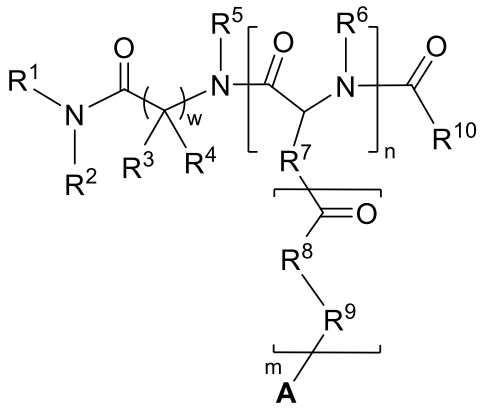
CLAIMS

1. A compound represented by general formula (1) for preparing lipid nanoparticles encapsulating a therapeutic, prophylactic and/or biological agent:



(1)

wherein

A comprises a carbohydrate and/or a derivative thereof;

R^1 and R^2 are each independently a hydrophobic group;

R^3, R^4, R^5, and R^6 are each independently H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

R^7, R^9 and R^{10} are each independently optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

R^8 is –O–, –S–, or $–NR^a–$, where R^a is selected from the group consisting of H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

m is 0 or 1;

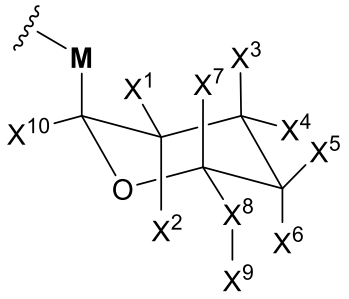
n ≥ 1; and

w ≥ 1,

optionally wherein the compound is capable of targeting carbohydrate receptors on a cell surface.

2. The compound of any one of the preceding claims, wherein **A** comprises a moiety selected from the group consisting of monosaccharide, disaccharide, oligosaccharide, polysaccharide and derivatives thereof.

3. The compound of any one of the preceding claims, wherein **A** is represented by general formula (2) having a 6-membered ring structure:



(2)

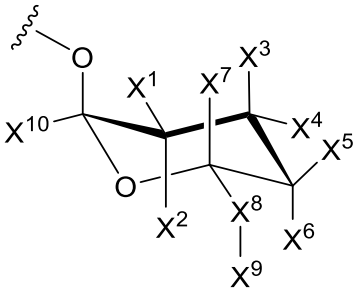
wherein

X^1 to X^7 and X^9 to X^{10} are each independently selected from –H or –OH;

X^8 is alkylene; and

M is –O– or –S–;

optionally wherein **A** is represented by general formula (2A) having a 6-membered ring structure:



(2A)

wherein

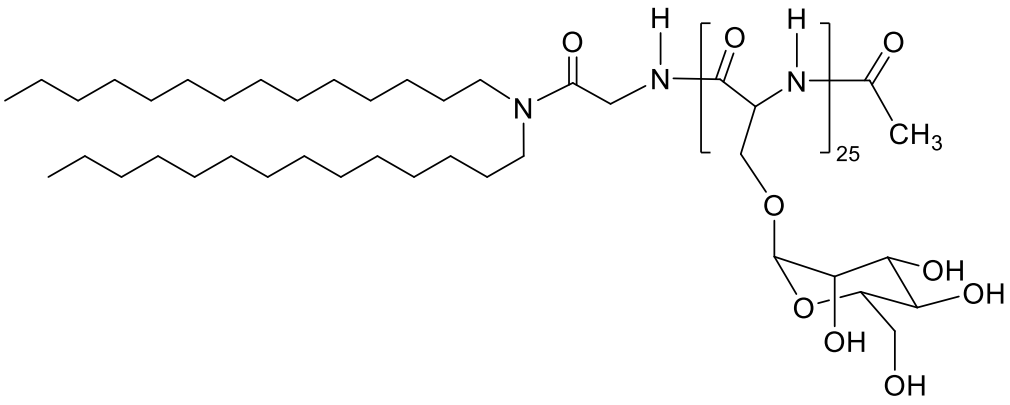
X^1 to X^7 and X^9 to X^{10} are each independently selected from –H or –OH; and

X^8 is alkylene.

4. The compound of any one of the preceding claims, wherein m = 1 and R^7 is $–CH_2CH_2–$;

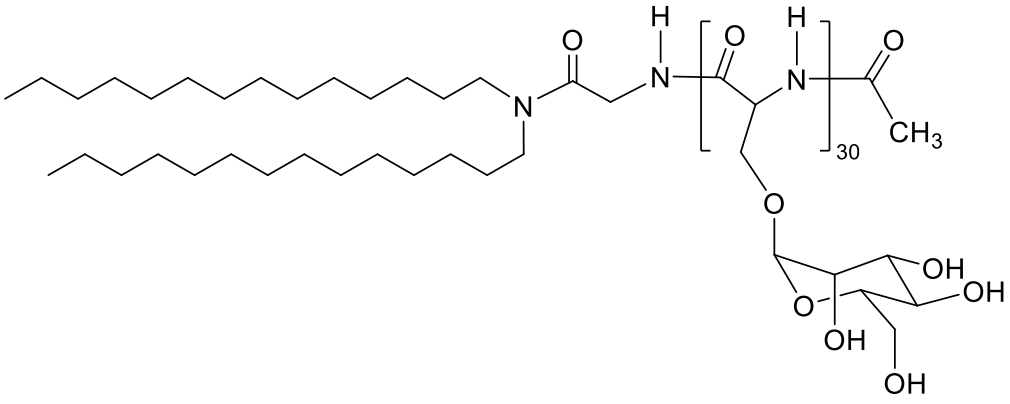
or m = 0 and R^7 is $–CH_2–$.

5. The compound of any one of the preceding claims, wherein the compound comprises a structure selected from one or more of the following:



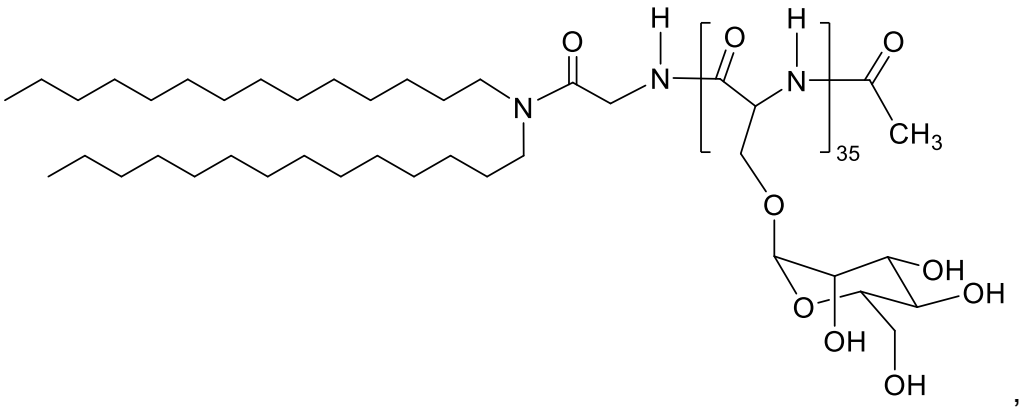
,

LPSM01 (n = 25)



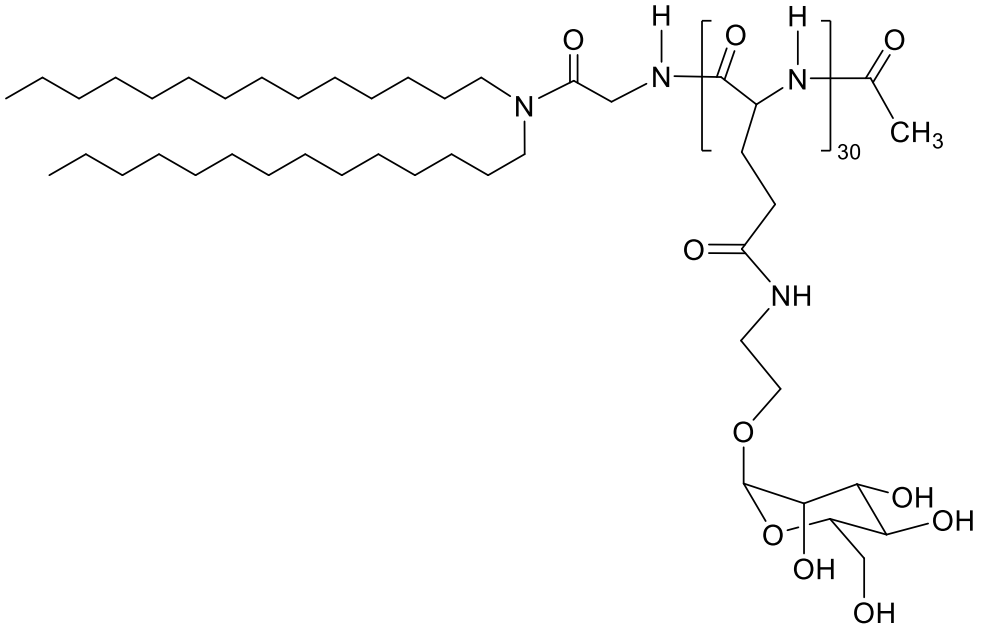
,

LPSM02 (n = 30)



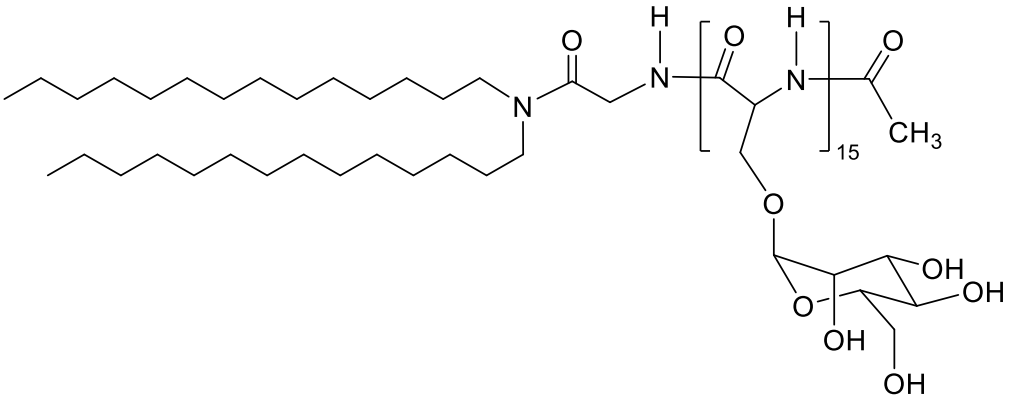
,

LPSM03 (n = 35)



, and

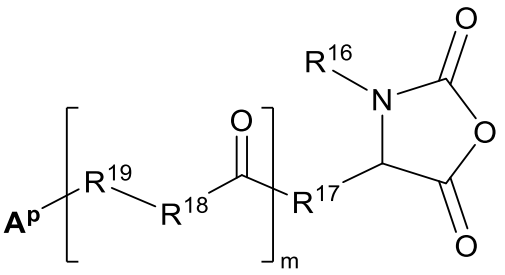
LPGM01 (n = 30)



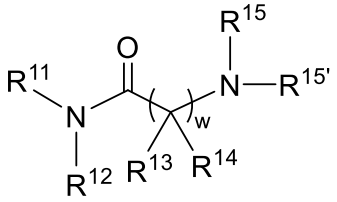
LPSM04 (n = 15)

6. A method of preparing a compound as claimed in any one of the preceding claims, the method comprising:

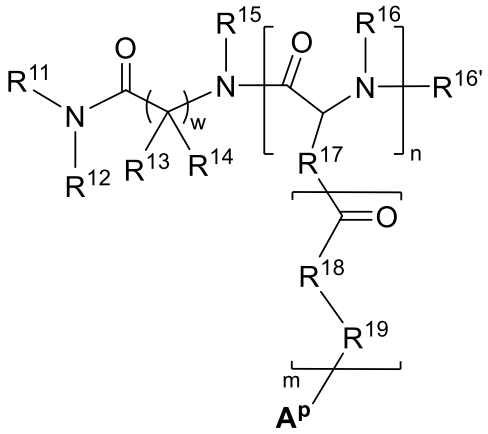
(i) reacting one or more N-carboxyanhydride (NCA) monomers represented by general formula (3) with a lipid initiator represented by general formula (4) to obtain a first intermediate compound represented by general formula (5):



(3)



(4)



(5)

wherein

$\mathbf{A^p}$ represents **A** protected with one or more protecting groups, where **A** comprises a carbohydrate and/or a derivative thereof;

R^{11} and R^{12} are each independently a hydrophobic group;

R^{13}, R^{14}, R^{15}, and R^{16} are each independently H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

R^{17} and R^{19} are each independently optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

R^{18} is –O–, –S–, or –NR^{a1}–, where R^{a1} is selected from the group consisting of H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

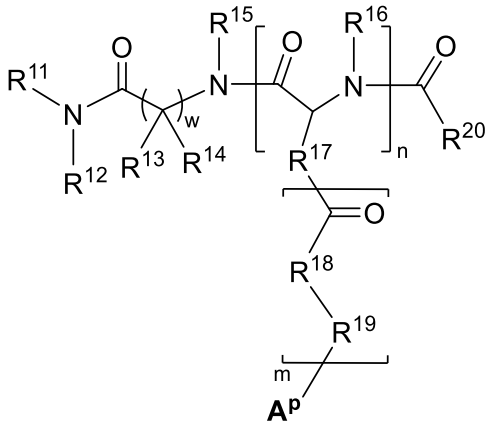
$R^{15'}$ and $R^{16'}$ are each independently H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl; and

m is 0 or 1;

n ≥ 1; and

w ≥ 1;

(ii) reacting the first intermediate compound represented by general formula (5) with an acylating agent to obtain a second intermediate compound represented by general formula (7):



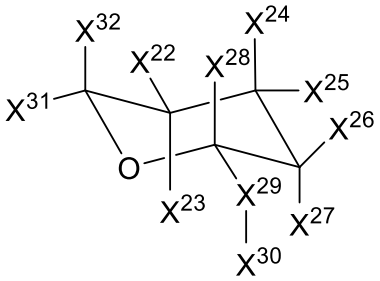
(7)

wherein R^{20} is optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

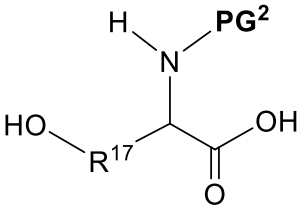
(iii) deprotecting the second intermediate compound represented by general formula (7) to obtain the compound represented by general formula (1).

7. The method of claim 6, wherein the method further comprises, prior to (i):

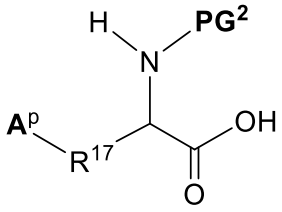
(a-i) reacting a protected monosaccharide represented by general formula (8^{p}) with a protected compound represented by general formula (10) in the presence of a Lewis acid to obtain a first intermediate compound represented by general formula (11):



(8^{p})



(10)



(11)

wherein

X^{22} to X^{28} and X^{30} to X^{32} are each independently selected from –H or –O**PG**^{1};

X^{29} is alkyl;

PG^{1} is –C(=O)–R^{22};

R^{22} is optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

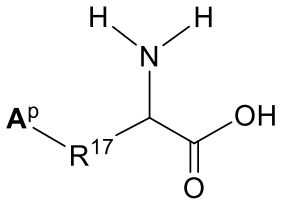
A^{p} represents **A** protected with one or more protecting groups, where **A** comprises a carbohydrate and/or a derivative thereof;

R^{17} is independently optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

PG^{2} is a protecting group selected from 9-Fluorenylmethoxycarbonyl (Fmoc), 2-(4-Nitrophenylsulfonyl)ethoxycarbonyl (Nsc), 2-Fluoro-Fmoc

(Fmoc(2F)), 2-Monoisooctyl-Fmoc (mio-Fmoc), 2,7-Diisooctyl-Fmoc (dio-Fmoc), N-carboxybenzyl (Cbz), or combinations thereof;

(a-ii) deprotecting the first intermediate compound represented by general formula (11) to obtain a second intermediate compound represented by general formula (12):

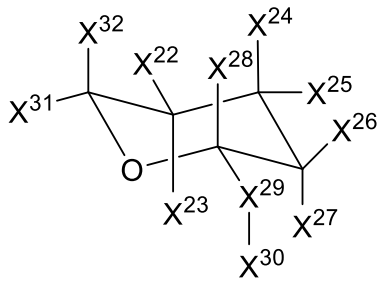


(12)

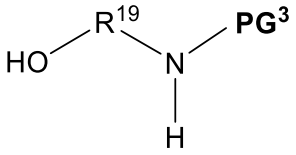
(a-iii) reacting the second intermediate compound represented by general formula (12) with a carbonylating agent to obtain the N-carboxyanhydride (NCA) monomer represented by general formula (3).

8. The method of claim 6, wherein the method further comprises, prior to (i):

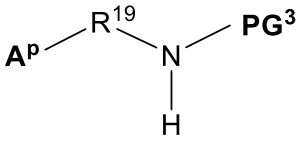
(b-i) optionally reacting a protected monosaccharide represented by general formula (8^{p}) with a protected alkanolamine compound represented by general formula (13) in the presence of a Lewis acid to obtain a first intermediate compound represented by general formula (14):



(8^{p})



(13)



(14)

wherein

X^{22} to X^{28} and X^{30} to X^{32} are each independently selected from –H or –O**PG**^{1};

X^{29} is alkyl;

PG^{1} is –C(=O)–R^{22};

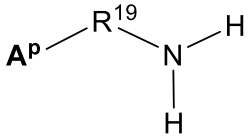
R^{22} is optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

A^{p} represents **A** protected with one or more protecting groups, where **A** comprises a carbohydrate and/or a derivative thereof;

R^{19} is independently optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

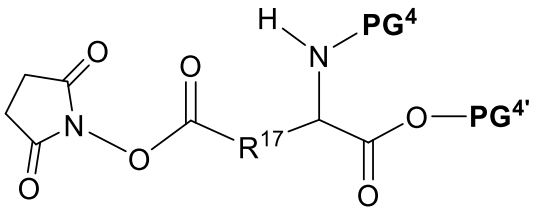
PG^{3} is a protecting group selected from N-carboxybenzyl, benzyloxycarbonyl (Cbz), or combinations thereof;

(b-ii) optionally deprotecting the first intermediate compound represented by general formula (14) to obtain a second intermediate compound represented by general formula (15):

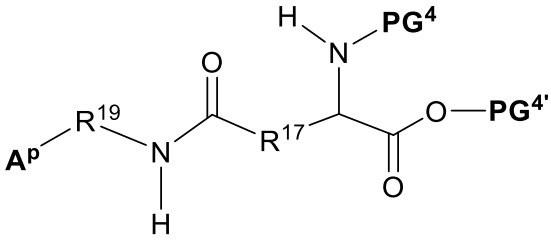


(15)

(b-iii) reacting the second intermediate compound represented by general formula (15) with a protected compound represented by general formula (16) in the presence of a base to obtain a third intermediate compound represented by general formula (17):



(16)



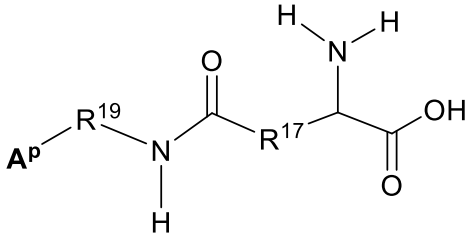
(17)

wherein

R^{17} is independently optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl; and

PG^4 and **PG$^{4'}$** are each independently a protecting group selected from *tert*-butyloxycarbonyl (Boc), *tert*-butyl, benzyloxycarbonyl protecting group (Cbz), or combinations thereof;

(b-iv) deprotecting the third intermediate compound represented by general formula (17) to obtain a fourth intermediate compound represented by general formula (18):



(18)

(b-v) reacting the fourth intermediate compound represented by general formula (18) with a carbonylating agent to obtain the N-carboxyanhydride (NCA) monomer represented by general formula (3).

9. A nanoparticle composition for delivery of a therapeutic, prophylactic and/or biological agent, the nanoparticle composition comprising:

a compound as claimed in any one of claims 1 to 5; and

a therapeutic, prophylactic and/or biological agent.

10. The nanoparticle composition of claim 9, wherein the composition further comprises:

(a) ionizable lipid;

(b) helper lipid; and

(c) cholesterol and/or derivatives thereof.

11. The nanoparticle composition of claim 10, wherein the ionizable lipid, helper lipid, cholesterol and/or derivatives thereof, and compound represented by general formula (1) are mixed at a mole ratio of 20 – 50 : 4 – 20 : 25 – 50 : 0.5 – 20;

optionally wherein the ionizable lipid is selected from ALC-0315, SM-102, Lipid 5, DLinDMA, D-Lin-MC2-DMA, DLin-MC3-DMA, D-Lin-MC4-DMA, Dlin-KC2-DMA, YSK05, AA3-Dlin, SSPalmM, SSPalmO-Phe, Lipid A9, L319, DODMA, CL1, BP Lipid 310, ATX-001, ATX-100, Lipid 2, 80-O16B, BP Lipid 309, BP Lipid 307, 93-O17S, 93-O17O, NT1-O14B, 306-O12B-3, 306-O12B, 113-O16B, 306Oi10, 306Oi9-cis2, BAMEA-O16B, Al-28, 113-O12B, 98N12-5, Ckk-E12, OF-02, C12-200, BP Lipid 311, BP Lipid 308, BP Lipid 314, BP Lipid 312, LP01, TCL053, Lipid C24, BP Lipid 315, Lipid 29, 9A1P9, C13-112-tri-tail, C13-113-tri-tail, C13-112-tetra-tail, or C13-113-tetra-tail, C12-200 or combinations thereof;

optionally wherein the helper lipid is selected from 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE), 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-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-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 or combinations thereof; and

optionally wherein the cholesterol and/or derivatives thereof is selected from cholesterol, fecosterol, sitosterol, ergosterol, campesterol, stigmasterol, brassicasterol, avenasterol or combinations thereof.

12. The nanoparticle composition of any one of claims 9 to 11, wherein the nanoparticle composition comprises nanoparticles having a N/P ratio from 1:1 to 20:1;

and/or the nanoparticle composition comprises nanoparticles having an average particle size of from 40 nm to 500 nm;

and/or the nanoparticle composition comprises nanoparticles having a zeta potential of from -20 mV to +20 mV.

13. The nanoparticle composition as claimed in any one of claims 9 to 12 for use in medicine.

14. The nanoparticle composition as claimed in any one of claims 9 to 12 for use in the treatment or prophylaxis of a disease, disorder or condition in a subject in need thereof;

optionally wherein an immune response in the subject is to be induced through the administration of the nanoparticle composition thereto;

optionally wherein the disease, disorder or condition is mediated by a coronavirus; and

optionally wherein the coronavirus is a SARS-CoV-2 coronavirus.

15. Use of a nanoparticle composition as claimed in any one of claims 9 to 12 in the manufacture of a medicament for inducing an immune response in a subject;

optionally wherein the immune response is against a coronavirus; and

optionally wherein the coronavirus is a SARS-CoV-2 coronavirus.