

ANTIBODIES AGAINST SARS-COV-2 AND METHODS OF USING THE SAME

STATEMENT REGARDING SEQUENCE LISTING

The Sequence Listing associated with this application is provided in text format
5 in lieu of a paper copy, and is hereby incorporated by reference into the specification.
The name of the text file containing the Sequence Listing is 930585_402WO
_SEQUENCE_LISTING.txt. The text file is 328 KB, was created on February 24,
2021, and is being submitted electronically via EFS-Web.

BACKGROUND

10 A novel betacoronavirus emerged in Wuhan, China, in late 2019. As of
February 19, 2021, approximately 110 million cases of infection by this virus (termed,
among other names, SARS-CoV-2 and originally identified as Wuhan coronavirus),
were confirmed worldwide, and had resulted in approximately 2.45 million deaths.
Modalities for preventing or treating SARS-CoV-2 infection, and diagnostic tools for
15 diagnosing a SARS-CoV-2 infection, are needed.

SUMMARY

In one aspect, the present disclosure refers to an isolated antibody, or an
antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) that
20 comprises the complementarity determining region (CDR)H1 amino acid sequence set
forth in SEQ ID NO.:106, the CDRH2 amino acid sequence set forth in SEQ ID
NO.:121, and the CDRH3 amino acid sequence set forth in SEQ ID NO.:108, and a
light chain variable domain (VL) that comprises the CDRL1 amino acid sequence set
forth in SEQ ID NO.:169, the CDRL2 amino acid sequence set forth in SEQ ID
25 NO.:170, and the CDRL3 amino acid sequence set forth in SEQ ID NO.:171,
wherein the antibody or antigen-binding fragment is capable of binding to a SARS-
CoV-2 surface glycoprotein (S).

In another aspect, the present disclosure refers to an isolated antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) and a light chain variable domain (VL), wherein the VH comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113 and the VL comprises or consists of the amino acid sequence set forth in SEQ ID NO.:168.

In another aspect, the present disclosure refers to the use of a SARS-CoV-2 neutralizing antibody or antigen-binding fragment in the manufacture of a medicament for treating a SARS-CoV-2 infection in a subject, wherein the SARS-CoV-2 neutralizing antibody or antigen-binding fragment comprises:

(i) a heavy chain variable domain (VH) that comprises: the complementarity determining region (CDR)H1 amino acid sequence set forth in SEQ ID NO.:106, the CDRH2 amino acid sequence set forth in SEQ ID NO.:121, and the CDRH3 amino acid sequence set forth in SEQ ID NO.:108; and

(ii) a light chain variable domain (VL) that comprises: the CDRL1 amino acid sequence set forth in SEQ ID NO.:169, the CDRL2 amino acid sequence set forth in SEQ ID NO.:170, and the CDRL3 amino acid sequence set forth in SEQ ID NO.:171.

In another aspect, the present disclosure refers to the use of a SARS-CoV-2 neutralizing antibody or antigen-binding fragment in the manufacture of a medicament for treating a SARS-CoV-2 infection in a subject, wherein the SARS-CoV-2 neutralizing antibody or antigen-binding fragment comprises a heavy chain variable domain (VH) and a light chain variable domain (VL), wherein the VH comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113 and the VL comprises or consists of the amino acid sequence set forth in SEQ ID NO.:168.

In another aspect, the present disclosure refers to an isolated antibody that comprises: (i) a heavy chain comprising (i)(1) a VH that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113, and (i)(2) a CH1-CH3 that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:173; and (ii) a light chain comprising (ii)(1) a VL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.: 168, and (ii)(2) a CL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:174.

In another aspect, the present disclosure refers to an isolated antibody that comprises: (i) a heavy chain comprising (i)(1) a VH that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113, and (i)(2) a CH1-CH3 that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:175; and (ii) a light chain comprising (ii)(1) a VL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.: 168, and (ii)(2) a CL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:174.

In another aspect, the present disclosure refers to the use of a SARS-CoV-2 neutralizing antibody in the manufacture of a medicament for treating a SARS-CoV-2 infection in a subject, wherein the SARS-CoV-2 neutralizing antibody comprises: (i) a heavy chain comprising (i)(1) a VH that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113, and (i)(2) a CH1-CH3 that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:173; and (ii) a light chain comprising (ii)(1) a VL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.: 168, and (ii)(2) a CL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:174.

In another aspect, the present disclosure refers to the use of a SARS-CoV-2 neutralizing antibody in the manufacture of a medicament for treating a SARS-CoV-2 infection in a subject, wherein the SARS-CoV-2 neutralizing antibody comprises: (i) a heavy chain comprising (i)(1) a VH that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113, and (i)(2) a CH1-CH3 that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:175; and (ii) a light chain comprising (ii)(1) a VL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.: 168, and (ii)(2) a CL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:174.

In another aspect, the present disclosure refers to an isolated polynucleotide encoding the antibody or antigen-binding fragment as disclosed herein, or encoding a VH, a heavy chain, a VL, and/or a light chain of the antibody or the antigen-binding fragment.

In another aspect, the present disclosure refers to a recombinant vector comprising the polynucleotide as disclosed herein.

In another aspect, the present disclosure refers to a method for producing an antibody or antigen-binding fragment as disclosed herein, wherein the method comprises culturing a host cell expressing the antibody or antigen-binding fragment under conditions and for a time sufficient to produce the antibody, or the antigen-binding fragment.

In another aspect, the present disclosure refers to a composition comprising the antibody or antigen-binding fragment as disclosed herein and a pharmaceutically acceptable carrier, excipient, or diluent.

In another aspect, the present disclosure refers to a composition comprising the polynucleotide as disclosed herein and a pharmaceutically acceptable carrier, excipient, or diluent.

In another aspect, the present disclosure refers to a composition comprising the recombinant vector as disclosed herein and a pharmaceutically acceptable carrier, excipient, or diluent.

In another aspect, the present disclosure refers to a host cell comprising the polynucleotide as disclosed herein and/or the vector as disclosed herein, wherein the polynucleotide is heterologous to the host cell.

5 In another aspect, the present disclosure refers to a human B cell comprising the polynucleotide as disclosed herein, wherein the polynucleotide is heterologous to the human B cell and/or wherein the human B cell is immortalized.

In yet another aspect, the present disclosure refers to a composition comprising the host cell as disclosed herein or the human B cell as disclosed herein and a pharmaceutically acceptable carrier, excipient, or diluent.

10 **BRIEF DESCRIPTION OF THE DRAWINGS**

Figures 1A and 1B show binding by antibodies (1A) S303 (VH SEQ ID NO.:63; VL SEQ ID NO.:67) and (1B) S309 (VH SEQ ID NO.:105; VL SEQ ID NO.:168) of the present disclosure to recombinant SARS-CoV-2 RBD, as described in Example 2.

15 **Figures 2A and 2B** show SARS-CoV-2 neutralization of infection by certain antibodies of the present disclosure, as described in Example 4.

Figures 3A-3I show SARS-CoV-2 neutralization of infection, as described in Example 4. Figure 3A shows neutralization by donor plasma from SARS-CoV-1 survivors. Figures 3B-3D and 3I show neutralization by supernatant from B cells
20 expressing certain antibodies of the present disclosure. Figures 3E-3H show neutralization by certain recombinant IgG1 antibodies.

CLAIMS

What is claimed is:

~~1. — An antibody, or an antigen binding fragment thereof, comprising a heavy chain variable domain (VH) comprising a CDRH1, a CDRH2, and a CDRH3, and a light chain variable domain (VL) comprising a CDRL1, a CDRL2, and a CDRL3, wherein:~~

~~(i) — the CDRH1 comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs.:106, 2, 56, 64, 80, 88, 96, 156, 179, 195, or 240, or a sequence variant thereof comprising one, two, or three acid substitutions, one or more of which substitutions is optionally a conservative substitution and/or is a substitution to a germline encoded amino acid;~~

~~(ii) — the CDRH2 comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs.:121, 3, 16, 22, 57, 65, 81, 89, 97, 107, 122, 126, 157, 180, 197, 199, or 241, or a sequence variant thereof comprising one, two, or three amino acid substitutions, one or more of which substitutions is optionally a conservative substitution and/or is a substitution to a germline encoded amino acid;~~

~~(iii) — the CDRH3 comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs.:108, 4, 25, 26, 58, 66, 82, 90, 98, 104, 127, 128, 158, 181, 201, 203, or 242, or a sequence variant thereof comprising one, two, or three amino acid substitutions, one or more of which substitutions is optionally a conservative substitution and/or is a substitution to a germline encoded amino acid;~~

~~(iv) — the CDRL1 comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs.:169, 6, 51, 54, 60, 68, 73, 74, 84, 92, 100, 110, 160, 183, 235, or 244, or a sequence variant thereof comprising one, two, or three amino acid substitutions, one or more of which substitutions is optionally a conservative substitution and/or is a substitution to a germline encoded amino acid;~~

~~(v) — the CDRL2 comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs.:170, 7, 61, 69, 85, 93, 101, 111, 161, 184, 236 or 245, or a sequence variant thereof comprising one, two, or three amino acid substitutions, one or~~

~~more of which substitutions is optionally a conservative substitution and/or is a substitution to a germline encoded amino acid; and/or~~

~~(vi) — the CDRL3 comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs.: 171, 8, 62, 70, 77, 78, 86, 94, 102, 112, 151-154, 162, 185, 237, or 246, or a sequence variant thereof comprising having one, two, or three amino acid substitutions, one or more of which substitutions is optionally a conservative substitution and/or is a substitution to a germline encoded amino acid;~~

~~wherein the antibody or antigen binding fragment is capable of binding to a SARS-CoV-2 surface glycoprotein (S) expressed on a cell surface of a host cell, on a SARS-CoV-2 virion, or both.~~

~~2. — The antibody or antigen binding fragment of claim 1, which is capable of neutralizing a SARS-CoV-2 infection in an *in vitro* model of infection and/or in an *in vivo* animal model of infection and/or in a human.~~

~~3. — The antibody or antigen binding fragment of any one of claims 1-2, comprising the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs.:~~

~~(i) — 106, 121, 108, 169, 170, and 171, respectively;~~

~~(ii) — 2-4 and 6-8 or 235-237, respectively;~~

~~(iii) — 2, any one of 16-22, 4, and 6-8 or 235-237, respectively;~~

~~(iv) — 2, 3, any one of 25-26, and 6-8 or 235-237, respectively;~~

~~(v) — 2-4, 51, 7 or 236, and 8 or 237, respectively;~~

~~(vi) — 2-4, 52, 7 or 236, and 8 or 237, respectively;~~

~~(vii) — 2-4, 53, 7 or 236, and 8 or 237, respectively;~~

~~(viii) — 2-5, 54, 7 or 236, and 8 or 237, respectively;~~

~~(ix) — 56-58 and 60-62, respectively;~~

~~(x) — 64-66 and 68-70, respectively;~~

~~(xi) — 64-66, 73 or 74, 69, and 70, respectively;~~

~~(xii) — 64-66, 68, 69, and 77 or 78, respectively;~~

~~(xiii) 80-82 and 84-86, respectively;~~
~~(xiv) 88-90 and 92-94, respectively;~~
~~(xv) 96-98 and 101-102, respectively;~~
~~(xvi) 96, 97, 104, and 100-102, respectively;~~
~~(xvii) 106-108 and 169-171, respectively;~~
~~(xviii) 106, any one of 121-126, 108, and 169-171, respectively;~~
~~(xix) 106, 107, 127 or 128, and 169-171, respectively;~~
~~(xx) 106, 107 or any one of 121-126, 108 and 169-171, respectively;~~
~~(xxi) 156-158 and 160-162, respectively;~~
~~(xxii) 106, 123, 127, and 169-171, respectively;~~
~~(xxiii) 2, 17, 25, 6 or 235 or any one of 51-54, 7 or 236, and 8 or 237,~~
~~respectively;~~
~~(xxiv) 2, 20, 25, 6 or 235 or any one of 51-54, 7 or 236, and 8 or 237,~~
~~respectively;~~
~~(xxv) 179-181 and 183-185, respectively~~
~~(xxvi) 195, 180, 181 and 183-185, respectively;~~
~~(xxvii) 195, 197, 181 and 183-185, respectively;~~
~~(xxviii) 195, 199, 181 and 183-185, respectively;~~
~~(xxiv) 195, 197, 201 and 183-185, respectively;~~
~~(xxx) 195, 197, 203 and 183-185, respectively;~~
~~(xxxi) 195, 199, 201 and 183-185, respectively;~~
~~(xxxii) 195, 199, 203 and 183-185, respectively;~~
~~(xxxiii) 179, 180, 181 and 183-185, respectively;~~
~~(xxxiv) 179, 197, 181 and 183-185, respectively;~~
~~(xxxv) 179, 199, 181 and 183-185, respectively;~~
~~(xxxvi) 179, 197, 201 and 183-185, respectively;~~
~~(xxxvii) 179, 197, 203 and 183-185, respectively;~~
~~(xxxviii) 179, 199, 201 and 183-185, respectively;~~
~~(xxxix) 179, 199, 203 and 183-185, respectively;~~
~~(xxxx) 179, 180, 201 and 183-185, respectively;~~

~~(xxxxxi) 179, 180, 203 and 183-185, respectively; or~~

~~(xxxixii) 240-242 and 244-246, respectively.~~

4. ~~The antibody or antigen-binding fragment of any one of claims 1-3, comprising:~~

~~(i) the CDRH1 amino acid sequence set forth in SEQ ID NO.:106;~~

~~(ii) the CDRH2 amino acid sequence set forth in SEQ ID NO.:121, SEQ ID NO.:107, SEQ ID NO.:122, SEQ ID NO.:123, SEQ ID NO.:124, SEQ ID NO.:125, or SEQ ID NO.:126;~~

~~(iii) the CDRH3 amino acid sequence set forth in SEQ ID NO.:108, SEQ ID NO.:127, or SEQ ID NO.:128;~~

~~(iv) the CDRL1 amino acid sequence set forth in SEQ ID NO.:169;~~

~~(v) the CDRL2 amino acid sequence set forth in SEQ ID NO.:170; and~~

~~(vi) the CDRL3 amino acid sequence set forth in SEQ ID NO.:171;~~

~~wherein, optionally, the antibody or antigen-binding fragment comprises the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in:~~

~~(a) SEQ ID NOs.:106, 121, 108, 169, 170, and 171, respectively;~~

~~(b) SEQ ID NOs.: 106, 121, 127, 169, 170, and 171, respectively;~~

~~(c) SEQ ID NOs.: 106, 121, 128, 169, 170, and 171, respectively;~~

~~(d) SEQ ID NOs.: 106, 107, 108, 169, 170, and 171, respectively;~~

~~(e) SEQ ID NOs.: 106, 107, 127, 169, 170, and 171, respectively;~~

~~(f) SEQ ID NOs.: 106, 107, 128, 169, 170, and 171, respectively;~~

~~(g) SEQ ID NOs.: 106, 122, 108, 169, 170, and 171, respectively;~~

~~(h) SEQ ID NOs.: 106, 122, 127, 169, 170, and 171, respectively;~~

~~(i) SEQ ID NOs.: 106, 122, 128, 169, 170, and 171, respectively;~~

~~(j) SEQ ID NOs.: 106, 123, 108, 169, 170, and 171, respectively;~~

~~(k) SEQ ID NOs.: 106, 123, 127, 169, 170, and 171, respectively;~~

~~(l) SEQ ID NOs.: 106, 123, 128, 169, 170, and 171, respectively;~~

~~(m) SEQ ID NOs.: 106, 124, 108, 169, 170, and 171, respectively;~~

- (n) ~~SEQ ID NOs.: 106, 124, 127, 169, 170, and 171, respectively;~~
- (o) ~~SEQ ID NOs.: 106, 124, 128, 169, 170, and 171, respectively;~~
- (p) ~~SEQ ID NOs.: 106, 125, 108, 169, 170, and 171, respectively;~~
- (q) ~~SEQ ID NOs.: 106, 125, 127, 169, 170, and 171, respectively;~~
- (r) ~~SEQ ID NOs.: 106, 125, 128, 169, 170, and 171, respectively;~~
- (s) ~~SEQ ID NOs.: 106, 126, 108, 169, 170, and 171, respectively;~~
- (t) ~~SEQ ID NOs.: 106, 126, 127, 169, 170, and 171, respectively; or~~
- (u) ~~SEQ ID NOs.: 106, 126, 128, 169, 170, and 171, respectively.~~

5. ~~An antibody or an antigen binding fragment thereof, comprising a heavy chain variable domain (VH) comprising the CDRH1 amino acid sequence set forth in SEQ ID NO.:106, the CDRH2 amino acid sequence set forth in SEQ ID NO.:121, and the CDRH3 amino acid sequence set forth in SEQ ID NO.:108, and a light chain variable domain (VL) comprising a CDRL1 amino acid sequence set forth in SEQ ID NO.:169, a CDRL2 amino acid sequence set forth in SEQ ID NO.:170, and the CDRL3 amino acid sequence set forth in SEQ ID NO.:171,~~

~~wherein the antibody or antigen binding fragment is capable of binding to a SARS-CoV-2 surface glycoprotein (S): expressed on a cell surface of a host cell; on a virion; or both.~~

6. ~~The antibody or antigen binding fragment of claim 5, which is capable of neutralizing a SARS-CoV-2 infection in an *in vitro* model of infection and/or in an *in vivo* animal model of infection and/or in a human.~~

7. ~~The antibody or antigen binding fragment of any one of claims 1-6, wherein:~~

(i) ~~the VH comprises or consists of an amino acid sequence having at least 85% identity to the amino acid sequence set forth in any one of SEQ ID NOs.:113, 1, 9-15, 23, 24, 27, 28-46, 55, 63, 79, 87, 95, 103, 105, 114-120, 129-146, 155, 172, 176-178, 194, 196, 198, 200, 202, 239 and 267, wherein the variation as compared to the~~

~~reference VH amino acid sequence, if present, is optionally limited to one or more framework regions and/or the variation comprises one or more substitution to a germline encoded amino acid; and/or~~

~~(ii) — the VL comprises or consists of an amino acid sequence having at least 85% identity to the amino acid sequence set forth in any one of SEQ ID NOs.:168, 5, 47-50, 59, 67, 71-72, 75, 76, 83, 91, 99, 109, 147-150, 159, 182, 190, 234, and 243, wherein the variation as compared to the reference VH amino acid sequence, if present, is optionally limited to one or more framework regions and/or the variation comprises one or more substitution to a germline encoded amino acid.~~

~~8. — The antibody or antigen binding fragment of any one of claims 1-7, wherein the VH comprises or consists of any VH amino acid sequence set forth in Table 2, and wherein the VL comprises or consists of any VL amino acid sequence set forth in Table 2, wherein, optionally, the VH and the VL comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:~~

- ~~(i) — 113 and 168, respectively;~~
- ~~(ii) — 1 and 5 or 234, respectively;~~
- ~~(iii) — any one of 9-15 and 5 or 234, respectively;~~
- ~~(iv) — 23 or 24 and 5 or 234, respectively;~~
- ~~(v) — 27 and 5 or 234, respectively;~~
- ~~(vi) — any one of 28-46 and 5 or 234, respectively;~~
- ~~(vii) — 1 and any one of 47-50, respectively;~~
- ~~(viii) — any one of 9-15 and any one of 47-50, respectively;~~
- ~~(ix) — 23 or 24 and any one of 47-50, respectively;~~
- ~~(x) — 27 and any one of 47-50, respectively;~~
- ~~(xi) — any one of 28-46 and any one of 47-50, respectively;~~
- ~~(xii) — 55 and 59, respectively;~~
- ~~(xiii) — 63 and 67, respectively;~~
- ~~(xiv) — 63 and 71 or 72, respectively;~~
- ~~(xv) — 63 and 75 or 76, respectively;~~

~~(xvi) — 79 and 83, respectively;~~
~~(xvii) — 87 and 91, respectively;~~
~~(xviii) — 95 and 99, respectively;~~
~~(xix) — 103 and 99, respectively;~~
~~(xx) — 105 and 168, respectively;~~
~~(xxi) — any one of 114 120 or 267 and 168, respectively;~~
~~(xxii) — 129 and 168, respectively;~~
~~(xxiii) — any one of 130 146 and 168, respectively;~~
~~(xxiv) — 105 and any one of 147 150, respectively;~~
~~(xxv) — any one of 113 120 and any one of 147 150, respectively;~~
~~(xxvi) — any one of 130 146 and any one of 147 150, respectively;~~
~~(xxvii) — 155 and 159, respectively;~~
~~(xxviii) — 172 and 168, respectively;~~
~~(xxix) — 176 or 177 and 5 or 234 or any one of 47 50, respectively;~~
~~(xxx) — 178 and 182 or 190, respectively;~~
~~(xxxi) — 194 and 182, respectively;~~
~~(xxxii) — 196 and 182, respectively;~~
~~(xxxiii) — 198 and 182, respectively;~~
~~(xxxiv) — 200 and 182, respectively;~~
~~(xxxv) — 202 and 182, respectively; or~~
~~(xxxvi) — 239 and 243, respectively.~~

9. — ~~An antibody, or an antigen binding fragment thereof, comprising a heavy chain variable domain (VH) and a light chain variable domain (VL), wherein the VH comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113 and the VL comprises or consists of the amino acid sequence set forth in SEQ ID NO.:168.~~

10. — ~~An antibody, or an antigen binding fragment thereof, comprising a heavy chain variable domain (VH) and a light chain variable domain (VL), wherein the VH comprises or consists of the amino acid sequence set forth in any one of SEQ ID~~

~~NOs.:105, 114-120, 129-146, 172, and 267, and the VL comprises or consists of the amino acid sequence set forth in SEQ ID NO.:168.~~

~~11.—An antibody, or antigen binding fragment thereof, comprising a heavy chain variable domain (VH) and a light chain variable domain (VL), wherein the VH comprises or consists of the amino acid sequence set forth in SEQ ID NO.:79 and the VL comprises or consists of the amino acid sequence set forth in SEQ ID NO.:83.~~

~~12.—An antibody, or antigen binding fragment thereof, comprising a heavy chain variable domain (VH) comprising a CDRH1, a CDRH2, and a CDRH3, and a light chain variable domain (VL) comprising a CDRL1, a CDRL2, and a CDRL3, wherein the CDRH1, CDRH2, and CDRH3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:80-82, respectively, and the CDRL1, CDRL2, and CDRL3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:84-86, respectively,~~

~~wherein the antibody or antigen binding fragment is capable of binding to a SARS-CoV-2 surface glycoprotein (S) expressed on a cell surface of a host cell, on a SARS-CoV-2 virion, or both.~~

~~13.—An antibody, or antigen binding fragment thereof, comprising a heavy chain variable domain (VH) and a light chain variable domain (VL), wherein the VH comprises or consists of the amino acid sequence set forth in SEQ ID NO.:105 and the VL comprises or consists of the amino acid sequence set forth in SEQ ID NO.:168.~~

~~14.—An antibody, or antigen binding fragment thereof, comprising a heavy chain variable domain (VH) comprising a CDRH1, a CDRH2, and a CDRH3, and a light chain variable domain (VL) comprising a CDRL1, a CDRL2, and a CDRL3, wherein the CDRH1, CDRH2, and CDRH3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:106-108, respectively, and the CDRL1, CDRL2,~~

and CDRL3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.: 169-171, respectively,

wherein the antibody or antigen binding fragment is capable of binding to a SARS-CoV-2 surface glycoprotein (S) expressed on a cell surface of a host cell, on a SARS-CoV-2 virion, or both.

15.—An antibody, or antigen binding fragment thereof, comprising a heavy chain variable domain (VH) and a light chain variable domain (VL), wherein the VH comprises or consists of the amino acid sequence set forth in SEQ ID NO.: 178 and the VL comprises or consists of the amino acid sequence set forth in SEQ ID NO.: 182 or SEQ ID NO.:190.

16.—An antibody, or antigen binding fragment thereof, comprising a heavy chain variable domain (VH) comprising a CDRH1, a CDRH2, and a CDRH3, and a light chain variable domain (VL) comprising a CDRL1, a CDRL2, and a CDRL3, wherein the CDRH1, CDRH2, and CDRH3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:179-181, respectively, and the CDRL1, CDRL2, and CDRL3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.: 183-185, respectively,

wherein the antibody or antigen binding fragment is capable of binding to a SARS-CoV-2 surface glycoprotein (S) expressed on a cell surface of a host cell, on a SARS-CoV-2 virion, or both.

17.—The antibody or antigen binding fragment of any one of claims 1-16, which:

(i) —recognizes an epitope in the ACE2 receptor binding motif (RBM, SEQ ID NO.:167) of a SARS-CoV-2;

(ii) —is capable of blocking an interaction between SARS-CoV-2 (e.g., a SARS-CoV-2 RBM) and ACE2;

~~(ii) — is capable of binding to SARS-CoV-2 S protein with greater avidity than to SARS-coronavirus S protein;~~

~~(iii) — recognizes an epitope that is conserved in the ACE2 RBM of SARS-CoV-2 and in an ACE2 RBM of SARS-coronavirus;~~

~~(vi) — is cross-reactive against SARS-CoV-2 and SARS-coronavirus;~~

~~(vii) — recognizes an epitope in the SARS-CoV-2 surface glycoprotein that is not in the ACE2 RBM;~~

~~or~~

~~(viii) — any combination of (i)–(vii).~~

~~18. — The antibody or antigen-binding fragment of any one of claims 1–17, which is capable of inhibiting an interaction between SARS-CoV-2 and any one or more of DC-SIGN, L-SIGN, and SIGLEC-1.~~

~~19. — The antibody or antigen-binding fragment of any one of claims 1–18, which is capable of inhibiting an interaction between SARS-CoV-2 and any one or more of: DC-SIGN; L-SIGN; SIGLEC-1; CD22; CD33; CLEC4M; SIGLEC-16; SIGLEC-15; SIGLEC-14; SIGLEC-12; SIGLEC-11; SIGLEC-10; SIGLEC-9; SIGLEC-8; SIGLEC-7; SIGLEC-6; SIGLEC-5; or any combination thereof.~~

~~20. — The antibody or antigen-binding fragment of any one of claims 1–19, which is a IgG, IgA, IgM, IgE, or IgD isotype.~~

~~21. — The antibody or antigen-binding fragment of any one of claims 1–20, which is an IgG isotype selected from IgG1, IgG2, IgG3, and IgG4.~~

~~22. — The antibody or antigen-binding fragment of any one of claims 1–21, which is human, humanized, or chimeric.~~

~~23.—The antibody or antigen binding fragment of any one of claims 1-22, wherein the antibody, or the antigen binding fragment, comprises a human antibody, a monoclonal antibody, a purified antibody, a single chain antibody, a Fab, a Fab', a F(ab')₂, a Fv, a scFv, or a scFab.~~

~~24.—The antibody or antigen binding fragment of claim 23, wherein the scFab comprises:~~

~~(i)—the amino acid sequence set forth in any one of SEQ ID NOs.:218-219 and 226-227;~~

~~(ii)—a VL comprising the amino acid sequence set forth in SEQ ID NO.:168 and a VH comprising the amino acid sequence set forth in SEQ ID NO.:105 or SEQ ID NO.:113; or~~

~~(iii)—a CDRH1 comprising the amino acid sequence set forth in SEQ ID NO.:106, a CDRH2 comprising the amino acid sequence set forth in SEQ ID NO.:107 or 121, a CDRH3 comprising the amino acid sequence set forth in SEQ ID NO.:108, a CDRL1 comprising the amino acid sequence set forth in SEQ ID NO.:169, a CDRL2 comprising the amino acid sequence set forth in SEQ ID NO.:170, and a CDRL3 comprising the amino acid sequence set forth in SEQ ID NO.:171.~~

~~25.—The antibody or antigen binding fragment of claim 23, wherein the scFv comprises:~~

~~(i)—the amino acid sequence set forth in any one of SEQ ID NOs.:220-221 or 228-229;~~

~~(ii)—a VL comprising the amino acid sequence set forth in SEQ ID NO.:168 and a VH comprising the amino acid sequence set forth in SEQ ID NO.:105 or SEQ ID NO.:113; or~~

~~(iii)—a CDRH1 comprising the amino acid sequence set forth in SEQ ID NO.:106, a CDRH2 comprising the amino acid sequence set forth in SEQ ID NO.:107 or 121, a CDRH3 comprising the amino acid sequence set forth in SEQ ID NO.:108, a CDRL1 comprising the amino acid sequence set forth in SEQ ID NO.:169, a CDRL2~~

~~comprising the amino acid sequence set forth in SEQ ID NO.:170, and a CDRL3 comprising the amino acid sequence set forth in SEQ ID NO.:171.~~

~~26. The antibody or antigen binding fragment of claim 25, wherein the scFv comprises more than one VH domain and more than one VL domain.~~

~~27. The antibody or antigen binding fragment of claim 26, wherein the scFv comprises:~~

~~(i) the amino acid sequence as set forth in any one of SEQ ID NOs.:222-225 or SEQ ID NOs.:230-233;~~

~~(ii) two VL domains, each comprising the amino acid sequence as set forth in SEQ ID NO.:168, and two VH domains, each comprising the amino acid sequence as set forth in SEQ ID NO.:105 or SEQ ID NO.:113; or~~

~~(iii) two VL domains, each comprising a CDRL1 comprising the amino acid sequence set forth in SEQ ID NO.:169, a CDRL2 comprising the amino acid sequence set forth in SEQ ID NO.:170, and a CDRL3 comprising the amino acid sequence set forth in SEQ ID NO.:171, and two VH domains, each comprising a CDRH1 comprising the amino acid sequence set forth in SEQ ID NO.:106, a CDRH2 comprising the amino acid sequence set forth in SEQ ID NO.:107 or 121, a CDRH3 comprising the amino acid sequence set forth in SEQ ID NO.:108.~~

~~28. The antibody or antigen binding fragment of any one of claims 1-27, wherein the antibody or antigen binding fragment is a multi-specific antibody or antigen binding fragment.~~

~~29. The antibody or antigen binding fragment of claim 28, wherein the antibody or antigen binding fragment is a bispecific antibody or antigen binding fragment.~~

~~30. The antibody or antigen binding fragment of claim 28 or 29, comprising:~~

~~(i) a first VH and a first VL; and~~

~~(ii) a second VH and a second VL;~~

~~wherein the first VH and the second VH are different and each independently comprise an amino acid sequence having at least 85% identity to the amino acid sequence set forth in any one of SEQ ID NOs.:113, 1, 9-15, 23, 24, 27-46, 55, 63, 79, 87, 95, 103, 105, 114-120, 129-146, 155, 172, 176-178, 194, 196, 198, 200, 202, 239, and 267,~~

~~wherein the first VL and the second VL are different and each independently comprise an amino acid sequence having at least 85% identity to the amino acid sequence set forth in any one of SEQ ID NOs.:168, 5, 47-50, 59, 67, 71, 72, 75, 76, 83, 91, 99, 109, 147-150, 159, 182, 190, 234, and 243;~~

~~and wherein the first VH and the first VL together form a first antigen binding site, and wherein the second VH and the second VL together form a second antigen binding site.~~

~~31. The antibody or antigen binding fragment of any one of claims 1-30, wherein the antibody or antigen binding fragment further comprises a Fc polypeptide or a fragment thereof.~~

~~32. The antibody or antigen binding fragment of claim 31, wherein the Fc polypeptide or fragment thereof comprises:~~

~~(i) a mutation that enhances binding to a FcRn as compared to a reference Fc polypeptide that does not comprise the mutation; and/or~~

~~(ii) a mutation that enhances binding to a FcγR as compared to a reference Fc polypeptide that does not comprise the mutation.~~

~~33. The antibody or antigen binding fragment of claim 32, wherein the mutation that enhances binding to a FcRn comprises: M428L; N434S; N434H; N434A;~~

N434S; M252Y; S254T; T256E; T250Q; P257I; Q311I; D376V; T307A; E380A; or any combination thereof.

34. ~~The antibody or antigen binding fragment of claim 32 or 33, wherein the mutation that enhances binding to FcRn comprises:~~

- ~~(i) — M428L/N434S;~~
- ~~(ii) — M252Y/S254T/T256E;~~
- ~~(iii) — T250Q/M428L;~~
- ~~(iv) — P257I/Q311I;~~
- ~~(v) — P257I/N434H;~~
- ~~(vi) — D376V/N434H;~~
- ~~(vii) — T307A/E380A/N434A; or~~
- ~~(viii) — any combination of (i)–(vii).~~

35. ~~The antibody or antigen binding fragment of any one of claims 32–34, wherein the mutation that enhances binding to FcRn comprises M428L/N434S.~~

36. ~~The antibody or antigen binding fragment of any one of claims 32–35, wherein the mutation that enhances binding to a Fc γ R comprises S239D; I332E; A330L; G236A; or any combination thereof.~~

37. ~~The antibody or antigen binding fragment of any one of claims 32–36, wherein the mutation that enhances binding to a Fc γ R comprises:~~

- ~~(i) — S239D/I332E;~~
- ~~(ii) — S239D/A330L/I332E;~~
- ~~(iii) — G236A/S239D/I332E; or~~
- ~~(iv) — G236A/A330L/I332E.~~

~~38. The antibody or antigen binding fragment of any one of claims 1-37, which comprises a mutation that alters glycosylation, wherein the mutation that alters glycosylation comprises N297A, N297Q, or N297G; and/or which is aglycosylated and/or afucosylated.~~

~~39. The antibody or antigen binding fragment of any one of claims 31-38, wherein the Fc polypeptide comprises a L234A mutation and a L235A mutation.~~

~~40. The antibody or antigen binding fragment of any one of claims 1-39, wherein the antibody or antigen binding fragment binds to the SARS-CoV-2 S protein, as measured using biolayer interferometry.~~

~~41. The antibody or antigen binding fragment of claim 40, wherein the antibody or antigen binding fragment binds to the SARS-CoV-2 S protein with a K_D of less than about 4.5×10^{-9} M, such as less than 4.5×10^{-9} M.~~

~~42. The antibody or antigen binding fragment of claim 40 or 41, wherein the antibody or antigen binding fragment binds to the SARS-CoV-2 S protein with a K_D of less than about 1.0×10^{-10} M, such as less than 1.0×10^{-10} M.~~

~~43. The antibody or antigen binding fragment of any one of claims 40-42, wherein the antibody or antigen binding fragment binds to the SARS-CoV-2 S protein with a K_D of less than about 1.0×10^{-11} M, such less than 1.0×10^{-11} M.~~

~~44. The antibody or antigen binding fragment of any one of claims 40-43, wherein the antibody or antigen binding fragment binds to the SARS-CoV-2 S protein with a K_D of less than about 1×10^{-12} M, such as less than 1×10^{-12} M.~~

~~45. The antibody or antigen binding fragment of any one of claims 1-44, wherein the antibody or antigen binding fragment is capable of neutralizing a SARS-~~

~~CoV-2 infection and/or of neutralizing an infection of a target cell with an IC50 of about 16 to about 20 µg/ml.~~

~~46.—The antibody or antigen binding fragment of any one of claims 1-45, wherein the antibody or antigen binding fragment is capable of neutralizing a SARS-CoV-2 infection and/or of neutralizing an infection of a target cell with an IC50 of about 0.3 to about 0.4 µg/ml or about 3 to about 4 nM.~~

~~47.—The antibody or antigen binding fragment of any one of claims 1-46, wherein the antibody or antigen binding fragment is capable of inducing antibody-dependent cell-mediated cytotoxicity (ADCC) and/or antibody-dependent cellular phagocytosis (ADCP) against a target cell infected by a SARS-CoV-2.~~

~~48.—The antibody or antigen binding fragment of any one of claims 40-47, wherein a Fab of the antibody or antigen binding fragment is capable of binding to SARS-CoV-2 S-protein with a KD of 2.0×10^{-9} or less, 1.9×10^{-9} or less, or 1.8×10^{-9} or less.~~

~~49.—The antibody or antigen binding fragment of any one of claims 1-48, wherein the antibody or antigen binding fragment is capable of neutralizing infection by the SARS-CoV-2 and does not compete with a human ACE2 for binding to the SARS-CoV-2 S-protein,~~

~~wherein, optionally, the neutralizing comprises neutralizing infection in an *in vitro* model of infection.~~

~~50.—The antibody or antigen binding fragment of any one of claims 1-49, wherein the antibody or antigen binding fragment is capable of neutralizing infection by the SARS-CoV-2 with an IC50 of 3.0 nM, 3.1 nM, 3.2 nM, 3.3 nM, 3.4 nM, 3.5 nM, 3.6 nM, 3.7 nM, 3.8 nM, 3.9 nM, or 4.0 nM.~~

~~51.—The antibody or antigen binding fragment of any one of claims 47-50, wherein the inducing ADCC comprises activating a Natural Killer cell that comprises a V158 FcγRIIIa variant, a Natural Killer cell that comprises a F158 FcγRIIIa variant, or both.~~

~~52.—The antibody or antigen binding fragment of any one of claims 47-51, wherein the ADCP comprises engaging a FcγRIIa and/or a FcγRIIIa expressed on the surface of a phagocytic cell, such as a monocyte, a macrophage, or a dendritic cell.~~

~~53.—An antibody, or an antigen binding fragment thereof, that competes for binding to a SARS-CoV-2 surface glycoprotein with the antibody or antigen binding fragment of any one of claims 1-52, wherein, optionally, the antibody or antigen binding fragment is capable of inhibiting an interaction between SARS-CoV-2 and any one or more of DC-SIGN, L-SIGN, and SIGLEC-1.~~

~~54.—An antibody, or an antigen binding fragment thereof, that competes for binding to a SARS-CoV-2 surface glycoprotein with antibody S309 (VH SEQ ID NO.:105; VL SEQ ID NO.:168) and/or antibody S303 (VH SEQ ID NO.:63; VL SEQ ID NO.:67), wherein, optionally, the antibody or antigen binding fragment is capable of inhibiting an interaction between SARS-CoV-2 and any one or more of DC-SIGN, L-SIGN, and SIGLEC-1.~~

~~55.—An antibody, or an antigen binding fragment thereof, that competes for binding to a SARS-CoV-2 surface glycoprotein with antibody S304 (VH SEQ ID NO.:79; VL SEQ ID NO.:81) and/or antibody S315 (VH SEQ ID NO.:178; VL SEQ ID NO.:182).~~

~~56.—The antibody or antigen binding fragment of any one of claims 1-55, which is capable of binding to the SARS-CoV-2 surface glycoprotein when the SARS-CoV-2 surface glycoprotein is comprised in a prefusion trimer.~~

~~57. The antibody or antigen binding fragment of any one of claims 1-56, which is capable of binding to a Receptor Binding Domain (RBD) of the SARS-CoV-2 surface glycoprotein when the RBD is glycosylated and/or when the RBD is deglycosylated, wherein the binding is determined using surface plasmon resonance (SPR), wherein, optionally:~~

~~(1) the SPR is performed using a Biacore T200 instrument using a single-cycle kinetics approach, further optionally with a 3 minute injection period and a 20 minute dissociation period;~~

~~(2) the antibody or antigen binding fragment is captured on a surface;~~

~~(3) the RBD is present at a concentration of were 0.8 nM, 3.1 nM, 12.5 nM, 50 nM, or 200 nM;~~

~~(4) the antibody or antigen binding fragment binds to the glycosylated RBD with a KD of about 2.0 nM, about 1.9 nM, about 1.8 nM, about 1.7 nM, about 1.6 nM, about 1.5 nM, about 1.4 nM, about 1.3 nM, about 1.2 nM, about 1.1 nM, about 1.0 nM, about 0.9 nM, about 0.8 nM, about 0.7 nM, about 0.6 nM, about 0.5 nM, about 0.4 nM, or about 0.3 nM, or with a KD of $0.4 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $0.45 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $0.5 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $0.6 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $0.7 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $1.7 \text{ nM} \pm 0.05 \text{ nM}$; and/or~~

~~(5) the antibody or antigen binding fragment binds to the deglycosylated RBD with a KD of about 37.0 nM, about 8.0 nM, about 2.0 nM, about 1.9 nM, about 1.8 nM, about 1.7 nM, about 1.6 nM, about 1.5 nM, about 1.4 nM, about 1.3 nM, about 1.2 nM, about 1.1 nM, about 1.0 nM, or about 0.9 nM, or with a KD of $37.0 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $8.0 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $1.0 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $0.9 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $1.3 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $1.8 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $1.7 \text{ nM} \pm 0.05 \text{ nM}$.~~

~~58. The antibody or antigen binding fragment of any one of claims 1-57, which is capable of neutralizing an infection by the SARS-CoV-2 in a human lung cell, wherein, optionally, the human lung cell comprises a Calu-3 cell, wherein, further~~

~~optionally, the antibody or antigen-binding fragment has a neutralization IC₅₀ of about 97 ng/mL.~~

~~59. The antibody or antigen-binding fragment of any one of claims 1-58, which is capable of binding to a human complement component C1q, wherein, optionally, binding to the C1q is determined using biolayer interferometry (BLI), such as using an Octet instrument.~~

~~60. The antibody or antigen-binding fragment of any one of claims 1-59, which is capable of inhibiting SARS-CoV-2 surface glycoprotein-mediated cell-cell fusion.~~

~~61. The antibody or antigen-binding fragment of any one of claims 1-60, which does not cause antibody-mediated enhancement of SARS-CoV-2 replication in a human donor-derived peripheral blood mononuclear cell (PBMC) or a dendritic cell.~~

~~62. The antibody or antigen-binding fragment of any one of claims 1-61, comprising:~~

~~(i) a CH1-CH3 comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:173 or 175; and/or~~

~~(ii) a CL comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:174 or SEQ ID NO.:193.~~

~~63~~1. An isolated antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) that comprises the complementarity determining region (CDR)H1 amino acid sequence set forth in SEQ ID NO.:106, the CDRH2 amino acid sequence set forth in SEQ ID NO.:121, and the CDRH3 amino acid sequence set forth in SEQ ID NO.:108, and a light chain variable domain (VL) that comprises the CDRL1 amino acid sequence set forth in SEQ ID NO.:169, the CDRL2

amino acid sequence set forth in SEQ ID NO.:170, and the CDRL3 amino acid sequence set forth in SEQ ID NO.:171,

wherein the antibody or antigen-binding fragment is capable of binding to a SARS-CoV-2 surface glycoprotein (S): ~~expressed on a cell surface of a host cell; on a SARS-CoV-2 virion; or both.~~

~~642.~~ The isolated antibody or antigen-binding fragment of ~~any one of claims 1-63~~claim 1, which is capable of binding to a surface glycoprotein (S) of:

(i) a SARS-CoV-2 Wuhan-Hu-1 (SEQ ID NO.:165);

(ii) a SARS-CoV-2 B.1.1.7;

(iii) a SARS-CoV-2 B.1.351;

(iv) a SARS-CoV-2 comprising any one or more of the following substitution mutations relative to SEQ ID NO.:165: N501Y; S477N; N439K; L452R; E484K; Y453F; A520S; K417N; K417V; S494P; N501T; S477R; V367F; P384L; A522S; A522V; V382L; P330S; T478I; S477I; P479S; or

(v) any combination of (i)-(iv).

3. An isolated antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) and a light chain variable domain (VL), wherein the VH comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113 and the VL comprises or consists of the amino acid sequence set forth in SEQ ID NO.:168.

~~654.~~ The isolated antibody or antigen-binding fragment of claim ~~63 or 64~~1 or 3, which is capable of neutralizing a SARS-CoV-2 infection:

(i) in an *in vitro* model of infection;

(ii) in an *in vivo* animal model of infection;

(iii) in a human; or

(iv) any combination of (i)-(iii).

5. Use of a SARS-CoV-2 neutralizing antibody or antigen-binding fragment in the manufacture of a medicament for treating a SARS-CoV-2 infection in a subject, wherein the SARS-CoV-2 neutralizing antibody or antigen-binding fragment comprises:

(i) a heavy chain variable domain (VH) that comprises: the complementarity determining region (CDR)H1 amino acid sequence set forth in SEQ ID NO.:106, the CDRH2 amino acid sequence set forth in SEQ ID NO.:121, and the CDRH3 amino acid sequence set forth in SEQ ID NO.:108; and

(ii) a light chain variable domain (VL) that comprises: the CDRL1 amino acid sequence set forth in SEQ ID NO.:169, the CDRL2 amino acid sequence set forth in SEQ ID NO.:170, and the CDRL3 amino acid sequence set forth in SEQ ID NO.:171.

6. The use of claim 5, wherein the SARS-CoV-2 comprises:

(i) a SARS-CoV-2 Wuhan-Hu-1;

(ii) a SARS-CoV-2 B.1.1.7;

(iii) a SARS-CoV-2 B.1.351;

(iv) a SARS-CoV-2 comprising, in a surface glycoprotein (S) thereof, any one or more of the following substitution mutations relative to SEQ ID NO.:165: N501Y; S477N; N439K; L452R; E484K; Y453F; A520S; K417N; K417V; S494P; N501T; S477R; V367F; P384L; A522S; A522V; V382L; P330S; T478I; S477I; P479S; or

(v) any combination of (i)-(iv).

7. Use of a SARS-CoV-2 neutralizing antibody or antigen-binding fragment in the manufacture of a medicament for treating a SARS-CoV-2 infection in a subject, wherein the SARS-CoV-2 neutralizing antibody or antigen-binding fragment comprises a heavy chain variable domain (VH) and a light chain variable domain (VL), wherein the VH comprises or consists of the amino acid sequence set forth in SEQ ID

NO.:113 and the VL comprises or consists of the amino acid sequence set forth in SEQ ID NO.:168.

8. The use of claim 5 or 7 wherein the SARS-CoV-2 neutralizing antibody or antigen-binding fragment is to be administered intravenously.

669. The isolated antibody or antigen-binding fragment of claim ~~any one of claims 63-651~~ or the use of claim 5, wherein:

- (i) the VH comprises or consists of an amino acid sequence having at least 85% identity to the amino acid sequence set forth in SEQ ID NO.:113; and/or
- (ii) the VL comprises or consists of an amino acid sequence having at least 85% identity to the amino acid sequence set forth in SEQ ID NO.:168.

6710. The isolated antibody or antigen-binding fragment of claim 9 or the use of any one of claims 63-669, wherein:

- (i) the VH comprises or consists of an amino acid sequence having at least 90% identity to the amino acid sequence set forth in SEQ ID NO.:113; and/or
- (ii) the VL comprises or consists of an amino acid sequence having at least 90% identity to the amino acid sequence set forth in SEQ ID NO.:168.

6811. The isolated antibody or antigen-binding fragment of claim 9 or the use of any one of claims 63-679, wherein:

- (i) the VH comprises or consists of an amino acid sequence having at least 95% identity to the amino acid sequence set forth in SEQ ID NO.:113; and/or
- (ii) the VL comprises or consists of an amino acid sequence having at least 95% identity to the amino acid sequence set forth in SEQ ID NO.:168.

6912. The isolated antibody or antigen-binding fragment of claim 9 or the use of any one of claims 63-689, wherein:

- (i) the VH comprises or consists of an amino acid sequence having at least 99% identity to the amino acid sequence set forth in SEQ ID NO.:113; and/or
- (ii) the VL comprises or consists of an amino acid sequence having at least 99% identity to the amino acid sequence set forth in SEQ ID NO.:168.

7013. The isolated antibody or antigen-binding fragment of ~~any one of claims 63-69~~ 1 or 3 or the use of claim 5 or 7, wherein the antibody or antigen-binding fragment ~~which~~ is capable of inhibiting an interaction between:

- (i) SARS-CoV-2 and a human DC-SIGN;
- (ii) SARS-CoV-2 and a human L-SIGN;
- (iii) SARS-CoV-2 and a human SIGLEC-1; or
- (iv) any combination of (i)-(iii).

7114. The isolated antibody or antigen-binding fragment of ~~any one of claim 1-63~~ 70 or the use of claim 5, wherein the antibody or antigen-binding fragment comprises a human antibody, a monoclonal antibody, a purified antibody, a single chain antibody, a Fab, a Fab', a F(ab')₂, a Fv, a scFv, or a scFab.

7215. The isolated antibody or antigen-binding fragment of ~~any one of claims 63-71~~ 1 or 3 or the use of claim 5 or 7, wherein the antibody or antigen-binding fragment further comprises a Fc polypeptide or a fragment thereof.

7316. The isolated antibody or antigen-binding fragment of claim 1 or 3 or the use of any one of claims 63-72 ~~5 or 7, wherein the antibody or antigen-binding fragment which~~ is a IgG, IgA, IgM, IgE, or IgD isotype.

7417. The isolated antibody or antigen-binding fragment of claim 15 or the use of claim 72 or 73 15, wherein the Fc polypeptide or fragment thereof comprises:

- (i) a mutation that enhances binding to a FcRn as compared to a reference Fc polypeptide that does not comprise the mutation; and/or

(ii) a mutation that enhances binding to a Fc γ R as compared to a reference Fc polypeptide that does not comprise the mutation.

~~75~~18. The isolated antibody or antigen-binding fragment [of claim 17 or the use of claim ~~74~~17](#), wherein the mutation that enhances binding to a FcRn comprises:

- (i) M428L/N434S;
- (ii) M252Y/S254T/T256E;
- (iii) T250Q/M428L;
- (iv) P257I/Q311I;
- (v) P257I/N434H;
- (vi) D376V/N434H;
- (vii) T307A/E380A/N434A; or
- (viii) any combination of (i)-(vii).

~~76~~19. The isolated antibody or antigen-binding fragment [of claim 18 or the use of claim ~~75~~18](#), wherein the mutation that enhances binding to [a](#) FcRn comprises M428L/N434S.

~~77~~20. The isolated antibody or antigen-binding fragment [of claim 17 or the use of ~~any one of~~ claims ~~74-76~~17](#), wherein the mutation that enhances binding to a Fc γ R comprises S239D, I332E, A330L, G236A, or any combination thereof.

~~78~~21. The isolated antibody or antigen-binding fragment [of claim 20 or the use of claim ~~77~~20](#), wherein the mutation that enhances binding to a Fc γ R comprises:

- (i) S239D/I332E;
- (ii) S239D/A330L/I332E;
- (iii) G236A/S239D/I332E; or
- (iv) G236A/A330L/I332E.

~~7922.~~ The isolated antibody or antigen-binding fragment of ~~any one of claims~~
~~63-78~~1 or 3 or the use of claim 5 or 7, wherein the antibody or antigen-binding
fragment further ~~comprising~~ comprises a CH1-CH3 that comprises or consists of the
amino acid sequence set forth in SEQ ID NO.:265 or 266.

~~80.—An isolated antibody, or an antigen-binding fragment thereof,~~
~~comprising a heavy chain variable domain (VH) and a light chain variable domain~~
~~(VL), wherein the VH comprises or consists of the amino acid sequence set forth in~~
~~SEQ ID NO.:113 and the VL comprises or consists of the amino acid sequence set forth~~
~~in SEQ ID NO.:168.~~

~~81.—The isolated antibody or antigen-binding fragment of claim 80, which is~~
~~capable of neutralizing a SARS-CoV-2 infection:~~

- ~~(i) —in an *in vitro* model of infection;~~
- ~~(ii) —in an *in vivo* animal model of infection;~~
- ~~(iii) —in a human; or~~
- ~~(iv) —any combination of (i)–(iii).~~

~~82.—The isolated antibody or antigen-binding fragment of claim 80 or 81,~~
~~which is capable of inhibiting an interaction between:~~

- ~~(i) —SARS-CoV-2 and a human DC-SIGN;~~
- ~~(ii) —SARS-CoV-2 and a human L-SIGN;~~
- ~~(iii) —SARS-CoV-2 and a human SIGLEC-1; or~~
- ~~(iv) —any combination of (i)–(iii).~~

~~83.—The isolated antibody or antigen-binding fragment of any one of claims~~
~~80-82, wherein the antibody or antigen-binding fragment further comprises a Fe~~
~~polypeptide or a fragment thereof.~~

~~84. The isolated antibody or antigen binding fragment of any one of claims 80-83, which is a IgG, IgA, IgM, IgE, or IgD isotype.~~

~~85. The isolated antibody or antigen binding fragment of any one of claims 83 or 84, wherein the Fc polypeptide or fragment thereof comprises:~~

~~(i) a mutation that enhances binding to a FcRn as compared to a reference Fc polypeptide that does not comprise the mutation; and/or~~

~~(ii) a mutation that enhances binding to a FcγR as compared to a reference Fc polypeptide that does not comprise the mutation.~~

~~86. The isolated antibody or antigen binding fragment of claim 85, wherein the mutation that enhances binding to a FcRn comprises:~~

- ~~(i) M428L/N434S;~~
- ~~(ii) M252Y/S254T/T256E;~~
- ~~(iii) T250Q/M428L;~~
- ~~(iv) P257I/Q311H;~~
- ~~(v) P257I/N434H;~~
- ~~(vi) D376V/N434H;~~
- ~~(vii) T307A/E380A/N434A; or~~
- ~~(viii) any combination of (i) (vii).~~

~~87. The isolated antibody or antigen binding fragment of claim 86, wherein the mutation that enhances binding to FcRn comprises M428L/N434S.~~

~~88. The isolated antibody or antigen binding fragment of any one of claims 85-87, wherein the mutation that enhances binding to a FcγR comprises S239D, I332E, A330L, G236A, or any combination thereof.~~

~~89. The isolated antibody or antigen binding fragment of claim 88, wherein the mutation that enhances binding to a FcγR comprises:~~

- ~~(i) — S239D/I332E;~~
- ~~(ii) — S239D/A330L/I332E;~~
- ~~(iii) — G236A/S239D/I332E; or~~
- ~~(iv) — G236A/A330L/I332E.~~

~~90. — The isolated antibody or antigen-binding fragment of any one of claims 80-89, further comprising a CH1-CH3 that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:265 or 266.~~

~~91~~23. An isolated antibody that comprises:

- (i) a heavy chain comprising (i)(1) a VH that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113, and (i)(2) a CH1-CH3 that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:173; and
- (ii) a light chain comprising (ii)(1) a VL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.: 168, and (ii)(2) a CL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:174.

~~92. — An isolated antibody, or an antigen-binding fragment thereof, that is capable of binding to a SARS-CoV-2 surface glycoprotein (S) and inhibiting an interaction between a SARS-CoV-2 and a human DC-SIGN, a human L-SIGN, a human SIGLEC-1, or any combination thereof.~~

~~93~~24. An isolated antibody that comprises:

- (i) a heavy chain comprising (i)(1) a VH that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113, and (i)(2) a CH1-CH3 that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:175; and
- (ii) a light chain comprising (ii)(1) a VL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.: 168, and (ii)(2) a CL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:174.

25. Use of a SARS-CoV-2 neutralizing antibody in the manufacture of a medicament for treating a SARS-CoV-2 infection in a subject, wherein the SARS-CoV-2 neutralizing antibody comprises:

(i) a heavy chain comprising (i)(1) a VH that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113, and (i)(2) a CH1-CH3 that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:173; and

(ii) a light chain comprising (ii)(1) a VL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.: 168, and (ii)(2) a CL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:174.

26. Use of a SARS-CoV-2 neutralizing antibody in the manufacture of a medicament for treating a SARS-CoV-2 infection in a subject, wherein the SARS-CoV-2 neutralizing antibody comprises:

(i) a heavy chain comprising (i)(1) a VH that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113, and (i)(2) a CH1-CH3 that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:175; and

(ii) a light chain comprising (ii)(1) a VL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.: 168, and (ii)(2) a CL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:174.

27. An isolated polynucleotide encoding the antibody or antigen-binding fragment of any one of claims 1 to 4 or 9 to 24, or encoding a VH, a heavy chain, a VL, and/or a light chain of the antibody or the antigen-binding fragment.

28. The isolated polynucleotide of claim 27, wherein the polynucleotide comprises deoxyribonucleic acid (DNA) or ribonucleic acid (RNA), wherein the RNA optionally comprises messenger RNA (mRNA).

29. The isolated polynucleotide of claim 27 or 28, which is codon-optimized for expression in a host cell.

30. The isolated polynucleotide of claim 29, which is codon-optimized for expression in a mammalian host cell.

31. The isolated polynucleotide of any one of claims 27 to 30, wherein the polynucleotide further comprises a nucleotide sequence encoding a signal peptide.

32. The isolated polynucleotide of any one of claims 27-31, comprising a polynucleotide having at least 50% identity to, or comprising the polynucleotide sequence of, any one of SEQ ID NOs.:257-262.

33. A recombinant vector comprising the polynucleotide of any one of claims 27-32.

34. A method for producing an antibody or antigen-binding fragment of any one of claims 1 to 4 or 9 to 24, wherein the method comprises culturing a host cell expressing the antibody or antigen-binding fragment under conditions and for a time sufficient to produce the antibody, or the antigen-binding fragment.

35. The method for producing an antibody or antigen-binding fragment of claim 34, wherein the host cell comprises a recombinant vector comprising a polynucleotide of any one of claims 27 to 32.

36. The method for producing an antibody or antigen-binding fragment of claim 34 or 35, wherein the host cell is a mammalian cell.

37. The method for producing an antibody or antigen-binding fragment of any one of claims 34-36, wherein the method comprises culturing the host cell in batch cell culture.

38. The method for producing an antibody or antigen-binding fragment of any one of claims 34-37, wherein the method further comprises purifying the antibody or antigen-binding fragment.

39. A composition comprising the antibody or antigen-binding fragment of any one of claims 1 to 4 or 9 to 24 and a pharmaceutically acceptable carrier, excipient, or diluent.

40. A composition comprising the polynucleotide of any one of claims 27-32 and a pharmaceutically acceptable carrier, excipient, or diluent.

41. A composition comprising the recombinant vector of claim 33 and a pharmaceutically acceptable carrier, excipient, or diluent.

42. A host cell comprising the polynucleotide of any one of claims 27-32 and/or the vector of claim 33, wherein the polynucleotide is heterologous to the host cell.

43. A human B cell comprising the polynucleotide of any one of claims 27-32, wherein the polynucleotide is heterologous to the human B cell and/or wherein the human B cell is immortalized.

44. A composition comprising the host cell of claim 42 or the human B cell of claim 43 and a pharmaceutically acceptable carrier, excipient, or diluent.

94. An isolated antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) that comprises the complementarity determining region (CDR)H1 amino acid sequence set forth in SEQ ID NO.:106, the CDRH2 amino acid sequence set forth in SEQ ID NO.:121, and the CDRH3 amino acid

sequence set forth in SEQ ID NO.:108, and a light chain variable domain (VL) that comprises the CDRL1 amino acid sequence set forth in SEQ ID NO.:169, the CDRL2 amino acid sequence set forth in SEQ ID NO.:170, and the CDRL3 amino acid sequence set forth in SEQ ID NO.:171,

wherein the antibody or antigen binding fragment is capable of binding to a SARS-CoV-2 surface glycoprotein (S); expressed on a cell surface of a host cell; on a SARS-CoV-2 virion; or both.

95. The antibody or antigen binding fragment of claim 94, which is capable of neutralizing a SARS-CoV-2 infection:

- (i) in an *in vitro* model of infection;
- (ii) in an *in vivo* animal model of infection;
- (iii) in a human; or
- (iv) any combination of (i) (iii).

96. The antibody or antigen binding fragment of claim 94 or 95, wherein:

- (i) the VH comprises or consists of an amino acid sequence having at least 85% identity to the amino acid sequence set forth in SEQ ID NO.:113; and/or
- (ii) the VL comprises or consists of an amino acid sequence having at least 85% identity to the amino acid sequence set forth in SEQ ID NO.:168.

97. The antibody or antigen binding fragment of any one of claims 94-96, wherein the VH comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113 and the VL comprises or consists of the amino acid sequence set forth in SEQ ID NO.:168.

98. The antibody or antigen binding fragment of any one of claims 94-97, which:

- (i) is capable of binding to SARS-CoV-2 surface glycoprotein with greater avidity than to a SARS coronavirus S protein;

- ~~(ii) — is cross reactive against SARS CoV 2 and SARS coronavirus;~~
- ~~(iii) — recognizes an epitope in the SARS CoV 2 surface glycoprotein that is not in the ACE2 RBM; or~~
- ~~(iv) — any combination of (i)–(iii).~~

~~99. — The antibody or antigen binding fragment of any one of claims 94–98, which is a IgG, IgA, IgM, IgE, or IgD isotype, and is preferably an IgG isotype selected from IgG1, IgG2, IgG3, and IgG4.~~

- ~~100. — The antibody or antigen binding fragment of any one of claims 94–99:~~
- ~~(i) — which is human, humanized, or chimeric;~~
 - ~~(ii) — wherein the antibody or the antigen binding fragment comprises a human antibody, a monoclonal antibody, a purified antibody, a single chain antibody, a Fab, a Fab', a F(ab')₂, a Fv, a scFv, or a scFab; and/or~~
 - ~~(iii) — wherein the antibody or antigen binding fragment is a multi-specific antibody or antigen binding fragment, wherein, optionally, the antigen binding fragment is a bispecific antibody or antigen binding fragment.~~

~~101. — The antibody or antigen binding fragment of any one of claims 94–100, wherein the antibody or antigen binding fragment further comprises a Fc polypeptide or a fragment thereof.~~

~~102. — The antibody or antigen binding fragment of claim 101, wherein the Fc polypeptide or fragment thereof comprises:~~

- ~~(1) — a mutation that enhances binding to a FeRn as compared to a reference Fc polypeptide that does not comprise the mutation, wherein, optionally, the mutation that enhances binding to a FeRn comprises M428L, N434S, N434H, N434A, N434S, M252Y, S254T, T256E, T250Q, P257I, Q311I, D376V, T307A, E380A, or any combination thereof, wherein, further optionally, the mutation that enhances binding to a FeRn comprises: (i) M428L/N434S; (ii) M252Y/S254T/T256E; (iii) T250Q/M428L;~~

(iv) P257I/Q311H; (v) P257I/N434H; (vi) D376V/N434H; (vii) T307A/E380A/N434A; or (viii) any combination of (i)–(vii); and/or

(2)——a mutation that enhances binding to a FcγR as compared to a reference Fe polypeptide that does not comprise the mutation, wherein, optionally, the mutation that enhances binding to a FcγR comprises S239D, I332E, A330L, G236A, or any combination thereof, wherein, further optionally, the mutation that enhances binding to a FcγR comprises: (i) S239D/I332E; (ii) S239D/A330L/I332E; (iii) G236A/S239D/I332E; or (iv) G236A/A330L/I332E.

~~103.——The antibody or antigen binding fragment of claim 102, wherein the mutation that enhances binding to a FcRn comprises M428L/N434S and/or the mutation that enhances binding to a FcγR comprises G236A/A330L/I332E.~~

~~104.——The antibody or antigen binding fragment of any one of claims 94–103, comprising:~~

~~(i)——a CH1–CH3 having 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO.:173 or 175; and/or~~

~~(ii)——a CL comprising an amino acid sequence having 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the amino acid sequence of SEQ ID NO.:174.~~

~~105.——The antibody or antigen binding fragment of any one of claims 94–104, which comprises a mutation that alters glycosylation of the antibody or antigen binding fragment, wherein the mutation that alters glycosylation of the antibody or antigen binding fragment comprises N297A, N297Q, or N297G, and/or wherein the antibody or antigen binding fragment is aglycosylated and/or afucosylated.~~

~~106.——The antibody or antigen binding fragment of any one of claims 94–105, wherein the antibody or antigen binding fragment binds to a SARS-CoV-2 surface glycoprotein with a KD of less than about 4.5×10^{-9} M, less than about 5×10^{-9} M, less~~

than about 1×10^{-10} M, less than about 5×10^{-10} M, less than about 1×10^{-11} M, less than about 5×10^{-11} M, or less than about 1×10^{-12} M, as measured by biolayer interferometry, wherein, optionally, the antibody or antigen binding fragment binds to the SARS-CoV-2 surface glycoprotein with a KD of less than 1×10^{-12} M, as measured by biolayer interferometry.

~~107.—The antibody or antigen binding fragment of any one of claims 94-106, wherein the antibody or antigen binding fragment is capable of inducing antibody-dependent cell-mediated cytotoxicity (ADCC) and/or antibody dependent cellular phagocytosis (ADCP) against a target cell infected by a SARS-CoV-2,~~

~~wherein, optionally, the inducing ADCC comprises activating a Natural Killer cell that comprises a V158 FcγRIIIa variant, a Natural Killer cell that comprises a F158 FcγRIIIa variant, or both, and/or the inducing ADCP comprises engaging a FcγRIIIa expressed on the surface of a phagocytic cell, such as a monocyte, a macrophage, or a dendritic cell.~~

~~108.—The antibody or antigen binding fragment of any one of claims 94-107, wherein the antibody or antigen binding fragment is a Fab and the Fab is capable of binding to a SARS-CoV-2 surface glycoprotein with a KD of 2.0×10^{-9} M or less, 1.9×10^{-9} M or less, or 1.8×10^{-9} M or less, as measured by biolayer interferometry.~~

~~109.—The antibody or antigen binding fragment of any one of claims 94-108, wherein the antibody or antigen binding fragment is capable of neutralizing infection by the SARS-CoV-2 and does not compete with a human ACE2 for binding to the SARS-CoV-2 surface glycoprotein.~~

~~110.—An antibody, or an antigen binding fragment thereof, that competes for binding to a SARS-CoV-2 surface glycoprotein with the antibody or antigen binding fragment of any one of claims 94-109.~~

~~111.—The antibody or antigen-binding fragment of any one of claims 94-110, which is capable of binding to the SARS-CoV-2 surface glycoprotein when the SARS-CoV-2 surface glycoprotein is comprised in a prefusion trimer.~~

~~112.—The antibody or antigen-binding fragment of any one of claims 94-111, which is capable of binding to a Receptor Binding Domain (RBD) of the SARS-CoV-2 surface glycoprotein when the RBD is glycosylated and/or when the RBD is deglycosylated, wherein the binding is determined using surface plasmon resonance (SPR), wherein, optionally:~~

~~(1)—the SPR is performed using a Biacore T200 instrument using a single-cycle kinetics approach, further optionally with a 3-minute injection period and a 20-minute dissociation period;~~

~~(2)—the antibody or antigen-binding fragment is captured on a surface;~~

~~(3)—the RBD is present at a concentration of 0.8 nM, 3.1 nM, 12.5 nM, 50 nM, or 200 nM;~~

~~(4)—the antibody or antigen-binding fragment binds to the glycosylated RBD with a KD of about about 0.6 nM, about 0.5 nM, about 0.4 nM, or about 0.3 nM, or with a KD of $0.3 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $0.4 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $0.45 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $0.5 \text{ nM} \pm 0.05 \text{ nM}$, or with a KD of $0.6 \text{ nM} \pm 0.05 \text{ nM}$; and/or~~

~~(5)—the antibody or antigen-binding fragment binds to the deglycosylated RBD with a KD of about 1.6 nM, about 1.5 nM, about 1.4 nM, about 1.3 nM, about 1.2 nM, about 1.1 nM, about 1.0.~~

~~113.—The antibody or antigen-binding fragment of any one of claims 94-112, which is capable of neutralizing an infection by the SARS-CoV-2 in a human lung cell, wherein, optionally, the human lung cell comprises a Calu-3 cell, wherein, further optionally, the antibody or antigen-binding fragment has a neutralization IC50 of about 97 ng/mL.~~

~~114.—The antibody or antigen binding fragment of any one of claims 94-113, which is capable of binding to a human complement component C1q, wherein, optionally, binding to the C1q is determined using biolayer interferometry (BLI), such as using an Octet instrument.~~

~~115.—The antibody or antigen binding fragment of any one of claims 94-114, which is capable of inhibiting SARS-CoV-2 surface glycoprotein mediated cell-cell fusion.~~

~~116.—The antibody or antigen binding fragment of any one of claims 94-115, which does not cause antibody-mediated enhancement of SARS-CoV-2 replication in a human donor-derived peripheral blood mononuclear cell (PBMC) or a dendritic cell.~~

~~117.—The antibody or antigen binding fragment of any one of claims 94-116, which is capable of inhibiting an interaction between:~~

- ~~(i) —SARS-CoV-2 and a human DC-SIGN;~~
- ~~(ii) —SARS-CoV-2 and a human L-SIGN;~~
- ~~(iii) —SARS-CoV-2 and a human SIGLEC-1; or~~
- ~~(iv) —any combination of (i)-(iii).~~

~~118.—The antibody or antigen binding fragment of any one of claims 94-117, which is capable of binding to a surface glycoprotein of:~~

- ~~(i) —a SARS-CoV-2 Wuhan Hu-1 (SEQ ID NO.:165);~~
- ~~(ii) —a SARS-CoV-2 B.1.1.7;~~
- ~~(iii) —a SARS-CoV-2 B.1.351;~~
- ~~(iv) —a SARS-CoV-2 comprising any one or more of the following substitution mutations relative to SEQ ID NO.:165: N501Y; S477N; N439K; L452R; E484K; Y453F; A520S; K417N; K417V; S494P; N501T; S477R; V367F; P384L; A522S; A522V; V382L; P330S; T478I; S477I; P479S; or~~
- ~~(v) —any combination of (i)-(iv).~~

~~119.—The antibody or antigen binding fragment of any one of claims 94-118, wherein the antibody or antigen binding fragment is capable of neutralizing infection by the SARS-CoV-2 with an IC50 of 3.0 nM, 3.1 nM, 3.2 nM, 3.3 nM, 3.4 nM, 3.5 nM, 3.6 nM, 3.7 nM, 3.8 nM, 3.9 nM, or 4.0 nM.~~

~~120.—The antibody or antigen binding fragment of any one of claims 94-119, comprising:~~

~~(i)—a heavy chain comprising (i)(1) a VH that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113, and (i)(2) a CH1-CH3 that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:173; and~~

~~(ii)—a light chain comprising (ii)(1) a VL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.: 168, and (ii)(2) a CL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:174.~~

~~121.—The antibody or antigen binding fragment of any one of claims 94-120, comprising:~~

~~(i)—a heavy chain comprising (i)(1) a VH that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:113, and (i)(2) a CH1-CH3 that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:175; and~~

~~(ii)—a light chain comprising (ii)(1) a VL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.: 168, and (ii)(2) a CL that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:174.~~

~~122.—The antibody or antigen binding fragment of any one of claims 94-121, comprising a CH1-CH3 that comprises or consists of the amino acid sequence set forth in SEQ ID NO.:265 or 266.~~

~~123.—An isolated polynucleotide encoding the antibody or antigen binding fragment of any one of claims 1-122, or encoding a VH, a heavy chain, a VL, and/or a light chain of the antibody or the antigen binding fragment.~~

~~124.—The isolated polynucleotide of claim 123, wherein the polynucleotide comprises deoxyribonucleic acid (DNA) or ribonucleic acid (RNA), wherein the RNA optionally comprises messenger RNA (mRNA).~~

~~125.—The isolated polynucleotide of claim 123 or 124, which is codon-optimized for expression in a host cell.~~

~~126.—The isolated polynucleotide of any one of claims 123-125, comprising a polynucleotide having at least 50% identity to the polynucleotide sequence according to any one or more of SEQ ID NOs.:186-189, 191-192, 238, 247, 248-255 and 257-262.~~

~~127.—The isolated polynucleotide of any one of claims 123-126, comprising the polynucleotide sequence set forth in any one or more of SEQ ID NOs.:249, 250, and 257-262.~~

~~128.—A recombinant vector comprising the polynucleotide of any one of claims 123-127.~~

~~129.—A host cell comprising the polynucleotide of any one of claims 123-127 and/or the vector of claim 128, wherein the polynucleotide is heterologous to the host cell.~~

~~130.—A human B cell comprising the polynucleotide of any one of claims 123-129, wherein polynucleotide is heterologous to the human B cell and/or wherein the human B cell is immortalized.~~

~~131.—A composition comprising:~~

- ~~(i) —the antibody or antigen binding fragment of any one of claims 1-122;~~
- ~~(ii) —the polynucleotide of any one of claims 123-127;~~
- ~~(iii) —the recombinant vector of claim 128;~~

- (iv) ~~the host cell of claim 129; and/or~~
- (v) ~~the human B cell of claim 130,~~
- ~~and a pharmaceutically acceptable excipient, carrier, or diluent.~~

~~132. The composition of claim 131, comprising two or more antibodies or antigen binding fragments of any one of claims 1-122.~~

~~133. The composition of claim 132, comprising:~~

~~(i) a first antibody or antigen binding fragment, comprising a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:79 and a VL comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:83; and~~

~~(ii) a second antibody or antigen binding fragment comprising, a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:105 and a VL comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:168.~~

~~134. The composition of claim 132, comprising:~~

~~(i) a first antibody or antigen binding fragment comprising a heavy chain variable domain (VH) comprising a CDRH1, a CDRH2, and a CDRH3, and a light chain variable domain (VL) comprising a CDRL1, a CDRL2, and a CDRL3, wherein the CDRH1, CDRH2, and CDRH3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:80-82, respectively, and the CDRL1, CDRL2, and CDRL3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:84-86, respectively; and~~

~~(ii) a second antibody or antigen binding fragment comprising a heavy chain variable domain (VH) comprising a CDRH1, a CDRH2, and a CDRH3, and a light chain variable domain (VL) comprising a CDRL1, a CDRL2, and a CDRL3, wherein the CDRH1, CDRH2, and CDRH3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:106-108, respectively, and the CDRL1, CDRL2, and CDRL3~~

~~comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:169-171, respectively.~~

~~135.—The composition of claim 132, comprising:~~

~~(i)——a first antibody or antigen-binding fragment, comprising a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:178 and a VL comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:182 or SEQ ID NO.:190; and~~

~~(ii)——a second antibody or antigen-binding fragment comprising, a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:105 and a VL comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:168.~~

~~136.—The composition of claim 135, comprising:~~

~~(i)——a first antibody or antigen-binding fragment comprising a heavy chain variable domain (VH) comprising a CDRH1, a CDRH2, and a CDRH3, and a light chain variable domain (VL) comprising a CDRL1, a CDRL2, and a CDRL3, wherein the CDRH1, CDRH2, and CDRH3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:179-181, respectively, and the CDRL1, CDRL2, and CDRL3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:183-185, respectively; and~~

~~(ii)——a second antibody or antigen-binding fragment comprising a heavy chain variable domain (VH) comprising a CDRH1, a CDRH2, and a CDRH3, and a light chain variable domain (VL) comprising a CDRL1, a CDRL2, and a CDRL3, wherein the CDRH1, CDRH2, and CDRH3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:106-108, respectively, and the CDRL1, CDRL2, and CDRL3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:169-171, respectively.~~

~~137.—The composition of claim 132, comprising:~~

~~(i) —a first antibody or antigen-binding fragment comprising a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:178 and a VL comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:182 or SEQ ID NO.:190; and~~

~~(ii) —a second antibody or antigen-binding fragment comprising a VH comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:63 and a VL comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:67, any one of SEQ ID NOs.:71-71, or any one of SEQ ID NOs.:75-76.~~

~~138.—The composition of claim 132, comprising:~~

~~(i) —a first antibody or antigen-binding fragment comprising a heavy chain variable domain (VH) comprising a CDRH1, a CDRH2, and a CDRH3, and a light chain variable domain (VL) comprising a CDRL1, a CDRL2, and a CDRL3, wherein the CDRH1, CDRH2, and CDRH3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:179-181, respectively, and the CDRL1, CDRL2, and CDRL3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:183-185, respectively; and~~

~~(ii) —a second antibody or antigen-binding fragment comprising a heavy chain variable domain (VH) comprising a CDRH1, a CDRH2, and a CDRH3, and a light chain variable domain (VL) comprising a CDRL1, a CDRL2, and a CDRL3, wherein the CDRH1, CDRH2, and CDRH3 comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:64-66, respectively, the CDRL1 comprises or consists of the amino acid sequences set forth in any one of SEQ ID NO.:68, SEQ ID NO.:73, or SEQ ID NO.:74, the CDRL2 comprises or consists of the amino acid sequences set forth in SEQ ID NO.:69, and the CDRL3 comprises or consists of the amino acid sequences set forth in SEQ ID NO.:70, SEQ ID NO.:77, or SEQ ID NO.:78.~~

~~139.—A composition comprising (i) the antibody or antigen-binding fragment of claim 8 or 9 and (ii) the antibody or antigen-binding fragment of claim 10 or 11,~~

wherein the composition is capable of neutralizing a SARS-CoV-2 infection with an IC₅₀ of about 0.07 to about 0.08 µg/ml.

~~140.—A composition comprising the polynucleotide of any one of claims 123–127 encapsulated in a carrier molecule, wherein the carrier molecule optionally comprises a lipid, a lipid-derived delivery vehicle, such as a liposome, a solid-lipid nanoparticle, an oily suspension, a submicron lipid emulsion, a lipid microbubble, an inverse-lipid micelle, a cochlear liposome, a lipid-microtubule, a lipid-microcylinder, lipid nanoparticle (LNP), or a nanoscale platform.~~

~~141.—A method of treating a SARS-CoV-2 infection in a subject, the method comprising administering to the subject an effective amount of:~~

- ~~(i) —the antibody or antigen-binding fragment of any one of claims 1–122;~~
- ~~(ii) —the polynucleotide of any one of claims 123–127;~~
- ~~(iii) —the recombinant vector of claim 128;~~
- ~~(iv) —the host cell of claim 129;~~
- ~~(v) —the human B cell of claim 130; and/or~~
- ~~(vi) —the composition of any one of claims 131–140.~~

~~142.—A method of inhibiting a SARS-CoV-2 infection in a subject, the method comprising administering to the subject an effective amount of:~~

- ~~(i) —the antibody or antigen-binding fragment of any one of claims 1–122;~~
- ~~(ii) —the polynucleotide of any one of claims 123–127;~~
- ~~(iii) —the recombinant vector of claim 128;~~
- ~~(iv) —the host cell of claim 129;~~
- ~~(v) —the human B cell of claim 130; and/or~~
- ~~(vi) —the composition of any one of claims 131–140.~~

~~143.—The antibody or antigen-binding fragment of any one of claims 1–122, the polynucleotide of any one of claims 123–127, the recombinant vector of claim 128, the host cell of claim 129, the human B cell of claim 130, and/or the composition of any~~

~~one of claims 131-140 for use in a method of treating a SARS-CoV-2 infection in a subject.~~

~~144.—The antibody or antigen binding fragment of any one of claims 1-122, the polynucleotide of any one of claims 123-127, the recombinant vector of claim 128, the host cell of claim 129, the human B cell of claim 130, and/or the composition of any one of claims 131-140 for use in a method of inhibiting a SARS-CoV-2 infection in a subject.~~

~~145.—The antibody or antigen binding fragment of any one of claims 1-122, the polynucleotide of any one of claims 123-127, the recombinant vector of claim 128, the host cell of claim 129, the human B cell of claim 130, and/or the composition of any one of claims 131-140, for use in the preparation of a medicament for the treatment of a SARS-CoV-2 infection in a subject.~~

~~146.—A method for *in vitro* diagnosis of a SARS-CoV-2 infection, the method comprising:~~

~~(i) —contacting a sample from a subject with an antibody or antigen binding fragment of any one of claims 1-122; and~~

~~(ii) —detecting a complex comprising an antigen and the antibody, or comprising an antigen and the antigen binding fragment.~~

~~147.—The method of claim 146, wherein the sample comprises blood isolated from the subject.~~

~~148.—A combination or composition comprising:~~

~~(i) —an antibody or antigen binding fragment comprising~~

~~(i)(a) —a CDRH1 amino acid sequence GYPFTSYG, a CDRH2 amino acid sequence ISTYNGNT or ISTYQGNT, a CDRH3 amino acid sequence ARDYTRGAWFGESLIGGFDN; a CDRL1 amino acid sequence or QTVSSTS, a CDRL2 amino acid sequence GAS, and a CDRL3 amino acid sequence QHDTSLT; or~~

~~(i)(b) —a VH amino acid sequence comprising or consisting of QVQLVQSGAEVKKPGASVKVSCKASGYPFTSYGISWVRQAPGQGLEWMGWIS TYNGNTNYAQKFQGRVTMTTDTSTTTGYMELRRLRSDDTAVYYCARDYTRG AWFGESLIGGFDNWGQGTLVTVSS~~

~~or comprising or consisting of~~
QVQLVQSGAEVKKPGASVKVSCKASGYPTSYGISWVRQAPGQGLEWMGWIS
TYQGNTNYAQKFQGRVTMTTDTSTTTGYMELRRLRSDDTAVYYCARDYTRG
AWFGESLIGGFNDNWGQGTLVTVSS;

~~and a VL amino acid sequence comprising or consisting of~~
EIVLTQSPGTLSLSPGERATLSCRASQTVSSTSLAWYQQKPGQAPRLLIYGASSR
ATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQHDTSLTFGGGGTKVEIK;

~~and~~

~~(ii) an antibody or antigen binding fragment comprising:~~

~~(ii)(a) VH and VL amino acid sequences according to SEQ ID NOs.:79 and 83,
respectively;~~

~~(ii)(b) CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid
sequences according to SEQ ID NOS.:80-82 and 84-86, respectively;~~

~~(ii)(c) VH and VL amino acid sequences according to SEQ ID NOs.:178 or 194
or 196 or 198 or 200 or 202 and 182 or 190, respectively; or~~

~~(ii)(d) CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid
sequences according to SEQ ID NOs.:179 or 195, 180 or 197 or 199, 181, 201 or 203,
and 183-185, respectively.~~

~~149.—A method of preventing or treating or neutralizing a coronavirus
infection in a subject, the method comprising administering to the subject the
combination or composition of claim 148, wherein, optionally, the antibody or antigen
binding fragment of (i) and the antibody or antigen binding fragment of (ii) are
administered concurrently, simultaneously, or consecutively.~~

~~150.—A method of preventing or treating or neutralizing a coronavirus
infection in a subject, the method comprising administering to a subject who has
received a first antibody or antigen binding fragment comprising:~~

~~(a) VH and VL amino acid sequences according to SEQ ID NOs.:79 and 83,
respectively; or~~

~~(b) CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid
sequences according to SEQ ID NOs.:80-82 and 84-86, respectively;~~

and a second antibody or antigen binding fragment comprising:

(a) — a VH amino acid sequence according to SEQ ID NO.:105 or 113, and a VL amino acid sequence according to SEQ ID NO.: 168; or

(b) — CDRH1, CDRH2, and CDRH3 amino acids according to SEQ ID NOs.: 106-108, respectively, or SEQ ID NOs.:106, 121, and 108, respectively, and CDRL1, CDRL2, and CDRL3 amino acid sequences according to SEQ ID NOs.:169-171, respectively.

151. — A method of preventing or treating or neutralizing a coronavirus infection in a subject, the method comprising administering to a subject who has received a first antibody or antigen binding fragment comprising:

(a) — a VH amino acid sequence according to SEQ ID NOs.:105 or 113, and a VL amino acid sequence according to SEQ ID NO.:168; or

(b) — CDRH1, CDRH2, and CDRH3 amino acids according to SEQ ID NOs.: 106-108, respectively, or SEQ ID NOs.:106, 121, and 108, respectively, and CDRL1, CDRL2, and CDRL3 amino acid sequences according to SEQ ID NOS.:169-171, respectively;

a second antibody or antigen binding fragment comprising:

(a) — VH and VL amino acid sequences according to SEQ ID NOs.:79 and 83, respectively; or

(b) — CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to SEQ ID NOS.:80-82 and 84-86, respectively.

152. — A method of preventing or treating or neutralizing a coronavirus infection in a subject, the method comprising administering to a subject who has received a first antibody or antigen binding fragment comprising:

(a) — VH and VL amino acid sequences according to SEQ ID NOs.:178 or 194 or 196 or 198 or 200 or 202 and 182 or 190, respectively; or

(b) — CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to SEQ ID NOS.:179 or 195, 180 or 197 or 199, 181-201 or 203, and 183-185, respectively;

a second antibody or antigen binding fragment comprising:

~~(a) — a VH amino acid sequence according to SEQ ID NOs.:105 or 113, and a VL amino acid sequence according to SEQ ID NO: 168; or~~

~~(b) — CDRH1, CDRH2, and CDRH3 amino acids according to SEQ ID NOs.: 106-108, respectively, or SEQ ID NOs.: 106, 121, and 108, respectively, and CDRL1, CDRL2, and CDRL3 amino acid sequences according to SEQ ID NOS.:169-171, respectively.~~

~~153. — A method of preventing or treating or neutralizing a coronavirus infection in a subject, the method comprising administering to a subject who has received a first antibody or antigen binding fragment comprising:~~

~~(a) — a VH amino acid sequence according to SEQ ID NOs.:105 or 113, and a VL amino acid sequence according to SEQ ID NO: 168; or~~

~~(b) — CDRH1, CDRH2, and CDRH3 amino acids according to SEQ ID NOs.: 106-108, respectively, or SEQ ID NOs.: 106, 121, and 108, respectively, and CDRL1, CDRL2, and CDRL3 amino acid sequences according to SEQ ID NOS.:169-171, respectively;~~

~~a second antibody or antigen binding fragment comprising:~~

~~(a) — VH and VL amino acid sequences according to SEQ ID NOs.:178 or 194 or 196 or 198 or 200 or 202 and 182 or 190, respectively; or~~

~~(b) — CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to SEQ ID NOS.:179 or 195, 180 or 197 or 199, 181-201 or 203, and 183-185, respectively.~~