-C8 alkyl group, an optionally substituted linear C2-C8 alkenyl group, an optionally substituted 5 to 10-membered heterocyclyl or an optionally substituted 5 to 10-membered heteroaryl;

wherein when any of R_3, R_4, R_5 and R_6 represents an alkenyl group, the alkenyl group independently comprises from one to six C=C bonds each independently having the E or Z configuration;

wherein when any of R_3, R_4, R_5 and R_6 represents an alkynyl group, the alkynyl group independently comprises from one to six C≡C bonds;

wherein when R_7 represents an alkenyl group, the alkenyl group comprises from one to two C=C bonds each independently having the E or Z configuration;

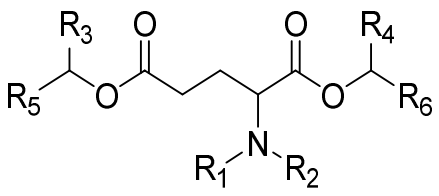
wherein when any alkyl and/or alkenyl group is substituted, this group is independently substituted with one or more -OH, -(C=O)-H, -(C=O)-CH_3, -(C=O)-$(CH_2)_pCH_3$, -(C=O)-$(CH_2)_p$-R_{19}, -O-(C=O)-CH_3, -O-(C=O)-$(CH_2)_pCH_3$, -O-(C=O)-$(CH_2)_p$-R_{19}, -(C=O)-OCH_3, -(C=O)-O-$(CH_2)_pCH_3$, -(C=O)-O-$(CH_2)_p$-R_{19}, -(C=O)-$(CH_2)_p$-(C=O)-R_{19}, -(C=O)-O-$(CH_2)_pN(CH_3)$-$(CH_2)_{p'}$-R_{19}, -(C=O)NH-$(CH_2)_p$-R_{19}, -(C=S)-CH_3, -O-CH_3, -O-$(CH_2)_pCH_3$, -NH_2, -$NHCH_3$, -$N(CH_3)_2$, -$N(CH_2CH_3)_2$, -$N(CH_2CH_2OH)_2$, -$N((CH_2)_pO$-(C=O)$CH_3)_2$, -$N(CH_3)$-$(CH_2)_p$-R_{19}, -(C=O)NH_2, -N_3, -NO_2, -SCH_3, -SCH_2CH_3, an optionally substituted 5 to 10-membered heterocyclyl, C5-C12 aralkyl, C5-C10 aryl or an optionally substituted 5 to 10-membered heteroaryl, with p and p' are independently from 1 to 5; and wherein R_{19} is -NH_2, -$NHCH_3$, -$N(CH_3)_2$, -$N(CH_2CH_3)_2$, an optionally substituted 5 to 10-membered heterocyclyl or an optionally substituted 5 to 10-membered heteroaryl;

wherein when any 5 to 10-membered heteroaryl and/or 5 to 10-membered heterocyclyl is substituted, this group is independently substituted with one or more substituents selected from the group consisting of C1-C4 alkyl group, -$(CH_2)_{p''}N(CH_3)_2$ and oxo (=O), with p'' from 1 to 5;

with the provisos that when A is absent, B is -CH_2CH_2-, X is -NR_1R_2, R_1 is -CH_3, and each of R_3, R_4, R_5, and R_6 is linear C18 alkyl groups with one C=C bond between carbons C_9 and C_{10} and one C=C bond between carbons C_{12} and C_{13}, then R_2 is different from -CH_3, -CH_2CH_2OH and -$CH_2CH_2NH_2$; and

wherein the compound or the pharmaceutically acceptable salt thereof is in the form of any enantiomers, any diastereoisomers, any cis or trans geometric isomers, or any mixtures thereof.

2. The compound of claim 1, wherein the compound of Formula (I) has a structure of Formula (I1):



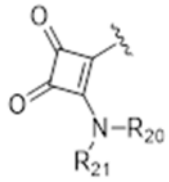
(I1)

or a pharmaceutically acceptable salt thereof,

wherein

R_1 is H or an optionally substituted linear C1-C4 alkyl group;

R_2 is H, an optionally substituted linear C1-C8 alkyl group, -C(=O)R_7, -$S(=O)_2$-R_7, or



;

R_{20} is H or an optionally substituted linear C1-C8 alkyl group;

R_{21} is an optionally substituted linear C1-C8 alkyl group or –(C=O)-R_{22}, wherein R_{22} is an optionally substituted C1-C8 alkyl group;

R_3 and R_4 are independently H, a linear or branched C4-C60 alkyl, a linear or branched C4-C60 alkenyl, or a linear or branched C4-C60 alkynyl group, wherein at least one of R_3 or R_4 is different from H;

R_5 and R_6 are independently a linear or branched C4-C60 alkyl, a linear or branched C4-C60 alkenyl, or a linear or branched C4-C60 alkynyl group;

R_7 is an optionally substituted linear C1-C8 alkyl group, an optionally substituted linear C2-C8 alkenyl group, an optionally substituted 5 to 10-membered heterocyclyl or an optionally substituted 5 to 10-membered heteroaryl;

wherein when any of R_3, R_4, R_5 and R_6 represents an alkenyl group, the alkenyl group independently comprises from one to six C=C bonds each independently having the E or Z configuration;

wherein when any of R_3, R_4, R_5 and R_6 represents an alkynyl group, the alkynyl group independently comprises from one to six C≡C bonds;

wherein when R_7 represents an alkenyl group, the alkenyl group comprises from one to two C=C bonds each independently having the E or Z configuration;

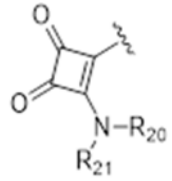
wherein when any alkyl and/or alkenyl group is substituted, this group is independently substituted with one or more -OH, -(C=O)-H, -(C=O)-CH_3, -(C=O)-$(CH_2)_pCH_3$, -(C=O)-$(CH_2)_p$-R_{19}, -O-(C=O)-CH_3, -O-(C=O)-$(CH_2)_pCH_3$, -O-(C=O)-$(CH_2)_p$-R_{19}, -(C=O)-OCH_3, -(C=O)-O-$(CH_2)_pCH_3$, -(C=O)-O-$(CH_2)_p$-R_{19}, -(C=O)-$(CH_2)_p$-(C=O)-R_{19}, -(C=O)-O-$(CH_2)_pN(CH_3)$-$(CH_2)_{p'}$-R_{19}, -(C=O)NH-$(CH_2)_p$-R_{19}, -(C=S)-CH_3, -O-CH_3, -O-$(CH_2)_pCH_3$, -NH_2, -$NHCH_3$, -$N(CH_3)_2$, -$N(CH_2CH_3)_2$, -$N(CH_2CH_2OH)_2$, -$N((CH_2)_pO$-(C=O)$CH_3)_2$, -$N(CH_3)$-$(CH_2)_p$-R_{19}, -(C=O)NH_2, -N_3, -NO_2, -SCH_3, -SCH_2CH_3, an optionally substituted 5 to 10-membered heterocyclyl, C5-C12 aralkyl, C5-C10 aryl or an optionally substituted 5 to 10-membered heteroaryl, with p and p' are independently from 1 to 5; and wherein R_{19} is -NH_2, -$NHCH_3$, -$N(CH_3)_2$, -$N(CH_2CH_3)_2$, an optionally substituted 5 to 10-membered heterocyclyl or an optionally substituted 5 to 10-membered heteroaryl,

wherein when any 5 to 10-membered heteroaryl and/or 5 to 10-membered heterocyclyl is substituted, this group is independently substituted with one or more substituents selected from the group consisting of C1-C4 alkyl group, $-(CH_2)_{p''}N(CH_3)_2$ and oxo (=O), with p'' from 1 to 5.

3. The compound of claim 1 or 2, or the pharmaceutically acceptable salt thereof, wherein:

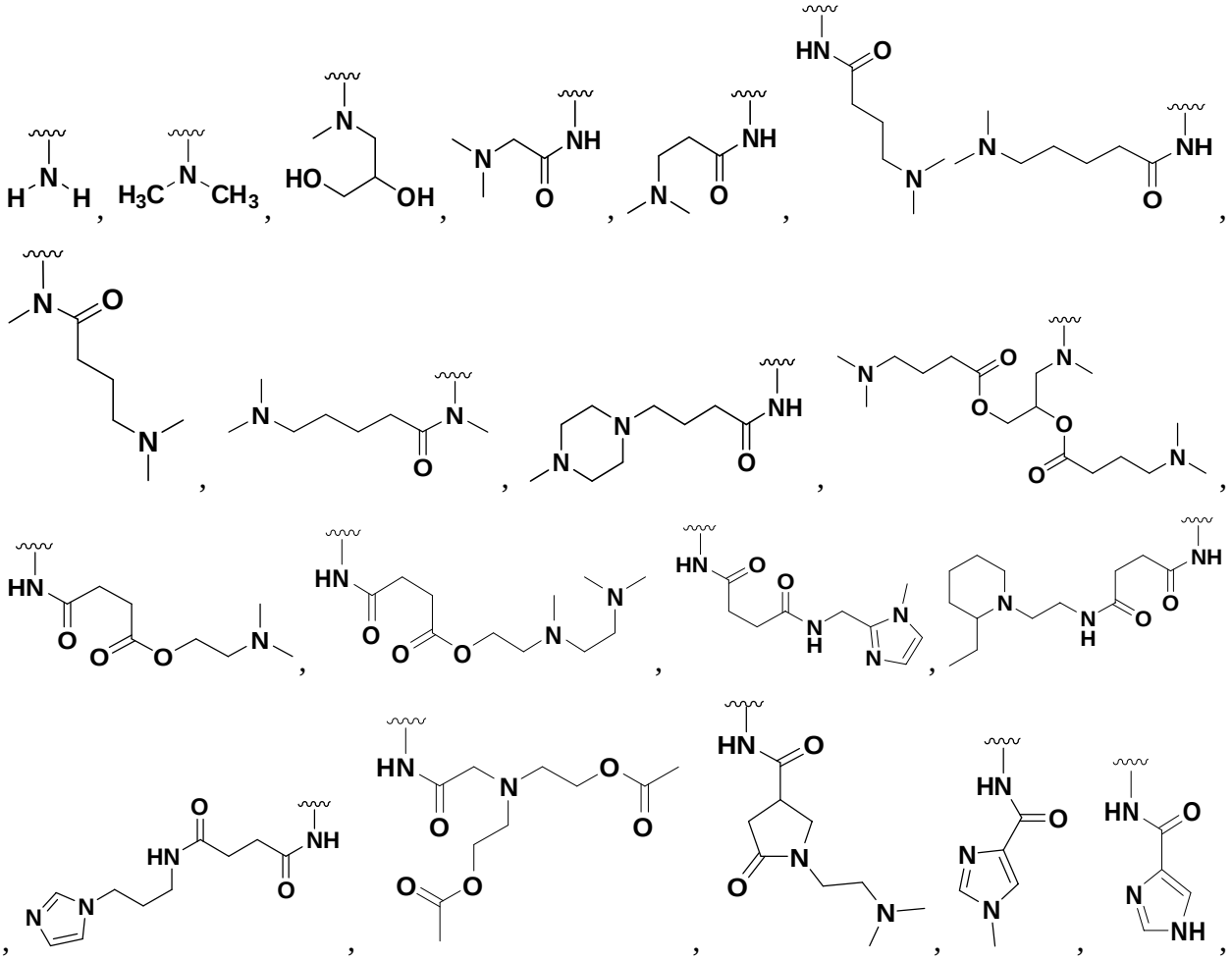
(i) R_1 is H or CH_3, preferably H; ~~.~~

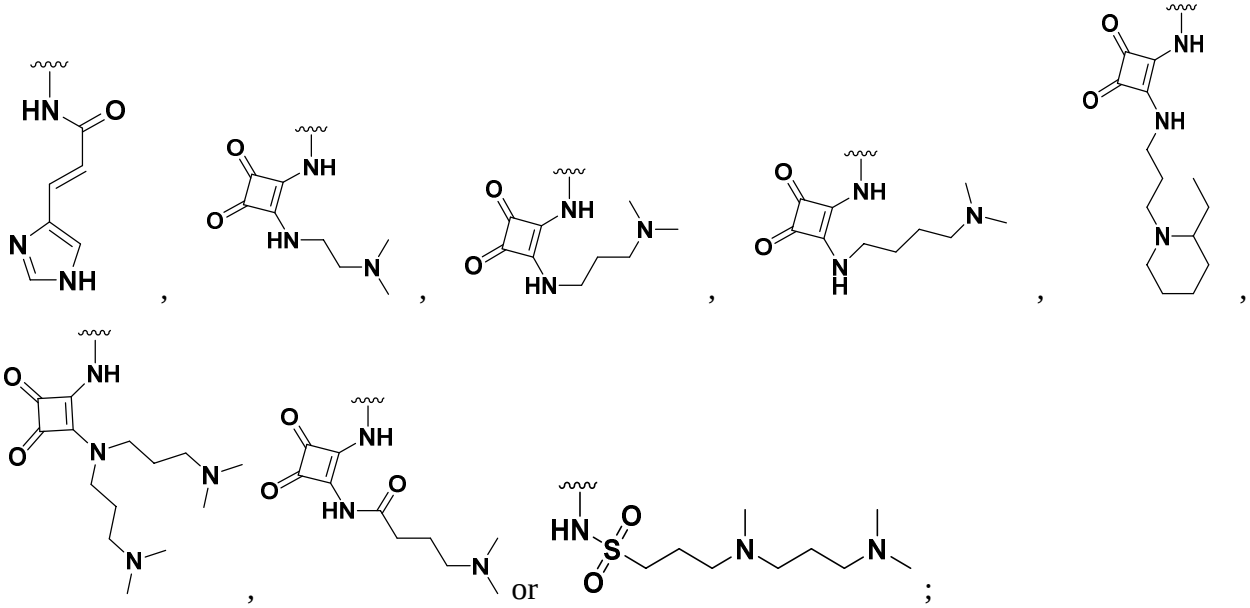
(ii) R_2 is H, an optionally substituted linear C3-C4 alkyl group, $-C(=O)R_7$, $-S(=O)_2-R_7$, or



;

(iii) $-NR_1R_2$ has one of the following structures:

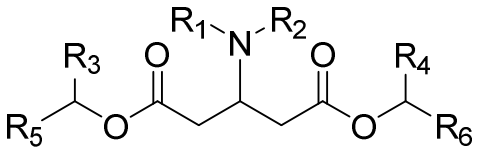




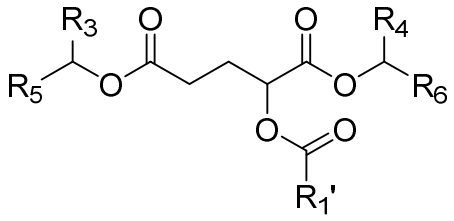
(iv) any of R_3, R_4, R_5 and R_6 is C6-C25 alkenyl, and the alkenyl group independently comprises one, two or three C=C bonds; or

(v) any combination of (i)-(iv).

4. The compound of claim 1, wherein the compound of Formula (I) has a structure of Formula (I2) or (I3):



(I2)



(I3)

or a pharmaceutically acceptable salt thereof,

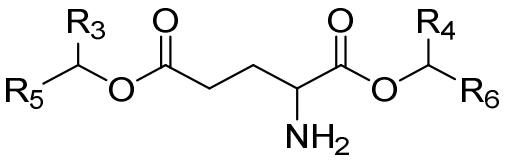
wherein R_1, R_2, R_3, R_4, R_5, R_6 and $R_{1'}$ are as defined in any one of claims 1 to 3.

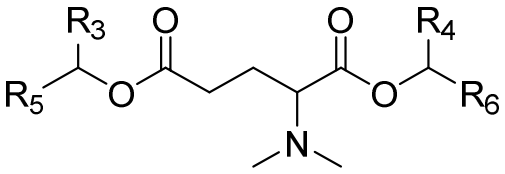
5. The compound of claim 4, wherein:

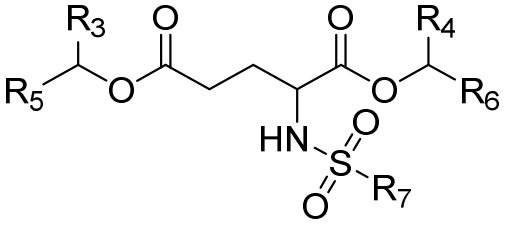
(i) the compound has a structure of formula (I2), or a pharmaceutically acceptable salt thereof, wherein R_1 is H or C1-C2 alkyl, and R_2 is -C(=O)R_7; and wherein R_3, R_4, R_5, R_6 and R_7 are as defined in any one of claims 1 to 3; or

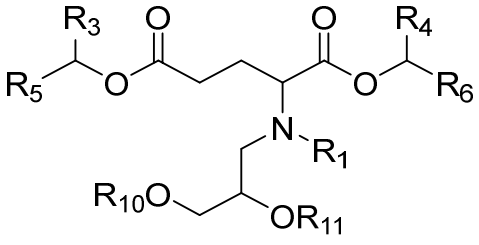
(ii) the compound has a structure of formula (I3), or a pharmaceutically acceptable salt thereof, wherein $R_{1'}$ is a linear C1-C4 alkyl group substituted with -(C=O)-$(CH_2)_p$-R_{19}, -O-(C=O)-$(CH_2)_p$-R_{19}, -(C=O)-O-$(CH_2)_p$-R_{19}, -(C=O)-$(CH_2)_p$-(C=O)-R_{19}, -(C=O)-O-$(CH_2)_p N(CH_3)$-$(CH_2)_{p'}$-$N(CH_3)_2$, -(C=O)NH-$(CH_2)_p$-R_{19}, -$N(CH_3)_2$, -$N((CH_2)_pO$-(C=O)$CH_3)_2$, -$N(CH_3)$-$(CH_2)_p N(CH_3)_2$, an optionally substituted 5 to 6-membered heterocyclyl or an optionally substituted 5 to 6-membered heteroaryl, with p and p' are independently from 1 to 5; and wherein R_{19} is -$N(CH_3)_2$, an optionally substituted 5 to 6-membered heterocyclyl or an optionally substituted 5 to 6-membered heteroaryl; wherein when the 5 to 6-membered heteroaryl and/or 5 to 6-membered heterocyclyl is substituted, this group is independently substituted with one substituent selected from the group consisting of C1-C2 alkyl group;
and wherein R_3, R_4, R_5 and R_6 are as defined in any one of claims 1 to 3.

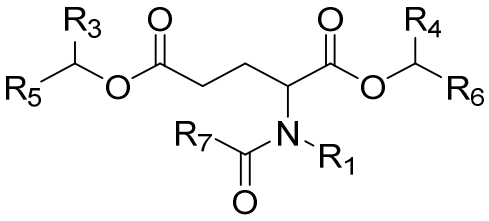
6. The compound of claim 1 or 2, wherein the compound has a structure of Formula (I1-1), (I1-2), (I1-3), (I1-4), (I1-5) or (I1-6):


(I1-1),

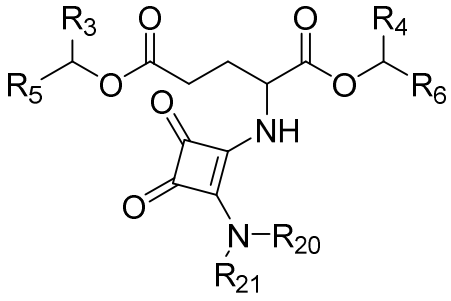

(I1-2),


(I1-3),


(I1-4),



(I1-5),



(I1-6),

or a pharmaceutically acceptable salt thereof,

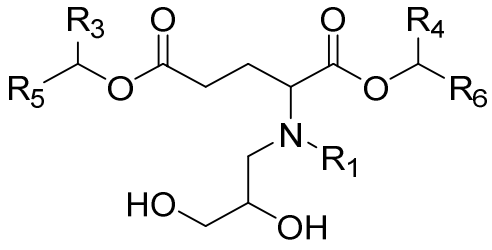
wherein R_1 is H or a linear C1-C4 alkyl;

wherein R_{10} and R_{11} are independently -H, -(C=O)-CH_3, -(C=O)-$(CH_2)_pCH_3$, -(C=O)-$(CH_2)_p$-R_{19}, or -(C=O)-$(CH_2)_p$-(C=O)-R_{19}; and

wherein R_3, R_4, R_5, R_6, R_7, R_{19}, R_{20} and R_{21} are as defined in any one of claims 1 to 3 and p is from 1 to 5.

7. The compound of claim 6, wherein the compound has a structure of

formula (I1-4a):

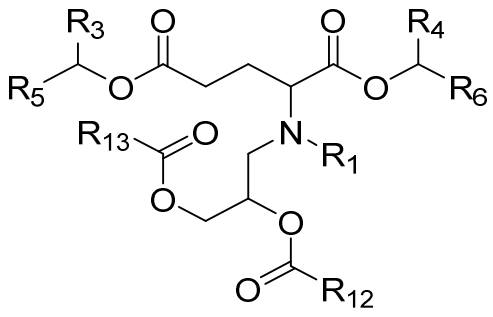


(I1-4a),

or a pharmaceutically acceptable salt thereof,

wherein R_1 is H or a linear C1-C4 alkyl, preferably R_1 is H or -CH_3, more preferably R_1 is -CH_3; and wherein R_3, R_4, R_5 and R_6 are as defined in any one of claims 1 to 3;

formula (I1-4b):



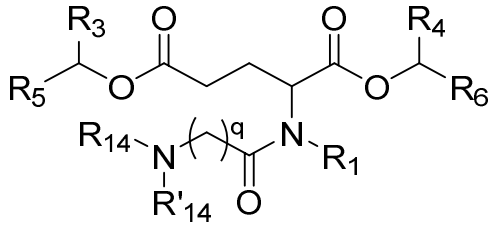
(I1-4b),

or a pharmaceutically acceptable salt thereof,

wherein R_1 is H or a linear C1-C4 alkyl, preferably R_1 is H or -CH_3, more preferably R_1 is -CH_3;

wherein R_{12} and R_{13} are independently an optionally substituted linear C1-C4 alkyl; wherein when the linear alkyl group is substituted, this group is independently substituted with -NH_2, -$NHCH_3$, -$N(CH_3)_2$, -$N(CH_2CH_3)_2$, or 5-6 membered heteroaryl, preferably R_{12} and R_{13} are independently linear C1-C4 alkyl substituted with -NH_2, -$NHCH_3$, -$N(CH_3)_2$ or -$N(CH_2CH_3)_2$, more preferably substituted with -$N(CH_3)_2$; and wherein R_3, R_4, R_5 and R_6 are as defined in any one of claims 1 to 3;

formula (I1-5a):



(I1-5a),

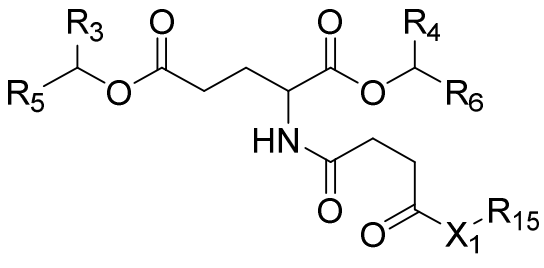
or a pharmaceutically acceptable salt thereof,

wherein R_1 is H or a linear C1-C4 alkyl, preferably R_1 is H or -CH_3, more preferably R_1 is H;

wherein q is from 1 to 5;

wherein R_{14} and R'_{14} independently represent -H, -CH_3, -CH_2CH_3, or -$(CH_2)_pO$-(C=O)CH_3 with p is from 1 to 5, preferably p is from 1 to 3, or R_{14} and R'_{14} are connected to form a 6-membered heterocyclyl optionally substituted with -CH_3 or -CH_2CH_3; and wherein R_3, R_4, R_5 and R_6 are as defined in any one of claims 1 to 3;

formula (I1-5b):



(I1-5b),

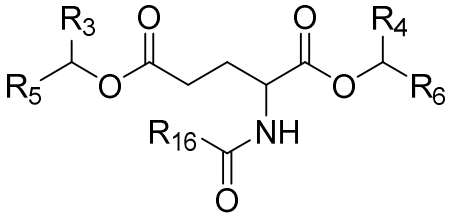
or a pharmaceutically acceptable salt thereof,

wherein X_1 is -NH- or -O-;

wherein R_{15} is a linear C1-C4 alkyl, $-(CH_2)_p-R_{19}$, or $–(CH_2)_pN(CH_3)-((CH_2)_{p'}-N(CH_3)_2)$ with p and p' are independently from 1 to 5, and R_{19} is as defined in claim 1 or 2;

preferably R_{15} is $–(CH_2)_2N(CH_3)-((CH_2)_2-N(CH_3)_2)$ or $-(CH_2)_p-R_{19}$ with p is from 1 to 3;
more preferably R_{15} is $–(CH_2)_2N(CH_3)-((CH_2)_2-N(CH_3)_2)$, $-(CH_2)_p-N(CH_3)_2$, or $-(CH_2)_p-R_{23}$ with p is from 1 to 3 and R_{23} is a 5 to 6-membered heteroaryl or 5 to 6-membered heterocyclyl, optionally substituted with C1-C2 alkyl;
even more preferably R_{15} is $–(CH_2)_2N(CH_3)-((CH_2)_2-N(CH_3)_2)$, $-(CH_2)_p-N(CH_3)_2$ or $-(CH_2)_p-R_{23}$ with p is from 1 to 3 and R_{23} is furanyl, thiophenyl, pyrrolyl, isoxazolyl, oxazolyl, isothiazolyl, thiazolyl, imidazolyl, pyrazolyl, pyrazinyl, pyridinyl, pyridazinyl, pyrimidinyl, piperidinyl or piperazinyl, wherein R_{23} is optionally substituted with C1-C2 alkyl;
most preferably R_{15} is $-(CH_2)_2N(CH_3)-((CH_2)_2-N(CH_3)_2)$, $-(CH_2)_p-N(CH_3)_2$ or $-(CH_2)_p-R_{23}$ with p is from 1 to 3 and R_{23} is imidazolyl or piperidinyl, wherein R_{23} is optionally substituted with a C1-C2 alkyl; and wherein R_3, R_4, R_5 and R_6 are as defined in any one of claim 1 to 3;

formula (I1-5c):



(I1-5c),

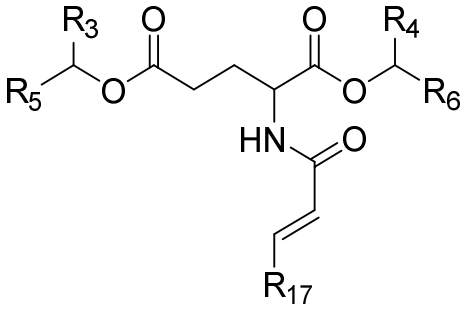
or a pharmaceutically acceptable salt thereof,

wherein

R_{16} is a 5 to 6-membered heteroaryl or a 5 to 6-membered heterocyclyl, optionally substituted with a linear C1-C4 alkyl, an oxo (=O) and/or a $–(CH_2)_p-N(CH_3)_2$ and wherein p is from 1 to 3, preferably R_{16} is furanyl, thiophenyl, pyrrolyl, pyrrolydinyl, isoxazolyl, oxazolyl, isothiazolyl, thiazolyl, imidazolyl, pyrazolyl, pyrazinyl, pyridinyl, pyridazinyl, piperazinyl,

piperidinyl or pyrimidinyl optionally substituted with a linear C1-C4 alkyl, an oxo (=O) and/or a $–(CH_2)p\text{-}N(CH_3)_2$ with p from 1 to 3, more preferably R_{16} is imidazolyl or pyrrolidinyl optionally substituted with a C1-C2 alkyl, an oxo (=O) and/or a $–(CH_2)p\text{-}N(CH_3)_2$ with p from 1 to 3; and wherein R_3, R_4, R_5 and R_6 are as defined in any one of claims 1 to 3;

formula (I1-5d):



(I1-5d),

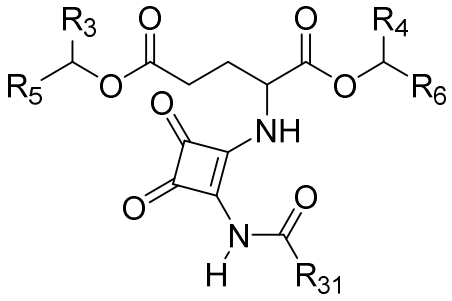
or a pharmaceutically acceptable salt thereof,

wherein

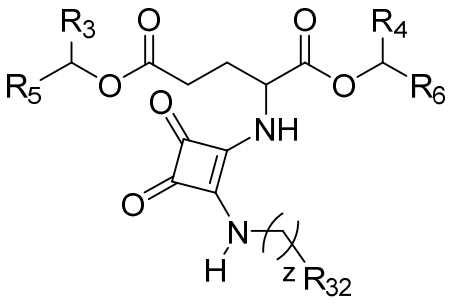
R_{17} is a 5 to 6-membered heteroaryl optionally substituted with a linear C1-C4 alkyl, or a $–(CH_2)_p\text{-}N(CH_3)_2$ and wherein p is from 1 to 3, preferably R_{17} is furanyl, thiophenyl, pyrrolyl, isoxazolyl, oxazolyl, isothiazolyl, thiazolyl, imidazolyl, pyrazolyl, pyrazinyl, pyridinyl, pyridazinyl or pyrimidinyl, optionally substituted with a C1-C2 alkyl, more preferably R_{17} is imidazolyl;

wherein the C=C bonds present in Formula (I1-5d) independently have the E or Z configuration; and wherein R_3, R_4, R_5 and R_6 are as defined in any one of claims 1 to 3; or

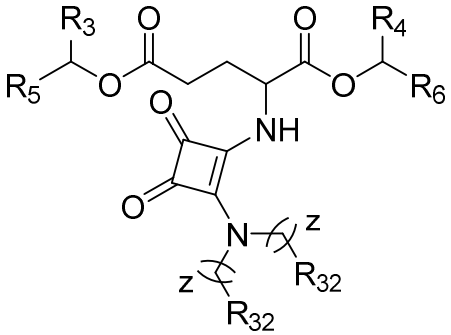
Formula (I1-6a), (I1-6b) or (I1-6c):



(I1-6a)



(I1-6b)



(I1-6c)

or a pharmaceutically acceptable salt thereof,

wherein

R_{31} is a linear C1-C4 alkyl group optionally substituted with -$N(CH_3)_2$; preferably R_{31} is –$(CH_2)_3$-$N(CH_3)_2$;

R_{32} is -$N(CH_3)_2$ or a 5 to 6-membered heterocyclyl optionally substituted with a linear C1-C4 alkyl group, and z is from 1 to 4; preferably R_{32} is -$N(CH_3)_2$, and z is from 2 to 4; more preferably R_{32} is piperazinyl or piperidinyl substituted with a C1-C2 alkyl group, and z is 3; and R_3, R_4, R_5 and R_6 are as defined in any one of claims 1 to 3.

8. A compound selected from the group consisting of Compounds **301**, **302**, **303, 304**, **305**, **306**, **307**, **308**, **309, 310, 311**, **312**, **313**, **314**, **315**, **316**, **317**, **318**, **319**, **320a**, **320b, 321a**, **321b, 322**, **323**, **324**, **325**, **326**, **328**, **329**, **330**, **331**, **332**, **333**, **334**, **335**, **336**, **339**, **340**, **341**, **342**, **343**, **344**, **345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 358, 359, 360** and **362** of Table 1, or a pharmaceutically acceptable salt thereof, wherein the compound or the pharmaceutically acceptable salt thereof is in the form of any enantiomers, any diastereoisomers, any cis or trans geometric isomers, or any mixtures thereof.

9. A lipid nanoparticle comprising at least one compound of any one of claims 1 to 8 or the pharmaceutically acceptable salt thereof.

10. A lipid nanoparticle comprising:

(a) from about 40 to about 100 mol % of an ionizable lipid;

(b) from 0 to about 20 mol % of a neutral lipid;

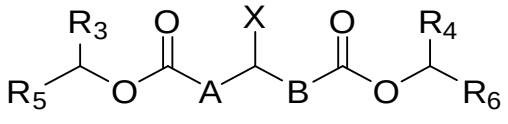
(c) from 0 to about 50 mol % of a helper lipid;

(d) from 0 to about 5 mol % of a polymer-conjugated lipid; and

(e) from 0 to about 10 mol % of a hydrophobic component;

wherein the mol % are based on the total lipids present in the nanoparticle; and

wherein the ionizable lipid is at least one compound of Formula (I):



(I)

or a pharmaceutically acceptable salt thereof,

wherein

A is absent or $-CH_2-$;

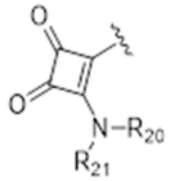
B is $-CH_2-$ or $-CH_2CH_2-$,;

wherein when A is absent then B is $-CH_2CH_2-$ and when A is $-CH_2-$ then B is $-CH_2-$;

X is $-NR_1R_2$ or $-O-(C=O)R_{1'}$;

R_1 is H or an optionally substituted linear C1-C4 alkyl group;

R_2 is H, an optionally substituted linear C1-C8 alkyl group, $-C(=O)R_7$, $-S(=O)_2-R_7$, or



;

$R_{1'}$ is an optionally substituted linear C1-C8 alkyl group;

R_{20} is H or an optionally substituted linear C1-C8 alkyl group;

R_{21} is an optionally substituted linear C1-C8 alkyl group or $–(C=O)-R_{22}$, wherein R_{22} is an optionally substituted C1-C8 alkyl group;

R_3 and R_4 are independently H, a linear or branched C4-C60 alkyl, a linear or branched C4-C60 alkenyl, or a linear or branched C4-C60 alkynyl group, wherein at least one of R_3 or R_4 is different from H;

R_5 and R_6 are independently a linear or branched C4-C60 alkyl, a linear or branched C4-C60 alkenyl, or a linear or branched C4-C60 alkynyl group;

R_7 is an optionally substituted linear C1-C8 alkyl group, an optionally substituted linear C2-C8 alkenyl group, an optionally substituted 5 to 10-membered heterocyclyl or an optionally substituted 5 to 10-membered heteroaryl;

wherein when any of R_3, R_4, R_5 and R_6 represents an alkenyl group, the alkenyl group independently comprises from one to six C=C bonds each independently having the E or Z configuration;

wherein when any of R_3, R_4, R_5 and R_6 represents an alkynyl group, the alkynyl group independently comprises from one to six C≡C bonds;

wherein when R_7 represents an alkenyl group, the alkenyl group comprises from one to two C=C bonds each independently having the E or Z configuration;

wherein when any alkyl and/or alkenyl group is substituted, this group is independently substituted with one or more -OH, -(C=O)-H, -(C=O)-CH_3, -(C=O)-$(CH_2)_pCH_3$, -(C=O)-$(CH_2)_p$-R_{19}, -O-(C=O)-CH_3, -O-(C=O)-$(CH_2)_pCH_3$, -O-(C=O)-$(CH_2)_p$-R_{19}, -(C=O)-OCH_3, -(C=O)-O-$(CH_2)_pCH_3$, -(C=O)-O-$(CH_2)_p$-R_{19}, -(C=O)-$(CH_2)_p$-(C=O)-R_{19}, -(C=O)-O-$(CH_2)_pN(CH_3)$-$(CH_2)_{p'}$-R_{19}, -(C=O)NH-$(CH_2)_p$-R_{19}, -(C=S)-CH_3, -O-CH_3, -O-$(CH_2)_pCH_3$, -NH_2, -$NHCH_3$, -$N(CH_3)_2$, -$N(CH_2CH_3)_2$, -$N(CH_2CH_2OH)_2$, -$N((CH_2)_pO$-(C=O)$CH_3)_2$, -$N(CH_3)$-$(CH_2)_p$-R_{19}, -(C=O)NH_2, -N_3, -NO_2, -SCH_3, -SCH_2CH_3, an optionally substituted 5 to 10-membered heterocyclyl, C5-C12 aralkyl, C5-C10 aryl or an optionally substituted 5 to 10-membered heteroaryl, with p and p' are independently from 1 to 5; and wherein R_{19} is -NH_2, -$NHCH_3$, -$N(CH_3)_2$, -$N(CH_2CH_3)_2$, an optionally substituted 5 to 10-membered heterocyclyl or an optionally substituted 5 to 10-membered heteroaryl;

wherein when any 5 to 10-membered heteroaryl and/or 5 to 10-membered heterocyclyl is substituted, this group is independently substituted with one or more substituents selected from the group consisting of C1-C4 alkyl group, -$(CH_2)_{p''}N(CH_3)_2$ and oxo (=O), with p'' from 1 to 5;

with the provisos that when A is absent, B is -CH_2CH_2-, X is -NR_1R_2, R_1 is -CH_3, and each of R_3, R_4, R_5, and R_6 is linear C18 alkyl groups with one C=C bond between carbons C_9 and C_{10} and one C=C bond between carbons C_{12} and C_{13}, then R_2 is different from -CH_3, -CH_2CH_2OH and -$CH_2CH_2NH_2$; and

wherein the compound or the pharmaceutically acceptable salt thereof is in the form of any enantiomers, any diastereoisomers, any cis or trans geometric isomers, or any mixtures thereof.

11. The lipid nanoparticle according to claim 10, comprising:

(1)

(a) from about 40 to about 85 mol % of the ionizable lipid;

(b) from about 5 to about 10 mol % of the neutral lipid;

(c) from about 1 to about 40 mol % of the helper lipid;

(d) from about 1 to about 4 mol % of the polymer-conjugated lipid; and

(e) from about 0 to about 5 mol % of the hydrophobic component; or

(2)

(a) from about 40 to about 85 mol % of the ionizable lipid;

(b) from about 5 to about 10 mol % of the neutral lipid;

(c) from about 1 to about 40 mol % of the helper lipid;

(d) from about 1 to about 4 mol % of the polymer-conjugated lipid; and

(e) from about 0.1 to about 5 mol % of the hydrophobic component.

12. The lipid nanoparticle according to claim 10 or 11, wherein

(i) the neutral lipid comprises at least one phospholipid selected from the group consisting of dipalmitoylphosphatidylcholine (DPPC), distearoylphosphatidylcholine (DSPC), phosphocholine (DOPC), dimyristoylphosphatidylcholine (DMPC), phosphatidylcholine (PLPC), 1,2-distearoyl-sn-glycero-3-phosphocholine (DAPC), phosphatidylethanolamine (PE), egg phosphatidylcholine (EPC), dilauryloylphosphatidylcholine (DLPC), 1-myristoyl-2-palmitoyl phosphatidylcholine (MPPC), 1-palmitoyl-2-myristoyl phosphatidylcholine (PMPC), 1-palmitoyl-2-stearoyl phosphatidylcholine (PSPC), 1,2-diarachidoyl-sn-glycero-3-phosphocholine (DBPC), 1-stearoyl-2-palmitoyl phosphatidylcholine (SPPC), 1,2-dieicosenoyl-sn-glycero-3-phosphocholine (DEPC), palmitoyloleoyl phosphatidylcholine (POPC), lysophosphatidyl choline, dioleoyl phosphatidylethanolamine (DOPE), dilinoleoylphosphatidylcholine distearoylphophatidylethanolamine (DSPE), dimyristoyl phosphatidylethanolamine (DMPE), dipalmitoyl phosphatidylethanolamine (DPPE), palmitoyloleoyl phosphatidylethanolamine (POPE), lysophosphatidylethanolamine and combinations thereof;

ii) the helper lipid comprises a sterol, an alkyl resorcinol or a combination thereof;

(iii) the polymer-conjugated lipid comprises polyethylene glycol (PEG), polypropylene glycol (PPG), poly(2-oxazoline) (POZ), polyamide (ATTA), cationic polymer, polysarcosine (Psar), polyglutamic acid (PGA), 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol (PEG-DMG), or any combination thereof;

(iv) the hydrophobic component comprises squalene, cardiolipin, α-tocopherol, withaferin A, vitamin A, retinol, β-carotene, or any combination thereof; or

(v) any combination of (i) to (iv).

13. The lipid nanoparticle according to any one of claims 9 to 12, further comprising at least one cargo, the cargo comprising at least one of a small molecule, an antibody, a polynucleotide such as mRNA or a polypeptide, preferably the cargo comprising at least one nucleic acid, such as mRNA.

14. A vaccine comprising the lipid nanoparticle according to any one of claims 9 to 13.

15. A lipid nanoparticle according to any one of claims 9 to 13 for use in:

(i) the treatment of cancer in a subject, wherein the lipid nanoparticle comprises an anti-cancer cargo or a cargo triggering an immune response against cancer cells,

wherein the cancer is preferably a lung cancer, breast cancer, colorectal cancer, ovarian cancer, pancreatic cancer, colorectal cancer, bladder cancer, prostate cancer, cervical cancer, renal cancer, leukemia, central nervous system cancers, myeloma, or melanoma; or

(ii) vaccination of a subject against an infectious agent, wherein the infectious agent is preferably:

(a) a virus, a bacterium, or a parasite; or

(b) campylobacter jejuni, clostridium difficile, entamoeba histolytica, enterotoxin B, Norwalk virus or norovirus, Helicobacter pylori, rotavirus, candida yeast, coronavirus including SARS-CoV, SARS-CoV-2, MERS-CoV, Enterovirus 71, Epstein-Barr virus, Gram-Negative Bacteria including Bordetella, Gram-Positive Bacteria including Clostridium Tetani, Francisella Tularensis, Streptococcus bacteria, Staphylococcus bacteria, Salmonella bacteria, Hepatitis, Human Cytomegalovirus, Human Immunodeficiency Virus, Human Papilloma Virus, Influenza, John Cunningham Virus, Mycobacterium, Poxviruses, Pseudomonas Aeruginosa, Respiratory Syncytial Virus, Rubella virus, Varicella zoster virus, Zika virus, Chikungunya virus, Dengue virus, Rabies virus, Trypanosoma cruzi disease, Chagas disease, Ebola virus, Plasmodium falciparum, Marburg virus, Japanese encephalitis virus, St. Louis encephalitis virus, West Nile Virus, Yellow Fever virus, Bacillus anthracis, Botulinum toxin, Ricin, Nipah, Shiga toxin and/or Shiga-like toxin.