Claims

What is claimed is:

1. An isolated antibody, or antigen-binding fragment thereof, which specifically binds to the spike protein of a coronavirus ("CoV-S"), wherein said antibody, or antigen-binding fragment thereof, comprises a heavy chain variable region (VH) comprising a ~~sequence having at least 90% identity to SEQ ID NO:22302 and a light chain variable region (VL) comprising a sequence having at least 90% identity to SEQ ID NO:22312.~~

~~2. The isolated antibody, or antigen-binding fragment thereof, of claim 1, comprising a VH comprising a sequence having at least 95% identity to SEQ ID NO:22302 and a VL comprising a sequence having at least 95% identity to SEQ ID NO:22312.~~

~~3. The isolated antibody, or antigen-binding fragment thereof, of claim 1 or claim 2, wherein the VH comprises a VH complementarity determining region 1 (~~VH CDR1~~)~~ comprising SEQ ID NO:22304, a VH ~~complementarity determining region 2 (~~CDR2~~)~~ comprising SEQ ID NO:22306, and a VH ~~complementarity determining region 3 (~~CDR3~~)~~ comprising SEQ ID NO:22308, and a light chain variable region (VL) comprising ~~and wherein the VL comprises~~ a VL CDR1 comprising SEQ ID NO:22314, a VL CDR2 comprising SEQ ID NO:22316, and a VL CDR3 comprising SEQ ID NO:22318.

~~4. An isolated antibody, or antigen-binding fragment thereof, which specifically binds to the spike protein of a coronavirus ("CoV-S"), wherein said antibody, or antigen-binding fragment thereof, comprises a heavy chain variable region (VH) comprising a VH CDR1 comprising SEQ ID NO:22304, a VH CDR2 comprising SEQ ID NO:22306, and a VH CDR3 comprising SEQ ID NO:22308, and a light chain variable region (VL) comprising a VL CDR1 comprising SEQ ID NO:22314, a VL CDR2 comprising SEQ ID NO:22316, and a VL CDR3 comprising SEQ ID NO:22318.~~

~~5. The isolated antibody, or antigen-binding fragment thereof, of claim 4, wherein the VH comprises a sequence having at least at least 90% identity to SEQ ID NO:22302 and VL comprising a sequence having at least 90% identity to SEQ ID NO:22312.~~

~~6. The isolated antibody, or antigen-binding fragment thereof, of claim 4 or claim 5, wherein the VH comprises a sequence having at least at least 95% identity to SEQ ID NO:22302 and VL comprising a sequence having at least 95% identity to SEQ ID NO:22312.~~

~~7~~2. The isolated antibody, or antigen-binding fragment thereof, of ~~any one of the previous~~ claim 1~~s~~, wherein the VH comprises SEQ ID NO:22302 and the VL comprises SEQ ID NO:22312.

3. The isolated antibody, or antigen-binding fragment thereof, of claim 2, wherein the VH consists of SEQ ID NO:22302 and the VL consists of SEQ ID NO:22312.

~~8. An isolated antibody, or antigen-binding fragment thereof, which specifically binds to the spike protein of a coronavirus ("CoV-S"), wherein said antibody, or antigen-binding fragment thereof, comprises~~

~~a heavy chain variable region (VH) comprising~~

~~a VH CDR3 having a sequence of ARDFSGHTAX$_1$AGTGFEY (SEQ ID NO: 23209), wherein X$_1$ is W or V;~~

~~a VH CDR2 having a sequence of SISX$_1$DGYX$_2$TYYPDSLKG (SEQ ID NO: 23208), wherein X$_1$ is S or E and X$_2$ is N or S; and~~

~~a VH CDR1 having a sequence of X$_1$TFX$_2$SYYX$_3$X$_4$ (SEQ ID NO: 23206), wherein X$_1$ is F or Y, X$_2$ is T or S, X$_3$ is M or I, and X$_4$ is H or N; and~~

~~a light chain variable region (VL) comprising~~

~~a VL CDR3 having a sequence of QSYDSSLSVLYX$_1$ (SEQ ID NO: 23214), wherein X$_1$ is T or V;~~

~~a VL CDR2 having a sequence of GX$_1$SSX$_2$X$_3$S (SEQ ID NO: 23212), wherein X$_1$ is S or A, X$_2$ is R or L, and X$_3$ is N, H, or Q; and~~

~~a VL CDR1 having a sequence of TSGX$_1$SNX$_2$GAGYX$_3$VH (SEQ ID NO: 23210), wherein X$_1$ is N or S, X$_2$ is I or V, and X$_3$ is D or Y.~~

~~9. An isolated antibody, or antigen-binding fragment thereof, which specifically binds to the spike protein of a coronavirus ("CoV-S"), wherein said antibody, or antigen-binding fragment thereof, comprises~~

~~a heavy chain variable region (VH) comprising a VH CDR3 having a sequence of VKDGGYYDSSGPGH (SEQ ID NO: 23218); a VH CDR2 having a sequence of AINLNGDSX$_1$YYTDSVRG (SEQ ID NO: 23217), wherein X$_1$ is K or T; and a VH CDR1 having a sequence of FTFS X$_1$X$_2$AMH (SEQ ID NO: 23215), wherein X$_1$ is R or K and X$_2$ is F or Y; and~~

~~a light chain variable region (VL) comprising a VL CDR3 having a sequence of QQRX$_1$NWPQN (SEQ ID NO: 23225), wherein X$_1$ is A or S; a VL CDR2 having a sequence of DX$_1$S X$_2$RAT (SEQ ID NO: 23223), wherein X$_1$ is A, S, or V, X$_2$ is K or R; and a VL CDR1 having a sequence of RASENIX$_1$HYLA (SEQ ID NO: 23220), wherein X$_1$ is L or A.~~

10. An isolated antibody, or antigen-binding fragment thereof, which specifically binds to the spike protein of a coronavirus ("CoV-S"), wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable region (VH) comprising a VH CDR1 of an antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36**, a VH CDR2 of the antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36**, and a VH CDR3 of the antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36**, and a light chain variable region (VL) comprising a VL CDR1 of the antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36**, a VL CDR2 of the antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36**, and a VL CDR3 of the antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36**.

11. The isolated antibody, or antigen-binding fragment thereof, of claim 10, wherein the VH comprises a sequence having at least at least 90% identity to the VL sequence of the antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36** and VL sequence having at least 90% identity to the VL sequence of the antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36**.

12. An isolated antibody, or antigen-binding fragment thereof, which specifically binds to the spike protein of a coronavirus ("CoV-S"), wherein said antibody, or antigen-binding fragment thereof, comprises a heavy chain variable region (VH) comprising a sequence having at least 90% identity to a VH protein sequence of an antibody selected from the group consisting of the antibodies listed in **Fig. 1** and **Fig. 36**, and a light chain variable region (VL) comprising a sequence having at least 90% identity to a VL protein sequence of the antibody listed in **Fig. 2**.

13. The isolated antibody, or antigen-binding fragment thereof, of claim 12,

wherein the heavy chain variable region (VH) comprises a VH CDR1 of the antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36**, a VH CDR2 of the antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36**, and a VH CDR3 of the antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36**, and

a light chain variable region (VL) comprising a VL CDR1 of the antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36**, a VL CDR2 of the antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36**, and a VL CDR3 of the antibody selected from the group consisting of the antibodies listed in **Fig. 1, Fig. 2**, or **Fig. 36**.

4. ~~14.~~ The isolated antibody, or antigen-binding fragment thereof, of ~~any one of the previous~~ claim 1~~s~~, wherein the ~~COV~~CoV-S is the spike protein of SARS-CoV ("SARS-CoV-S") or the spike protein of SARS-CoV-2 ("SARS-CoV-2-S").

5. ~~15.~~ The isolated antibody, or antigen-binding fragment thereof, of claim 1~~any one of the previous claims~~, wherein the antibody, or antigen-binding fragment thereof, cross-reacts with SARS-CoV-S and SARS-CoV-2-S.

6. ~~16.~~ The isolated antibody, or antigen-binding fragment thereof, of claim 5~~14 or claim 15~~, wherein SARS-CoV-S comprises an~~a sequence having at least 95% identity to the~~ amino acid sequence of SEQ ID NO:1, and wherein SARS-CoV-2-S comprises an ~~a sequence having at least 95% identity to the~~ amino acid sequence of SEQ ID NO:5.

~~17. The isolated antibody, or antigen-binding fragment thereof, of any one of claims 14-16, wherein the SARS-CoV-2-S is a B.1.1.7 variant, a B. 1.351 variant, a B.1.1.28 variant, a B. 1.429 variant, a B. 1.427 variant, or a B.1.525 variant.~~

7. ~~18.~~ The isolated antibody, or antigen-binding fragment thereof, of ~~any one of the previous~~ claim 1~~s~~, which neutralizes SARS-CoV and/or SARS-CoV-2.

8. ~~19.~~ The isolated antibody, or antigen-binding fragment thereof, of claim 7~~18~~, which neutralizes SARS-CoV and/or SARS-CoV-2 with an IC50 of about 100 nM or lower.

9. ~~20.~~ The isolated antibody, or antigen-binding fragment thereof, of claim 1~~any one of the previous claims~~, which binds to SARS-CoV-S with a KD value of about 100 nM or lower.

10. ~~21.~~ The isolated antibody, or antigen-binding fragment thereof, of claim 1~~any one of the previous claims~~, wherein the antibody is human, humanized, primatized, chimeric, bispecific or multispecific.

11. ~~22.~~ The isolated antibody, or antigen-binding fragment thereof, of claim 1~~any one of the previous claims~~, wherein the antigen-binding fragment thereof comprises a Fab, Fab2, or scFv.

~~23. An isolated antibody, or antigen-binding fragment thereof, which competes for binding with the isolated antibody, or antigen-binding fragment thereof, of any one of the previous claims.~~

~~24. An isolated antibody, or antigen-binding fragment thereof, which binds the same epitope as the isolated antibody, or antigen-binding fragment thereof, of any one of the previous claims.~~

~~25. An antibody drug conjugate ("ADC") comprising the antibody, or antigen-binding fragment thereof, of any one of the previous claims, and a drug.~~

~~26. A chimeric antigen receptor ("CAR") comprising at least one antibody, or antigen-binding portion thereof, of any one of claims 1-24.~~

~~27. An isolated nucleic acid encoding the antibody, or antigen-binding fragment thereof, of any one of claims 1-24, or the CAR of claim 26.~~

~~28. An isolated cell comprising the isolated nucleic acid of claim 27, or expressing the isolated antibody or antigen-binding fragment thereof, of any one of claims 1-24, or the CAR of claim 26.~~

~~29. A composition comprising the antibody, or antigen-binding fragment thereof, of any one of claims 1-24, the ADC of claim 25, or the CAR of claim 26.~~

12. ~~30.~~ A pharmaceutical composition comprising the antibody, or antigen-binding fragment thereof, of any one of claims 1-11~~24, the ADC of claim 25, or the CAR of claim 26~~, and a pharmaceutically acceptable carrier.

~~31. The pharmaceutical composition of claim 30, further comprising a second antibody, or antigen-binding fragment thereof, wherein the second antibody, or antigen-binding fragment thereof, is selected from the group consisting of ADI-58122, ADI-58127, ADI-58129 or ADI-58131.~~

~~32. A kit comprising the antibody of any one of claims 1-24, the ADC of claim 25, the CAR of claim 26, the composition of claim 29, or the pharmaceutical composition of claim 30 or claim 31, and instructions for use.~~

~~33. A method of producing the antibody, or antigen-binding fragment thereof, of any one of claims 1-24, or the CAR of claim 26, the method comprising (a) culturing a cell expressing the antibody, or antigen-binding fragment thereof, or the CAR under conditions that permit expression and (b) isolating the antibody, or antigen-binding fragment thereof, or the CAR from the cell, or the culture medium comprising the cell.~~

~~34. A method of determining whether a subject has been infected with SARS-CoV or SARS-CoV-2, the method comprising detecting whether a biological sample from said subject comprises SARS-CoV-S protein or SARS-CoV-2-S protein based on an immunoreaction with at least one of the antibodies, or antigen-binding fragments thereof, of any one of claims 1-24.~~

~~35. A method of inducing an immune response against SARS-CoV, SARS-CoV-2, or another coronavirus selected from the group consisting of MERS-CoV, HCoV-HKU1, HCoV-OC43, HCoV-229E, and HCoV-NL63 in a subject in need thereof, the method comprising administering at least one antibody, or antigen-binding fragment thereof, of any one of claims 1-24, at least one ADC of claim 25, or at least one CAR of claim 26, or the pharmaceutical composition of claim 30 or claim 31.~~

~~36. A method of preventing infection of susceptible cells by SARS-CoV, SARS-CoV-2, or another coronavirus selected from the group consisting of MERS-CoV, HCoV-HKU1, HCoV-OC43, HCoV-229E, and HCoV-NL63 in a subject in need thereof, the method comprising administering the antibody, or antigen-binding fragment thereof, of any one of claims 1-22, at least one ADC of claim 23, or at least one CAR of claim 26, or the pharmaceutical composition of claim 30 or claim 31.~~

~~37. A method of treating a coronavirus infection of a subject by SARS-CoV, SARS-CoV-2, or another coronavirus selected from the group consisting of MERS-CoV, HCoV-HKU1, HCoV-OC43, HCoV-229E, and HCoV-NL63 in a subject in need thereof, the method comprising administering the antibody, or antigen-binding fragment thereof, of any one of claims 1-24, at least one ADC of claim 25, or at least one CAR of claim 26, or the pharmaceutical composition of claim 30 or claim 31.~~

13. Use of an antibody, or antigen-binding fragment thereof in the manufacture of a medicament for treating an infection of a subject by a coronavirus, wherein the antibody, or antigen-binding fragment thereof binds to a spike protein of the coronavirus, wherein the antibody, or antigen-binding fragment thereof, comprises

a heavy chain variable region (VH) comprising a VH complementarity-determining region 1 (CDR1) comprising SEQ ID NO:22304, a VH complementarity-determining region 2 (CDR2) comprising SEQ ID NO:22306, and a VH complementarity-determining region 3 (CDR3) comprising SEQ ID NO:22308; and

a light chain variable region (VL) comprising a VL CDR1 comprising SEQ ID NO:22314, a VL CDR2 comprising SEQ ID NO:22316, and a VL CDR3 comprising SEQ ID NO:22318.

14. The use of claim 13, wherein the VH comprises SEQ ID NO:22302 and the VL comprises SEQ ID NO:22312.

15. The use of claim 14, wherein the VH consists of SEQ ID NO:22302 and the VL consists of SEQ ID NO:22312.

~~38. A method of treating a symptom of an infection of a subject by SARS-CoV, SARS-CoV-2, or another coronavirus selected from the group consisting of MERS-CoV, HCoV-HKU1, HCoV-OC43, HCoV-229E, and HCoV-NL63 in a subject in need thereof, the method comprising administering the antibody, or antigen-binding fragment thereof, of any one of claims 1-24, at least one ADC of claim 25, or at least one CAR of claim 26, or the pharmaceutical composition of claim 30 or claim 31.~~

~~39. The method of claim 38, wherein the symptom comprises at least one of bronchitis, pneumonia, respiratory failure, acute respiratory failure, organ failure, multi-organ system failure, pediatric inflammatory multisystem syndrome, acute respiratory distress syndrome, blood clot, a cardiac condition, myocardial injury, myocarditis, heart failure, cardiac arrest, acute myocardial infarction, dysrhythmia, venous thromboembolism, post intensive care syndrome, shock, anaphylactic shock, cytokine release syndrome, septic shock, disseminated intravascular coagulation, ischemic stroke, intracerebral hemorrhage, microangiopathic thrombosis, psychosis, seizure, nonconvulsive status epilepticus, traumatic brain injury, stroke, anoxic brain injury, encephalitis, posterior reversible leukoencephalopathy, necrotizing encephalopathy, post infectious encephalitis, autoimmune mediated encephalitis, acute disseminated encephalomyelitis, acute kidney injury, acute liver injury, pancreatic injury, immune thrombocytopenia, subacute thyroiditis, a gastrointestinal complication, aspergillosis, increased susceptibility to infection with another virus or bacteria, and/or a pregnancy related complication.~~

~~40. A method of decreasing the risk of mortality, hospitalization, mechanical ventilation, or a combination thereof, in a subject infected by SARS-CoV, SARS-CoV-2, or another coronavirus selected from the group consisting of MERS-CoV, HCoV-HKU1, HCoV-OC43, HCoV-229E, and HCoV-NL63, the method comprising administering to the subject a therapeutically effective amount of the antibody, or antigen-binding fragment thereof, of any one of claims 1-24, the ADC of claim 25, or the CAR of claim 26.~~

16. ~~41.~~ The use~~method~~ of ~~any one of claims 13-15~~34-~~40~~, wherein the subject is a human subject.

17. ~~42.~~ The use~~method~~ of ~~any one of claims 13-16~~34-~~41~~, wherein the subject has at least one risk factor which renders them more prone to a poor clinical outcome.

18. ~~43.~~ The use~~method~~ of ~~claim~~ 17~~42~~, wherein the at least one risk factor is selected from the group consisting of: an old age selected from the group consisting of over 55, over 60 or over 65 years old; diabetes~~;~~, a chronic respiratory condition~~;~~, obesity~~;~~, hypertension~~;~~, a cardiac or cardiovascular condition~~;~~, a chronic inflammatory or autoimmune condition~~;~~, and an immune compromised status.

19. ~~44.~~ The use~~method~~ of ~~any one of claims~~ 13-15~~34-43~~, wherein the antibody, or the antigen-binding fragment thereof, is to be administered intramuscularly or intravenously.

20. ~~45.~~ The use~~method~~ of ~~any one of claims~~ 13-15~~34-44~~, wherein the antibody, or the antigen-binding fragment thereof, is to be administered at a dose of ~~about 100 mg to about 2000 mg, about 200 mg to about 1500 mg, about~~ 300 mg to ~~about 600 mg, about 500 mg to about~~ 1200 mg~~., or about 300 mg to about 1200 mg.~~

21. ~~46.~~ The use~~method~~ of ~~any one of claims~~ 13-15~~34-45~~, wherein the antibody, or antigen-binding fragment thereof, is to be administered once or is administered weekly.

22. The use of any one of claims 13-15, wherein the coronavirus is SARS-CoV or SARS-CoV-2.