~~Claims~~CLAIMS

1. A ~~nucleic acid~~purified mRNA comprising ~~at least one coding sequence encoding at least one antigenic peptide or protein that is from or is derived from~~ :

(a ~~SARS-CoV-2 coronavirus, or an immunogenic fragment or immunogenic variant thereof, wherein the nucleic acid comprises at least one~~) a 5' cap structure;

(b) a heterologous 5' untranslated region (UTR~~).~~);

~~2. Nucleic acid of claim 1, wherein the nucleic acid is suitable for a vaccine.~~

~~3. Nucleic acid of claim 1 or 2, wherein the at least one antigenic peptide or protein comprises or consists of at least one peptide or protein that is or is derived from a structural protein, an accessory protein, or~~(c) a ~~replicase protein, or an immunogenic fragment or immunogenic variant of any of these.~~

~~4. Nucleic acid of claim 3, wherein the structural protein is or is derived from a~~ coding sequence encoding a SARS-CoV-2 spike protein (S~~), an envelope protein (E), a membrane protein (M) or a nucleocapsid protein (N), or an immunogenic fragment or immunogenic variant of any of these.~~

~~5. Nucleic acid of any one of claims 1 to 4, wherein the at least one antigenic peptide or protein is or is derived from a spike protein (S), or an immunogenic fragment or immunogenic variant thereof.~~

~~6. Nucleic acid of any of the preceding claims, wherein the at least one antigenic peptide or protein comprises or consists of at least one of the amino acid sequences being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%,~~) at least 95~~%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 1-111, 274-11663, 13176-13510, 13521-14123, 22732-22758, 22917, 22923, 22929-22964, 26938, 26939or an immunogenic fragment or immunogenic variant of any of these.~~

~~7. Nucleic acid of any one of claims 4 to 6, wherein the spike protein (S) comprises or consists of spike protein fragment S1, or an immunogenic fragment or immunogenic variant thereof.~~

~~8. Nucleic acid of any one of the preceding claims, wherein the at least one antigenic peptide or protein comprises or consists of at least one of the amino acid sequences being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 1-27, 29, 31-48, 58-111, 274-1345, 1480-1546, 1614-11663, 13377-13510, 13521-14123, 22732, 22737-22758, 22929-22964or an immunogenic fragment or immunogenic variant of any of these.~~

~~9. Nucleic acid of any one of the preceding claims, wherein the at least one antigenic peptide or protein comprises or consists of at least one of the amino acid sequences being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 27, 1279-1345, 29, 1480-1546, 13243-13309, 22733-22736, 26938, 26939or an immunogenic fragment or immunogenic variant of any of these.~~

~~10. Nucleic acid of any one of claims 4 to 9, wherein the spike protein (S) comprises or consists of a spike protein fragment S1 or an immunogenic fragment or immunogenic variant thereof, and spike protein fragment S2 or an immunogenic fragment or immunogenic variant thereof.~~

~~11. Nucleic acid of any one of the preceding claims, wherein the at least one antigenic peptide or protein comprises or consists of at least one of the amino acid sequences being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 1-26, 31-48, 58-111, 274-1278, 1614-11663, 13377-13510, 13521-14177, 22732, 22737-22758, 22929-22964 or an immunogenic fragment or immunogenic variant of any of these.~~

~~12. Nucleic acid of any one of claims 4 to 11, wherein the spike protein (S) is~~ % identical to SEQ ID NO: 10 that is a pre-fusion stabilized spike protein (S_stab) comprising ~~at least one pre-fusion stabilizing mutation.~~

~~13. Nucleic acid of claim 12, wherein the at least one pre-fusion stabilizing mutation comprises the following amino acid substitutions:~~ K986P and V987P~~.~~

~~14. Nucleic acid of claim 12 or 13, wherein the at least one pre-fusion stabilizing mutation comprises a cavity filling mutation.~~

~~15. Nucleic acid of claim 14, wherein the at least one cavity filling mutation is selected from the list~~ stabilizing substitutions and further comprising ~~T887W; A1020W; T887W and A1020W; or P1069F.~~a D614G amino acid substitution relative to SEQ ID NO: 10; and

~~16. Nucleic acid of any one of claims 12 to 15,~~ (d) a heterologous 3' UTR,

wherein the ~~at least one pre-fusion stabilizing mutation~~mRNA optionally comprises a ~~mutated protonation site.~~ nucleotide substitution at one or more uracil position(s) selected from a 1-methylpseudouridine or a pseudouridine substitution.

~~17. Nucleic acid of claim 16, wherein the at least one mutated protonation site is selected from the list comprising H1048Q and H1064N; H1083N and H1101N; or H1048Q and H1064N and H1083N and H1101N.~~

~~18. Nucleic acid of any one of claims 12 to 17, wherein the at least one pre-fusion stabilizing mutation generates at least one artificial intramolecular disulfide bond.~~

~~19. Nucleic acid of claim 18, wherein the at least one artificial intramolecular disulfide bond is generated by the following amino acid substitutions: I712C and T1077C; I714C and Y1110C; P715C and P1069C; G889C and L1034C; I909C and Y1047C; Q965C and S1003C; F970C and G999C; A972C and R995C; A890C and V1040C; T874C and S1055C, or N914C and S1123C.~~

~~20. Nucleic acid of any one of the preceding claims, wherein the at least one antigenic peptide or protein comprises or consists of at least one of the amino acid sequences being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 10-26, 40-48, 85-111, 341-1278, 1681-2618, 2686-3623, 3691-4628, 4696-5633, 5701-6638, 6706-7643, 7711-8648, 8716-9653, 9721-10658, 10726-11663, 13377-13510, 13521-14123, 22732, 22738, 22740,~~

~~22742, 22744, 22746, 22748, 22750, 22752, 22754, 22756, 22758, 22947-22964or an immunogenic fragment or immunogenic variant of any of these.~~

~~21. Nucleic acid of any one of the preceding claims, wherein the at least one antigenic peptide or protein comprises or consists of at least one of the amino acid sequences being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 10-26, 341-407, 609-1278, 13521-13587, 22738, 22740, 22742, 22744, 22746, 22748, 22750, 22752, 22754, 22756, 22758, 22947-22964or an immunogenic fragment or immunogenic variant of any of these.~~

~~22. Nucleic acid of any one of the preceding claims, wherein the at least one coding sequence additionally encodes one or more heterologous peptide or protein elements selected from a signal peptide, a linker, a helper epitope, an antigen clustering element, a trimerization element, a transmembrane element, and/or a VLP-forming sequence.~~

~~23. Nucleic acid of claim 22, wherein the at least one heterologous peptide or protein element is a heterologous antigen-clustering element, a heterologous trimerization element, and/or a VLP-forming sequence.~~

~~24. Nucleic acid of claim 22 or 23, wherein the at least one heterologous antigen clustering element is selected from a ferritin element, a lumazine synthase element, a surface antigen of Hepatitis B virus (HBsAg), or encapsulin.~~

~~25. Nucleic acid of any one of the preceding claims, wherein the at least one antigenic peptide or protein comprises or consists of at least one of the amino acid sequences being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 58-75, 85-102, 3624-5633, 7644-9653, 13588-13721, 13856-13989, 22733, 22735, 22736 or an immunogenic fragment or immunogenic variant of any of these.~~

~~26. Nucleic acid of claim 22 or 23, wherein the at least one heterologous trimerization element is a foldon element, preferably a fibritin foldon element.~~

~~27. Nucleic acid of any one of the preceding claims, wherein the at least one antigenic peptide or protein comprises or consists of at least one of the amino acid sequences being identical~~

~~or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 76-84, 103-111, 5634-6638, 9654-10658, 13722-13788, 13990-14056, 22734, 26938, 26939 or an immunogenic fragment or immunogenic variant of any of these.~~

~~28. Nucleic acid of claim 22 or 23, wherein the at least one VLP-forming sequence is a Woodchuck hepatitis core antigen element (WhcAg).~~

~~29. Nucleic acid of any one of the preceding claims, wherein the at least one antigenic peptide or protein comprises or consists of at least one of the amino acid sequences being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 6639-7643, 10659-11663, 13789-13855, 14057-14123 or an immunogenic fragment or immunogenic variant of any of these.~~

~~30. Nucleic acid of any one of the preceding claims, wherein the at least one antigenic peptide or protein comprises or consists of at least one of the amino acid sequences being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 1, 10, 21, 22, 25, 27, 274, 341, 408, 475, 542, 743, 810, 1011, 1145, 1212, 1279, 8716, 10726, 22732-22758, 22929-22942, 22947-22964 or an immunogenic fragment or immunogenic variant of any of these.~~

~~31. Nucleic acid of any one of the preceding claims, wherein the at least one antigenic peptide or protein comprises or consists of at least one of the amino acid sequences being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 10, 22960, 22961 or 22963 or an immunogenic fragment or immunogenic variant of any of these.~~

~~32. Nucleic acid of any one of the preceding claims, wherein the at least one coding sequence comprises or consists of at least one nucleic acid sequence being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 116-132, 134-138, 140-143, 145-175, 11664-11813, 11815, 11817-12050, 12052, 12054-13147, 13514, 13515, 13519, 13520, 14124-14177, 22759, 22764-22786, 22791-22813, 22818-22839, 22969-23184, 23189-23404, 23409-23624, 23629-23844, 23849-24064, 24069-24284, 24289-24504, 24509-24724,~~

~~24729-24944, 24949-25164, 25169-25384, 25389-25604, 25609-25824, 25829-26044, 26049-26264, 26269-26484, 26489-26704, 26709-26937 or a fragment or variant of any of these sequences.~~

~~33. Nucleic acid of any one of the preceding claims, wherein the at least one antigenic peptide or protein is an S protein comprising a pre-fusion stabilizing K986P and V987P mutation comprising or consisting of the amino acid sequence being identical to SEQ ID NO: 10, or an immunogenic fragment or immunogenic variant of any of these.~~

~~34. Nucleic acid of any one of the preceding claims, wherein the at least one coding sequence is a codon modified coding sequence, wherein the amino acid sequence encoded by the at least one codon modified coding sequence is preferably not being modified compared to the amino acid sequence encoded by the corresponding wild type or reference coding sequence.~~

~~35. Nucleic acid of claim 34, wherein the at least one codon modified coding sequence is 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.~~

~~36. Nucleic acid of claim 34 or 35, wherein the at least one codon modified coding sequence is a G/C optimized coding sequence, a human codon usage adapted coding sequence, or a G/C content modified coding sequence.~~

~~37. Nucleic acid of any one of the preceding claims, wherein the at least one coding sequence comprises or consists of a G/C optimized coding sequence comprising a nucleic acid sequence being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one SEQ ID NOs: 136-138, 140, 141, 148, 149, 152, 155, 156, 159, 162, 163, 166, 169, 170, 173, 11731-11813, 11815, 11817-11966, 12271-12472, 12743-12944, 13514, 13515, 14124-14132, 14142-14150, 14160-14168, 22759, 22764-22786, 22791-22813, 22818-22839, 22969-23040, 23077-23148, 23189-23260, 23297-23368, 23409-23480, 23517-23588, 23629-23700, 23737-23808, 23849-23920, 23957-24028, 24069-24140, 24177-24248, 24289-24360, 24397-24468, 24509-24580, 24617-24688, 24729-24800, 24837-24908, 24949-25020,~~

~~25057-25128, 25169-25240, 25277-25348, 25389-25460, 25497-25568, 25609-25680, 25717-25788, 25829-25900, 25937-26008, 26049-26120, 26157-26228, 26269-26340, 26377-26448, 26489-26560, 26597-26668, 26709-26780, 26817-26888, 26925-26937 or a fragment or variant of any of these sequences.~~

~~38. Nucleic acid of any one of the preceding claims, wherein the at least one coding sequence comprises or consists of a human codon usage adapted coding sequence comprising a nucleic acid sequence being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 142, 143, 145, 150, 153, 157, 160, 164, 167, 171, 174, 11967-12033, 12473-12539, 12945-13011 or a fragment or variant of any of these sequences.~~

~~39. Nucleic acid of any one of the preceding claims, wherein the at least one coding sequence comprises or consists of a G/C content modified coding sequence comprising a nucleic acid sequence being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one SEQ ID NOs: 146, 147, 151, 154, 158, 161, 165, 168, 172, 175, 12034-12050, 12052, 12054-12203, 12540-12675, 13012-13147, 13519, 13520, 14133-14141, 14151-14159, 14169-14177, 23041-23076, 23149-23184, 23261-23296, 23369-23404, 23481-23516, 23589-23624, 23701-23736, 23809-23844, 23921-23956, 24029-24064, 24141-24176, 24249-24284, 24361-24396, 24469-24504, 24581-24616, 24689-24724, 24801-24836, 24909-24944, 25021-25056, 25129-25164, 25241-25276, 25349-25384, 25461-25496, 25569-25604, 25681-25716, 25789-25824, 25901-25936, 26009-26044, 26121-26156, 26229-26264, 26341-26376, 26449-26484, 26561-26596, 26669-26704, 26781-26816, 26889-26924 or a fragment or variant of any of these sequences.~~

~~40. Nucleic acid of any one of the preceding claims, wherein the at least one coding sequence has a G/C content of at least about 50%, 55%, or 60%, preferably of about 63.9%.~~

~~41. Nucleic acid of any one of the preceding claims, wherein the at least one coding sequence encodes an S protein comprising a pre-fusion stabilizing K986P and V987P mutation, wherein the coding sequence comprises or consists of a G/C optimized coding sequence comprising a nucleic acid sequence being identical to SEQ ID NOs: 137, 23090, 23091, 23093, 23094 or a fragment or variant thereof.~~

~~42. Nucleic acid of any one of the preceding claims, wherein the at least one heterologous untranslated region is selected from at least one heterologous 5'-UTR and/or at least one heterologous 3' UTR.~~

~~43. Nucleic acid of claim 42, wherein the at least one heterologous 3'-UTR comprises or consists of a nucleic acid sequence derived from a 3'-UTR of a gene selected from PSMB3, ALB7, alpha-globin, CASP1, COX6B1, GNAS, NDUFA1 and RPS9, or from a homolog, a fragment or a variant of any one of these genes.~~

~~44. Nucleic acid of claim 42, 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.~~

~~45. Nucleic acid of claim 42, wherein the at least one heterologous 5' UTR and the at least one heterologous 3' UTR is selected from UTR design a-1 (HSD17B4/PSMB3), a-3 (SLC7A3/PSMB3), e-2 (RPL31/RPS9), and i-3 (-/muag), wherein UTR design a-1 (HSD17B4/PSMB3) and i-3 (-/muag) are particularly preferred.~~

~~46. Nucleic acid of any one of the preceding claims, wherein the nucleic acid~~2.

The purified mRNA of claim 1, wherein the 3' UTR comprises at least one poly(A) sequence~~, preferably~~ comprising 30 to 200 adenosine nucleotides~~ and/or at least one poly(C) sequence, preferably comprising 10 to 40 cytosine nucleotides.~~.

~~47. Nucleic acid of any one of the preceding claims~~3. The purified mRNA of claim 2, wherein the ~~nucleic acid comprises at least one histone stem-loop.~~

~~48. Nucleic acid of any one of the preceding claims, wherein the nucleic acid is a DNA or an RNA.~~

~~49. Nucleic acid of any one of the preceding claims, wherein the nucleic acid is a coding RNA.~~

~~50. Nucleic acid of claim 49, wherein the coding RNA is an mRNA, a self-replicating RNA, a circular RNA, or a replicon RNA.~~

~~51. Nucleic acid of any one of the preceding claims, wherein the nucleic acid, preferably the coding RNA, is an mRNA.~~

~~52. Nucleic acid of claim 51, wherein the mRNA is not a replicon RNA or a self-replicating RNA.~~

~~53. Nucleic acid of claim 51, wherein the mRNA comprises at least one poly(A) sequence comprising 30 to 200 adenosine nucleotides and the 3' terminal nucleotide is an adenosine.~~

~~54. Nucleic acid of any one of claims 48 to 51, wherein the RNA, preferably the coding RNA, comprises a~~ 5' ~~-~~cap ~~structure, preferably~~is a m7G, cap0, cap1, cap2, a modified cap0 or a modified cap1 structure~~, preferably a 5' .~~

4. The purified mRNA of claim 3, wherein the 5' cap is a cap1 structure.

~~55. Nucleic acid of any one of claims 48 to 54~~5. The purified mRNA of claim 2, wherein the ~~nucleic acid, preferably the mRNA,~~mRNA comprises ~~the following elements in 5'- to 3'-direction:~~

~~A) 5' cap1 structure;~~

~~B) coding sequence according to SEQ ID NO. 137, or~~ a ~~fragment or variant thereof;~~

~~C) 3' UTR derived from a 3' UTR of an alpha-globin gene, preferably according to SEQ ID NO: 267 or 268;~~

~~D)~~terminal poly(A) sequence ~~comprising about 64 A nucleotides;~~

~~E) poly(C) sequence comprising about~~ of 30 ~~C nucleotides;~~

~~F) histone stem-loop according to SEQ ID NOs: 178 or 179.~~

~~56. Nucleic acid of any one of claims 48 to 54, wherein the nucleic acid, preferably the mRNA, comprises the following elements in 5'- to 3'-direction:~~

~~A) 5' cap1 structure;~~

~~B) 5'-UTR derived from a 5'-UTR of a HSD17B4 gene, preferably according to SEQ ID NO: 231 or 232;~~

~~C) coding sequence according to SEQ ID NO. 137, or a fragment or variant thereof;~~

~~D) 3' UTR derived from a 3' UTR of a PSMB3 gene, preferably according to SEQ ID NO: 253 or 254;~~

~~E) a histone stem-loop selected from SEQ ID NOs: 178 or 179;~~

~~F) poly(A) sequence comprising about 100 A nucleotides.~~

~~57. Nucleic acid of claim 56, wherein the 3' terminal nucleotide is an~~to 200 adenosine nucleotides.

~~58. Nucleic acid of any one of claims 48 to 54~~6. The purified mRNA of claim 2, wherein the ~~nucleic acid, preferably~~ at least one coding sequence of the mRNA~~,~~ has a G/C content of at least about 50%.

7. The purified mRNA of claim 6, wherein the mRNA comprises ~~the following elements in 5'- to 3'-direction:~~an RNA sequence at least 80% identical to SEQ ID NO: 23092.

~~A) 5' cap1 structure;~~

~~B) coding sequence according to SEQ ID NO. 23090 or 23091, or a fragment or variant thereof;~~

~~C) 3' UTR derived from a 3' UTR of an alpha-globin gene, preferably according to SEQ ID NO: 267 or 268;~~

~~D) poly(A) sequence comprising about 64 A nucleotides;~~

~~E) poly(C) sequence comprising about 30 C nucleotides;~~

~~F) histone stem-loop according to SEQ ID NOs: 178 or 179.~~

~~59. Nucleic acid of any one of claims 48 to 54, wherein the nucleic acid, preferably the mRNA,~~8. The purified mRNA of claim 2, wherein the spike protein comprises the D614G amino acid substitution and a E484K amino acid substitution relative to SEQ ID NO: 10.

9. The purified mRNA of claim 8, comprising at least one of the following amino acid substitutions relative to SEQ ID NO: 10: L18F, D80A, D215G, delL242, delA243, delL244, R246I, K417N, N501Y and/or A701V.

10. The purified mRNA of claim 9, wherein the spike protein comprises the following ~~elements in 5'- to 3'-direction:~~

~~A) 5' cap1 structure;~~

~~B) 5'-UTR derived from a 5'-UTR of a HSD17B4 gene, preferably according~~amino acid substitutions relative to SEQ ID NO: ~~231 or 232;~~

~~C) coding sequence according to SEQ ID NO. 23090 or 23091, or a fragment or variant thereof;~~

~~D) 3' UTR derived from a 3' UTR of a PSMB3 gene, preferably according to SEQ ID NO: 253 or 254;~~

~~E) a histone stem-loop selected from SEQ ID NOs: 178 or 179;~~

~~F) poly(A) sequence comprising about 100 A nucleotides.~~

~~60. Nucleic acid of any one of the preceding claims, wherein the nucleic acid comprises or consists of a nucleic acid sequence, preferably an RNA sequence, which is identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 148-175, 12204-13147, 14142-14177, 22786-22839, 23189-23404, 23409-23624, 23629-23844, 23849-24064, 24069-24284, 24289-24504, 24509-24724, 24729-24944, 24949-25164, 25169-25384, 25389-25604, 25609-25824, 25829-26044, 26049-26264, 26269-26484, 26489-26704, 26709-26937148 or a fragment or variant of any of these sequences.~~

~~61. Nucleic acid of any one of the preceding claims, wherein the nucleic acid comprises or consists of a nucleic acid sequence, preferably an RNA sequence, which is identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence selected from the group consisting~~

~~of SEQ ID NOs: 149, 156, 12338, 150, 157, 151, 158, 12541, 163, 170, 12810, 164, 171, 165, 172, 13013, 12342-12351, 12545-12554, 12814-12823, 13017-13026, 14133 or a fragment or variant of any of these sequences, preferably selected from SEQ ID NOs: 149, 150, 151, 163, 164, 165 or a fragment or variant of any of these sequences.~~

~~62. Nucleic acid of any one of the preceding claims, wherein the nucleic acid comprises or consists of a nucleic acid sequence, preferably an RNA sequence, which is identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence selected from SEQ ID NOs: 163 or a fragment or variant thereof.~~

~~63. Nucleic acid of any one of the preceding claims, wherein the nucleic acid comprises or consists of a nucleic acid sequence, preferably an RNA sequence, which is identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence selected from SEQ ID NOs: 149 or a fragment or variant thereof.~~

~~64. Nucleic acid of any one of the preceding claims, wherein the nucleic acid comprises or consists of a nucleic acid sequence, preferably an RNA sequence, which is identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence selected from SEQ ID NOs: 24837 or a fragment or variant thereof.~~

~~65. Nucleic acid of any one of the preceding claims, wherein the nucleic acid comprises or consists of a nucleic acid sequence, preferably an RNA sequence, which is identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 23311, 23531, 24851 or a fragment or variant thereof.~~

~~66. Nucleic acid of any one of the preceding claims, wherein the nucleic acid comprises or consists of a nucleic acid sequence, preferably an RNA sequence, which is identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 23310, 23530, 24850 or a fragment or variant thereof.~~

67. ~~Nucleic acid of any one of the preceding claims, wherein the nucleic acid comprises or consists of a nucleic acid sequence, preferably an RNA sequence, which is identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 23313, 23533, 24853, 23314, 23534, 24854 or a fragment or variant thereof.~~

68. ~~Nucleic acid of any one of the preceding claims, wherein the nucleic acid is an RNA that does not comprise a 1-methylpseudouridine substitution.~~

69. ~~Nucleic acid of any one of the preceding claims, wherein the nucleic acid is an RNA that does not comprise chemically modified nucleotides.~~

70. ~~Nucleic acid of any one of the preceding claims, wherein the nucleic acid is an in vitro transcribed RNA, wherein RNA in vitro transcription has been performed in the presence of a sequence optimized nucleotide mixture and a cap analog, preferably wherein the sequence optimized nucleotide mixture does not comprise chemically modified nucleotides.~~

71. ~~Nucleic acid of any one of the preceding claims, wherein the nucleic acid is a purified RNA, preferably an RNA that has been purified by RP-HPLC and/or TFF.~~

72. ~~Nucleic acid of any one of the preceding claims, wherein the nucleic acid is a purified RNA that has been purified by RP-HPLC and/or TFF and comprises about 5%, 10%, or 20% less double stranded RNA side products as an RNA that has not been purified with RP-HPLC and/or TFF.~~

73. ~~Nucleic acid of any one of the preceding claims, wherein the nucleic acid is a purified RNA that has been purified by RP-HPLC and/or TFF and comprises about 5%, 10%, or 20% less double stranded RNA side products as an RNA that has been purified with Oligo dT purification, precipitation, filtration and/or anion exchange chromatography.~~

74. ~~A composition comprising at least one nucleic acid as defined in any one of claims 1 to 73, wherein the composition optionally comprises at least one pharmaceutically acceptable carrier.~~

~~75. Composition of claims 74, wherein the composition comprises an mRNA according to SEQ ID NOs: 149,163, 24837, 23311, 23531, 23310, 23530, 23313 or 23533 or a fragment or variant of any of these sequences.~~

~~76. Composition of claim 74, wherein the composition is a multivalent composition comprising a plurality or at least more than one of the nucleic acid as defined in in any one of claims 1 to 73.~~

~~77. Composition of claim 76, wherein the plurality or at least more than one of the nucleic acid sequences of the multivalent composition each encode a different spike protein, preferably a prefusion stabilized spike protein.~~

~~78. Composition of claim 77, wherein the different spike proteins or prefusion stabilized spike proteins are derived from different SARS-CoV-2 virus variants/isolates~~

~~79. Composition of claim 78, wherein the different spike proteins or prefusion stabilized spike proteins are derived from at least B.1.1.7, B.1.351, P.1, or CAL.20C.~~

~~80. Composition of claim 78, wherein the different spike proteins or prefusion stabilized spike proteins have~~

~~amino acid changes in the S protein comprising:~~

~~(i) delH69, delV70, Y453F, D614G, I692V and M1229I;~~

~~(ii) delH69, delV70, delY144, N501Y, A570D, D614G, P681H, T716I, S982A and D1118H;~~

~~(iii)~~10: L18F, D80A, D215G, delL242, delA243, delL244, R246I, K417N, E484K, N501Y, D614G and A701V~~;~~.

(iv) L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y and T1027I; and/or

(v) S13I, W152C, L452R, and D614G.

81. Composition of any one of claims 76 to 78, wherein the multivalent composition comprises at least two nucleic acid species comprising a coding sequence encoding an amino acid sequence being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 10, 22961; 22960, 22963, 22941, 22964.

82. Composition of any one of claims 76 to 78, wherein the multivalent composition comprises at least two RNA species being identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 149 or 24837, 23531 or 24851, 23530 or 24850, 23533 or 24853, 23439 or 24759 or 23534 or 24854.

83. Composition of any one of claims 74 to 80, wherein the composition comprises mRNA with an RNA integrity of 70% or more.

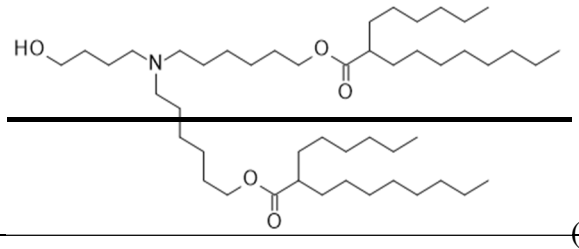
84. Composition of any one of claims 74 to 83, wherein the composition comprises mRNA with a capping degree of 70% or more, preferably wherein at least 70%, 80%, or 90% of the mRNA species comprise a Cap1 structure.

85. Composition of any one of claims 74 to 84, wherein the at least one nucleic acid is complexed or associated with or at least partially complexed or partially associated with one or more cationic or polycationic compound, preferably cationic or polycationic polymer, cationic or polycationic polysaccharide, cationic or polycationic lipid, cationic or polycationic protein, cationic or polycationic peptide, or any combinations thereof.

86. Composition of claim 85, wherein the at least one nucleic acid is complexed or associated with one or more lipids or lipid-based carriers, thereby forming liposomes, lipid nanoparticles (LNP), lipoplexes, and/or nanoliposomes, preferably encapsulating the at least one nucleic acid.

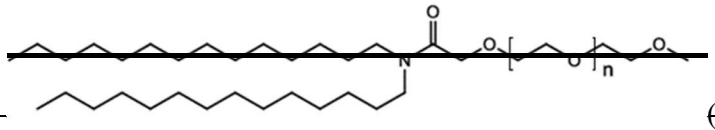
87. Composition of claims 85 or 86, wherein the at least one nucleic acid is complexed with one or more lipids thereby forming lipid nanoparticles.

88. Composition of claim 86 or 87, wherein the LNP comprises a cationic lipid according to formula III-3:



(III-3).

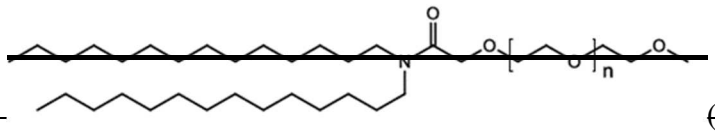
89. Composition of any one of claims 86-88, wherein the LNP comprises a PEG lipid of formula (IVa):



(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.

90. Composition of any one of claims 86-88, wherein the LNP comprises a PEG lipid of formula (IVa):



(IVa),

wherein n is an integer selected such that the average molecular weight of the PEG lipid is about 2500g/mol.

~~91. Composition of any one of claims 86-90, wherein the LNP comprises one or more~~

11. The purified mRNA of claim 2, wherein the mRNA comprises a 1-methylpseudouridine nucleotide substitution at one or more uracil position(s).

12. The purified mRNA of claim 11, wherein 100% of the uracil positions in the coding sequence are replaced with 1-methylpseudouridine.

13. The purified mRNA of claim 2, wherein the mRNA is a purified mRNA that has been purified by RP-HPLC and/or TFF.

14. A pharmaceutical composition comprising the purified mRNA of claim 1 and at least one pharmaceutically acceptable carrier.

15. The composition of claim 14, wherein the composition comprises at least two different mRNA encoding at least two different SARS-CoV-2 spike proteins.

16. The composition of claim 15, wherein the at least two different SARS-CoV-2 spike proteins are each at least 95% identical to SEQ ID NO: 10 and comprise the K986P and V987P stabilizing substitutions.

17. The composition of claim 16, wherein the at least two different SARS-CoV-2 spike proteins are from different SARS CoV-2 variants.

18. The composition of claim 14, wherein the mRNA is complexed or associated with lipid nanoparticles (LNPs).

19. The composition of claim 18, wherein the LNPs comprises:

(i) at least one cationic lipid;

(ii) at least one neutral ~~lipids and/or one or more steroid or steroid analogues.~~

~~92. Composition of claim 91, wherein the neutral lipid is 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), preferably wherein the molar ratio of the cationic lipid to DSPC is in the range from about 2:1 to about 8:1.~~

~~93. Composition of claim 91, wherein the steroid is cholesterol, preferably wherein the molar ratio of the cationic lipid to cholesterol is in the range from about 2:1 to about 1:1.~~

~~94. Composition of any one of claims 86-93, wherein the LNP comprises~~

~~(i) at least one cationic lipid, preferably a lipid of formula (III), more preferably lipid III-3;~~

~~(ii) at least one neutral lipid, preferably 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC);~~ lipid;

(iii) at least one steroid or steroid analogue~~, preferably cholesterol;~~ ; and

(iv) at least one ~~polymer conjugated lipid, preferably a~~ PEG-lipid ~~derived from formula (IVa, with n = 49),~~,

wherein (i) to (iv) are in a molar ratio of about 20-60% cationic lipid, 5-25% neutral lipid, 25-55% sterol, and 0.5-~~15~~10% PEG-lipid.

~~95. Composition of any one of claims 86-93~~20. The composition of claim 19, wherein the ~~LNP~~at least one PEG-lipid is present in the LNPs in a molar ratio of about 0.5% to 5%.

21. The composition of claim 20, wherein the at least one PEG-lipid comprises PEG-DMG or PEG-cDMA.

22. (Original) The composition of claim 21, wherein the at least one PEG-lipid comprises PEG-2000-DMG.

23. The composition of claim 18, wherein the LNPs have a mean diameter of from about 60nm to 200nm.

24. The composition of claim 18, wherein the composition has a lipid to RNA molar ratio (N/P ratio) of from about 2 to about 12.

25. The composition of claim 20, further comprising sucrose.

26. A composition comprising:

(I) a purified mRNA comprising:

(a) a 5’ cap structure;

(b) a heterologous 5’ untranslated region (UTR);

(c) a coding sequence encoding a SARS-CoV-2 spike protein (S) at least 95% identical to SEQ ID NO: 10 that is a pre-fusion stabilized spike protein (S_stab) comprising K986P and V987P stabilizing substitutions and further comprising a D614G amino acid substitution relative to SEQ ID NO: 10; and

(d) a heterologous 3’ UTR, comprising a terminal poly(A) sequence of 30 to 200 adenosine nucleotides,

wherein 100% of the uracil positions in the mRNA are replaced with 1-methylpseudouridine; and

(II) at least one pharmaceutically acceptable carrier,

wherein the mRNA is complexed or associated with lipid nanoparticles (LNPs).

27. The composition of claim 26, wherein the LNPs comprises:

(i) at least one cationic lipid~~, preferably a lipid of formula (III), more preferably lipid III-3; ~~;

(ii) at least one neutral lipid~~, preferably 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC); ~~;

(iii) at least one steroid or steroid analogue~~, preferably cholesterol; ~~; and

(iv) at least one ~~polymer conjugated lipid, preferably a PEG-lipid derived from formula (IVa, with n = 45),~~PEG-lipid,

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

96. Composition of claim 94 or 95, wherein (i) to (iv) are 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% PEG-lipid.

97. Composition of any one of claims 87 to 96, wherein the nucleic acid is RNA and the composition comprises less than about 20% free (non complexed or non-encapsulated) RNA, preferably less than about 15% free RNA, more preferably less than about 10% free RNA.

98. Composition of any one of claims 87 to 97, wherein the wt/wt ratio of lipid to nucleic acid is from about 10:1 to about 60:1, preferably from about 20:1 to about 30:1, for example about 25:1.

99. Composition of any one of claims 87 to 98, wherein the n/p ratio of the LNPs encapsulating the nucleic acid is in a range from about 1 to about 10, preferably in a range from about 5 to about 7, more preferably about 6.

100. Composition of any one of claims 87 to 99, wherein the composition has a polydispersity index (PDI) 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.

101. Composition of any one of claims 86 to 100, wherein the LNPs have a Z-average size in a range of about 60nm to about 120nm, preferably less than about 120nm, more preferably less than about 100nm, most preferably less than about 80nm.

102. Composition of any one of claims 86 to 101, wherein the LNPs comprise less than about 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1% LNPs that have a particle size exceeding about 500nm.

103. Composition of any one of claims 86 to 102, wherein the LNPs comprise less than about 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1% LNPs that have a particle size smaller than about 20nm.

104. Composition of any one of claims 86 to 103, wherein at least about 80%, 85%, 90%, 95% of lipid-based carriers have a spherical morphology, preferably comprising a solid core or partially solid core.

105. Composition of any one of claims 86 to 104, wherein the composition has a turbidity ranging from about 150 FNU to about 0.0 FNU, preferably of about 50 FNU or less, more preferably of about 25 FNU or less.

106. Composition of any one of claims 74 to 105, further comprising a sugar in a concentration of about 50 to about 300mM, preferably sucrose in a concentration of about 150mM.

107. Composition of any one of claims 74 to 106, further comprising a salt in a concentration of about 10mM to about 200mM, preferably NaCl in a concentration of about 75mM.

108. Composition of any one of claims 74 to 107, further comprising a buffering agent in a concentration 1mM to about 100mM, preferably Na_3PO_4 in a concentration of about 10mM.

109. Composition of any one of claims 74 to 108, wherein the composition has a pH in a range of about pH 7.0 to about pH 8.0, preferably of about pH 7.4.

110. Composition of any one of claims 86 to 109, comprising lipid nanoparticles encapsulating an RNA encoding a SARS-CoV-2 S protein comprising a pre-fusion stabilizing K986P and V987P mutation

wherein the LNPs comprise

(i) cationic lipid of formula III-3;

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

(iii) cholesterol; and

(iv) PEG-lipid of fromula IVa (n=49)),

wherein (i) to (iv) are in a molar ratio of about 47.4% cationic lipid, 10% DSPC, 40.9 cholesterol, 1.7% PEG-lipid;

wherein the RNA is identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence of SEQ ID NO. 163 or 149;

wherein the RNA is not chemically modified;

~~wherein the RNA comprises a 5'-Cap1 structure;~~

~~wherein the intergity of the RNA is at least about 70%;~~

~~wherein the n/p ratio of the LNPs encapsulating the RNA is about 6;~~

~~wherein the LNPs encapsulating the RNA have a Z-average size of about 60nm to about 120nm;~~

~~wherein the composition comprises less than about 20% free (non complexed; non-encapsulated) RNA;~~

~~optionally, wherein the composition further comprises sucrose in a concentration of about 150mM, NaCl in a concentration of about 75mM, Na_3PO_4 in a concentration of about 10mM;~~

~~optionally, wherein the composition has a pH of about pH 7.4.~~

~~111. Composition of any one of claims 86 to 109, comprising lipid nanoparticles encapsulating an RNA encoding a SARS-CoV-2 S protein comprising a pre-fusion stabilizing K986P and V987P mutation~~

~~wherein the LNPs comprise~~

~~(i) cationic lipid of formula III-3;~~

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

~~(iii) cholesterol; and~~

~~(iv) PEG-lipid of fromula IVa (n=45)),~~

~~wherein (i) to (iv) are in a molar ratio of about 47.4% cationic lipid, 10% DSPC, 40.9 cholesterol, 1.7% PEG-lipid;~~

~~wherein the RNA is identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence of SEQ ID NO. 163 or 149;~~

~~wherein the RNA is not chemically modified;~~

~~wherein the RNA comprises a 5'-Cap1 structure;~~

~~wherein the intergity of the RNA is at least about 70%;~~

~~wherein the n/p ratio of the LNPs encapsulating the RNA is about 6;~~

~~wherein the LNPs encapsulating the RNA have a Z-average size of about 60nm to about 120nm;~~

~~wherein the composition comprises less than about 20% free (non complexed) RNA;~~

~~optionally, wherein the composition further comprises sucrose in a concentration of about 150mM, NaCl in a concentration of about 75mM, Na_3PO_4 in a concentration of about 10mM;~~

~~optionally, wherein the composition has a pH of about pH 7.4.~~

~~112. Composition of any one of claims 86 to 110, comprising an RNA that is not chemically modified, which is identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence of SEQ ID NO. 163 formulated in lipid nanoparticles (LNPs), which have a molar ratio of approximately 50:10:38.5:1.5, preferably 47.5:10:40.8:1.7 or more preferably 47.4:10:40.9:1.7 proportion (mol%) of cationic lipid III-3, DSPC, cholesterol and PEG-lipid of formula (IVa).~~

~~113. Composition of any one of claims 86 to 110, comprising an RNA that is not chemically modified, which is identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence of SEQ ID NO. 149 formulated in lipid nanoparticles (LNPs), which have a molar ratio of approximately 50:10:38.5:1.5, preferably 47.5:10:40.8:1.7 or more preferably 47.4:10:40.9:1.7 proportion (mol%) of cationic lipid III-3, DSPC, cholesterol and PEG-lipid of formula (IVa).~~

~~114. Composition any one of claims 74 to 112, wherein the composition comprises a mRNA encoding a SARS-CoV-2 spike protein (S) that is a pre-fusion stabilized spike protein (S_stab) comprising at least one pre-fusion stabilizing mutation.~~

~~115. Composition of claim 114, wherein the mRNA encodes a SARS-CoV-2 spike protein at least 95% identical to SEQ ID NO: 163 or encodes~~ 28. The composition of claim 27, wherein the at least one PEG-lipid comprises PEG-2000-DMG.

29. The composition of claim 27, wherein the spike protein comprises the D614G substitution and a E484K substitution relative to SEQ ID NO: 10.

30. Use of an effective amount of a composition according to claim 27 in the manufacture of a medicament for stimulating an immune response to a coronavirus spike protein ~~identical to SEQ ID NO: 163.~~

~~116. Composition of claim 114, wherein the LNP comprises~~

~~(i) at least one cationic lipid;~~

~~(ii) at least one neutral lipid;~~

~~(iii) at least one steroid or steroid analogue; and~~

~~(iv) at least one PEG-lipid,~~

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

~~117. Composition of claim 114, wherein the LNP comprises~~

~~(i) at least one cationic lipid according to formula III-3;~~

~~(ii) DSPC;~~

~~(iii) cholesterol; and~~

~~(iv) a PEG-lipid, according to formula IVa,~~

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

~~118. Composition of claim 114, wherein the LNP comprises~~

~~(i) at least one cationic lipid according to formula III-3;~~

~~(ii) DSPC;~~

~~(iii) cholesterol; and~~

~~(iv) a PEG-lipid, according to formula IVa,~~

~~wherein (i) to (iv) are in a molar ratio of about 47.5:10:40.8:1.7.~~

~~119. Composition of claim 114, wherein the LNP comprises:~~

~~(i) at least one cationic lipid according to formula III-3;~~

~~(ii) DSPC;~~

~~(iii) cholesterol; and~~

~~(iv) a PEG-lipid, according to formula IVa,~~

~~wherein (i) to (iv) are in a molar ratio of 47.4:10:40.9:1.7.~~

~~120. Composition of anyone of claims 107-118, wherein the ratio of mRNA to total lipid is about 0.03-0.04 w/w.~~

~~121. Composition of claim 120, wherein the mRNA is complexed with one or more lipids thereby forming lipid nanoparticles (LNP), wherein the LNP comprises~~

~~(i) at least one cationic lipid according to formula III-3;~~

~~(ii) DSPC;~~

~~(iii) cholesterol; and~~

~~(iv) a PEG-lipid, according to formula IVa,~~

~~wherein (i) to (iv) are in a molar ratio of about 47.5:10:40.8:1.7, and~~

~~wherein the ratio of mRNA to total lipid is about 0.03-0.04 w/w.~~

~~122. Composition of claim 120, wherein the mRNA is complexed with one or more lipids thereby forming lipid nanoparticles (LNP), wherein the LNP comprises:~~

~~(i) at least one cationic lipid according to formula III-3;~~

~~(ii) DSPC;~~

~~(iii) cholesterol; and~~

~~(iv) a PEG-lipid, according to formula IVa,~~

~~wherein (i) to (iv) are in a molar ratio of 47.4:10:40.9:1.7, and~~

~~wherein the ratio of mRNA to total lipid is about 0.03-0.04 w/w.~~

~~123. Composition of any one of claims 74-99 or 110-122, wherein the composition is a lyophilized composition.~~

~~124. Composition of claim 123, wherein the lyophilized composition has a water content of less than about 10%.~~

~~125. Composition of claim 124, wherein the lyophilized composition has a water content of between about 0.5% and 5%.~~

~~126. Composition any one of claims 86 to 122, wherein the nucleic acid is RNA and wherein the composition is stable for at least about two weeks after storage as a liquid at temperatures of about 5°C.~~

~~127. Composition of claim 126, wherein the nucleic acid is RNA and wherein the composition is stable for at least 1 month after storage as a liquid at temperatures of about 5°C.~~

~~128. Composition of claim 126, wherein the nucleic acid is RNA and wherein the composition is stable for about 2 weeks to about 1 month, 2 months, 3 months, 4 months, 5 months, 6 months or 1 year after storage as a liquid at temperatures of about 5°C.~~

~~129. Composition of claim 126, wherein the nucleic acid is RNA and wherein at least 70%, 75%, 80%, 85%, 90% or 95% of the RNA is intact at least about two weeks after storage as a liquid at temperatures of about 5°C.~~

~~130. Composition of claim 129, wherein the nucleic acid is RNA and wherein at least 70%, 75%, 80%, 85%, 90% or 95% of the RNA is intact at least 1 month after storage as a liquid at temperatures of about 5°C.~~

131. Composition of claim 126, wherein the nucleic acid is RNA and wherein at least 70%, 75%, 80%, 85%, 90% or 95% of the RNA is intact about 2 weeks to about 1 month, 2 months, 3 months, 4 months, 5 months, 6 months or 1 year after storage as a liquid at temperatures of about 5°C.

132. Composition of claim 126, wherein the nucleic acid is RNA and wherein at least 80% of the RNA is intact after about two weeks of storage as a liquid at temperatures of about 5°C.

133. Composition any one of claims 86 to 132, wherein the composition comprises an aggregation reducing lipid.

134. Composition any one of claims 86 to 133, wherein the nucleic acid is RNA and wherein the concentration of the RNA is in a range from about 10 µg/ml to about 10 mg/ml, preferably in a range from about 100 µg/ml to about 1 mg/ml.

135. Composition any one of claims 86 to 133, wherein the nucleic acid is RNA and wherein the concentration of the RNA is at least 100 µg/ml, more preferably at least 200 µg/ml, most preferably at least 500 µg/ml.

136. Composition any one of claims 86 to 135, wherein the nucleic acid is RNA and 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%.

137. Composition any one of claims 86 to 136, wherein the nucleic acid is RNA and wherein the composition comprises less than about 20% free RNA, preferably less than about 15% free RNA, more preferably less than about 10% free RNA.

138. Composition any one of claims 86 to 137, wherein the nucleic acid is RNA and wherein the composition comprises less than about 100nM divalent cations per g RNA, preferably less than about 50nM divalent cations per g RNA, more preferably less than about 10nM divalent cations per g RNA.

139. Composition of claim 138, wherein the divalent cations are selected from Mg2+ and/or Ca2+.

~~140. Composition of any one of claims 86 to 139, wherein the concentration of lipid is in a range from about 250 µg/ml to about 250 mg/ml, preferably in a range from about 2.5mg/ml to about 25mg/ml.~~

~~141. Composition of any one of claims 86 to 140, wherein the concentration of lipid is at least about 2.5mg/ml, preferably at least 5 mg/ml, more preferably at least 12.5 mg/ml.~~

~~142. Composition of any one of claims 133 to 142, wherein the concentration of aggregation reducing lipid is in a range from about 17.5 µg/ml to about 17.5 mg/ml, preferably in a range from about 175 µg/ml to about 1.75 mg/ml.~~

~~143. Composition of any one of claims 133 to 142, wherein the concentration of aggregation reducing lipid is at least about 175 µg/ml, preferably at least about 350 µg/ml, more preferably at least 875 µg/ml.~~

~~144. Composition of any one of claims 86 to 143, wherein the nucleic acid is RNA and wherein the wt/wt ratio of lipid to the RNA is from about 10:1 to about 60:1, preferably from about 20:1 to about 30:1, more preferably about 25:1.~~

~~145. Composition of any one of claims 86 to 144, wherein the nucleic acid is RNA and wherein the N/P ratio of the lipid-based carriers to the RNA is in a range from about 1 to about 10, preferably in a range from about 5 to about 7, more preferably about 6.~~

~~146. Composition of any one of claim 86 to 143, wherein the nucleic acid is RNA and wherein the lipid-based carriers encapsulating the RNA comprise an aggregation reducing lipid in a molar ratio of about 0.5% 15%, preferably in a molar ratio of about 1.0% to about 2.5 %, more preferably in a molar ratio of about 1.7%.~~

~~147. Composition of any one of claim 133 to 143, wherein the aggregation reducing lipid is a polymer conjugated lipid, e.g. a PEG-conjugated lipid.~~

~~148. Composition of any one of claim 86 to 147, wherein the nucleic acid is RNA and wherein the RNA and lipid-based carrier encapsulating the RNA have been purified by at least one purification step, preferably by at least one step of TFF and/or at least one step of clarification and/or at least one step of filtration.~~

~~149. Composition of any one of claim 86 to 148, wherein the composition comprises less than about 500ppM ethanol, preferably less than about 50ppM ethanol, more preferably less than about 5ppM ethanol.~~

~~150. Composition of any one of claim 86 to 154, wherein the composition has an osmolarity of about 250 mOsmol/kg to about 450 mOsmol/kg, preferably of about 335 mOsmol/kg.~~

~~151. Composition of any one of claim 86 to 150, wherein the composition is stable for at least 1 week, preferably for at least 2 weeks, more preferably for at least 3 weeks, most preferably for at least 4 weeks after storage as a liquid at about 25 °C.~~

~~152. Composition of any one of claim 86 to 151, wherein the composition is stable for at least 1 day, preferably for at least 2 days, more preferably for at least 3 days, most preferably for at least 4 days after storage as a liquid at about 40°C.~~

~~153. Composition of any one of claim 86 to 152, wherein upon storage as a liquid, the integrity of the RNA decreases less than about 30%, preferably less than about 20%, more preferably less than about 10%.~~

~~154. Composition of any one of claim 86 to 153, wherein upon storage as a liquid, the amount of free RNA does not increase by more than 10%, preferably by not more than 5%.~~

~~155. Composition of any one of claim 86 to 154, wherein the nucleic acid is RNA and wherein upon storage as a liquid, the PDI value of the lipid-based carriers encapsulating the RNA does not increase by more than a value of about 0.2, preferably by not more than a value of about 0.1.~~

~~156. Composition of any one of claim 86 to 155, wherein the nucleic acid is RNA and wherein upon storage as a liquid, the Z-average size of the lipid-based carriers encapsulating the RNA does not increase by more than 20%, preferably by not more than 10%.~~

~~157. Composition of any one of claim 86 to 156, wherein upon storage as a liquid, the turbidity of the composition does not increase by more than 20%, preferably by not more than 10%.~~

~~158. Composition of any one of claim 86 to 157, wherein upon storage as a liquid, the pH and/or the osmolality does not increase or decrease by more than 20%, preferably by not more than 10%.~~

159. ~~Composition of any one of claim 86 to 158, wherein upon storage as a liquid, the potency of the composition decreases less than about 30%, preferably less than about 20%, more preferably less than about 10%.~~

160. ~~Composition of any one of claims 86 to 133, wherein the nucleic acid is RNA and wherein the RNA is a purified RNA, preferably an RP-HPLC purified RNA and/or a tangential flow filtration (TFF) purified RNA.~~

161. ~~Composition of any one of claims 74 to 160, additionally comprising at least one antagonist of at least one RNA sensing pattern recognition receptor, preferably at least one antagonist of a TLR7 receptor and/or a TLR8 receptor.~~

162. ~~Composition of claim 161, wherein the at least one antagonist of a TLR7 receptor and/or a TLR8 receptor is a single stranded oligonucleotide, preferably p5'-GAG-CGmG-CCA-3'.~~

163. ~~A polypeptide for a vaccine comprising at least one antigenic peptide or protein that is or is derived from a coronavirus SARS-CoV-2, or an immunogenic fragment or immunogenic variant thereof, preferably wherein the amino acid sequences of said antigenic peptide or protein is identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to any one of amino acid sequences SEQ ID NOs: 1-111, 274-11663, 13176-13510, 13521-14123, 22732-22758, 22917, 22923, 22929-22964, 26938, 26939, or an immunogenic fragment or immunogenic variant of any of these.~~

164. ~~A vaccine comprising the nucleic acid of any one of claims 1 to 73, and/or the composition of any one of claims 74 to 162, and/or the polypeptide of claim 163.~~

165. ~~A vaccine of claim 164, wherein the vaccine elicits an adaptive immune response, preferably a protective adaptive immune response against a coronavirus, preferably against coronavirus SARS-CoV-2.~~

166. ~~A vaccine of claim 164 or 165, wherein the vaccine is a multivalent vaccine comprising a plurality or at least more than one of the nucleic acid as defined in any one of claims 1 to 73, or a plurality or at least more than one of the compositions as defined in any one of claims 74 to 162.~~

~~167. A Kit or kit of parts, comprising the nucleic acid of any one of claims 1 to 73, and/or the composition of any one of claims 74 to 162, and/or the polypeptide of claim 163, and/or the vaccine of claim 164 to 166, optionally comprising a liquid vehicle for solubilising, and, optionally, technical instructions providing information on administration and dosage of the components.~~

~~168. Nucleic acid of any one of claims 1 to 73, the composition of any one of claims 74 to 162 the polypeptide of claim 163, the vaccine of claim 164 to 166, the kit or kit of parts of claim 167, for use as a medicament.~~

~~169. Nucleic acid of any one of claims 1 to 73, the composition of any one of claims 74 to 162, the polypeptide of claim 163, the vaccine of claim 164 to 166, the kit or kit of parts of claim 167, for use in the treatment or prophylaxis of an infection with a coronavirus, preferably a SARS-CoV-2 coronavirus, or of a disorder related to such an infection, preferably COVID-19.~~

~~170. A method of treating or preventing a disorder, wherein the method comprises applying or administering to a~~ in a subject ~~in need thereof the nucleic acid of any one of claims 1 to 73, the composition of any one of claims 74 to 162, the polypeptide of claim 163, the vaccine of claim 164 to 166, and/or the kit or kit of parts of claim 167.~~

~~171. The method of treating or preventing a disorder of claim 170, wherein the disorder is an infection with a coronavirus, preferably a SARS-CoV-2 coronavirus, or a disorder related to such an infection, preferably COVID-19.~~

~~172. The method of treating or preventing a disorder of claim 170 or 171, wherein the subject in need is a mammalian subject, preferably a human subject.~~

~~173. The method of treating or preventing a disorder of any one of claims 170 to 172, wherein the human subject is an elderly human subject, preferably of an age of at least 50, 60, 65, or 70 years.~~

~~174. The method of treating or preventing a disorder of claim 173, wherein the human subject is 61 years of age or older.~~

~~175. The method of treating or preventing a disorder of any one of claims 170 to 172, wherein the human subject is 18 to 60 years of age.~~

~~176. The method of treating or preventing a disorder of any one of claims 170 to 172, wherein the subject is pregnant.~~

~~177. The method of any one of claims 170 to 175, wherein no more than 25% of subjects experience a Grade 3 systemic adverse event after a first dose of the composition or wherein no more than 30% of subjects experience a Grade 2 or higher local adverse event after a first dose of the composition.~~

~~178. The method of any one of claims 170 to 175, wherein no more than 40% of subjects experience a Grade 3 systemic adverse event after a second dose of the composition.~~

~~179. The method of treating or preventing a disorder of any one of claims 170 to 172, wherein the human subject is a newborn or infant, preferably of an age of not more than 3 years, of not more than 2 years, of not more than 1.5 years, of not more than 1 year (12 months), of not more than 9 months, 6 months or 3 months, or of an age between 6 months and 2 years~~

~~180. The method of claim 170, further defined as a method of reducing disease burden in the subject.~~

~~181. The method of claim 180, wherein the method reduces the severity of one or more symptom of COVID-19 disease.~~

~~182. The method of claim 181, wherein the method reduces the probability that the subject will require hospital admission, intensive care unit admission, treatment with supplemental oxygen and/or treatment with a ventilator.~~

~~183. The method of claim 181, wherein the method reduces the probability that the subject will develop severe or moderate COVID-19 disease.~~

~~184. The method of claim 181, wherein the method prevents severe COVID-19 disease in the subject for at least about 6 months.~~

185. The method of claim 184, wherein the method prevents severe COVID-19 disease in the subject when the subject is exposed to a SARS-CoV-2 variant having a least a first amino acid change in the S protein as compared to SEQ ID NO: 1.

186. The method of claim 185, wherein the SARS-CoV-2 variant has amino acid changes in the S protein comprising:

(i) delH69, delV70, Y453F, D614G, I692V and M1229I;

(ii) delH69, delV70, delY144, N501Y, A570D, D614G, P681H, T716I, S982A and D1118H;

(iii) L18F, D80A, D215G, delL242, delA243, delL244, R246I, K417N, E484K, N501Y, D614G and A701V;

(iv) L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y and T1027I; and/or

(v) S13I, W152C, L452R, and D614G.

187. The method of claim 181, wherein the method reduces the probability that the subject will develop a fever, breathing difficulties; loss of smell and/or loss of taste.

188. The method of claim 181, wherein the method reduces the probability that the subject will develop a fever, breathing difficulties; loss of smell and/or loss of taste.

189. The method of claim 170, wherein the subject has a disease or is immune compromised.

190. The method of claim 189, wherein the subject has liver disease, kidney disease diabetes, hypertension, heart disease, lung disease, cancer or is HIV positive.

191. The method of claim 170, wherein the subject has not been treated with an immunosuppressant drug for more than 14 days in the last 6 months.

192. The method of claim 170, wherein the subject has not received a live vaccine for at least 28 days prior to the administration and/or has not received an inactivated vaccine for at least 14 days prior to the administration.

~~193. A method of stimulating an immune response in a subject, wherein the method comprises administering to the subject at least a first composition comprising the nucleic acid, preferably mRNA of any one of claims 1 to 73, the composition of any one of claims 74 to 162, the polypeptide of claim 163, the vaccine of claim 164 to 166, and/or the kit or kit of parts of claim 167.~~

~~194. The method of claim 193, wherein the subject was previously infected with SARS CoV-2.~~

~~195. The method of claim 193, wherein the subject was previously treated with at least a first SARS-CoV-2 vaccine composition.~~

~~196. The method of claim 195, wherein the first SARS-CoV-2 vaccine composition was a mRNA vaccine.~~

~~197. The method of claim 196, wherein the first SARS-CoV-2 vaccine composition was BNT162 or mRNA-1273.~~

~~198. The method of claim 195, wherein the first SARS-CoV-2 vaccine composition was a protein subunit vaccine.~~

~~199. The method of claim 198, wherein the first SARS-CoV-2 vaccine composition was NVX-CoV2373 or COVAX.~~

~~200. The method of claim 195, wherein the first SARS-CoV-2 vaccine composition was an adenovirus vector vaccine.~~

~~201. The method of claim 200, wherein the first SARS-CoV-2 vaccine composition was ADZ1222 or Ad26.COV-2.S.~~

~~202. The method of any one of claims 193-201, wherein the subject has detectable SARS-CoV-2 binding antibodies.~~

~~203. The method of claim 202, wherein the subject has detectable SARS-CoV-2 S protein-binding antibodies.~~

~~204. The method of claim 202, wherein the subject has detectable SARS-CoV-2 N protein-binding antibodies.~~

~~205. The method of any one of claims 195-201, wherein the first SARS-CoV-2 vaccine composition was~~, wherein the said medicament is to be administered to the ~~patient at least about 3 month, 6 months, 9 months, 1 year, 1.5 years, 2 years or 3 years ago.~~

~~206. The method of any one of claims 195-201, wherein the first SARS-CoV-2 vaccine composition was administered to the patient between about 3 months and 2 years ago or between about 6 months and 2 years ago.~~

~~207. The method of any one of claims 193-206, wherein the method prevents moderate and severe COVID-19 disease in at least 80%, 85%, 90% or 95% of treated subjects.~~

~~208. The method of claim 207, wherein the method prevents moderate and severe COVID-19 disease in at least 80%, 85%, 90% or 95% of treated subjects from about 2 weeks to about 1 year after said administration.~~

~~209. The method of claim 207, wherein the method 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.~~

~~210. The method of any one of claims 193-209, wherein the method prevents SARS-CoV-2 infection of the subject and/or SARS-CoV-2 transmission from the subject in at least 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90% or 95% of treated subjects.~~

~~211. The method of claim 210, wherein the prevents SARS-CoV-2 infection of the subject and/or SARS-CoV-2 transmission from the subject in at least 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90% or 95% of treated subjects from about 2 weeks to about 1 year after said administration.~~

~~212. The method of claim 211, wherein the method prevents SARS-CoV-2 infection of the subject and/or SARS-CoV-2 transmission from the subject in at least 50%, 55%, 60%, 65%, 70%, 75%, 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.~~

~~213. The method of any one of claims 193-212, further comprising administering at least a second composition to the subject, the second composition comprising the nucleic acid, preferably mRNA of any one of claims 1 to 61, the composition of any one of claims 74 to~~

~~128, the polypeptide of claim 163, the vaccine of claim 164 to 166, and/or the kit or kit of parts of claim 167.~~

~~214. The method of claim 213, wherein the second composition is administered at least about 7 days after said first composition.~~

~~215. The method of claim 214, wherein the second composition is administered at least about 10 days, 14 days, 21 days, 28 days, 35 days, 42 days, 49 days or 56 days after said first composition.~~

~~216. The method of claim 213, wherein the second composition is administered between about 7 days and about 56 days after said first composition.~~

~~217. The method of claim 216, wherein the second composition is administered between: about 14 days and about 56 days; about 21 days and about 56 days; or about 28 days and about 56 days after said first composition.~~

~~218. The method of any one of claims 193-212, further comprising administering at least a third composition to the subject, the third composition comprising the nucleic acid of any one of claims 1 to 61, the composition of any one of claims 74 to 162, the polypeptide of claim 163, the vaccine of claim 164 to 166, and/or the kit or kit of parts of claim 167.~~

~~219. The method of any one of claims 213-218, wherein the method prevents moderate and severe COVID-19 disease in at least 80%, 85%, 90% or 95% of treated subjects.~~

~~220. The method of claim 219, wherein the method prevents moderate and severe COVID-19 disease in at least 80%, 85%, 90% or 95% of treated subjects from about 2 weeks to about 1 year after administering the second or subsequent composition.~~

~~221. The method of claim 219, wherein the method 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 administering the second or subsequent composition.~~

~~222. The method of any one of claims 193-221, further defined as a method of stimulating an antibody, a CD4+ T cell response or a CD8+ T-cell response in the subject.~~

~~223. The method of any one of claims 193-221, further defined as a method of stimulating a neutralizing antibody response in the subject.~~

~~224. The method of any one of claims 193-221, wherein the method stimulates an antibody response that produces between about 10 and about 500 coronavirus spike protein-binding antibodies for every coronavirus neutralizing antibody in the subject.~~

~~225. The method of claim 224, wherein the method stimulates an antibody response that produces no more than about 200 spike protein-binding antibodies for every coronavirus neutralizing antibody.~~

~~226. The method of claim 224, wherein the method stimulates an antibody response that produces between about 10 and about 300; about 20 and about 300; about 20 and about 200; or about 30 and about 100 coronavirus spike protein-binding antibodies for every coronavirus neutralizing antibody.~~

~~227. The method of claim 226, wherein the method stimulates an antibody response that produces between about 30 and about 80 coronavirus spike protein-binding antibodies for every coronavirus neutralizing antibody.~~

~~228. The method of claim 223, wherein the method stimulates an antibody response that produces between about 1 and about 500 coronavirus spike protein receptor binding domain (RBD)-binding antibodies for every coronavirus neutralizing antibody in the subject.~~

~~229. The method of claim 228, wherein the method stimulates an antibody response that produces no more than about 50 spike protein RBD-binding antibodies for every coronavirus neutralizing antibody.~~

~~230. The method of claim 228, wherein the method stimulates an antibody response that produces between about 1 and about 200; about 2 and about 100; about 3 and about 200; about 5 and about 100; or about 5 and about 50 spike protein RBD-binding antibodies for every coronavirus neutralizing antibody.~~

~~231. The method of claim 230, wherein the method stimulates an antibody response that produces between about 5 and about 20 coronavirus spike protein RBD-binding antibodies for every coronavirus neutralizing antibody.~~

~~232. The method of claim 222, wherein the subject has been previously infected with SARS-CoV-2.~~

~~233. The method of claim 222, further defined as a method stimulating a protective immune response in the subject.~~

~~234. The method of any one of claims 193-233, wherein the subject is a human subject.~~

~~235. The method of claim 234, wherein the subject is between the ages of 6 months and 100 years, 6 months and 80 years, 1 year and 80 years, 1 year and 70 years, 2 years and 80 years or 2 years and 60 years.~~

~~236. The method of claim 234, wherein the subject is a newborn or infant of an age of not more than 3 years, of not more than 2 years, of not more than 1.5 years, of not more than 1 year (12 months), of not more than 9 months, 6 months or 3 months, or is between 6 months and 2 years.~~

~~237. The method of claim 234, wherein the subject is an elderly subject of an age of at least 50, 60, 65, or 70 years.~~

~~238. The method of claim 237, wherein the subject is an elderly subject of an age of at least 60 years.~~

~~239. The method of any one of claims 234 to 238, wherein the subject has native American, African, Asian or European heritage.~~

~~240. The method of claim 238, wherein the subject has at least about 10%, 25%, or 50% native American, African, Asian or European heritage.~~

~~241. The method of claim 238, wherein the subject has native American heritage.~~

~~242. The method of claim 238, wherein the subject has at least about 10%, 25% or 50% native American heritage.~~

~~243. The method of any one of claims 193-242, wherein the method induces essentially no increase in Th2 cytokines, preferably IL-4, IL-13, TNF and/or IL-1β in the subject~~

~~244. The method of any one of claims 193-242, further defined as a method of inducing a Th1 directed immune response in the subject.~~

~~245. The method of any one of claims 193-244, wherein the subject is receiving anti-coagulation therapy.~~

~~246. The method of any one of claims 193-245, wherein the composition is administered by intramuscular injection.~~

~~247. The method of any one of claims 193-246, wherein the composition comprises a mRNA encoding a coronavirus spike protein (S) that is a pre-fusion stabilized spike protein (S_stab) comprising at least one pre-fusion stabilizing mutation.~~

~~248. The method of claim 247, wherein the mRNA encodes a coronavirus spike protein at least 95% identical to SEQ ID NO: 163.~~

~~249. The method of claim 248, wherein the mRNA encodes a coronavirus spike protein identical to SEQ ID NO: 163.~~

~~250. The method of claim 247, wherein the mRNA encodes a coronavirus spike protein at least 95% identical to SEQ ID NO: 149.~~

~~251. The method of claim 248, wherein the mRNA encodes a coronavirus spike protein identical to SEQ ID NO: 149.~~

~~252. The method of claim 250 or 251, wherein a single dose of the composition provides a sufficient immune response to protect the subject from severe COVID-19 disease for at least about 6 months.~~

~~253. The method of claim 252, wherein a single dose of the composition provides a sufficient immune response to protect the subject from severe COVID-19 disease for about 6 months to about 1 year, 1.5 years, 2 years, 2.5 years, 3 years, 4 years or 5 years.~~

~~254. The method of any one of claims 247-249, wherein the mRNA is complexed with one or more lipids thereby forming LNP.~~

~~255. The method of claim 254, wherein the LNP comprises~~

~~(i) at least one cationic lipid;~~

~~(ii) at least one neutral lipid;~~

~~(iii) at least one steroid or steroid analogue; and~~

~~(iv) at least one PEG-lipid,~~

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

~~256. The method of claim 255, wherein the LNP comprises~~

~~(i) at least one cationic lipid according to formula III-3;~~

~~(ii) DSPC;~~

~~(iii) cholesterol; and~~

~~(iv) a PEG-lipid, according to formula IVa,~~

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

~~257. The method of claim 256, wherein the LNP comprises~~

~~(i) at least one cationic lipid according to formula III-3;~~

~~(ii) DSPC;~~

~~(iii) cholesterol; and~~

~~(iv) a PEG-lipid, according to formula IVa,~~

~~wherein (i) to (iv) are in a molar ratio of about 47.5:10:40.8:1.7.~~

~~258. The method of claim 256, wherein the LNP comprises~~

~~(i) at least one cationic lipid according to formula III-3;~~

~~(ii) DSPC;~~

~~(iii) cholesterol; and~~

~~(iv) a PEG-lipid, according to formula IVa,~~

~~wherein (i) to (iv) are in a molar ratio of 47.4:10:40.9:1.7.~~

~~259. The method of anyone of claims 254-258, wherein the ratio of mRNA to total lipid is about 0.03-0.04 w/w.~~

~~260. The method of claim 249, wherein the mRNA is complexed with one or more lipids thereby forming lipid nanoparticles (LNP), wherein the LNP comprises~~

~~(i) at least one cationic lipid according to formula III-3;~~

~~(ii) DSPC;~~

~~(iii) cholesterol; and~~

~~(iv) a PEG-lipid, according to formula IVa,~~

~~wherein (i) to (iv) are in a molar ratio of about 47.5:10:40.8:1.7, and~~

~~wherein the ratio of mRNA to total lipid is about 0.03-0.04 w/w.~~

~~261. The method of claim 249, wherein the mRNA is complexed with one or more lipids thereby forming lipid nanoparticles (LNP), wherein the LNP comprises~~

~~(i) at least one cationic lipid according to formula III-3;~~

~~(ii) DSPC;~~

~~(iii) cholesterol; and~~

~~(iv) a PEG-lipid, according to formula IVa,~~

~~wherein (i) to (iv) are in a molar ratio of 47.4:10:40.9:1.7, and~~

~~wherein the ratio of mRNA to total lipid is about 0.03-0.04 w/w.~~

~~262. The method of any one of claims 247-261, wherein the subject is administered a composition that comprises between about 2 µg and about 50 µg of mRNA.~~

~~263. The method of claim 262, wherein the subject is administered a composition that between about 10 µg and about 50 µg of mRNA.~~

~~264. The method of claim 263, wherein the subject is administered a composition that between about 10 µg and about 30 µg of mRNA.~~

~~265. The method of claim 264, wherein the subject is administered a composition that comprises about 12 µg of mRNA.~~

~~266. The method of any one of claims 264 to 265, wherein the administration provides seroconversion in 100% of subjects to which the composition is administered.~~

~~267. The method of any one of claims 193 to 266, wherein the human subject is 61 years of age or older.~~

~~268. The method of any one of claims 193 to 266, wherein the human subject is 18 to 60 years of age.~~

~~269. The method of any one of claims 193 to 268, wherein the human subject has had a previous vaccine allergy.~~

~~270. The method of any one of claims 193 to 269, wherein the subject has detectable anti-PEG antibodies.~~

~~271. The method of the any one of claims 193 to 270 comprising:~~

~~(i) obtaining a composition of any one of claims 74 to 162, wherein the composition is lyophilized;~~

~~(ii) solubilizing the lyophilized composition in a pharmaceutically acceptable liquid carrier to produce a liquid composition; and~~

~~(iii) administering an effective amount of the liquid composition to the subject.~~

~~272. A method of stabilizing a composition of any one of claims 74 to 162 comprising lyophilizing the composition to a produce a stabilized composition.~~

~~273. The method of claim 272, wherein the stabilized composition has a water content of less than about 10%.~~

~~274. The method of claim 273, wherein the stabilized composition has a water content of between about 0.5% and 5.0%.~~

~~275. A stabilized, lyophilized composition produced by a method of any one of claims 272-274~~subject.