

WHAT IS CLAIMED IS:

1. An isolated antibody or antibody fragment that binds to a SARS-CoV-2 surface spike protein, wherein the antibody or fragment comprises
 - 5 (a) a CDRH1 comprising the amino acid sequence of SEQ ID NO:59, a CDRH2 comprising the amino acid sequence of SEQ ID NO:60, a CDRH3 comprising the amino acid sequence of SEQ ID NO:61, a CDRL1 comprising the amino acid sequence of SEQ ID NO:89, a CDRH2 comprising the amino acid sequence of SEQ ID NO:90, a CDRH3 comprising the amino acid sequence of SEQ ID
10 NO:91;
 - (b) a CDRH1 comprising the amino acid sequence of SEQ ID NO:68, a CDRH2 comprising the amino acid sequence of SEQ ID NO:69, a CDRH3 comprising the amino acid sequence of SEQ ID NO:70, a CDRL1 comprising the amino acid sequence of SEQ ID NO:98, a CDRH2 comprising the amino acid sequence of SEQ ID NO:99, a CDRH3 comprising the amino acid sequence of SEQ ID
15 NO:100;
 - (c) a CDRH1 comprising the amino acid sequence of SEQ ID NO:41, a CDRH2 comprising the amino acid sequence of SEQ ID NO:42, a CDRH3 comprising the amino acid sequence of SEQ ID NO:43, a CDRL1 comprising the amino acid sequence of SEQ ID NO:71, a CDRH2 comprising the amino acid sequence of SEQ ID NO:72, a CDRH3 comprising the amino acid sequence of SEQ ID
20 NO:73;
 - (d) a CDRH1 comprising the amino acid sequence of SEQ ID NO:44, a CDRH2 comprising the amino acid sequence of SEQ ID NO:45, a CDRH3 comprising the amino acid sequence of SEQ ID NO:46, a CDRL1 comprising the amino acid sequence of SEQ ID NO:74, a CDRH2 comprising the amino acid sequence of SEQ ID NO:75, a CDRH3 comprising the amino acid sequence of SEQ ID
25 NO:76;
 - (e) a CDRH1 comprising the amino acid sequence of SEQ ID NO:47, a CDRH2 comprising the amino acid sequence of SEQ ID NO:48, a CDRH3 comprising the amino acid sequence of SEQ ID NO:49, a CDRL1 comprising the amino acid sequence of SEQ ID NO:77, a CDRH2 comprising the amino acid sequence of SEQ ID NO:78, a CDRH3 comprising the amino acid sequence of SEQ ID
30 NO:79;

- 5 (f) a CDRH1 comprising the amino acid sequence of SEQ ID NO:50, a CDRH2 comprising the amino acid sequence of SEQ ID NO:51, a CDRH3 comprising the amino acid sequence of SEQ ID NO:52, a CDRL1 comprising the amino acid sequence of SEQ ID NO:80, a CDRH2 comprising the amino acid sequence of SEQ ID NO:81, a CDRH3 comprising the amino acid sequence of SEQ ID NO:82;
- 10 (g) a CDRH1 comprising the amino acid sequence of SEQ ID NO:53, a CDRH2 comprising the amino acid sequence of SEQ ID NO:54, a CDRH3 comprising the amino acid sequence of SEQ ID NO:55, a CDRL1 comprising the amino acid sequence of SEQ ID NO:83, a CDRH2 comprising the amino acid sequence of SEQ ID NO:84, a CDRH3 comprising the amino acid sequence of SEQ ID NO:85;
- 15 (h) a CDRH1 comprising the amino acid sequence of SEQ ID NO:56, a CDRH2 comprising the amino acid sequence of SEQ ID NO:57 a CDRH3 comprising the amino acid sequence of SEQ ID NO:58, a CDRL1 comprising the amino acid sequence of SEQ ID NO:86, a CDRH2 comprising the amino acid sequence of SEQ ID NO:87, a CDRH3 comprising the amino acid sequence of SEQ ID NO:88;
- 20 (i) a CDRH1 comprising the amino acid sequence of SEQ ID NO:62, a CDRH2 comprising the amino acid sequence of SEQ ID NO:63 a CDRH3 comprising the amino acid sequence of SEQ ID NO:64, a CDRL1 comprising the amino acid sequence of SEQ ID NO:65, a CDRH2 comprising the amino acid sequence of SEQ ID NO:66, a CDRH3 comprising the amino acid sequence of SEQ ID NO:67; or
- 25 (j) a CDRH1 comprising the amino acid sequence of SEQ ID NO:65, a CDRH2 comprising the amino acid sequence of SEQ ID NO:66, a CDRH3 comprising the amino acid sequence of SEQ ID NO:67, a CDRL1 comprising the amino acid sequence of SEQ ID NO:95, a CDRH2 comprising the amino acid sequence of SEQ ID NO:96, a CDRH3 comprising the amino acid sequence of SEQ ID
- 30 NO:97.
2. The antibody or antibody fragment of claim 1, wherein the antibody or fragment comprises heavy and light chain variable sequences having at least 70%, 80%, 90%, or 95% identity to

- (a) the amino acid sequence of SEQ ID NO:33 and the amino acid sequence of SEQ ID NO:34;
- (b) the amino acid sequence of SEQ ID NO:39 and the amino acid sequence of SEQ ID NO:40;
- 5 (c) the amino acid sequence of SEQ ID NO:21 and the amino acid sequence of SEQ ID NO:22;
- (d) the amino acid sequence of SEQ ID NO:23 and the amino acid sequence of SEQ ID NO:24;
- (e) the amino acid sequence of SEQ ID NO:25 and the amino acid sequence of SEQ ID NO:26;
- 10 (f) the amino acid sequence of SEQ ID NO:27 and the amino acid sequence of SEQ ID NO:28;
- (g) the amino acid sequence of SEQ ID NO:29 and the amino acid sequence of SEQ ID NO:30;
- 15 (h) the amino acid sequence of SEQ ID NO:31 and the amino acid sequence of SEQ ID NO:32;
- (i) the amino acid sequence of SEQ ID NO:35 and the amino acid sequence of SEQ ID NO:36; or
- (j) the amino acid sequence of SEQ ID NO:37 and the amino acid sequence of SEQ ID NO:38.
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3. The antibody or antibody fragment of claim 1 or 2, wherein the antibody or fragment comprises
- (a) a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO:33 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:34;
- 25 (b) a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO:39 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:40;
- 30 (c) a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO:21 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:22;

- (d) a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO:23 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:24;
- 5 (e) a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO:25 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:26;
- (f) a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO:27 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:28;
- 10 (g) a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO:29 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:30;
- (h) a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO:31 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:32;
- 15 (i) a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO:35 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:36; or
- (j) a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO:37 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:38.
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4. The antibody or antibody fragment of any one of claims 1-3, wherein the antibody or fragment is monoclonal.
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5. The antibody or antibody fragment of any one of claims 1-4, wherein the antibody fragment is a recombinant scFv (single chain fragment variable) antibody, Fab fragment, F(ab')₂ fragment, or Fv fragment.
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6. The antibody or antibody fragment of any one of claims 1-5, wherein the antibody or fragment comprises a YTE mutation.

7. The antibody or antibody fragment of any one of claims 1-6, wherein the antibody or fragment is an IgG, or a recombinant IgG antibody or antibody fragment comprising an Fc portion mutated to alter (eliminate or enhance) FcR interactions, to increase half-life and/or increase therapeutic efficacy, such as a LALA, LALA PG, N297, GASD/ALIE, DHS, YTE or LS mutation or glycan modified to alter (eliminate or enhance) FcR interactions such as enzymatic or chemical addition or removal of glycans or expression in a cell line engineered with a defined glycosylating pattern.
8. The antibody or antibody fragment of any one of claims 1-7, wherein the antibody or antibody fragment is capable of neutralizing live BSL3 SARS-CoV-2 virus in a focus reduction neutralization test (FRNT) assay using Vero-E2 cell culture monolayers, optionally wherein the antibody or antibody fragment is capable of neutralizing 96% of the live BSL3 SARS-CoV-2 virus at a concentration of 250 ng/mL.
9. The antibody or antibody fragment of any one of claims 1-8, wherein the antibody or antibody fragment blocks receptor binding domain (RBD) binding to human receptor angiotensin converting enzyme 2 (ACE2), optionally wherein the antibody or antibody fragment blocks activity against hACE2 with an $IC_{50} < 150$ ng/mL.
10. The antibody or antibody fragment of any one of claims 1-9, wherein the antibody or antibody fragment is capable of neutralizing SARS-CoV-2 virus comprising a spike protein comprising a D614G substitution, optionally wherein the spike protein does not comprise a E484K substitution.
11. The antibody or antibody fragment of any one of claims 1-10, wherein the antibody or antibody fragment is able to bind RBD in the “up” conformation.
12. The antibody or antibody fragment of any one of claims 1-11 wherein the antibody or antibody fragment is able to bind RBD in the “up” and “down” conformations.
13. The antibody or antibody fragment of any one of claims 1-11, wherein the antibody or antibody fragment is not able to bind RBD in the “down” conformation.

14. The antibody or antibody fragment of any one of claims 1-13, wherein the antibody or fragment is able to bind a trimeric spike protein ectodomain and is able to bind to a monomeric spike protein RBD, optionally wherein the binding to the trimeric spike protein ectodomain and/or the binding to the monomeric spike protein RBD is with an $EC_{50} < 2$ ng/mL.
15. The antibody or antibody fragment of any one of claims 1-14, wherein the antibody or antibody fragment further comprises a detectable label.
16. A method of treating a subject infected with SARS-CoV-2 or reducing the likelihood of infection of a subject at risk of contracting SARS-CoV-2, comprising delivering to the subject a first antibody or antibody fragment of any one of claims 1-15.
17. A method of protecting the health of a subject of age 60 or older, an immunocompromised, subject or a subject suffering from a respiratory and/or cardiovascular disorder that is infected with or at risk of infection with SARS-CoV-2 comprising delivering to the subject a first antibody or antibody fragment of any one of claims 1-15.
18. The method of claim 16 or 17, wherein the method further comprises delivering to the subject a second antibody or antibody fragment, optionally wherein the second antibody or antibody fragment is an antibody or antibody fragment of any one of claims 1-15.
19. A method of treating a subject infected with SARS-CoV-2 or reducing the likelihood of infection of a subject at risk of contracting SARS-CoV-2, comprising delivering to the subject a first antibody or antibody fragment and a second antibody or antibody fragment, wherein the first and second antibodies or antibody fragments are synergistic in neutralizing neutralizing SARS-CoV-2.
20. The method of claim 18 or 19 wherein the first antibody or antibody fragment and the second antibody or antibody fragment have a synergy score of 17.4.

21. The method of any one of claims 18-20, wherein the dose of the first antibody or antibody fragment and the second antibody or antibody fragment can be reduced by more than 3 times the dose of the first antibody or antibody fragment or the second antibody or antibody fragment alone to achieve the same potency in virus neutralization.
22. The method of any one of claims 18-21, wherein the first antibody or antibody fragment is able to bind to RBD in the “up” confirmation and is not able to bind to RBD in the “down” confirmation.
23. The method of any one of claims 18-22, wherein the second antibody or antibody fragment is able to bind RBD in both “up” and “down” conformations.
24. The method of any one of claims 18-23, wherein the first antibody or antibody fragment and the second antibody or antibody fragment do not compete for binding to RBD.
25. The method of any one of claims 18-24, wherein the first antibody or antibody fragment comprises a CDRH1 comprising the amino acid sequence of SEQ ID NO:59, a CDRH2 comprising the amino acid sequence of SEQ ID NO:60, a CDRH3 comprising the amino acid sequence of SEQ ID NO:61, a CDRL1 comprising the amino acid sequence of SEQ ID NO:89, a CDRH2 comprising the amino acid sequence of SEQ ID NO:90, a CDRH3 comprising the amino acid sequence of SEQ ID NO:91.
26. The method of any one of claims 18-25, wherein the second antibody or antibody fragment comprises a CDRH1 comprising the amino acid sequence of SEQ ID NO:68, a CDRH2 comprising the amino acid sequence of SEQ ID NO:69, a CDRH3 comprising the amino acid sequence of SEQ ID NO:70, a CDRL1 comprising the amino acid sequence of SEQ ID NO:98, a CDRH2 comprising the amino acid sequence of SEQ ID NO:99, a CDRH3 comprising the amino acid sequence of SEQ ID NO:100.
27. The method of any one of claims 18-26, wherein the first antibody or antibody fragment comprises a heavy chain variable sequence comprising the amino acid

sequence of SEQ ID NO:33 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:34.

- 5 28. The method of any one of claims 18-27, wherein the second antibody or antibody fragment comprises a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO:39 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:40.
- 10 29. The method of any one of claims 16-28, wherein the delivering reduces the expression of INF- γ , IL-6, CXCL10 and CCL2 in the subject.
30. The method of any one of claims 16-29, wherein the delivering is intravenous.
- 15 31. The method of any one of claims 16-30, wherein the subject is of age 60 or older, is immunocompromised, or suffers from a respiratory and/or cardiovascular disorder.
32. The method of any one of claims 16-31, wherein the delivering improves the subject's respiration as compared to an untreated control.
- 20 33. The method of any one of claims 16-32, wherein the delivering reduces viral load as compared to an untreated control.
34. The method of any one of claims 17-33, wherein the delivering is prior to infection.
- 25 35. The method of any one of claims 17-33, wherein the delivering is after infection.
36. A vaccine formulation comprising one or more antibodies or antibody fragments of any one of claims 1-15.
- 30 37. The vaccine formulation of claim 36, further comprising a second antibody or antibody fragment that binds to a SARS-CoV-2 surface spike protein, optionally wherein the second antibody or antibody fragment is an antibody or antibody fragment of any one of claims 1-15.

38. A vaccine formulation comprising one or more expression vectors encoding a first antibody or antibody fragment according to any one of claims 1-15.
- 5 39. The vaccine formulation of claim 38, wherein the expression vector(s) is/are Sindbis virus or VEE vector(s).
40. The vaccine formulation of claim 38 or 39, formulated for delivery by needle injection, jet injection, or electroporation.
- 10 41. The vaccine formulation of claim 40, further comprising one or more expression vectors encoding for a second antibody or antibody fragment that binds to a SARS-CoV-2 surface spike protein, optionally wherein the second antibody or antibody fragment is an antibody or antibody fragment of any one of claims 1-15.
- 15 42. A method of detecting COVID-19 infection with SARS-CoV-2 in a subject comprising
(a) contacting a sample from the subject with the antibody or fragment of any one of claims 1-15; and
20 (b) detecting SARS-CoV-2 in the sample by binding of the antibody or antibody fragment to a SARS-CoV-2 antigen in the sample.
43. The method of claim 42, wherein the sample is a body fluid.
- 25 44. The method of claim 42 or 43, wherein the sample is blood, sputum, tears, saliva, mucous or serum, semen, cervical or vaginal secretions, amniotic fluid, placental tissues, urine, exudate, transudate, tissue scrapings or feces.
45. The method of any one of claims 42-44, wherein the detection comprises ELISA, RIA, lateral flow assay or western blot.
- 30 46. A method of determining the antigenic integrity, correct conformation and/or correct sequence of a SARS-CoV-2 surface spike protein comprising:

- (a) contacting a sample comprising the antigen with the antibody or fragment of any one of claims 1-15; and
- (b) determining antigenic integrity, correct conformation and/or correct sequence of the antigen by detectable binding of the antibody or antibody fragment to the antigen.
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47. The method of claim 46, wherein the sample comprises recombinantly produced antigen.
- 10 48. The method of claim 46, wherein the sample comprises a vaccine formulation or vaccine production batch.
49. The method of any one of claims 46-48, wherein the detection comprises ELISA, RIA, western blot, a biosensor using surface plasmon resonance or biolayer interferometry, or flow cytometric staining.
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50. The method of any one of claims 46-49, further comprising performing steps (a) and (b) a second time to determine the antigenic stability of the antigen over time.
- 20 51. A hybridoma or engineered cell comprising a polynucleotide encoding the antibody or antibody fragment of any one of claims 1-15.
52. An isolated human monoclonal antibody or antibody fragment, or hybridoma or engineered cell producing the same, wherein the antibody binds to a SARS-CoV-2 surface spike protein.
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53. An isolated polynucleotide comprising a nucleic acid sequence encoding the heavy chain variable region of the antibody or antibody fragment of any one of claims 1-15 and/or a nucleic acid sequence encoding the light chain variable region of the antibody or antibody fragment.
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54. The polynucleotide of claim 53, wherein the polynucleotide comprises the sequence of any one of SEQ ID NOs: 1-20.

55. A vector comprising the polynucleotide of claim 54.
56. A host cell comprising the polynucleotide of claim 53 or 54, the vector of claim 55,
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 antibody fragment thereof of any
one of claims 1-15.
57. A method of making an antibody or antibody fragment comprising (a) culturing the
cell of claim 56; and (b) isolating the antibody or antibody fragment thereof from
the cultured cell.
58. A composition comprising a first antibody or antibody fragment that binds to a
SARS-CoV-2 surface spike protein and a second antibody or antibody fragment
that binds to a SARS-CoV-2 surface spike protein, optionally wherein the
composition is a pharmaceutically acceptable composition.
59. A kit comprising a first antibody or antibody fragment that binds to a SARS-CoV-
2 surface spike protein and a second antibody or antibody fragment that binds to a
SARS-CoV-2 surface spike protein, optionally wherein the kit further comprises
instructions for using the first antibody or antibody fragment and the second
antibody or antibody fragment for treating a subject infected with SARS-CoV-2 or
for reducing the likelihood of infection of a subject at risk of contracting SARS-
CoV-2.
60. The composition or kit of claim 58 or 59 wherein the first antibody or antibody
fragment and the second antibody or antibody fragment have a synergy score of
17.4.
61. The composition or kit of any one of claims 58-60, wherein the dose of the first
antibody or antibody fragment and the second antibody or antibody fragment can
be reduced by more than 3 times the dose of the first antibody or antibody fragment
or the second antibody or antibody fragment alone to achieve the same potency in
virus neutralization.

- 5 62. The composition or kit of any one of claims 58-61, wherein the first antibody or antibody fragment is able to bind to RBD in the “up” confirmation and is not able to bind to RBD in the “down” confirmation.
63. The composition or kit of any one of claims 58-62, wherein the second antibody or antibody fragment is able to bind RBD in both “up” and “down” conformations.
- 10 64. The composition or kit of any one of claims 58-63, wherein the first antibody or antibody fragment and the second antibody or antibody fragment do not compete for binding to RBD.
- 15 65. The composition or kit of any one of claims 58-64, wherein the first antibody or antibody fragment comprises a CDRH1 comprising the amino acid sequence of SEQ ID NO:59, a CDRH2 comprising the amino acid sequence of SEQ ID NO:60, a CDRH3 comprising the amino acid sequence of SEQ ID NO:61, a CDRL1 comprising the amino acid sequence of SEQ ID NO:89, a CDRH2 comprising the amino acid sequence of SEQ ID NO:90, a CDRH3 comprising the amino acid sequence of SEQ ID NO:91.
- 20 66. The composition or kit of any one of claims 58-65, wherein the second antibody or antibody fragment comprises a CDRH1 comprising the amino acid sequence of SEQ ID NO:68, a CDRH2 comprising the amino acid sequence of SEQ ID NO:69, a CDRH3 comprising the amino acid sequence of SEQ ID NO:70, a CDRL1 comprising the amino acid sequence of SEQ ID NO:98, a CDRH2 comprising the amino acid sequence of SEQ ID NO:99, a CDRH3 comprising the amino acid sequence of SEQ ID NO:100.
- 25 67. The composition or kit of any one of claims 58-66, wherein the first antibody or antibody fragment comprises a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO:33 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:34.
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68. The composition or kit of any one of claims 58-67, wherein the second antibody or antibody fragment comprises a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO:39 and/or a light chain variable sequence comprising the amino acid sequence of SEQ ID NO:40.

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69. The kit of any one of claims 59-68, wherein the first antibody or antibody fragment and the second antibody or antibody fragment are in separate containers.

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