Claims

1. A pharmaceutical composition comprising or consisting of
   - at least one component A comprising at least one mRNA comprising at least one coding sequence encoding at least one antigenic peptide or protein selected or derived from a SARS-CoV-2 virus, wherein the at least one antigenic peptide or protein is a SARS-CoV-2 spike protein comprising or consisting of at least one amino acid sequence being identical or at least 90% identical to SEQ ID NO: 10, wherein the SARS-CoV-2 spike protein comprises a pre-fusion stabilizing K986P and V987P mutation, and
   - at least one component B comprising a plurality of mRNAs, wherein the plurality of mRNAs encodes at least one, preferably 2, 3, 4, 5, 6 antigenic peptide or protein selected or derived from HA and at least one, preferably 2, 3, 4, 5, 6 antigenic peptide or protein selected or derived from NA of at least one Influenza A virus and at least one Influenza B virus,

   wherein the at least one mRNA of component A and/or the plurality of mRNAs of component B is/are complexed or associated with one or more lipids, thereby forming lipid nanoparticles (LNPs).

2. Pharmaceutical composition of claim 1, wherein the SARS-CoV-2 spike protein comprises the amino acid substitution D614G.

3. Pharmaceutical composition of claims 2 to 5,
   wherein the at least one mRNA of component A comprises or consists of a nucleic acid sequence encoding a SARS-CoV-2 antigen which is identical or at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence selected from SEQ ID NOs: 149, 163, 24837, 26633, 26907.

4. Pharmaceutical composition of any one claims 1 to 3, wherein at least one Influenza virus is selected from Influenza A, Influenza B or Influenza C, *preferably* wherein the at least one Influenza virus is selected from at least one Influenza A virus and/or at least one Influenza B virus.

5. Pharmaceutical composition of claim 4, wherein the at least one Influenza virus is selected from at least one Influenza A virus selected from at least one of the list comprising H1 N1, H1 N2, H2N2, H3N1, H3N2,H3N8,H5N1,H5N2,H5N3,H5N8,H5N9,H7N1,H7N2, H7N3, H7N4, H7N7, H7N9,H9N2,H10N7 and H10N8, *preferably* from at least one of H1 N1, H3N2, H5N1, H5N8.

6. Pharmaceutical composition of claim 4 or 5, wherein the at least one antigenic peptide or protein selected or derived from at least one Influenza virus encoded by the at least one mRNA of component B comprises or consists of at least one of the amino acid sequences being identical or at least 90%, 91 %, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 14178-14229,

and/or

wherein the at least one coding sequence of the at least one mRNA of component B comprises or consists at least one nucleic acid sequence encoding an Influenza virus antigen being identical or at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of the nucleic acid sequences selected from SEQ ID NOs: 14230-14333, 14334-14541, 26946, 26947-26955, preferably
wherein the at least one mRNA of component B comprises or consists of a nucleic acid sequence encoding an Influenza virus antigen which is identical or at least 90%, 91 %, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence selected from SEQ ID NOs: 14334-14541, 26947-26955.

7. Pharmaceutical composition of any one of claims 4 to 6, wherein component B comprises a plurality of mRNA sequences encoding an Influenza virus antigen, *preferably* 2, 3, 4, 5, 6, 7, 6, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, or 100 of nucleic acid sequences encoding an Influenza virus antigen.

8. Pharmaceutical composition of any one of claims 4 to 7, wherein component B comprises a plurality of mRNA sequences encoding an Influenza virus antigen, wherein the Influenza virus is selected from the list comprising FLUAV/H 1 N1/A/California/7 /2009, FLUAV/H 1 N1/A/Michigan/45/2015, FLUAV/H1 N1/A/Netherlands/602/2009, FLUAV/H3N2/A/Hong Kong/4801/2014, FLUBV/HONO/B/Brisbane/60/2008, FLUBV/HONO/B/Phuket/3073/2013

or

wherein component B comprises a plurality of mRNA sequences, *preferably* seven mRNA sequences, encoding a plurality of Influenza virus antigens, *preferably* seven Influenza virus antigens, wherein the influenza virus antigens are selected from

- HA protein of FLUAV/H3N2/A/Hong Kong/4801/2014,
- HA protein of FLUAV/H1 N1/A/California/7/2009,
- HA protein of FLUBV/HONO/B/Phuket/3073/2013,
- HA protein of FLUBV/HONO/B/Brisbane/60/2008,
- NA protein of FLUAV/H3N2/A/Hong Kong/4801/2014,

- NA protein of FLUAV/H1 N1/A/California/7/2009, and
- NA protein of FLUBV/HONO/B/Brisbane/60/2008.

9. Pharmaceutical composition of any one of the preceding claims, wherein the at least one coding sequence of the mRNA of component A and/or the at least one coding sequence of the mRNA of component B is a codon modified coding sequence, *preferably* wherein the amino acid sequence encoded by the at least one codon modified coding sequence is not being modified compared to the amino acid sequence encoded by the corresponding wild type or reference coding sequence,

   wherein (i) the at least one codon modified coding sequence is preferably selected from C maximized coding sequence, CAI maximized coding sequence, human codon usage adapted coding sequence, G/C content modified coding sequence, and G/C optimized coding sequence, or any combination thereof

   and/or

   wherein (ii) the at least one codon modified coding sequence is preferably a G/C optimized coding sequence, a human codon usage adapted coding sequence, or a G/C content modified coding sequence

10. Pharmaceutical composition of any one of the preceding claims, wherein (iii) the at least one coding sequence of component A and/or the at least one mRNA of component B has a G/C content of at least about 50%, 55%, or 60%.

11. Pharmaceutical composition of any one of the preceding claims, wherein the at least one mRNA of component A and/or the at least one mRNA of component B comprises at least one heterologous untranslated region selected from at least one heterologous 5'-UTR and/or at least one heterologous 3'UTR.

12. Pharmaceutical composition of claim 11, wherein the at least one heterologous 3'-UTR comprises or consists a nucleic acid sequence derived from a 3'-UTR of a gene selected from PSMB3, ALB?, alphaglobin, CASP1, COX6B1, GNAS, NDUFA 1 and RPS9, or from a homolog, a fragment or a variant of any one of these genes

    and/or

    wherein the at least one heterologous 5'-UTR comprises or consists of a nucleic acid sequence derived from a 5'-UTR of a gene selected from HSD17B4, RPL32, ASAH1,

ATP5A1, MP68, NDUFA4, NOSIP, RPL31, SLC7A3, TUBB4B and UBQLN2, or from a homolog, a fragment or variant of any one of these genes.

13. Pharmaceutical composition of any one of the preceding claims, wherein the mRNA of component A and/or component B comprises at least one coding sequence operably linked to

- an alpha-globin 3'-UTR; or
- a HSD17B4 5'-UTR and a PSMB3 3'-UTR (HSD17B4/PSMB3); or
- a SLC7A3 5'-UTR and a PSMB3 3'-UTR (SLC7A3/PSMB3); or
- a RPL31 5'-UTR and a RPS9 3'-UTR (RPL31/RPS9)

and/or

wherein the mRNA of component A and/or component B comprises at least one coding sequence operably linked to a HSD1784 5'-UTR and a PSMB3 3'-UTR (HSD17B4/PSMB3).

14. Pharmaceutical composition of any one of the preceding claims, wherein the at least one mRNA of component A and/or the at least one mRNA of component B comprises at least one poly(A) sequence, *preferably* comprising 30 to 200 adenosine nucleotides, *optionally* wherein the at least one mRNA of component A and/or the at least one mRNA of component B comprises at least one poly(C) sequence, *preferably* comprising 10 to 40 cytosine nucleotides and/or

wherein the at least one mRNA of component A and/or the at least one mRNA of component B comprises at least one histone stem-loop or histone stem-loop structure.

15. Pharmaceutical composition of any one of the preceding claims, wherein the at least one mRNA of component A and/or the at least one mRNA of component B is a purified mRNA

and/or

wherein the at least one mRNA of component A and/or the at least one mRNA of component B is an RNA, wherein the RNA has an RNA integrity of at least about 50%, preferably of at least about 60%, more preferably of at least about 70%, most preferably of at least about 80%.

16. Pharmaceutical composition of any one of the preceding claims, wherein the at least one mRNA of component A and/or the at least one mRNA of component B comprises a 5'-cap structure, *preferably* m7G, cap0, cap1, cap2, a modified capo or a modified cap1 structure.

17. Pharmaceutical composition of any one of the preceding claims, wherein the at least one mRNA of component A and/or the at least one mRNA of component B comprises at least one modified nucleotide,

    wherein the at least one mRNA of component A and/or the at least one mRNA of component B preferably comprises at least one modified nucleotide selected from pseudouridine (Ψ) and N1-methylpseudouridine (m1Ψ), *optionally* wherein all uracil nucleotides are replaced by pseudouridine (Ψ) nucleotides and/or N1-methylpseudouridine (m1Ψ) nucleotides.

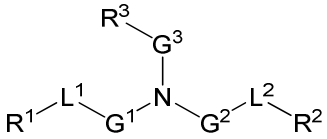
18. Pharmaceutical composition of any one of the preceding claims, comprising at least one pharmaceutically acceptable carrier.

19. Pharmaceutical composition of any one of the preceding claims, wherein the at least one mRNA of component A and/or the at least one mRNA of component B are formulated separately, *preferably* wherein the at least one mRNA component A and/or the at least mRNA acid component B are formulated in separate lipid nanoparticles (LNP).

    and/or

    wherein the at least one mRNA of component A and/or the at least one mRNA of component B are co-formulated, *preferably* wherein the at least one mRNA of component A and/or the at least one mRNA of component B are co-formulated in lipid nanoparticles (LNP).

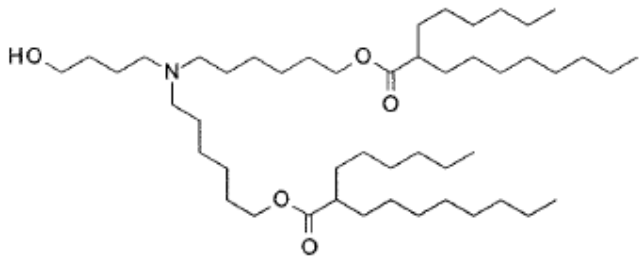
20. Pharmaceutical composition of any one of the preceding claims, wherein the LNP comprises at least one cationic lipid according to formula III:



or a pharmaceutically acceptable salt, tautomer, prodrug or stereoisomer thereof, wherein:
L1 or L2 is each independently -O(C=O)-, -(C=O)O-, -C(=O)-, -O-, -S(O)x-, -S-S-, -C(=O)S-, -SC(=O)-, -NRaC(=O)-, -C(=O)NRa-, -NRaC(=O)NRa-, -OC(=O)NRa- or -NRaC(=O)O-, preferably L1 or L2 is -O(C=O)- or -(C=O)O-;
G1 and G2 are each independently unsubstituted C1-C12 alkylene or C1-C12 alkenylene;
G3 is C1-C24 alkylene, C1-C24 alkenylene, C3-C8 cycloalkylene, or C3-C8 cycloalkenylene;
Ra is H or C1-C12 alkyl;

R1 and R2 are each independently C6-C24 alkyl or C6-C24 alkenyl;
R3 is H, OR5, CN, -C(=O)OR4, -OC(=O)R4 or -NR5C(=O)R4;
R4 is C1-C12 alkyl;
R5 is H or C1-C6 alkyl; and
x is 0, 1 or 2.

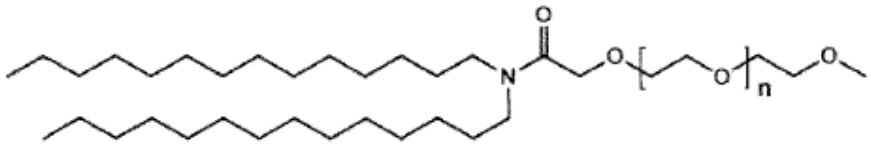
21. Pharmaceutical composition of any one of the preceding claims, wherein the lipid nanoparticles (LNP) comprises at least one cationic lipid, *preferably* a cationic lipid according to formula III-3:



(III-3)

and/or

(1) wherein the lipid nanoparticles (LNP) comprises at least one polymer conjugated lipid, *preferably* a PEG lipid, *preferably* a PEG-lipid according to formula (IVa):

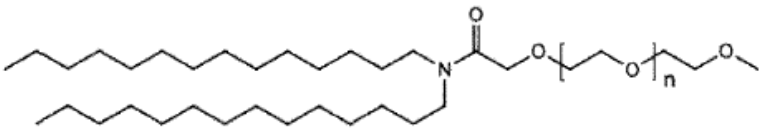


(IVa)

wherein n has a mean value ranging from 30 to 60, *preferably* wherein n has a mean value of about 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, *most preferably* wherein n has a mean value of 49 or 45

or

(2) wherein the lipid nanoparticles (LNP) comprises at least one polymer conjugated lipid, *preferably* a PEG lipid, *preferably* a PEG-lipid according to formula (IVa):



(IVa)

wherein n is an integer selected such that the average molecular weight of the PEG lipid is about 2000g/mol to about 3000g/mol or about 2300g/mol to about 2700g/mol, preferably about 2500g/mol.

22. Pharmaceutical composition of any one of the preceding claims, wherein the lipid nanoparticles (LNP) comprise one or more neutral lipids and/or one or more steroid or steroid analogues,

wherein the neutral lipid is preferably 1,2-distearoyl-sn-glycero-3 phosphocholine (DSPC), *more preferably* wherein the molar ratio of the cationic lipid to DSPC is in the range from about 2: 1 to about 8:1

and/or

wherein the steroid is preferably cholesterol, *more preferably* wherein the molar ratio of the cationic lipid to cholesterol is in the range from about 2:1 to about 1:1

23. Pharmaceutical composition of any one of the preceding claims, wherein the lipid nanoparticle (LNP) comprises or consists of

(i) at least one cationic lipid, *preferably* at least one cationic lipid as defined in claim 21;
(ii) a neutral lipid, *preferably* a neutral lipid as defined in claim 22;
(iii) a steroid or steroid analogue, *preferably* a steroid or steroid analogue as defined in claim 22; and
(iv) polymer conjugated lipid, *preferably* a PEG-lipid, e.g. PEG-DMG or PEG-cDMA, *preferably* a PEG-lipid as defined in claim 21 (1) or (2),

wherein (i) to (iv) are preferably in a molar ratio of about 20-60% cationic lipid, 5-25% neutral lipid, 25-55% sterol, and 0.5-15% polymer-conjugated lipid, *preferably* PEG-lipid

and/or

wherein (i) to (iv) are preferably in a molar ratio of about 50:10:38.5:1.5, preferably 47.5:10:40.8:1.7 or more preferably 47.4:10:40.9:1.7.

24. Pharmaceutical composition of any of the preceding claims, wherein the wt/wt ratio of lipid to mRNA is from about 10:1 to about 60:1, preferably from about 20:1 to about 30:1, for example about 25:1

and/or

wherein the n/p ratio of the lipid nanoparticle (LNP) encapsulating the mRNA is in a range from about 1 to about 10, preferably in a range from about 5 to about 7, more preferably about 6

and/or

wherein the composition has a polydispersity index (POI) value of less than about 0.4, preferably of less than about 0.3, more preferably of less than about 0.2, most preferably of less than about 0.1

and/or

wherein the LNPs have a Z-average size in a range of about 60nm to about 120nm, preferably less than about 120nm

and/or

wherein the composition comprises less than about 20% free (non complexed) RNA, preferably less than about 15% free (non complexed) RNA, more preferably less than about 10% free (non complexed) RNA.

25. Pharmaceutical composition of any one of the preceding claims, wherein the composition is a lyophilized composition, a spray-dried composition, or a spray-freeze dried composition, *optionally* comprising at least one pharmaceutically acceptable lyoprotectant,

wherein the lyophilized or spray-dried composition preferably has a water content of less than about 10%, *preferably* a water content of between about 0.5% and 5%.

26. Pharmaceutical composition of any one of the preceding claims, wherein when administered to a subject, the at least one mRNA of component A and the at least one mRNA of component B are translated into an antigenic peptide or protein suitable for inducing an immune response.

27. Pharmaceutical composition of any one of the preceding claims, wherein when administered to a subject, an antigen-specific humeral immune responses against the peptide or protein encoded by component A and an antigen-specific humoral immune responses against the peptide or protein encoded by component B is induced in said subject.

28. Pharmaceutical composition of any one of the preceding claims, wherein when administered to a subject, an antigen-specific T-cell responses against the peptide or protein encoded by component A and an antigen-specific T-cell responses against the peptide or protein encoded by component B is induced in said subject.

29. Pharmaceutical composition of any one of the preceding claims, wherein upon administration to a subject, an antigen-specific B-cell memory against the peptide or protein encoded by component A and an antigen-specific B-cell memory against the peptide or protein encoded by component B is established in said subject.

30. A combination vaccine comprising at least one component A and at least one component B as defined in claims 1 to 29,

    wherein the combination vaccine is preferably against at least one SARS-CoV-2, at least one influenza virus, at least one RSV virus, and, optionally, against at least one PIV and/or at least one hMPV.

31. A Kit or kit of parts, comprising at least one pharmaceutical composition of claims 1 to 29, and/or at least one combination vaccine of claim 30, *optionally* comprising at least one liquid vehicle for solubilising, and, *optionally,* technical instructions providing information on administration and dosage of the kit components.

32. Pharmaceutical composition of claims 1 to 29, combination vaccine of claim 30, kit or kit of parts of claim 31, for use as a medicament,

    preferably for use in the treatment or prophylaxis of an infection with SARS-CoV-2, and at least one influenza virus, or of a disorder caused by such an infection

    or

preferably for use in the treatment or prophylaxis of an infection with at least one coronavirus, *preferably* SARS-CoV-2, at least one RSV, and at least one influenza virus, or a disorder caused by such an infection,

for use in treating or preventing a disorder caused by such an infection, wherein the subject in need is a mammalian subject, *preferably* a human subject, *more preferably* an elderly human subject,

or

for use in treating or preventing a disorder caused by an infection with SARS-CoV-2 and at least one influenza virus, wherein the use prevents moderate and severe COVID-19 disease in at least 80%, 85%, 90% or 95% of treated subjects from about 2 weeks to about 3 month, 6 months, 9 months, 1 year, 1.5 years, 2 years or 3 years after said administration and prevents at least one further disease associated with a Coronavirus infection, or an Influenza virus infection.

33. Pharmaceutical composition of claims 1 to 29, combination vaccine of claim 30, kit or kit of parts of claim 31 for use as a medicament in treating or preventing a disorder caused by such an infection, wherein the subject is to be administered a single dose that comprises between about 5µg and about 50µg of RNA

or

for use in treating or preventing a disorder of caused by such an infection, wherein the subject is to be administered a two doses that comprise between about 5µg and about 50µg of RNA.

34. A method of stabilizing a pharmaceutical composition of claims 1 to 29 or a combination vaccine of claim 30 comprising lyophilizing the composition or vaccine to produce a stabilized composition or vaccine,

wherein the stabilized composition or vaccine has preferably a water content of less than about 10%, preferably a water content of between about 0.5% and 5.0%.