

WHAT IS CLAIMED:

1. An antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the antibody or antigen-binding fragment thereof specifically binds to an epitope of the spike protein comprising amino acid F486 and/or N487.
2. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof competitively inhibits binding to the spike protein of SARS-CoV-2 of an antibody comprising (i) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:39 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:40; (ii) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:31 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:32; (iii) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:47 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:48; or (iv) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:61 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:62.
3. The antibody or antigen-binding fragment thereof of claim 1 or 2, wherein the antibody or antigen-binding fragment thereof binds to the same epitope of the spike protein of SARS-CoV-2 as an antibody comprising (i) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:39 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:40; (ii) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:31 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:32; (iii) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:47 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:48; or (iv) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:61 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:62.
4. The antibody or antigen-binding fragment thereof of any one of claims 1-3, wherein the antibody or antigen-binding fragment comprises (i) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:39 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:40; (ii) a variable heavy chain (VH)

comprising the amino acid sequence of SEQ ID NO:31 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:32; (iii) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:47 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:48; or (iv) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:61 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:62.

5. The antibody or antigen-binding fragment thereof of any one of claims 1-4, wherein the antibody or antigen-binding fragment thereof comprises the VH-CDR1, VH-CDR2, VH-CDR3, VL-CDR1, VL-CDR2, and VL-CDR3 of SEQ ID NOs:41-46, respectively or SEQ ID NOs: 55-60, respectively.
6. The antibody or antigen-binding fragment thereof of any one of claims 1-5, wherein the antibody or antigen-binding fragment thereof comprises the VH of SEQ ID NO:47 and/or the VL of SEQ ID NO:48 or comprises the VH of SEQ ID NO:61 and/or the VL of SEQ ID NO:62;
optionally wherein the antibody or antigen-binding fragment thereof comprises the VH of SEQ ID NO:47 and the VL of SEQ ID NO:48 or comprises the VH of SEQ ID NO:61 and the VL of SEQ ID NO:62.
7. An antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the antibody or antigen-binding fragment thereof specifically binds to an epitope of the spike protein comprising amino acid G447 and/or K444.
8. The antibody or antigen-binding fragment thereof of claim 7, wherein the antibody the antibody or antigen-binding fragment thereof competitively inhibits binding to the spike protein of SARS-CoV-2 of an antibody comprising (i) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:15 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:16; or (ii) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:23 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:24.
9. The antibody or antigen-binding fragment thereof of claim 7 or 8, wherein the antibody or antigen-binding fragment thereof binds to the same epitope of the spike protein of SARS-

CoV-2 as an antibody comprising (i) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:15 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:16; or (ii) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:23 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:24.

10. The antibody or antigen-binding fragment thereof of any one of claims 7-9, wherein the antibody or antigen-binding fragment thereof comprises (i) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:15 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:16; or (ii) a variable heavy chain (VH) comprising the amino acid sequence of SEQ ID NO:23 and a variable light chain (VL) comprising the amino acid sequence of SEQ ID NO:24.
11. The antibody or antigen-binding fragment thereof of any one of claims 1-10, wherein the antibody or antigen-binding fragment thereof cross-reacts with SARS-CoV.
12. The antibody or antigen-binding fragment thereof of any one of claims 1-10, wherein the antibody or antigen-binding fragment thereof does not cross-react with SARS-CoV.
13. The antibody or antigen-binding fragment thereof of any one of claims 1-12, wherein the antibody or antigen-binding fragment inhibits binding of SARS-CoV-2 to angiotensin converting enzyme 2 (ACE2).
14. The antibody or antigen-binding fragment thereof of any one of claims 1-13, wherein the antibody or antigen-binding fragment neutralizes SARS-CoV-2.
15. The antibody or antigen-binding fragment thereof of any one of claims 1-14, wherein the antibody or antigen-binding fragment is fully human.
16. The antibody or antigen-binding fragment thereof of any one of claims 1-14, wherein the antibody or antigen-binding fragment is humanized.
17. The antibody or antigen-binding fragment thereof of any one of claims 1-16, wherein the antibody or antigen-binding fragment comprises a heavy chain constant region.

18. The antibody or antigen-binding fragment thereof of claim 17, wherein the heavy chain constant region is selected from the group consisting of human immunoglobulins IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2 heavy chain constant regions, optionally wherein the heavy chain constant region is a human IgG1.
19. The antibody or antigen-binding fragment thereof of any one of claims 1-18, wherein the antibody or antigen-binding fragment comprises a light chain constant region.
20. The antibody or antigen-binding fragment thereof of claim 19, wherein the light chain constant region is selected from the group consisting of human immunoglobulins IgG κ and IgG λ light chain constant regions, optionally wherein the light chain constant region is a human IgG κ light chain constant region.
21. The antibody or antigen-binding fragment thereof of any one of claims 1-20, wherein the antibody or antigen-binding fragment comprises (i) a human IgG1 heavy chain constant region and (ii) a human IgG κ light chain constant region.
22. The antibody or antigen-binding fragment thereof of any one of claims 1-21, wherein the antibody or antigen-binding fragment further comprises a heavy chain constant region comprising a YTE mutation, optionally wherein the heavy chain constant region is a human IgG1 heavy chain constant region, and a light chain constant region, optionally wherein the light chain constant region is a human IgG κ light chain constant region.
23. The antibody or antigen-binding fragment thereof of any one of claims 1-18, wherein the antibody or antigen-binding fragment further comprises a heavy chain constant region comprising a TM mutation, optionally wherein the heavy chain constant region is a human IgG1 heavy chain constant region, and a light chain constant region, optionally wherein the light chain constant region is a human IgG κ light chain constant region.
24. The antibody or antigen binding fragment thereof of any one of claims 1-23, which is a full length antibody.
25. The antibody or antigen binding fragment thereof of any one of claims 1-23, which is an antigen binding fragment.

26. The antigen binding fragment of claim 25, wherein the antigen binding fragment comprises a Fab, Fab', F(ab')₂, single chain Fv (scFv), disulfide linked Fv, V-NAR domain, IgNar, IgGΔCH2, minibody, F(ab')₃, tetrabody, triabody, diabody, single-domain antibody, (scFv)₂, or scFv-Fc.
27. The antibody or antigen binding fragment thereof of any one of claims 1-26, wherein the antibody or antigen-binding fragment is isolated.
28. The antibody or antigen binding fragment thereof of any one of claims 1-27, wherein the antibody or antigen-binding fragment is monoclonal.
29. The antibody or antigen binding fragment thereof of any one of claims 1-28, wherein the antibody or antigen-binding fragment is recombinant.
30. The antibody or antigen-binding fragment thereof of any one of claims 1-29, further comprising a detectable label.
31. An isolated polynucleotide comprising a nucleic acid molecule encoding the heavy chain variable region and/or a nucleic acid molecule encoding the light chain variable region of the antibody or antigen-binding fragment thereof of any one of claims 1-30.
32. An isolated vector comprising the polynucleotide of claim 31.
33. A host cell comprising the polynucleotide of any one of claim 31, the vector of claim 32, or a first vector comprising a nucleic acid molecule encoding the heavy chain variable region and a second vector comprising a nucleic acid molecule encoding the light chain variable region of the antibody or antigen-binding fragment thereof of any one of claims 1-30.
34. A method of producing an antibody or antigen-binding fragment thereof that binds to the spike protein of SARS-CoV-2 comprising culturing the host cell of claim 33 so that the nucleic acid molecule is expressed and the antibody or antigen-binding fragment thereof is produced, optionally wherein the method further comprises isolating the antibody or antigen-binding fragment.

35. An antibody or antigen-binding fragment thereof produced by the method of claim 34.
36. A method of selecting an antibody or antigen-binding fragment thereof comprising determining that the antibody or antigen-binding fragment thereof binds to an epitope of the spike protein of SARS-CoV-2 comprising amino acid F486 and/or N487 and selecting the antibody or antigen-binding fragment thereof.
37. The method of claim 36, wherein the determining comprises measuring the ability of the antibody or antigen-binding fragment thereof to bind to a mutant spike protein of SARS-CoV-2 comprising F486A and/or N487A, and wherein the antibody or antigen-binding fragment thereof is not selected if it binds to the mutant protein.
38. An antibody or antigen-binding fragment thereof selected by the method of claim 36 or 37.
39. A method of selecting an antibody or antigen-binding fragment thereof comprising determining that the antibody or antigen-binding fragment thereof binds to an epitope of the spike protein of SARS-CoV-2 comprising amino acid G447 and/or K444 and selecting the antibody or antigen-binding fragment thereof.
40. The method of claim 39, wherein the determining comprises measuring the ability of the antibody or antigen-binding fragment thereof to bind to a mutant spike protein of SARS-CoV-2 comprising G447R and/or K444A, and wherein the antibody or antigen-binding fragment thereof is not selected if it binds to the mutant protein.
41. An antibody or antigen-binding fragment thereof selected by the method of claim 38 or claim 39.
42. A composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-30, 35, 38, and 41, optionally wherein the composition is a pharmaceutical composition further comprising a pharmaceutically acceptable excipient.
43. A composition comprising (i) a first antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the first antibody or antigen-binding fragment thereof specifically binds to the ACE2-interface of the receptor binding domain (RBD) of the spike protein of SARS-CoV-2 and (ii) a second antibody or

antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the second antibody or antigen-binding fragment thereof specifically binds to the apex domain of the RBD of the spike protein.

44. A composition comprising (i) a first antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the first antibody or antigen-binding fragment thereof specifically binds to an epitope of the spike protein comprising F486 and/or N487 and (ii) a second antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the second antibody or antigen-binding fragment thereof specifically binds to an epitope of the spike protein comprising G447 and/or K444.
45. The composition of claim 43 or 44, wherein the first antibody or antigen-binding fragment thereof and the second antibody or antigen-binding fragment thereof bind to non-overlapping epitopes and/or wherein the first antibody or antigen-binding fragment thereof and the second antibody or antigen-binding fragment thereof can bind to a trimer of the spike domain of SARS-CoV-2 concurrently.
46. The composition of any one of claims 43-45, wherein the first antibody or antigen-binding fragment thereof is the antibody or antigen-binding fragment thereof of any one of claims 1-3, 7-28, 33, and 36.
47. The composition of any one of claims 43-46, wherein the second antibody or antigen-binding fragment thereof is the antibody or antigen-binding fragment thereof of any one of claims 5-28, 33, and 39.
48. The composition of any one of claims 43-47, wherein the composition is a pharmaceutical composition further comprising a pharmaceutically acceptable carrier.
49. A method of selecting a combination of antibodies or antigen-binding fragments thereof for use in the treatment or prevention of a SARS-CoV-2 infection, the method, comprising determining that a first antibody or antigen-binding fragment thereof binds to an epitope of the spike protein of SARS-CoV-2 comprising amino acid F486 and/or N487, determining that a second antibody or antigen-binding fragment thereof binds to an epitope of the spike

protein of SARS-CoV-2 comprising amino acid G447 and/or K444, and selecting the two antibodies or antigen-binding fragments thereof.

50. The method of claim 49, wherein the determining comprising measuring the ability of the first antibody or antigen-binding fragment thereof to bind to a mutant spike protein of SARS-CoV-2 comprising F486A and/or N487A and/or measuring the ability of the second antibody or antigen-binding fragment thereof to bind to a mutant spike protein of SARS-CoV-2 comprising G447R and/or K444A, and wherein the antibody or antigen-binding fragment thereof is not selected if it binds to the mutant protein.
51. A composition comprising the combination of antibodies or antigen-binding fragments thereof selected by the method of claim 49 or 50.
52. A method for inhibiting the binding of SARS-CoV-2 to ACE2 comprising contacting the SARS-CoV-2 with the antibody or antigen-binding fragment thereof of any one of claims 1-30, 35, 38, and 41 or the composition of any one of claims 42-48 and 51.
53. A method for inhibiting the binding of SARS-CoV-2 to ACE2 comprising contacting the SARS-CoV-2 with (i) a first antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the first antibody or antigen-binding fragment thereof specifically binds to the ACE2-interface of the receptor binding domain (RBD) of the spike protein of SARS-CoV-2 and (ii) a second antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the second antibody or antigen-binding fragment thereof specifically binds to the apex domain of the RBD of the spike protein.
54. A method for inhibiting the binding of SARS-CoV-2 to ACE2 comprising contacting the SARS-CoV-2 with (i) a first antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the first antibody or antigen-binding fragment thereof specifically binds to an epitope of the spike protein comprising F486 and/or N487 and (ii) a second antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the second antibody or antigen-binding fragment thereof specifically binds to an epitope of the spike protein comprising G447 and/or K444.

55. A method for neutralizing SARS-CoV-2 comprising contacting the SARS-CoV-2 with the antibody or antigen-binding fragment thereof of any one of claims 1-30, 35, 38, and 41 or the composition of any one of claims 42-48 and 51.
56. A method for neutralizing SARS-CoV-2 comprising contacting the SARS-CoV-2 with (i) a first antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the first antibody or antigen-binding fragment thereof specifically binds to the ACE2-interface of the receptor binding domain (RBD) of the spike protein of SARS-CoV-2 and (ii) a second antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the second antibody or antigen-binding fragment thereof specifically binds to the apex domain of the RBD of the spike protein.
57. A method for neutralizing SARS-CoV-2 comprising contacting the SARS-CoV-2 with (i) a first antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the first antibody or antigen-binding fragment thereof specifically binds to an epitope of the spike protein comprising F486 and/or N487 and (ii) a second antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the second antibody or antigen-binding fragment thereof specifically binds to an epitope of the spike protein comprising G447 and/or K444.
58. The method of any one of claims 55-57, wherein the contacting is *in vitro*.
59. The method of any one of claims 55-57, wherein the contacting is in a subject.
60. A method of treating or preventing a SARS-CoV-2 infection in a subject, the method comprising administering to the subject an effective amount of the antibody or antigen-binding fragment thereof of any one of claims 1-30, 35, 38, and 41 or the composition of any one of claims 42-48 and 51.
61. A method of treating or preventing a SARS-CoV-2 infection in a subject, the method comprising administering to the subject (i) a first antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the first antibody or antigen-binding fragment thereof specifically binds to the ACE2-interface of

the receptor binding domain (RBD) of the spike protein of SARS-CoV-2 and (ii) a second antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the second antibody or antigen-binding fragment thereof specifically binds to the apex domain of the RBD of the spike protein.

62. A method of treating or preventing a SARS-CoV-2 infection in a subject, the method comprising administering to the subject (i) a first antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the first antibody or antigen-binding fragment thereof specifically binds to an epitope of the spike protein comprising F486 and/or N487 and (ii) a second antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the second antibody or antigen-binding fragment thereof specifically binds to an epitope of the spike protein comprising G447 and/or K444.
63. A method of reducing the viral load in a subject infected with SARS-CoV-2, the method comprising administering to the subject an effective amount of the antibody or antigen-binding fragment thereof of any one of claims 1-30, 35, 38, and 41 or the composition of any one of claims 42-48 and 51.
64. A method of reducing the viral load in a subject infected with SARS-CoV-2, the method comprising administering to the subject (i) a first antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the first antibody or antigen-binding fragment thereof specifically binds to the ACE2-interface of the receptor binding domain (RBD) of the spike protein of SARS-CoV-2 and (ii) a second antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the second antibody or antigen-binding fragment thereof specifically binds to the apex domain of the RBD of the spike protein.
65. A method of reducing the viral load in a subject infected with SARS-CoV-2, the method comprising administering to the subject (i) a first antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the first antibody or antigen-binding fragment thereof specifically binds to an epitope of the spike protein comprising F486 and/or N487 and (ii) a second antibody or antigen-binding fragment thereof that specifically binds to the spike protein of SARS-CoV-2, wherein the

second antibody or antigen-binding fragment thereof specifically binds to an epitope of the spike protein comprising G447 and/or K444.

66. The method of any one of claims 53-65, wherein the first antibody or antigen-binding fragment thereof and the second antibody or antigen-binding fragment thereof bind to non-overlapping epitopes and/or wherein the first antibody or antigen-binding fragment thereof and the second antibody or antigen-binding fragment thereof can bind to a trimer of the spike domain of SARS-CoV-2 concurrently.
67. The method of any one of claims 53-66, wherein the first antibody or antigen-binding fragment thereof is the antibody or antigen-binding fragment thereof of any one of claims 1-3, 8-30, 35, and 38.
68. The method of any one of claims 53-67, wherein the second antibody or antigen-binding fragment thereof is the antibody or antigen-binding fragment thereof of any one of claims 6-30, 35, and 41.
69. The method of any one of claims 53-68, wherein the first antibody or antigen-binding fragment thereof and the second antibody or antigen-binding fragment thereof are administered simultaneously, optionally wherein the first antibody or antigen-binding fragment thereof and the second antibody or antigen-binding fragment thereof are administered in separate pharmaceutical compositions.
70. The method of any one of claims 53-68, wherein the first antibody or antigen-binding fragment thereof and the second antibody or antigen-binding fragment thereof are administered sequentially.
71. The method of any one of claims 59-70, wherein the subject has been exposed to SARS-CoV-2 or is at risk of exposure to SARS-CoV-2.
72. The method of any one of claims 59-71, wherein the subject is human.
73. A method for detecting SARS-CoV-2 in a sample comprising contacting the sample with the antibody or antigen-binding fragment thereof of any one of claims 1-30, 35, 38, and 41 or the composition of any one of claims 42-48 and 51.

74. A kit comprising the antibody or antigen-binding fragment thereof of any one of claims of any one of claims 1-30, 35, 38, and 41 or the composition of any one of claims 42-48 and 51 and a) a detection reagent, b) a SARS-Co-V2 spike protein antigen, c) a notice that reflects approval for use or sale for human administration, or d) a combination thereof.