CLAIMS

1. A combination comprising a sequence encoding a SARS-CoV-2 Spike protein antigen and a sequence encoding a SARS-CoV-2 Nucleocapsid antigen, wherein the sequence encoding the SARS-CoV-2 Spike protein antigen and the sequence encoding the SARS-CoV-2 Nucleocapsid protein antigen are comprised in one or more self-replicating RNA molecules and wherein the one or more self-replicating RNA molecules further comprise a sequence encoding nonstructural alphavirus proteins.

2. The combination of claim 1, wherein the sequence encoding the SARS-CoV-2 Spike protein antigen and the sequence encoding the SARS-CoV-2 Nucleocapsid protein antigen are comprised in the same self-replicating RNA molecule, or wherein the sequence encoding the SARS-CoV-2 Spike protein antigen and the sequence encoding the SARS-CoV-2 Nucleocapsid protein antigen are comprised in different self-replicating RNA molecules.

3. The combination of claim 1 or claim 2, wherein the alphavirus is a Venezuelan Equine Encephalitis Virus (VEEV), such as strain TC-83 or a strain having at least 90% sequence identity, preferably at least 95%, more preferably at least 97% thereto.

4. The combination of any one of the previous claims, wherein the one or more self-replicating RNA molecules comprise an A3G mutation in the 5'UTR and/or a Q739L mutation in Nonstructural Protein 2 (nsP2).

5. The combination of any one of the previous claims, wherein the Spike protein antigen is a truncated form of the Spike protein comprising the Receptor-Binding Domain (RBD).

6. The combination of claim 5, wherein the RBD corresponds to SEQ ID NO: 1 or an amino acid sequence having at least 95% identity, preferably at least 97% sequence identity, more preferably at least 99% sequence identity thereto.

7. The combination of any of the previous claims,wherein the one or more self-replicating RNA molecules comprise the nonstructural proteins of VEEV strain TC-83, an A3G mutation in the 5'UTR and a Q739L mutation in nsP2.

8. The combination of any of the previous claims wherein said sequence encoding the SARS-CoV-2 Spike protein antigen comprises a 5' cap, followed by a sequence

encoding nonstructural alphavirus proteins nsP1, nsP2, nsP3 and nsP4, a subgenomic promoter followed by a sequence encoding for the SARS-CoV-2 Spike protein antigen or a truncated form of the Spike protein comprising the Receptor-Binding Domain (RBD) and a poly-A tail downstream of said SARS-CoV-2 Spike protein antigen or truncated form.

9. The combination of any of the previous claims wherein said sequence encoding a SARS-CoV-2 Nucleocapsid (N) antigen comprises a 5′ cap, followed by a sequence encoding nonstructural alphavirus proteins nsP1, nsP2, nsP3 and nsP4, a subgenomic promoter followed by a sequence encoding for the SARS-CoV-2 N protein antigen and a poly-A tail downstream of said SARS-CoV-2 N protein antigen.

10. A pharmaceutical composition comprising the combination according to any one of the previous claims and a pharmaceutically acceptable carrier and/or a pharmaceutically acceptable vehicle.

11. The pharmaceutical composition of claim 10, further comprising at least one adjuvant.

12. The pharmaceutical composition of claim 10 or 11, further comprising a cationic lipid, a liposome, a lipid nanoparticle, a cochleate, a virosome, an immune-stimulating complex, a microparticle, a microsphere, a nanosphere, a unilamellar vesicle, a multilamellar vesicle, an oil-in water emulsion, a water-in-oil emulsion, an emulsome, and a polycationic peptide, or a cationic nano-emulsion.

13. The pharmaceutical composition of any one of claims 10 to 12, wherein the one or more self-replicating RNA molecules are encapsulated in, bound to or adsorbed on a cationic lipid, a liposome, a lipid nanoparticle, a cochleate, a virosome, an immune-stimulating complex, a microparticle, a microsphere, a nanosphere, a unilamellar vesicle, a multilamellar vesicle, an oil-in-water emulsion, a water-in-oil emulsion, an emulsome, and a polycationic peptide, a cationic nano-emulsion and combinations thereof.

14. A vaccine, comprising a combination according to any of the previous claims wherein said RNA molecules are encapsulated in, bound to or adsorbed on a cationic lipid, a lipid nanoparticle, a liposome, a cochleate, a virosome, an immune-stimulating complex, a microparticle, a microsphere, a nanosphere, a unilamellar vesicle, a multilamellar vesicle, an oil-in-water emulsion, a water-in-oil emulsion,

an emulsome, and a polycationic peptide, a cationic nano-emulsion and combinations thereof and wherein the effective dose of said RNA in said vaccine is between 0.1 and 100 µg.

15. The combination of any one of claims 1 to 9 or the pharmaceutical composition of any one of claims 10 to 13 or the vaccine according to claim 14, for use as a medicine.

16. The combination of any one of claims 1 to 9 or the pharmaceutical composition of any one of claims 10 to 13 or the vaccine according to claim 14, for use in the prevention and/or treatment of an infectious disease.

17. The combination of any one of claims 1 to 9 or the pharmaceutical composition of any one of claims 10 to 13 or the vaccine for use according to claim 14, for use in inducing an immune response in a subject.

18. The combination of any one of claims 1 to 9 or the pharmaceutical composition of any one of claims 10 to 13 or vaccine according to claim 14, for use in vaccinating a subject against a coronaviral disease, such as SARS-CoV, SARS-CoV-2 or MERS-CoV.

19. The combination, the pharmaceutical composition or the vaccine for use according to any of the claims 15 to 18 wherein an effective dose of said RNA is between 0.1 and 100 µg.

20. The combination, the pharmaceutical composition or the vaccine for use according to any of the claims 15 to 19, wherein said combination, composition or vaccine is administered intramuscular, intradermal or subcutaneous.

21. The combination, the pharmaceutical composition or the vaccine for use according to any of the claims 15 to 20, wherein said combination, composition or vaccine is administered as a single dose or as a multi-dose, requiring a serie of two or more doses, administered within a pre-defined timespan.

22. The combination, the pharmaceutical composition or the vaccine for use according to any of the claims 15 to 21, wherein said combination, composition or vaccine is administered periodically, such as annually or bi-annually.

23. The combination, the pharmaceutical composition or the vaccine for use according to any of the previous claims, wherein a dose of said vaccine is between 0.05 and 1 ml.

24. A coronavirus vaccine comprising self-replicating RNA molecules, said each self replicating RNA molecule comprises a sequence encoding nonstructural alphavirus proteins and a sequence encoding a SARS-CoV-2 Spike protein antigen, wherein said RNA molecules are encapsulated in, bound to or adsorbed on a cationic lipid, a lipid nanoparticle, a liposome, a cochleate, a virosome, an immune-stimulating complex, a microparticle, a microsphere, a nanosphere, a unilamellar vesicle, a multilamellar vesicle, an oil-in-water emulsion, a water-in-oil emulsion, an emulsome, and a polycationic peptide, a cationic nano-emulsion and combinations thereof.

25. The vaccine of claim 24, wherein the alphavirus is a Venezuelan Equine Encephalitis Virus (VEEV), such as strain TC-83 or a strain having at least 90% sequence identity, preferably at least 95%, more preferably at least 97% thereto.

26. The vaccine of claim 24 or 25 comprising an A3G mutation in the 5'UTR and/or a Q739L mutation in Nonstructural Protein 2 (nsP2).

27. The vaccine of any one of the previous claims 24 to 26, wherein the Spike protein antigen is a truncated form of the Spike protein comprising the Receptor-Binding Domain (RBD), wherein the RBD corresponds to SEQ ID NO: 1 or an amino acid sequence having at least 95% identity, preferably at least 97% sequence identity, more preferably at least 99% sequence identity thereto.

28. The vaccine of any one of the previous claims 24 to 27, wherein the Spike protein is fused to an immune stimulating protein, such as C3d-p28.

29. The vaccine of any one of the previous claims 24 to 28, further comprising a sequence encoding a SARS-CoV-2 Nucleocapsid protein antigen and/or a SARS-Cov-2 Membrane protein antigen.

30. The vaccine of any one of the previous claims 24 to 29, comprising the nonstructural proteins of VEEV strain TC-83, an A3G mutation in the 5'UTR and a Q739L mutation in nsP2, and a 25 sequence encoding a truncated form of the SARS-CoV-2 Spike protein comprising the RBD.

31. The vaccine of any of the previous claims, wherein said each self-amplifying RNA molecule comprises a 5' cap, followed by a sequence encoding nonstructural alphavirus proteins nsP1, nsP2, nsP3 and nsP4, a subgenomic promoter followed by a sequence encoding for the SARS-CoV-2 Spike protein antigen or a truncated form of the Spike protein comprising the Receptor-Binding Domain (RBD) and a poly-A tail downstream of said SARS-CoV-2 Spike protein antigen or truncated form.

32. The vaccine of any of the previous claims 24 to 31, wherein said vaccine, when administered to a subject, preferably a human subject, is able to elicit or induce an immune response to SARS-COV-2 and/or variants thereof in said subject.

33. The vaccine according to any of the previous claims 24 to 32, wherein the vaccine is formulated such that one dose of said vaccine comprises between 0.1 µg and 100 µg of RNA.

34. The vaccine according to any of the previous claims 24 to 33, wherein a dose of said vaccine is between 0.05 and 1 ml.

35. The vaccine according to any of the previous claims, further comprising an adjuvant.

36. A method of treatment or prophylaxis of coronavirus infection, preferably SARS-CoV-2, said method comprises administering a combination according to any of the claims 1 to 9, a pharmaceutical composition according or a vaccine according to any of the claims 10 to 13 or 14 to 35 to a subject, preferably a human subject.

37. A method of inducing an immuneresponse in a subject against a coronavirus infection, preferably SARS-CoV-2, said method comprises administering a combination according to any of the claims 1 to 9, a pharmaceutical composition according or a vaccine according to any of the claims 10 to 13 or 14 to 35 to a subject, preferably a human subject.

38. The method according to claim 36 or 37, wherein said combination, pharmaceutical composition or vaccine is administered to said subject by subcutaneous, intramuscular or intradermal injection.

39. The method according to any of the previous claims wherein an administered dose comprises between 0.1 and 100 µg RNA.

40. Method according to any of the previous claims wherein said combination, pharmaceutical composition or vaccine is administered as a single dose or as a multi-dose, requiring a serie of two or more doses, administered within a pre-defined timespan.

41. Method according to any of the previous claims, wherein said combination, composition or vaccine is administered periodically, such as annually or bi-annually

42. A vector, said vector comprises:
- an antigen sequence, wherein said antigen sequence encodes for an antigen of SARS-CoV-2 and wherein said antigen is downstream of a promoter sequence, preferably an alphavirus derived subgenomic promoter (SGP);
- a poly(A) sequence downstream of said antigen sequence; and
- sequences encoding for non-structural proteins nsP1 to4 of the Venezuelan Equine Encephalitis Virus.

43. The vector according to claim 42, wherein said antigen sequence encodes for a SARS-CoV-2 Spike protein or a truncated form thereof, or wherein said antigen sequence encodes for a SARS-CoV-2 Nucleocapsid (N) antigen.

44. The vector according to claims 42 and 43, wherein said truncated form of the Spike protein comprising the Receptor-Binding Domain (RBD).

45. The vector according to any of the previous claims, wherein the sequence of nsP2 is such that it encodes for an nsP2 protein having a Q739L mutation and/or an A3G mutation in the 5'UTR of said vector.

46. The vector according to any of the previous claims, wherein said vector is a plasmid or linearized DNA.