CLAIMS

1. 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 90% 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.

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

3. The purified mRNA of claim 1 or 2, wherein the coding sequence encoding the SARS-CoV-2 spike protein (S) is at least 94% identical to SEQ ID NO: 10.

4. The purified mRNA of any one of claims 1 to 3, wherein the at least one heterologous 3′-UTR comprises or consists of a nucleic acid sequence derived from a 3′-UTR of PSMB3.

5. The purified mRNA of any one of claims 1 to 4, wherein the 3’ UTR comprises at least one poly(A) sequence comprising 30 to 200 adenosine nucleotides.

6. The purified mRNA of any one of claims 1 to 5, wherein the 5’ cap is a m7G, cap0, cap1, cap2, a modified cap0 or a modified cap1 structure.

7. The purified mRNA of any one of claims 1 to 6, wherein the 5’ cap is a cap1 structure.

8. The purified mRNA of any one of claims 1 to 7, further comprising at least one heterologous 5’ UTR.

9. The purified mRNA of claim 8, wherein the at least one heterologous 5’ UTR comprises or consists of a nucleic acid sequence derived from a 5′-UTR of HSD17B4.

10. The purified mRNA of any one of claims 1 to 9, wherein the mRNA comprises a terminal poly(A) sequence of 30 to 200 adenosine nucleotides.

11. The purified mRNA of claim 10, wherein at least one poly(A) sequence comprises 100 consecutive adenosine nucleotides.

12. The purified mRNA of claim 11, wherein at least one poly(A) sequence is 100 consecutive adenosine nucleotides in length.

13. The purified mRNA of any one of claims 1 to 12, wherein the at least one coding sequence of the mRNA has a G/C content of at least 50%.

14. The purified mRNA of any one of claims 1 to 13, wherein the mRNA comprises an RNA sequence at least 80% identical to SEQ ID NO: 23092.

15. The purified mRNA of any one of claims 1 to 14, wherein the spike protein comprises the D614G amino acid substitution and a E484K amino acid substitution relative to SEQ ID NO: 10.

16. The purified mRNA of any one of claims 1 to 15, 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.

17. The purified mRNA of any one of claims 1 to 16, wherein the spike protein comprises the following amino acid substitutions relative to SEQ ID NO: 10: L18F, D80A, D215G, delL242, delA243, delL244, R246I, K417N, E484K, N501Y, D614G, A701V, K986P and V987P.

18. The purified mRNA of any one of claims 1 to 17, wherein the mRNA comprises a 1-methylpseudouridine nucleotide substitution at one or more uracil position(s).

19. The purified mRNA of any one of claims 1 to 18, wherein 100% of the uracil positions in the coding sequence are replaced with 1-methylpseudouridine.

20. The purified mRNA of any one of claims 1 to 19, wherein the protein that is derived from a SARS-CoV-2 coronavirus spike protein comprises K417N, E484K, N501Y and D614G amino acid substitutions relative to SEQ ID NO: 10.

21. The purified mRNA of any one of claims 1 to 20, wherein the protein that is derived from a SARS-CoV-2 coronavirus spike protein comprises a S2 sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 28.

22. The purified mRNA of any one of claims 1 to 21, wherein the protein that is derived from a SARS-CoV-2 coronavirus spike protein comprises a secretory signal peptide sequence of SEQ ID NO: 28.

23. The purified mRNA of any one of claims 1 to 22, wherein the at least one coding sequence comprises a nucleic acid sequence at least 80% identical to SEQ ID NO: 137.

24. The purified mRNA of claim 23, wherein the at least one coding sequence comprises a nucleic acid sequence at least 90% identical to SEQ ID NO: 137.

25. The purified mRNA of any one of claims 1 to 24, wherein the at least one coding sequence comprises a nucleic acid sequence at least 85% identical to SEQ ID NO: 141.

26. The purified mRNA of claim 25, wherein the at least one coding sequence comprises a nucleic acid sequence at least 90% identical to SEQ ID NO: 141.

27. The purified mRNA of any one of claims 1 to 26, wherein the mRNA is a purified mRNA that has been purified by RP-HPLC and/or TFF.

28. A pharmaceutical composition comprising the purified mRNA of any one of claims 1 to 27 and at least one pharmaceutically acceptable carrier.

29. The composition of claim 28, wherein the composition comprises at least two different mRNA encoding at least two different SARS-CoV-2 spike proteins.

30. The composition of claim 29, 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.

31. The composition of claim 29 or 30, wherein the at least two different SARS-CoV-2 spike proteins are from different SARS CoV-2 variants.

32. The composition of any one of claims 28 to 31, wherein the mRNA is complexed or associated with lipid nanoparticles (LNPs).

33. The composition of claim 32, wherein the LNPs comprises:

(i) at least one cationic lipid;

(ii) at least one neutral lipid;

(iii) at least one steroid; and

(iv) at least one PEG-lipid.

34. 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;

(d) a heterologous 3’ UTR; and

(e) 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).

35. The composition of claim 34, wherein the LNPs comprises:

(i) at least one cationic lipid;

(ii) at least one neutral lipid;

(iii) at least one steroid; and

(iv) at least one PEG-lipid.

36. The composition of claim 34 or 35, wherein the spike protein comprises the D614G substitution and a E484K substitution relative to SEQ ID NO: 10.

37. Use of the purified mRNA or composition of any one of claims 1 to 36 in the manufacture of a medicament for the treatment or prevention of coronavirus infection.

38. A method of producing a pharmaceutical composition comprising obtaining a purified mRNA according to any one of claims 1 to 27 and formulating the purified mRNA in at least one pharmaceutically acceptable carrier.

39. The method of claim 38, wherein the at least one pharmaceutically acceptable carrier comprises lipid nanoparticles (LNPs).