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(54) **ANTIBODY THERAPIES FOR SARS-COV-2 INFECTION**

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ABSTRACT

The instant disclosure provides methods of treating or preventing a SARS-CoV-2 infection, e.g., in a subject having or at risk for developing COVID-19, using an antibody (or antigen-binding fragment) compositions. Disclosed methods include prophylaxis against SARS-CoV-2 infection or transmission, as well as treatment of a subject having a SARS-CoV-2 infection. A SARS-CoV-2 infection (e.g., causing COVID-19) to be treated can be at any stage of infection and/or can result in any stage of disease, for example, mild, mild-to-moderate, severe, or critical.

Specification includes a Sequence Listing.

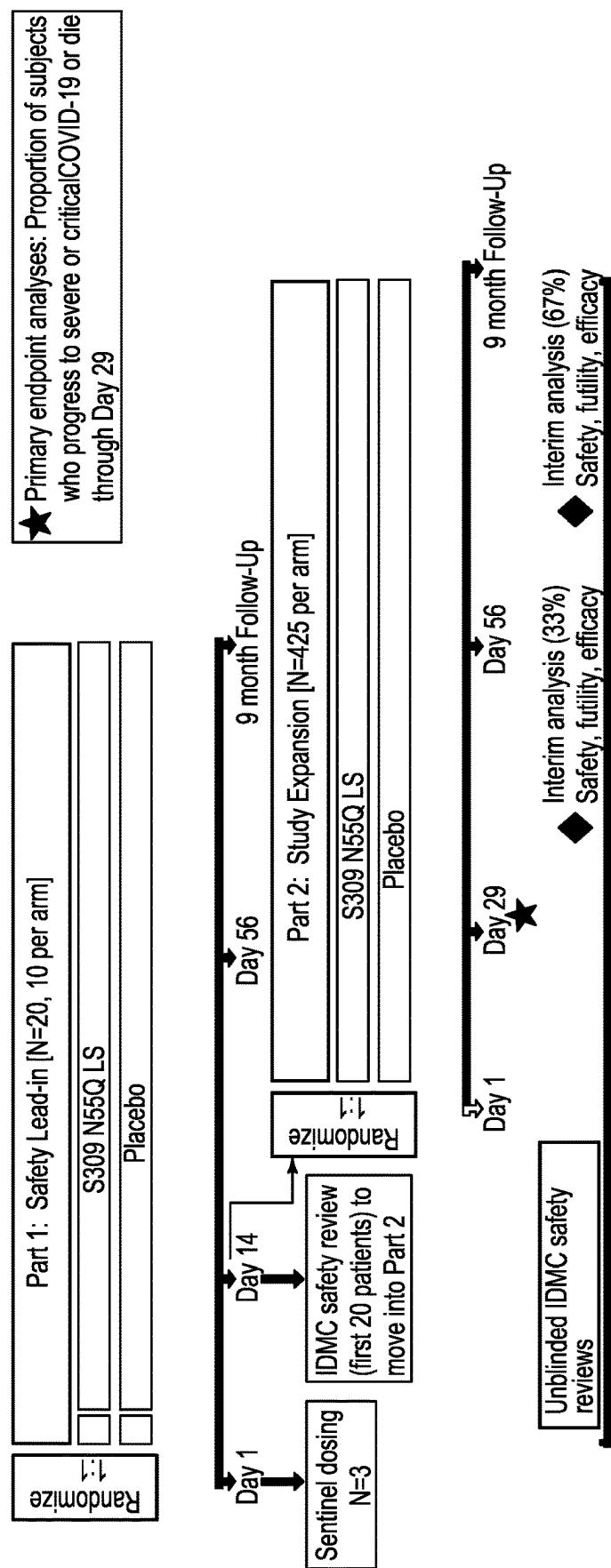


FIG. 1

Lead-In Phase	Study Visit Week	Screening	In-patient	W2	W3	W4	W6	W8	W12	W16	W20	W24-W32	W36 (EOS/ET)
Study Visit Day ± Visit Window	D-1	D1	D2	D5	D8	D11	D15±2	D18±2	D22±2	D29±2	D43±3	D57±4	D85±7 D113±7 D141±7 D252±7
Informed consent	X												
Demography	X												
Medical history	X												
Inclusion criteria	X												
Physical examination (full physical on D1 and W36; symptom-directed on other days)	X	X	X (Daily)		X	X	X	X					X
Body weight, height, and BMI	X												
Vital signs (including O2 saturation)	X	X ^a	X (every 8 hrs)		X	X	X	X					
Laboratory assessments (safety)	X	X						X	X				
Pregnancy test	X												
Randomization	X												
Study drug administration	X												
Electrocardiogram	X		X (Daily)										
Blood sample for PK analysis (intensive) ^b		X ^c	X	X	X			X	X	X	X	X	X
Anti-drug Antibody (serum) (intensive) ^b		X ^d						X		X	X	X	X
Blood sample for anti-SARS-CoV-2 antibody		X		X		X		X		X	X	X	X
Blood sample for virology (e.g. viral analysis)		X		X		X		X		X		X	
Blood sample for FcR and IgG analysis		X ^d											
Blood sample for RNA Paxgene analysis		X ^d											
SARS-CoV-2 diagnostic test (point-of-care or local laboratory test)	X												

FIG. 2A

Study Stage	Screening	In-patient	Follow-up Period								
			W2	W3	W4	W6	W8	W12	W16	W20	W24-W32 (EOS/ET)
Study Visit Day ± Visit Window	D-1	D1 D2 D5 D8 D11 D15±2	D18±2	D22±2	D29±2	D43±3	D57±4	D85±7	D113±7	D141±7	D252±7
Nasal swab for virology	X X X X X X	X X X X X X	X X X X X X								
Nasopharyngeal swab for virology	X X X X X X	X X X X X X	X X X X X X								
Symptom self-assessment (daily)				X							
Monthly Phone call - safety assessment						X	X	X	X	X	X
Review/record AEs ^e				X							
Concomitant medications			X	X	X						
Blood sample for exploratory immunology (serum)	X ^d										
PBMC sample for immunology substudy ^f	X ^d					X					X

^a^b^c^d^e^f

^a Vital signs on day 1 will be q15 mins during IV infusion of drug, q1hr x 2hrs after infusion
^b All 20 participants in the lead-in (N=10/arm) will be included in an intensive PK and ADA sub study.
^c On Day 1, blood samples will be collected pre-dose and at end infusion, 1, 2, 6, and 12 hours following end of infusion
^d On Day 1, samples will be collected pre-dose
^e Adverse events will be assessed up to Week 12 post dose. Serious adverse events (SAEs) will be assessed up Week 36 (EOS) post dose.
^f Samples for optional immunology sub-study

Expansion Phase

Study Stage	Screening	Dosing	Follow-up Period								
			W2	W3	W4	W6	W8	W12	W16	W20	W24-W32 (EOS/ET)
Study Visit Day ± Visit Window	D-1	D1 D2 D5 D8±2	D11±2	D15±2	D18±2	D22±2	D29±2	D57±4	D85±7	D113±7	D141±7
Informed consent	X										D252±7
Demography	X										
Medical history	X										
Inclusion criteria	X										

FIG. 2B

Study Stage	Screening/Dosing	Follow-up Period													
		W1	W2	W3	W4	W8	W12	W16	W20	W24- W32	W36 (EOS/ET)	D252±7			
Study Visit Day	Visit Window	D-1	D1	D2	D5	D8±2	D11±2	D15±2	D18±2	D22±2	D29±2	D57±4	D85±7	D113±7	D141±7
Physical examination (full physical on D1 and W36; symptom-directed on other days)	X	X	X	X		X		X	X						X
Body weight, height, and BMI	X														
Vital signs (including O2 saturation)	X ^a					X		X	X						
Laboratory assessments	X					X		X	X						
Pregnancy test	X														
Randomization	X														
Study drug administration	X														
Blood sample for PK analysis (Sparse)	X ^c		X				X		X		X		X		X
Anti-drug Antibody (serum) (Sparse)	X ^b								X		X		X		X
Blood sample for anti-SARS-CoV-2 antibody	X					X		X		X		X		X	
Blood sample for virology (e.g. viral load)	X			X			X		X		X		X		X
Blood sample for FcR and IgG analysis	X ^b														
Blood sample for RNA Paxgene	X ^b		X												
SARS-CoV-2 diagnostic test (point-of-care or local laboratory test)	X														
Nasal swab for virology	X	X	X	X	X		X	X	X	X	X				
Nasopharyngeal swab for virology	X	X	X	X	X		X	X	X	X	X				
Symptom self-assessment (daily)	X	X	X	X	X		X	X	X	X	X				
Phone call - clinical symptom assessment							X (daily) ^d								

FIG. 2C

Study Stage	Screening Dosing		Follow-up Period										W36 (EOS/ET)			
			W1	W2	W3	W4	W6	W8	W12	W16	W20	W24-W32				
Study Visit Week	D-1	D1	D2	D5	D8±2 ^b	D11±2 ^b	D15±2 ^b	D18±2 ^b	D22±2 ^b	D29±2 ^b	D43±3 ^b	D57±4 ^b	D85±7 ^b	D113±7 ^b	D141±7 ^b	D252±7 ^b
Study Visit Day	Visit Window															
Home Oxygen Saturation assessment					X (daily) ^d											
Monthly Phone call-safety assessment																
Review/record AEs ^e										X	X	X	X	X	X	
Concomitant medications										X	X					
Work Productivity (WPAI)		X			X		X		X	X	X					
EQ-5D-5L		X			X		X		X	X	X					
Blood sample for exploratory immunology		X ^c			X					X				X		
PBMC sample for immunology substudy ^f		X								X				X		

a Vital signs on day 1 will be q15 mins during IV infusion of drug, q1hr x 2hrs after infusion
b On Day 1, samples will be collected pre-dose
c On Day 1, collection will occur pre-dose and at the end of infusion
d Phone calls only on days when not evaluated in clinic.
e Adverse events will be assessed up to Week 12 post dose. Serious adverse events (SAEs) will be assessed up Week 36 (EOS) post dose.
f Samples for optional immunology sub-study

FIG. 2D

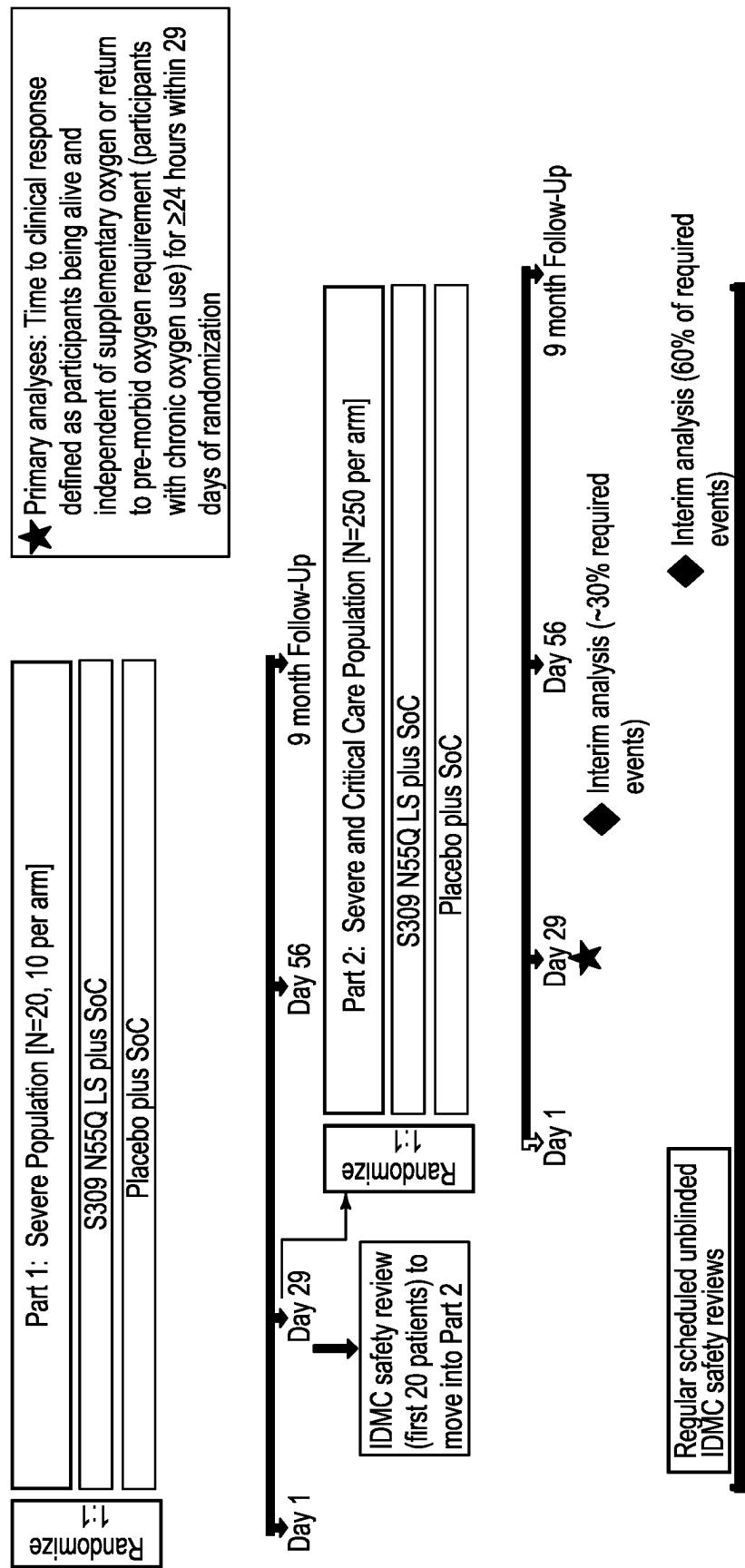


FIG. 3

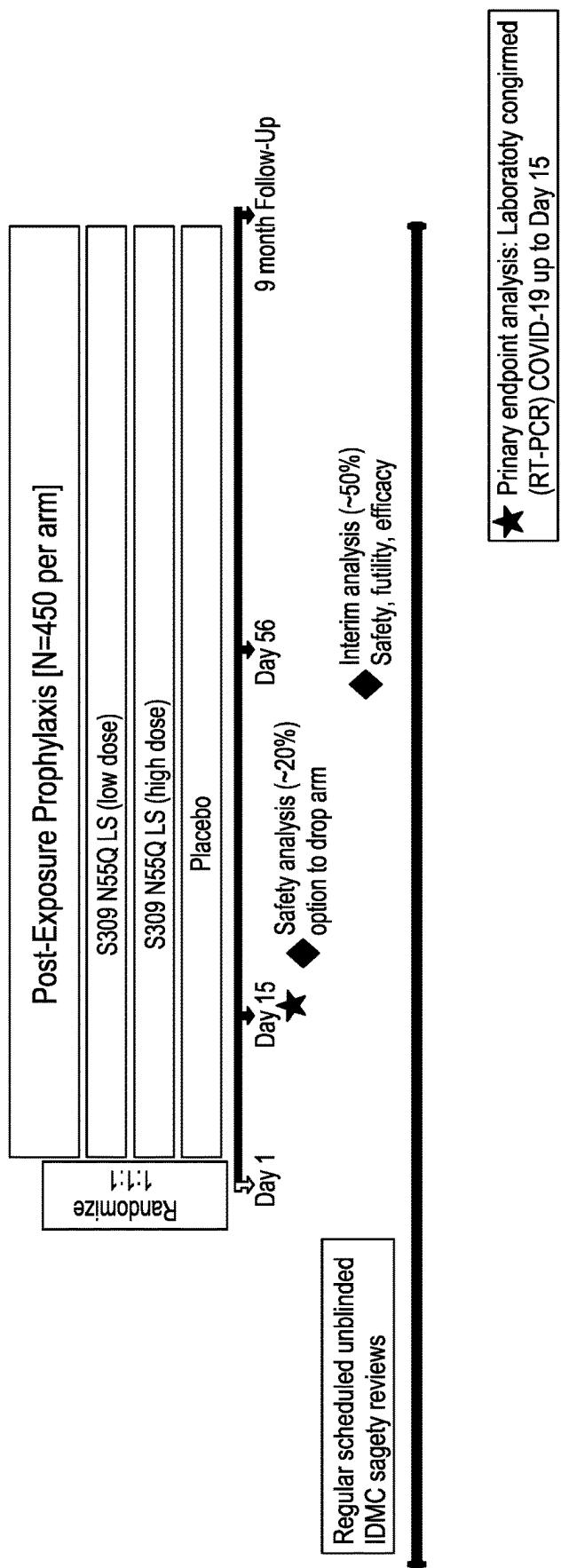


FIG. 4

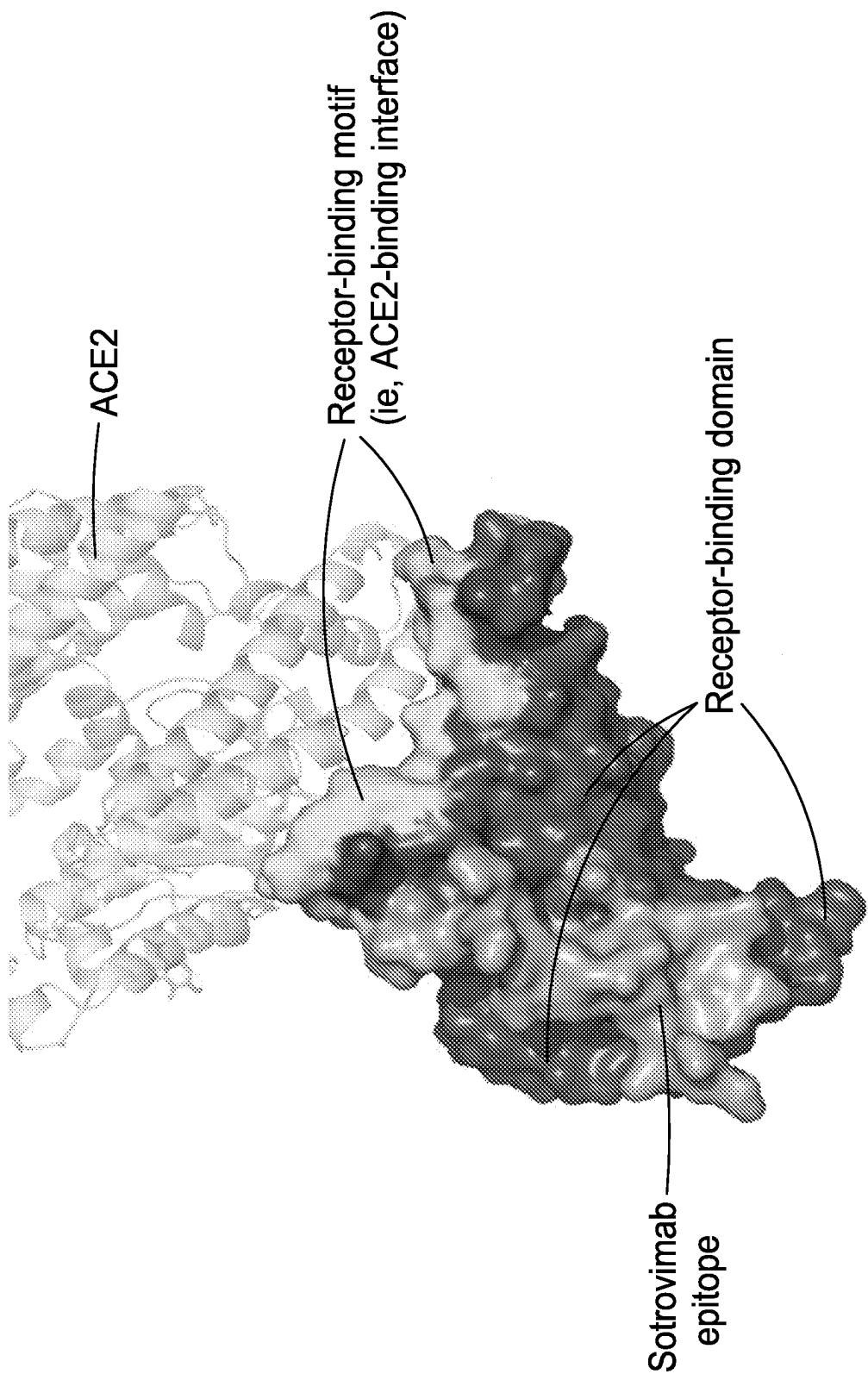


FIG. 5

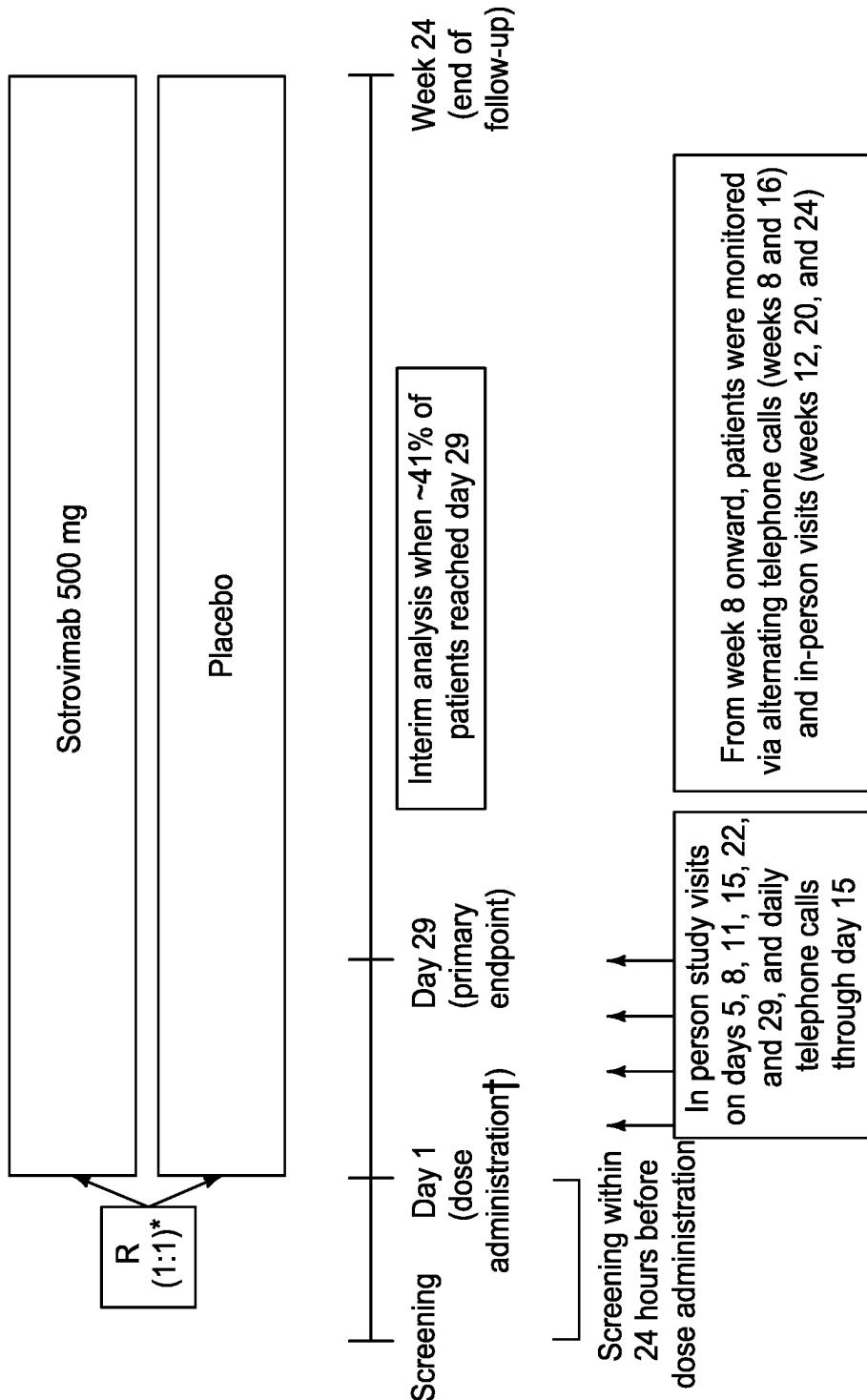


FIG. 6

ANTIBODY THERAPIES FOR SARS-COV-2 INFECTION

STATEMENT REGARDING SEQUENCE LISTING

[0001] The Sequence Listing associated with this application is provided in text format 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_413WO_SEQUENCE_LISTING.txt. The text file is 327 KB, was created on Jun. 10, 2021, and is being submitted electronically via EFS-Web.

BACKGROUND

[0002] A novel betacoronavirus emerged in Wuhan, China, in late 2019. As of Jun. 9, 2021, approximately 174 million cases of infection by this virus (termed, among other names, SARS-CoV-2 and Wuhan coronavirus) were confirmed worldwide, and had resulted in approximately 3.7 million deaths. Therapies for preventing or treating SARS-CoV-2 infection and COVID-19 are needed.

BRIEF DESCRIPTION OF THE DRAWINGS

[0003] FIG. 1 shows the design of a clinical study of recombinant monoclonal IgG1 antibody sotrovimab (also called, e.g., S309 N55Q LS herein) for treatment of mild to moderate COVID-19 disease.

[0004] FIGS. 2A-2D show a timeline of events for a clinical study of sotrovimab for treatment of mild to moderate COVID-19 disease.

[0005] FIG. 3 shows the study design for a clinical study of sotrovimab for treatment of severe to critical COVID-19 disease.

[0006] FIG. 4 shows the study design for a clinical study of sotrovimab for post-exposure prophylaxis of COVID-19 disease.

[0007] FIG. 5 shows the binding site of sotrovimab on the spike protein of SARS-CoV-2. The SARS-CoV-2 receptor-binding domain is shown, with the ACE2 receptor-binding motif in green and the sotrovimab epitope in orange. ACE2 denotes angiotensin-converting enzyme 2.

[0008] FIG. 6 shows the design of a clinical study using sotrovimab described herein. R denotes randomization. *Patients were stratified by age (≤ 70 vs. >70 years), symptom duration (≤ 3 days vs. 4-5 days), and region. †Study pharmacists reconstituted and dispensed all study medications within equal time frames to maintain blinding.

DETAILED DESCRIPTION

[0009] Provided herein are methods of treating or preventing a SARS-CoV-2 infection, e.g., in a subject having or at risk for developing COVID-19, using an antibody, an antigen-binding fragment, or composition that comprises the same. Certain antibodies and antigen-binding fragments for use in the methods recognize a conserved epitope in SARS-CoV-2 S glycoprotein and potently neutralize SARS-CoV-2 in vitro and in vivo. Non-limiting examples of antibodies include S309 and engineered variants of S309 (e.g., sotrovimab, VIR-7832). In some embodiments, a variant of S309 comprises a N55Q substitution in the VH region. In some embodiments, an antibody or antigen-binding fragment comprises an Fc polypeptide comprising one or more amino acid mutations that, for example, can extend in vivo half-life

of the antibody or antigen-binding fragment and/or can promote a vaccinal effect of the antibody or antigen-binding fragment.

[0010] Presently disclosed methods include prophylaxis against SARS-CoV-2 infection or transmission, as well as treatment of a subject having a SARS-CoV-2 infection. A SARS-CoV-2 infection (e.g., causing COVID-19) can be at any stage of infection and/or can result in any stage of disease, for example, mild, mild-to-moderate, severe, or critical. For example, as described further herein, a single dose of an antibody of the present disclosure can be sufficient to reduce hospitalization or death in subjects with mild-to-moderate COVID-19.

[0011] Administration of the antibody or antigen-binding fragment can be performed using any method, such as for example, intravenous injection and intramuscular injection. In some contexts, a single dose of the antibody or antigen-binding fragment (or composition comprising the same) is administered to a subject. Subjects may be characterized in accordance with one or more criteria, and/or possess one or more characteristics, as provided herein. Also provided are antibodies, antigen-binding fragments, and compositions for use in methods of treating or preventing a SARS-CoV-2 infection (or COVID-19), as well as in the preparation of a medicament for the treatment or treating or prevention of a SARS-CoV-2 infection.

[0012] Prior to setting forth this disclosure in more detail, it may be helpful to an understanding thereof to provide definitions of certain terms to be used herein. Additional definitions are set forth throughout this disclosure.

[0013] As used herein, "SARS-CoV-2", also originally referred to as "Wuhan coronavirus", "Wuhan seafood market pneumonia virus", or "Wuhan CoV", "novel CoV", or "nCoV", or "2019 nCoV", or "Wuhan nCoV", or a variant thereof, is a betacoronavirus of lineage B (sarbecovirus). SARS-CoV-2 was first identified in Wuhan, Hubei province, China, in late 2019 and spread within China and to other parts of the world by early 2020. SARS CoV-2 infection can result in a disease known as COVID-19; symptoms of COVID-19 include fever or chills, dry cough, dyspnea, fatigue, body aches, headache, new loss of taste or smell, sore throat, congestions or runny nose, nausea or vomiting, diarrhea, persistent pressure or pain in the chest, new confusion, inability to wake or stay awake, and bluish lips or face.

[0014] The genomic sequence of SARS-CoV-2 isolate Wuhan-Hu-1 is provided in SEQ ID NO.: 163 (see also GenBank MN908947.3, Jan. 23, 2020), and the amino acid translation of the genome is provided in SEQ ID NO.: 164 (see also GenBank QHD43416.1, Jan. 23, 2020). Like other coronaviruses (e.g., SARS CoV), SARS-CoV-2 comprises a "spike" or surface ("S") type I transmembrane glycoprotein containing a receptor binding domain (RBD). RBD is believed to mediate entry of the lineage B SARS coronavirus to respiratory epithelial cells by binding to the cell surface receptor angiotensin-converting enzyme 2 (ACE2). In particular, a receptor binding motif (RBM) in the virus RBD is believed to interact with ACE2.

[0015] The amino acid sequence of the SARS-CoV-2 Wuhan-Hu-1 surface glycoprotein is provided in SEQ ID NO.: 165. The amino acid sequence of SARS-CoV-2 Wuhan coronavirus RBD is provided in SEQ ID NO.: 166. Wuhan coronavirus S protein has approximately 73% amino acid sequence identity with SARS-CoV. The amino acid

sequence of Wuhan coronavirus RBM is provided in SEQ ID NO.: 167. Wuhan coronavirus RBD has approximately 75% to 77% amino acid sequence similarity to SARS coronavirus RBD, and Wuhan coronavirus RBM has approximately 50% amino acid sequence similarity to SARS coronavirus RBM.

[0016] Unless otherwise indicated herein, SARS-CoV-2 Wu-Hu-1 refers to a virus comprising the amino acid sequence set forth in any one or more of SEQ ID NOs.: 164, 165, and 166, optionally with the genomic sequence set forth in SEQ ID NO.: 163.

[0017] There have been a number of emerging SARS-CoV-2 variants. Some SARS-CoV-2 variants contain an N439K mutation, which has enhanced binding affinity to the human ACE2 receptor (Thomson, E. C., et al., *The circulating SARS-CoV-2 spike variant N439K maintains fitness while evading antibody-mediated immunity*. bioRxiv, 2020). Some SARS-CoV-2 variants contain an N501Y mutation, which is associated with increased transmissibility, including the lineages B.1.1.7 (also known as 201/501Y.V1 and VOC 202012/01) and B.1.351 (also known as 20H/501Y.V2), which were discovered in the United Kingdom and South Africa, respectively (Tegally, H., et al., *Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) lineage with multiple spike mutations in South Africa*. medRxiv, 2020: p. 2020.12.21.20248640; Leung, K., et al., *Early empirical assessment of the N501Y mutant strains of SARS-CoV-2 in the United Kingdom, October to November 2020*. medRxiv, 2020: p. 2020.12.20.20248581). B.1.351 also include two other mutations in the RBD domain of SARS-CoV2 spike protein, K417N and E484K (Tegally, H., et al., *Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) lineage with multiple spike mutations in South Africa*. medRxiv, 2020: p. 2020.12.21.20248640). Other SARS-CoV-2 variants include the Lineage B.1.1.28, which was first reported in Brazil; the Variant P.1, lineage B.1.1.28 (also known as 20J/501Y.V3), which was first reported in Japan; Variant L452R, which was first reported in California in the United States (Pan American Health Organization, *Epidemiological update: Occurrence of variants of SARS-CoV-2 in the Americas*, Jan. 20, 2021, available at <https://reliefweb.int/sites/reliefweb.int/files/resources/2021-jan-20-phe-epi-update-SARS-CoV-2.pdf>). Other SARS-CoV-2 variants include a SARS CoV-2 of clade 19A; SARS CoV-2 of clade 19B; a SARS CoV-2 of clade 20A; a SARS CoV-2 of clade 20B; a SARS CoV-2 of clade 20C; a SARS CoV-2 of clade 20D; a SARS CoV-2 of clade 20E (E1U); a SARS CoV-2 of clade 20F; a SARS CoV-2 of clade 20G; and SARS CoV-2 B1.1.207; and other SARS CoV-2 lineages described in Rambaut, A., et al., *A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology*. Nat Microbiol 5, 1403-1407 (2020). A SARS CoV-2 infection in accordance with the present disclosure includes infection by any one or more of the aforementioned SARS-CoV-2 viruses and variants thereof.

[0018] In the present description, any concentration range, percentage range, ratio range, or integer range is to be understood to include the value of any integer within the recited range and, when appropriate, fractions thereof (such as one tenth and one hundredth of an integer), unless otherwise indicated. Also, any number range recited herein relating to any physical feature, such as polymer subunits,

size or thickness, are to be understood to include any integer within the recited range, unless otherwise indicated. As used herein, the term "about" means $\pm 20\%$ of the indicated range, value, or structure, unless otherwise indicated. It should be understood that the terms "a" and "an" as used herein refer to "one or more" of the enumerated components. The use of the alternative (e.g., "or") should be understood to mean either one, both, or any combination thereof of the alternatives. As used herein, the terms "include," "have," and "comprise" are used synonymously, which terms and variants thereof are intended to be construed as non-limiting.

[0019] "Optional" or "optionally" means that the subsequently described element, component, event, or circumstance may or may not occur, and that the description includes instances in which the element, component, event, or circumstance occurs and instances in which they do not.

[0020] In addition, it should be understood that the individual constructs, or groups of constructs, derived from the various combinations of the structures and subunits described herein, are disclosed by the present application to the same extent as if each construct or group of constructs was set forth individually. Thus, selection of particular structures or particular subunits is within the scope of the present disclosure.

[0021] The term "consisting essentially of" is not equivalent to "comprising" and refers to the specified materials or steps of a claim, or to those that do not materially affect the basic characteristics of a claimed subject matter. For example, a protein domain, region, or module (e.g., a binding domain) or a protein "consists essentially of" a particular amino acid sequence when the amino acid sequence of a domain, region, module, or protein includes extensions, deletions, mutations, or a combination thereof (e.g., amino acids at the amino- or carboxy-terminus or between domains) that, in combination, contribute to at most 20% (e.g., at most 15%, 10%, 8%, 6%, 5%, 4%, 3%, 2% or 1%) of the length of a domain, region, module, or protein and do not substantially affect (i.e., do not reduce the activity by more than 50%, such as no more than 40%, 30%, 25%, 20%, 15%, 10%, 5%, or 1%) the activity of the domain(s), region(s), module(s), or protein (e.g., the target binding affinity of a binding protein).

[0022] "Treat," "treatment," or "ameliorate" refers to medical management of a disease, disorder, or condition of a subject (e.g., a human or non-human mammal, such as a primate, horse, cat, dog, goat, mouse, or rat). In general, an appropriate dose or treatment regimen comprising an antibody, antigen-binding fragment, or composition of the present disclosure is administered in an amount sufficient to elicit a therapeutic or prophylactic benefit. Therapeutic or prophylactic/preventive benefit includes, for example, improved clinical outcome; lessening or alleviation of symptoms associated with a disease; decreased occurrence of symptoms; improved quality of life; longer disease-free status; diminishment of extent of disease, stabilization of disease state; delay or prevention of disease progression; remission; survival; prolonged survival; or any combination thereof. In certain embodiments, therapeutic or prophylactic/preventive benefit includes reduction or prevention of hospitalization for treatment of a SARS-CoV-2 infection or COVID-19 (i.e., in a statistically significant manner). In certain embodiments, therapeutic or prophylactic/preventive benefit includes a reduced duration of hospitalization for treatment of a SARS-CoV-2 infection or COVID-19 (i.e., in

a statistically significant manner). In certain embodiments, therapeutic or prophylactic/preventive benefit includes a reduced or abrogated need for respiratory intervention, such as intubation and/or the use of a respirator device. In certain embodiments, therapeutic or prophylactic/preventive benefit includes reversing a late-stage disease pathology and/or reducing mortality. In certain embodiments, therapeutic and/or prophylactic benefit comprises a reduction in viral load and/or viral shedding in, e.g., a respiratory sample (lung tissue, nasal swab, sputum, or the like) from the subject. In certain embodiments, therapeutic and/or prophylactic benefit comprises preventing progression of COVID-19, e.g., from mild-to-moderate to severe, or from severe to critical, as described herein. In certain embodiments, therapeutic and/or prophylactic comprises preventing contraction and/or transmission of a SARS-CoV-2 infection, e.g., which can be symptomatic or asymptomatic.

[0023] A “therapeutically effective amount” or “effective amount” of an antibody, antigen-binding fragment, or composition of this disclosure refers to an amount of the composition or molecule sufficient to result in a therapeutic effect, including improved clinical outcome; lessening or alleviation of symptoms associated with a disease; decreased occurrence of symptoms; improved quality of life; longer disease-free status; diminishment of extent of disease, stabilization of disease state; delay of disease progression; remission; survival; or prolonged survival in a statistically significant manner. When referring to an individual active ingredient, administered alone, a therapeutically effective amount refers to the effects of that ingredient or cell expressing that ingredient alone. When referring to a combination, a therapeutically effective amount refers to the combined amounts of active ingredients or combined adjunctive active ingredient with a cell expressing an active ingredient that results in a therapeutic effect, whether administered serially, sequentially, or simultaneously. A combination may comprise, for example, two different antibodies that specifically bind a SARS-CoV-2 antigen, which in certain embodiments, may be the same or different SARS-CoV-2 antigen, and/or can comprise the same or different epitopes.

[0024] As used herein, “amino acid” refers to naturally occurring and synthetic amino acids, as well as amino acid analogs and amino acid mimetics that function in a manner similar to the naturally occurring amino acids. Naturally occurring amino acids are those encoded by the genetic code, as well as those amino acids that are later modified, e.g., hydroxyproline, γ -carboxyglutamate, and O-phosphoserine. Amino acid analogs refer to compounds that have the same basic chemical structure as a naturally occurring amino acid, i.e., an α -carbon that is bound to a hydrogen, a carboxyl group, an amino group, and an R group, e.g., homoserine, norleucine, methionine sulfoxide, methionine methyl sulfonium. Such analogs have modified R groups (e.g., norleucine) or modified peptide backbones, but retain the same basic chemical structure as a naturally occurring amino acid. Amino acid mimetics refer to chemical compounds that have a structure that is different from the general chemical structure of an amino acid, but that functions in a manner similar to a naturally occurring amino acid.

[0025] As used herein, “mutation” refers to a change in the sequence of a nucleic acid molecule or polypeptide molecule as compared to a reference or wild-type nucleic acid molecule or polypeptide molecule, respectively. A mutation can

result in several different types of change in sequence, including substitution, insertion or deletion of nucleotide(s) or amino acid(s).

[0026] A “conservative substitution” refers to amino acid substitutions that do not significantly affect or alter binding characteristics of a particular protein. Generally, conservative substitutions are ones in which a substituted amino acid residue is replaced with an amino acid residue having a similar side chain. Conservative substitutions include a substitution found in one of the following groups: Group 1: Alanine (Ala or A), Glycine (Gly or G), Serine (Ser or S), Threonine (Thr or T); Group 2: Aspartic acid (Asp or D), Glutamic acid (Glu or Z); Group 3: Asparagine (Asn or N), Glutamine (Gln or Q); Group 4: Arginine (Arg or R), Lysine (Lys or K), Histidine (His or H); Group 5: Isoleucine (Ile or I), Leucine (Leu or L), Methionine (Met or M), Valine (Val or V); and Group 6: Phenylalanine (Phe or F), Tyrosine (Tyr or Y), Tryptophan (Trp or W). Additionally or alternatively, amino acids can be grouped into conservative substitution groups by similar function, chemical structure, or composition (e.g., acidic, basic, aliphatic, aromatic, or sulfur-containing). For example, an aliphatic grouping may include, for purposes of substitution, Gly, Ala, Val, Leu, and Ile. Other conservative substitutions groups include: sulfur-containing: Met and Cysteine (Cys or C); acidic: Asp, Glu, Asn, and Gln; small aliphatic, nonpolar or slightly polar residues: Ala, Ser, Thr, Pro, and Gly; polar, negatively charged residues and their amides: Asp, Asn, Glu, and Gln; polar, positively charged residues: His, Arg, and Lys; large aliphatic, nonpolar residues: Met, Leu, Ile, Val, and Cys; and large aromatic residues: Phe, Tyr, and Trp. Additional information can be found in Creighton (1984) Proteins, W.H. Freeman and Company.

[0027] As used herein, “protein” or “polypeptide” refers to a polymer of amino acid residues. Proteins apply to naturally occurring amino acid polymers, as well as to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of a corresponding naturally occurring amino acid, and non-naturally occurring amino acid polymers. Variants of proteins, peptides, and polypeptides of this disclosure are also contemplated. In certain embodiments, variant proteins, peptides, and polypeptides comprise or consist of an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 99.9% identical to an amino acid sequence of a defined or reference amino acid sequence as described herein.

[0028] “Nucleic acid molecule” or “polynucleotide” or “polynucleic acid” refers to a polymeric compound including covalently linked nucleotides, which can be made up of natural subunits (e.g., purine or pyrimidine bases) or non-natural subunits (e.g., morpholine ring). Purine bases include adenine, guanine, hypoxanthine, and xanthine, and pyrimidine bases include uracil, thymine, and cytosine. Nucleic acid molecules include polyribonucleic acid (RNA), which includes mRNA, microRNA, siRNA, viral genomic RNA, and synthetic RNA, and polydeoxyribonucleic acid (DNA), which includes cDNA, genomic DNA, and synthetic DNA, either of which may be single or double stranded. If single-stranded, the nucleic acid molecule may be the coding strand or non-coding (anti-sense) strand. A nucleic acid molecule encoding an amino acid sequence includes all nucleotide sequences that encode the same amino acid sequence. Some versions of the nucleotide

sequences may also include intron(s) to the extent that the intron(s) would be removed through co- or post-transcriptional mechanisms. In other words, different nucleotide sequences may encode the same amino acid sequence as the result of the redundancy or degeneracy of the genetic code, or by splicing.

[0029] Variants of nucleic acid molecules of this disclosure are also contemplated. Variant nucleic acid molecules are at least 70%, 75%, 80%, 85%, 90%, and are preferably 95%, 96%, 97%, 98%, 99%, or 99.9% identical a nucleic acid molecule of a defined or reference polynucleotide as described herein, or that hybridize to a polynucleotide under stringent hybridization conditions of 0.015M sodium chloride, 0.0015M sodium citrate at about 65-68° C. or 0.015M sodium chloride, 0.0015M sodium citrate, and 50% formamide at about 42° C. Nucleic acid molecule variants retain the capacity to encode a binding domain thereof having a functionality described herein, such as binding a target molecule.

[0030] "Percent sequence identity" refers to a relationship between two or more sequences, as determined by comparing the sequences. Preferred methods to determine sequence identity are designed to give the best match between the sequences being compared. For example, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment). Further, non-homologous sequences may be disregarded for comparison purposes. The percent sequence identity referenced herein is calculated over the length of the reference sequence, unless indicated otherwise. Methods to determine sequence identity and similarity can be found in publicly available computer programs. Sequence alignments and percent identity calculations may be performed using a BLAST program (e.g., BLAST 2.0, BLASTP, BLASTN, or BLASTX). The mathematical algorithm used in the BLAST programs can be found in Altschul et al., *Nucleic Acids Res.* 25:3389-3402, 1997. Within the context of this disclosure, it will be understood that where sequence analysis software is used for analysis, the results of the analysis are based on the "default values" of the program referenced. "Default values" mean any set of values or parameters which originally load with the software when first initialized.

[0031] The term "isolated" means that the material is removed from its original environment (e.g., the natural environment if it is naturally occurring). For example, a naturally occurring nucleic acid or polypeptide present in a living animal is not isolated, but the same nucleic acid or polypeptide, separated from some or all of the co-existing materials in the natural system, is isolated. Such nucleic acid could be part of a vector and/or such nucleic acid or polypeptide could be part of a composition (e.g., a cell lysate), and still be isolated in that such vector or composition is not part of the natural environment for the nucleic acid or polypeptide.

[0032] The term "gene" means the segment of DNA or RNA involved in producing a polypeptide chain; in certain contexts, it includes regions preceding and following the coding region (e.g., 5' untranslated region (UTR) and 3' UTR) as well as intervening sequences (introns) between individual coding segments (exons).

[0033] A "functional variant" refers to a polypeptide or polynucleotide that is structurally similar or substantially similar to a parent or reference compound of this

disclosure, but differs slightly in composition (e.g., one base, atom or functional group is different, added, or removed), such that the polypeptide or encoded polypeptide is capable of performing at least one function of the parent polypeptide with at least 50% efficiency, preferably at least 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, 99.9%, or 100% level of activity of the parent polypeptide. In other words, a functional variant of a polypeptide or encoded polypeptide of this disclosure has "similar binding," "similar affinity" or "similar activity" when the functional variant displays no more than a 50% reduction in performance in a selected assay as compared to the parent or reference polypeptide, such as an assay for measuring binding affinity (e.g., Biacore® or tetramer staining measuring an association (K_a) or dissociation (K_D) constant).

[0034] As used herein, a "functional portion" or "functional fragment" refers to a polypeptide or polynucleotide that comprises only a domain, portion or fragment of a parent or reference compound, and the polypeptide or encoded polypeptide retains at least 50% activity associated with the domain, portion or fragment of the parent or reference compound, preferably at least 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, 99.9%, or 100% level of activity of the parent polypeptide, or provides a biological benefit (e.g., effector function). A "functional portion" or "functional fragment" of a polypeptide or encoded polypeptide of this disclosure has "similar binding" or "similar activity" when the functional portion or fragment displays no more than a 50% reduction in performance in a selected assay as compared to the parent or reference polypeptide (preferably no more than 20% or 10%, or no more than a log difference as compared to the parent or reference with regard to affinity).

[0035] As used herein, the term "engineered," "recombinant," or "non-natural" refers to an organism, microorganism, cell, nucleic acid molecule, or vector that includes at least one genetic alteration or has been modified by introduction of an exogenous or heterologous nucleic acid molecule, wherein such alterations or modifications are introduced by genetic engineering (i.e., human intervention). Genetic alterations include, for example, modifications introducing expressible nucleic acid molecules encoding functional RNA, proteins, fusion proteins or enzymes, or other nucleic acid molecule additions, deletions, substitutions, or other functional disruption of a cell's genetic material. Additional modifications include, for example, non-coding regulatory regions in which the modifications alter expression of a polynucleotide, gene, or operon.

[0036] As used herein, "heterologous" or "non-endogenous" or "exogenous" refers to any gene, protein, compound, nucleic acid molecule, or activity that is not native to a host cell or a subject, or any gene, protein, compound, nucleic acid molecule, or activity native to a host cell or a subject that has been altered. Heterologous, non-endogenous, or exogenous includes genes, proteins, compounds, or nucleic acid molecules that have been mutated or otherwise altered such that the structure, activity, or both is different as between the native and altered genes, proteins, compounds, or nucleic acid molecules. In certain embodiments, heterologous, non-endogenous, or exogenous genes, proteins, or nucleic acid molecules (e.g., receptors, ligands, etc.) may not be endogenous to a host cell or a subject, but instead nucleic acids encoding such genes, proteins, or nucleic acid molecules may have been added to a host cell

by conjugation, transformation, transfection, electroporation, or the like, wherein the added nucleic acid molecule may integrate into a host cell genome or can exist as extra-chromosomal genetic material (e.g., as a plasmid or other self-replicating vector). The term “homologous” or “homolog” refers to a gene, protein, compound, nucleic acid molecule, or activity found in or derived from a host cell, species, or strain. For example, a heterologous or exogenous polynucleotide or gene encoding a polypeptide may be homologous to a native polynucleotide or gene and encode a homologous polypeptide or activity, but the polynucleotide or polypeptide may have an altered structure, sequence, expression level, or any combination thereof. A non-endogenous polynucleotide or gene, as well as the encoded polypeptide or activity, may be from the same species, a different species, or a combination thereof.

[0037] In certain embodiments, a nucleic acid molecule or portion thereof native to a host cell will be considered heterologous to the host cell if it has been altered or mutated, or a nucleic acid molecule native to a host cell may be considered heterologous if it has been altered with a heterologous expression control sequence or has been altered with an endogenous expression control sequence not normally associated with the nucleic acid molecule native to a host cell. In addition, the term “heterologous” can refer to a biological activity that is different, altered, or not endogenous to a host cell. As described herein, more than one heterologous nucleic acid molecule can be introduced into a host cell as separate nucleic acid molecules, as a plurality of individually controlled genes, as a polycistronic nucleic acid molecule, as a single nucleic acid molecule encoding a fusion protein, or any combination thereof.

[0038] As used herein, the term “endogenous” or “native” refers to a polynucleotide, gene, protein, compound, molecule, or activity that is normally present in a host cell or a subject.

[0039] The term “expression”, as used herein, refers to the process by which a polypeptide is produced based on the encoding sequence of a nucleic acid molecule, such as a gene. The process may include transcription, post-transcriptional control, post-transcriptional modification, translation, post-translational control, post-translational modification, or any combination thereof. An expressed nucleic acid molecule is typically operably linked to an expression control sequence (e.g., a promoter).

[0040] The term “operably linked” refers to the association of two or more nucleic acid molecules on a single nucleic acid fragment so that the function of one is affected by the other. For example, a promoter is operably linked with a coding sequence when it is capable of affecting the expression of that coding sequence (i.e., the coding sequence is under the transcriptional control of the promoter). “Unlinked” means that the associated genetic elements are not closely associated with one another and the function of one does not affect the other.

[0041] As described herein, more than one heterologous nucleic acid molecule can be introduced into a host cell as separate nucleic acid molecules, as a plurality of individually controlled genes, as a polycistronic nucleic acid molecule, as a single nucleic acid molecule encoding a protein (e.g., a heavy chain of an antibody), or any combination thereof. When two or more heterologous nucleic acid molecules are introduced into a host cell, it is understood that the two or more heterologous nucleic acid molecules can be

introduced as a single nucleic acid molecule (e.g., on a single vector), on separate vectors, integrated into the host chromosome at a single site or multiple sites, or any combination thereof. The number of referenced heterologous nucleic acid molecules or protein activities refers to the number of encoding nucleic acid molecules or the number of protein activities, not the number of separate nucleic acid molecules introduced into a host cell.

[0042] The term “construct” refers to any polynucleotide that contains a recombinant nucleic acid molecule (or, when the context clearly indicates, a fusion protein of the present disclosure). A (polynucleotide) construct may be present in a vector (e.g., a bacterial vector, a viral vector) or may be integrated into a genome. A “vector” is a nucleic acid molecule that is capable of transporting another nucleic acid molecule. Vectors may be, for example, plasmids, cosmids, viruses, a RNA vector or a linear or circular DNA or RNA molecule that may include chromosomal, non-chromosomal, semi-synthetic or synthetic nucleic acid molecules. Vectors of the present disclosure also include transposon systems (e.g., Sleeping Beauty, see, e.g., Geurts *et al.*, *Mol. Ther.* 8:108, 2003; Mátés *et al.*, *Nat. Genet.* 41:753, 2009). Exemplary vectors are those capable of autonomous replication (episomal vector), capable of delivering a polynucleotide to a cell genome (e.g., viral vector), or capable of expressing nucleic acid molecules to which they are linked (expression vectors).

[0043] As used herein, “expression vector” or “vector” refers to a DNA construct containing a nucleic acid molecule that is operably linked to a suitable control sequence capable of effecting the expression of the nucleic acid molecule in a suitable host. Such control sequences include a promoter to effect transcription, an optional operator sequence to control such transcription, a sequence encoding suitable mRNA ribosome binding sites, and sequences which control termination of transcription and translation. The vector may be a plasmid, a phage particle, a virus, or simply a potential genomic insert. Once transformed into a suitable host, the vector may replicate and function independently of the host genome, or may, in some instances, integrate into the genome itself or deliver the polynucleotide contained in the vector into the genome without the vector sequence. In the present specification, “plasmid,” “expression plasmid,” “virus,” and “vector” are often used interchangeably.

[0044] The term “introduced” in the context of inserting a nucleic acid molecule into a cell, means “transfection”, “transformation,” or “transduction” and includes reference to the incorporation of a nucleic acid molecule into a eukaryotic or prokaryotic cell wherein the nucleic acid molecule may be incorporated into the genome of a cell (e.g., chromosome, plasmid, plastid, or mitochondrial DNA), converted into an autonomous replicon, or transiently expressed (e.g., transfected mRNA).

[0045] In certain embodiments, polynucleotides of the present disclosure may be operatively linked to certain elements of a vector. For example, polynucleotide sequences that are needed to effect the expression and processing of coding sequences to which they are ligated may be operatively linked. Expression control sequences may include appropriate transcription initiation, termination, promoter, and enhancer sequences; efficient RNA processing signals such as splicing and polyadenylation signals; sequences that stabilize cytoplasmic mRNA; sequences that enhance translation efficiency (i.e., Kozak consensus sequences);

sequences that enhance protein stability; and possibly sequences that enhance protein secretion. Expression control sequences may be operatively linked if they are contiguous with the gene of interest and expression control sequences that act in trans or at a distance to control the gene of interest.

[0046] In certain embodiments, the vector comprises a plasmid vector or a viral vector (e.g., a lentiviral vector or a γ -retroviral vector). Viral vectors include retrovirus, adenovirus, parvovirus (e.g., adeno-associated viruses), coronavirus, negative strand RNA viruses such as orthomyxovirus (e.g., influenza virus), rhabdovirus (e.g., rabies and vesicular stomatitis virus), paramyxovirus (e.g., measles and Sendai), positive strand RNA viruses such as picornavirus and alphavirus, and double-stranded DNA viruses including adenovirus, herpesvirus (e.g., Herpes Simplex virus types 1 and 2, Epstein-Barr virus, cytomegalovirus), and poxvirus (e.g., vaccinia, fowlpox, and canarypox). Other viruses include, for example, Norwalk virus, togavirus, flavivirus, reoviruses, papovavirus, hepadnavirus, and hepatitis virus. Examples of retroviruses include avian leukosis-sarcoma, mammalian C-type, B-type viruses, D type viruses, HTLV-BLV group, lentivirus, spumavirus (Coffin, J. M., Retroviridae: The viruses and their replication, In Fundamental Virology, Third Edition, B. N. Fields et al., Eds., Lippincott-Raven Publishers, Philadelphia, 1996).

[0047] "Retroviruses" are viruses having an RNA genome, which is reverse-transcribed into DNA using a reverse transcriptase enzyme, the reverse-transcribed DNA is then incorporated into the host cell genome. "Gammaretrovirus" refers to a genus of the retroviridae family. Examples of gammaretroviruses include mouse stem cell virus, murine leukemia virus, feline leukemia virus, feline sarcoma virus, and avian reticuloendotheliosis viruses.

[0048] "Lentiviral vectors" include HIV-based lentiviral vectors for gene delivery, which can be integrative or non-integrative, have relatively large packaging capacity, and can transduce a range of different cell types. Lentiviral vectors are usually generated following transient transfection of three (packaging, envelope, and transfer) or more plasmids into producer cells. Like HIV, lentiviral vectors enter the target cell through the interaction of viral surface glycoproteins with receptors on the cell surface. On entry, the viral RNA undergoes reverse transcription, which is mediated by the viral reverse transcriptase complex. The product of reverse transcription is a double-stranded linear viral DNA, which is the substrate for viral integration into the DNA of infected cells.

[0049] In certain embodiments, the viral vector can be a gammaretrovirus, e.g., Moloney murine leukemia virus (MLV)-derived vectors. In other embodiments, the viral vector can be a more complex retrovirus-derived vector, e.g., a lentivirus-derived vector. HIV-1-derived vectors belong to this category. Other examples include lentivirus vectors derived from HIV-2, FIV, equine infectious anemia virus, SIV, and Maedi-Visna virus (ovine lentivirus). Methods of using retroviral and lentiviral viral vectors and packaging cells for transducing mammalian host cells with viral particles containing transgenes are known in the art and have been previously described, for example, in: U.S. Pat. No. 8,119,772; Walchli et al., *PLoS One* 6:327930, 2011; Zhao et al., *J. Immunol.* 174:4415, 2005; Engels et al., *Hum. Gene Ther.* 14:1155, 2003; Frecha et al., *Mol. Ther.* 18:1748, 2010; and Verhoeven et al., *Methods Mol. Biol.* 506:97, 2009. Retroviral and lentiviral vector constructs and expression

systems are also commercially available. Other viral vectors also can be used for polynucleotide delivery including DNA viral vectors, including, for example adenovirus-based vectors and adeno-associated virus (AAV)-based vectors; vectors derived from herpes simplex viruses (HSVs), including amplicon vectors, replication-defective HSV and attenuated HSV (Krisky et al., *Gene Ther.* 5:1517, 1998).

[0050] Other vectors that can be used with the compositions and methods of this disclosure include those derived from baculoviruses and α -viruses. (Jolly, D J. 1999. Emerging Viral Vectors. pp 209-40 in Friedmann T. ed. The Development of Human Gene Therapy. New York: Cold Spring Harbor Lab), or plasmid vectors (such as sleeping beauty or other transposon vectors).

[0051] When a viral vector genome comprises a plurality of polynucleotides to be expressed in a host cell as separate transcripts, the viral vector may also comprise additional sequences between the two (or more) transcripts allowing for bicistronic or multicistronic expression. Examples of such sequences used in viral vectors include internal ribosome entry sites (IRES), furin cleavage sites, viral 2A peptide, or any combination thereof.

[0052] Plasmid vectors, including DNA-based antibody or antigen-binding fragment-encoding plasmid vectors for direct administration to a subject, are described further herein.

[0053] As used herein, the term "host" refers to a cell or microorganism targeted for genetic modification with a heterologous nucleic acid molecule to produce a polypeptide of interest (e.g., an antibody of the present disclosure).

[0054] A host cell may include any individual cell or cell culture which may receive a vector or the incorporation of nucleic acids or express proteins. The term also encompasses progeny of the host cell, whether genetically or phenotypically the same or different. Suitable host cells may depend on the vector and may include mammalian cells, animal cells, human cells, simian cells, insect cells, yeast cells, and bacterial cells. These cells may be induced to incorporate the vector or other material by use of a viral vector, transformation via calcium phosphate precipitation, DEAE-dextran, electroporation, microinjection, or other methods. See, for example, Sambrook et al., *Molecular Cloning: A Laboratory Manual* 2d ed. (Cold Spring Harbor Laboratory, 1989).

[0055] In the context of a SARS-CoV-2 infection, a "host" refers to a cell or a subject infected with the SARS-CoV-2.

[0056] "Antigen" or "Ag", as used herein, refers to an immunogenic molecule that provokes an immune response. This immune response may involve antibody production, activation of specific immunologically-competent cells, activation of complement, antibody dependent cytotoxicity, or any combination thereof. An antigen (immunogenic molecule) may be, for example, a peptide, glycopeptide, polypeptide, glycopolypeptide, polynucleotide, polysaccharide, lipid, or the like. It is readily apparent that an antigen can be synthesized, produced recombinantly, or derived from a biological sample. Exemplary biological samples that can contain one or more antigens include tissue samples, stool samples, cells, biological fluids, or combinations thereof. Antigens can be produced by cells that have been modified or genetically engineered to express an antigen. Antigens can also be present in a SARS-CoV-2 (e.g., a surface glycoprotein or portion thereof), such as present in

a virion, or expressed or presented on the surface of a cell infected by the SARS-CoV-2.

[0057] The term “epitope” or “antigenic epitope” includes any molecule, structure, amino acid sequence, or protein determinant that is recognized and specifically bound by a cognate binding molecule, such as an immunoglobulin, or other binding molecule, domain, or protein. Epitopic determinants generally contain chemically active surface groupings of molecules, such as amino acids or sugar side chains, and can have specific three-dimensional structural characteristics, as well as specific charge characteristics. Where an antigen is or comprises a peptide or protein, the epitope can be comprised of consecutive amino acids (e.g., a linear epitope), or can be comprised of amino acids from different parts or regions of the protein that are brought into proximity by protein folding (e.g., a discontinuous or conformational epitope), or non-contiguous amino acids that are in close proximity irrespective of protein folding.

Antibodies, Antigen-Binding Fragments, and Compositions

[0058] Certain presently disclosed methods and uses comprise administering to a subject antibody, or an antigen-binding fragment thereof, that comprises 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, and is capable of binding to a surface glycoprotein of a SARS-CoV-2 (e.g. as expressed on a cell surface of a host cell and/or on a SARS-CoV-2 virion).

[0059] In certain preferred embodiments, described further herein, an antibody or antigen-binding fragment thereof used in a method comprises the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs.: 106, 121, 108, 169, 170, and 171, respectively, or set forth in SEQ ID NOs.: 106, 107, 108, 169, 170, and 171, respectively. In certain embodiments, an antibody or antigen-binding fragment thereof used in a method comprises the VH amino acid sequence set forth in SEQ ID NO.: 113 or 105 and the VL amino acid sequence set forth in SEQ ID NO.: 168.

[0060] In certain embodiments, an antibody or antigen-binding fragment of used in a method associates with or unites with a SARS-CoV-2 surface glycoprotein epitope or antigen comprising the epitope, while not significantly associating or uniting with any other molecules or components in a sample.

[0061] In certain embodiments, an antibody or antigen-binding fragment of the present disclosure associates with or unites (e.g., binds) to a SARS-CoV-2 surface glycoprotein epitope, and can also associate with or unite with an epitope from another coronavirus (e.g., SARS CoV) present in the sample, but not significantly associating or uniting with any other molecules or components in the sample. In other words, in certain embodiments, an antibody or antigen binding fragment of the present disclosure is cross-reactive for SARS-CoV-2 and one or more additional coronavirus.

[0062] In certain embodiments, an antibody or antigen-binding fragment of the present disclosure specifically binds to a SARS-CoV-2 surface glycoprotein. As used herein, “specifically binds” refers to an association or union of an antibody or antigen-binding fragment to an antigen with an affinity or K_a (i.e., an equilibrium association constant of a particular binding interaction with units of 1/M) equal to or greater than 10^5 M^{-1} (which equals the ratio of the on-rate

$[K_{on}]$ to the off rate $[K_{off}]$ for this association reaction), while not significantly associating or uniting with any other molecules or components in a sample. Alternatively, affinity may be defined as an equilibrium dissociation constant (K_d) of a particular binding interaction with units of M (e.g., 10^{-5} M to 10^{-13} M). Antibodies may be classified as “high-affinity” antibodies or as “low-affinity” antibodies. “High-affinity” antibodies refer to those antibodies having a K_a of at least 10^7 M^{-1} , at least 10^8 M^{-1} , at least 10^9 M^{-1} , at least 10^{10} M^{-1} , at least 10^{11} M^{-1} , at least 10^{12} M^{-1} , or at least 10^{13} M^{-1} . “Low-affinity” antibodies refer to those antibodies having a K_a of up to 10^7 M^{-1} , up to 10^6 M^{-1} , up to 10^5 M^{-1} . Alternatively, affinity may be defined as an equilibrium dissociation constant (K_d) of a particular binding interaction with units of M (e.g., 10^{-5} M to 10^{-13} M).

[0063] A variety of assays are known for identifying antibodies of the present disclosure that bind a particular target, as well as determining binding domain or binding protein affinities, such as Western blot, ELISA (e.g., direct, indirect, or sandwich), analytical ultracentrifugation, spectroscopy, and surface plasmon resonance (Biacore®) analysis (see, e.g., Scatchard et al., *Ann. N.Y. Acad. Sci.* 51:660, 1949; Wilson, *Science* 295:2103, 2002; Wolff et al., *Cancer Res.* 53:2560, 1993; and U.S. Pat. Nos. 5,283,173, 5,468, 614, or the equivalent). Assays for assessing affinity or apparent affinity or relative affinity are also known.

[0064] Binding can be determined by, for example, recombinantly expressing a SARS-CoV-2 antigen in a host cell (e.g., by transfection) and immunostaining the (e.g., fixed, or fixed and permeabilized) host cell with antibody and analyzing binding by flow cytometry (e.g., using a ZE5 Cell Analyzer (BioRad®) and FlowJo software (TreeStar)). In some embodiments, positive binding can be defined by differential staining by antibody of SARS-CoV-2-expressing cells versus control (e.g., mock) cells.

[0065] In some embodiments an antibody or antigen-binding fragment of the present disclosure binds to SARS-CoV-2 S protein, as measured using biolayer interferometry. In certain embodiments, an antibody or antigen-binding fragment of the present disclosure binds to SARS-CoV-2 S protein with a K_D of less than about $4.5 \times 10^{-9} \text{ M}$, less than about $5 \times 10^{-9} \text{ M}$, less than about $1 \times 10^{-10} \text{ M}$, less than about $5 \times 10^{-10} \text{ M}$, less than about $1 \times 10^{-11} \text{ M}$, less than about $5 \times 10^{-11} \text{ M}$, less than about $1 \times 10^{-12} \text{ M}$, or less than about $5 \times 10^{-12} \text{ M}$. In some embodiments, an antibody or antigen-binding fragment of the present disclosure binds to SARS-CoV-2 S protein RBD with a K_D of less than about $4.5 \times 10^{-9} \text{ M}$, less than about $5 \times 10^{-9} \text{ M}$, less than about $1 \times 10^{-10} \text{ M}$, less than about $5 \times 10^{-10} \text{ M}$, less than about $1 \times 10^{-11} \text{ M}$, less than about $5 \times 10^{-11} \text{ M}$, less than about $1 \times 10^{-12} \text{ M}$, or less than about $5 \times 10^{-12} \text{ M}$. In certain embodiments, an antibody or antigen-binding fragment of the present disclosure binds to SARS-CoV-2 S protein (e.g., a glycosylated or a deglycosylated S protein RBD) with a K_D , a k_a , and/or a k_d as shown herein. In particular embodiments, an antibody or antigen-binding fragment is capable of binding to a glycosylated S protein RBD with a K_D of about 0.35, about 0.36, about 0.37, about 0.38, about 0.39, about 0.40, about 0.41, about 0.42, about 0.43, about 0.44, or about 0.45 nM, a k_a of about $8.5 \times 10^4 \text{ l/Ms}$, and/or a k_d of about $3.3 \times 10^{-5} \text{ l/S}$. In certain embodiments, an antibody or antigen-binding fragment is capable of binding to a deglycosylated S protein RBD with a K_D of about 0.95, about 0.96 nM, about 0.97 nM, about 0.98 nM, about 0.99 nM, about 1.0 nM, about 1.1

nM, about 1.2 nM, about 1.3 nM, about 1.4 nM, about 1.5 nM, or about 1.6 nM, a k_a of about 3.1e5 l/Ms, and/or a k_d of about 3.2e-4 1/S.

[0066] In certain embodiments, an antibody or antigen-binding fragment is capable of neutralizing infection by SARS-CoV-2. As used herein, a “neutralizing antibody” is one that can neutralize, i.e., prevent, inhibit, reduce, impede, or interfere with, the ability of a pathogen to initiate and/or perpetuate an infection in a host. The terms “neutralizing antibody” and “an antibody that neutralizes” or “antibodies that neutralize” are used interchangeably herein. In any of the presently disclosed embodiments, the antibody or antigen-binding fragment is capable of preventing and/or 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. In some embodiments, an antibody or antigen-binding fragment of the present disclosure is capable of neutralizing a SARS-CoV-2 infection with an IC₅₀ of about 16 to about 20 µg/ml. In some embodiments, an antibody or antigen-binding fragment is capable of neutralizing a SARS-CoV-2 infection, or a virus pseudotyped with SARS-CoV-2, with an IC₅₀ of about 0.3 to about 0.4 µg/ml. In some embodiments, an antibody or antigen-binding fragment, or a composition comprising two or more antibodies or antigen-binding fragments, of the present disclosure is capable of neutralizing a SARS-CoV-2 infection, or a virus pseudotyped with SARS-CoV-2, with an IC₅₀ of about 0.07 to about 0.08 µg/ml.

[0067] In certain embodiments, the antibody or antigen-binding fragment (i) recognizes an epitope in the ACE2 receptor binding motif (RBM, SEQ ID NO.: 167) of SARS-CoV-2; (ii) is capable of blocking an interaction between SARS-CoV-2 and ACE2; (ii) is capable of binding to SARS-CoV-2 S protein with greater avidity than to SARS coronavirus S protein; (iv) is capable of staining about 30%, about 35%, about 40%, about 50%, about 55%, about 56%, about 57%, about 58%, about 59%, about 60%, or more of target cells expressing SARS-CoV-2 surface glycoprotein in a sample comprising about 50,000 of the target cells (e.g., ExpiCHO cells) in approximately 100 µL when the antibody or antigen-binding fragment is present at 10 µg/ml (e.g., staining as determined by a flow cytometry ELISA); (v) 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).

[0068] Terms understood by those in the art of antibody technology are each given the meaning acquired in the art, unless expressly defined differently herein. For example, the term “antibody” refers to an intact antibody comprising at least two heavy (H) chains and two light (L) chains interconnected by disulfide bonds, as well as any antigen-binding portion or fragment of an intact antibody that has or retains the ability to bind to the antigen target molecule recognized by the intact antibody, such as an scFv, Fab, or Fab'2 fragment. Thus, the term “antibody” herein is used in the broadest sense and includes polyclonal and monoclonal antibodies, including intact antibodies and functional (antigen-binding) antibody fragments thereof, including fragment antigen binding (Fab) fragments, F(ab')2 fragments, Fab' fragments, Fv fragments, recombinant IgG (rIgG) fragments, single chain antibody fragments, including single

chain variable fragments (scFv), and single domain antibodies (e.g., sdAb, sdFv, nanobody) fragments. The term encompasses genetically engineered and/or otherwise modified forms of immunoglobulins, such as intrabodies, peptibodies, chimeric antibodies, fully human antibodies, humanized antibodies, and heteroconjugate antibodies, multispecific, e.g., bispecific antibodies, diabodies, triabodies, tetrabodies, tandem di-scFv, and tandem tri-scFv. Unless otherwise stated, the term “antibody” should be understood to encompass functional antibody fragments thereof. The term also encompasses intact or full-length antibodies, including antibodies of any class or sub-class, including IgG and sub-classes thereof (IgG1, IgG2, IgG3, IgG4), IgM, IgE, IgA, and IgD.

[0069] The terms “V_L” or “VL” and “V_H” or “VH” refer to the variable binding region from an antibody light chain and an antibody heavy chain, respectively. In certain embodiments, a VL is a kappa (κ) class (also “VK” herein). In certain embodiments, a VL is a lambda (λ) class. The variable binding regions comprise discrete, well-defined sub-regions known as “complementarity determining regions” (CDRs) and “framework regions” (FRs). The terms “complementarity determining region,” and “CDR,” are synonymous with “hypervariable region” or “HVR,” and refer to sequences of amino acids within antibody variable regions, which, in general, together confer the antigen specificity and/or binding affinity of the antibody, wherein consecutive CDRs (i.e., CDR1 and CDR2, CDR2 and CDR3) are separated from one another in primary structure by a framework region. There are three CDRs in each variable region (HCDR1, HCDR2, HCDR3; LCDR1, LCDR2, LCDR3; also referred to as CDRHs and CDRLs, respectively). In certain embodiments, an antibody VH comprises four FRs and three CDRs as follows: FR1-HCDR1-FR2-HCDR2-FR3-HCDR3-FR4; and an antibody VL comprises four FRs and three CDRs as follows: FR1-LCDR1-FR2-LCDR2-FR3-LCDR3-FR4. In general, the VH and the VL together form the antigen-binding site through their respective CDRs.

[0070] As used herein, a “variant” of a CDR refers to a functional variant of a CDR sequence having up to 1-3 amino acid substitutions (e.g., conservative or non-conservative substitutions), deletions, or combinations thereof.

[0071] Numbering of CDR and framework regions may be according to any known method or scheme, such as the Kabat, Chothia, EU, IMGT, and AHo numbering schemes (see, e.g., Kabat et al., “Sequences of Proteins of Immunological Interest, US Dept. Health and Human Services, Public Health Service National Institutes of Health, 1991, 5th ed.; Chothia and Lesk, *J. Mol. Biol.* 196:901-917 (1987)); Lefranc et al., *Dev. Comp. Immunol.* 27:55, 2003; Honegger and Plückthun, *J. Mol. Bio.* 309:657-670 (2001)). Equivalent residue positions can be annotated and for different molecules to be compared using Antigen receptor Numbering And Receptor Classification (ANARCI) software tool (2016, Bioinformatics 15:298-300).

[0072] Accordingly, identification of CDRs of an exemplary variable domain (VH or VL) sequence as provided herein according to one numbering scheme is not exclusive of an antibody comprising CDRs of the same variable domain as determined using a different numbering scheme. In certain embodiments, an antibody or antigen-binding fragment is provided that comprises CDRs identified in a VH sequence according to any one of SEQ ID NOS.: 1, 9-15,

23, 24, 27, 28-46, 55, 63, 79, 87, 95, 103, 105, 113-120, 129-146, 155, 172, 176-178, 194, 196, 198, 200, 202, and 239, and in a VL sequence according to any one of SEQ ID NOs.: 5, 47-50, 59, 67, 71-72, 75, 76, 83, 91, 99, 109, 147-150, 159, 168, 182, 190, 234, and 243, as determined using any known CDR numbering method, including the Kabat, Chothia, EU, IMGT, Martin (Enhanced Chothia), Contact, and AHo numbering methods. In certain embodiments, CDRs are according to the IMGT numbering method. In certain embodiments, CDRs are according to the antibody numbering method developed by the Chemical Computing Group (CCG); e.g., using Molecular Operating Environment (MOE) software.

[0073] In certain embodiments, the antibody or antigen-binding fragment comprises CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to SEQ ID NOs.: 106, 121 or 107, 108, 169, 170, and 171, respectively.

[0074] In some embodiments, an antibody or an antigen-binding fragment is provided that comprises 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 according to any one of SEQ ID NOs.: 2, 56, 64, 80, 88, 96, 106, 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 according to any one of SEQ ID NOs.: 3, 16-22, 57, 65, 81, 89, 97, 107, 121-126, 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 according to any one of SEQ ID NOs.: 4, 25, 26, 58, 66, 82, 90, 98, 104, 108, 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 according to any one of SEQ ID NOs.: 6, 51-54, 60, 68, 73, 74, 84, 92, 100, 110, 160, 169, 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 according to any one of SEQ ID NOs.: 7, 61, 69, 85, 93, 101, 111, 161, 170, 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 according to any one of SEQ ID NOs.: 8, 62, 70, 77, 78, 86, 94, 102, 112, 151, 152, 153, 154, 162, 171, 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 surface glycoprotein of a SARS-CoV-2 expressed on a cell surface of a host cell.

[0075] In any of the presently disclosed embodiments, the antibody or antigen-binding fragment is capable of preventing and/or 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.

[0076] The term “CL” refers to an “immunoglobulin light chain constant region” or a “light chain constant region,” i.e., a constant region from an antibody light chain. The term “CH” refers to an “immunoglobulin heavy chain constant region” or a “heavy chain constant region,” which is further divisible, depending on the antibody isotype into CH1, CH2, and CH3 (IgA, IgD, IgG), or CH1, CH2, CH3, and CH4 domains (IgE, IgM). The Fc region of an antibody heavy chain is described further herein. In any of the presently disclosed embodiments, an antibody or antigen-binding fragment of the present disclosure comprises any one or more of CL, a CH1, a CH2, and a CH3. In certain embodiments, a CL comprises 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 or SEQ ID NO.: 193. In certain embodiments, a CH1-CH2-CH3 comprises 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.: 173 or SEQ ID NO.: 175.

[0077] It will be understood that, for example, production in a mammalian cell line can remove one or more C-terminal lysine of an antibody heavy chain (see, e.g., Liu et al. *mAbs* 6 (5): 1145-1154 (2014)). Accordingly, an antibody or antigen-binding fragment of the present disclosure can comprise a heavy chain, a CH1-CH3, a CH3, or an Fc polypeptide wherein a C-terminal lysine residue is present or is absent; in other words, encompassed are embodiments where the C-terminal residue of a heavy chain, a CH1-CH3, or an Fc polypeptide is not a lysine, and embodiments where a lysine is the C-terminal residue. Examples of CH1-CH3 amino acid sequences that lack a C-terminal lysine are provided in SEQ ID NOs.: 265 and 266.

[0078] In certain embodiments, a composition comprises a plurality of an antibody and/or an antigen-binding fragment of the present disclosure, wherein one or more antibody or antigen-binding fragment does not comprise a lysine residue at the C-terminal end of the heavy chain, CH1-CH3, or Fc polypeptide, and wherein one or more antibody or antigen-binding fragment comprises a lysine residue at the C-terminal end of the heavy chain, CH1-CH3, or Fc polypeptide.

[0079] A “Fab” (fragment antigen binding) is the part of an antibody that binds to antigens and includes the variable region and CH1 of the heavy chain linked to the light chain via an inter-chain disulfide bond. Each Fab fragment is monovalent with respect to antigen binding, i.e., it has a single antigen-binding site. Pepsin treatment of an antibody yields a single large F(ab')2 fragment that roughly corresponds to two disulfide linked Fab fragments having divalent antigen-binding activity and is still capable of cross-linking antigen. Both the Fab and F(ab')2 are examples of “antigen-binding fragments.” Fab' fragments differ from Fab fragments by having additional few residues at the carboxy terminus of the CH1 domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. F(ab')2 antibody

fragments originally were produced as pairs of Fab' fragments that have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

[0080] Fab fragments may be joined, e.g., by a peptide linker, to form a single chain Fab, also referred to herein as "scFab." In these embodiments, an inter-chain disulfide bond that is present in a native Fab may not be present, and the linker serves in full or in part to link or connect the Fab fragments in a single polypeptide chain. A heavy chain-derived Fab fragment (e.g., comprising, consisting of, or consisting essentially of VH+CH1, or "Fd") and a light chain-derived Fab fragment (e.g., comprising, consisting of, or consisting essentially of VL+CL) may be linked in any arrangement to form a scFab. For example, a scFab may be arranged, in N-terminal to C-terminal direction, according to (heavy chain Fab fragment-linker-light chain Fab fragment) or (light chain Fab fragment-linker-heavy chain Fab fragment). Peptide linkers and exemplary linker sequences for use in scFabs are discussed in further detail herein.

[0081] A scFab can be comprise any combination of VH and VL sequences or any combination of the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 sequences disclosed herein. In certain embodiments, a scFab comprises the VH sequence as provided in SEQ ID NO: 105 or SEQ ID NO: 113 and the VL sequence as provided in SEQ ID NO: 168. In certain embodiments, a scFab comprises a CDRH1 sequence as provided in SEQ ID NO: 106, a CDRH2 sequence as provided in SEQ ID NO: 107 or 121, a CDRH3 sequence as provided in SEQ ID NO: 108, a CDRL1 sequence as provided in SEQ ID NO: 169, a CDRL2 sequence as provided in SEQ ID NO: 170, and a CDRL3 sequence as provided in SEQ ID NO: 171. In certain embodiments, a scFab comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the amino acid sequence provided in any one of SEQ ID NOs.: 218-219 or 226-227.

[0082] "Fv" is a small antibody fragment that contains a complete antigen-recognition and antigen-binding site. This fragment generally consists of a dimer of one heavy- and one light-chain variable region domain in tight, non-covalent association. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although typically at a lower affinity than the entire binding site.

[0083] "Single-chain Fv" also abbreviated as "sFv" or "scFv", are antibody fragments that comprise the VH and VL antibody domains connected into a single polypeptide chain. In some embodiments, the scFv polypeptide comprises a polypeptide linker disposed between and linking the VH and VL domains that enables the scFv to retain or form the desired structure for antigen binding. Such a peptide linker can be incorporated into a fusion polypeptide using standard techniques well known in the art. For a review of scFv, see Pluckthun in *The Pharmacology of Monoclonal Antibodies*, vol. 113, Rosenburg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994); Borrebaeck 1995, infra. In certain embodiments, the antibody or antigen-binding fragment comprises a scFv comprising a VH domain, a VL domain, and a peptide linker linking the VH domain to the VL domain. In particular embodiments, a scFv comprises a VH domain linked to a VL domain by a peptide linker, which can be in a VH-linker-VL orientation or in a VL-linker-VH orientation. Any scFv of the present disclosure may be engineered so that the C-terminal end of the VL

domain is linked by a short peptide sequence to the N-terminal end of the VH domain, or vice versa (i.e., (N)VL(C)-linker-(N)VH(C) or (N)VH(C)-linker-(N)VL(C)). Alternatively, in some embodiments, a linker may be linked to an N-terminal portion or end of the VH domain, the VL domain, or both.

[0084] Peptide linker sequences may be chosen, for example, based on: (1) their ability to adopt a flexible extended conformation; (2) their inability or lack of ability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides and/or on a target molecule; and/or (3) the lack or relative lack of hydrophobic or charged residues that might react with the polypeptides and/or target molecule. Other considerations regarding linker design (e.g., length) can include the conformation or range of conformations in which the VH and VL can form a functional antigen-binding site. In certain embodiments, peptide linker sequences contain, for example, Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala, may also be included in a linker sequence. Other amino acid sequences which may be usefully employed as linker include those disclosed in Maratea et al., Gene 40:39-46 (1985); Murphy et al., Proc. Natl. Acad. Sci. USA 83:8258-8262 (1986); U.S. Pat. No. 4,935,233, and U.S. Pat. No. 4,751,180. Other illustrative and non-limiting examples of linkers may include, for example, Glu-Gly-Lys-Ser-Ser-Gly-Ser-Gly-Ser-Glu-Ser-Lys-Val-Asp (SEQ ID NO: 215) (Chaudhary et al., Proc. Natl. Acad. Sci. USA 87:1066-1070 (1990)) and Lys-Glu-Ser-Gly-Ser-Val-Ser-Ser-Glu-Gln-Leu-Ala-Gln-Phe-Arg-Ser-Leu-Asp (SEQ ID NO: 216) (Bird et al., Science 242: 423-426 (1988)) and the pentamer Gly-Gly-Gly-Gly-Ser (SEQ ID NO: 217) when present in a single iteration or repeated 1 to 5 or more times, or more; see, e.g., SEQ ID NO: 213. Any suitable linker may be used, and in general can be about 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 15 23, 24, 25, 26, 27, 28, 29, 30, 40, 50, 60, 70, 80, 90, 100 amino acids in length, or less than about 200 amino acids in length, and will preferably comprise a flexible structure (can provide flexibility and room for conformational movement between two regions, domains, motifs, fragments, or modules connected by the linker), and will preferably be biologically inert and/or have a low risk of immunogenicity in a human. Exemplary linkers include those comprising or consisting of the amino acid sequence set forth in any one or more of SEQ ID NOs: 206-217. In certain embodiments, the linker comprises or consists of an amino acid sequence having at least 75% (i.e., at least about 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more) identity to the amino acid sequence set forth in any one of SEQ ID NOs: 206-217.

[0085] scFv can be constructed using any combination of the VH and VL sequences or any combination of the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 sequences disclosed herein. In certain embodiments, a scFv comprises the VH sequence provided in SEQ ID NO: 105 or SEQ ID NO: 113 and the VL sequence provided in SEQ ID NO: 168. In certain embodiments, a scFab comprises a CDRH1 sequence as provided in SEQ ID NO: 106, a CDRH2 sequence as provided in SEQ ID NO: 107 or 121, a CDRH3 sequence as provided in SEQ ID NO: 108, a CDRL1 sequence as provided in SEQ ID NO: 169, a CDRL2 sequence as provided in SEQ ID NO: 170, and a CDRL3 sequence as provided in SEQ ID NO: 171. In certain

embodiments, a scFv can comprise the amino acid sequence as provided in SEQ ID NO: 220-221 or SEQ ID NO: 228-229.

[0086] In some embodiments, linker sequences are not required; for example, when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

[0087] Also provided herein are variant antibodies that comprise one or more amino acid alterations in a variable region (e.g., VH, VL, framework or CDR) as compared to a presently disclosed ("parent") antibody, wherein the variant antibody is capable of binding to a SARS-CoV-2 antigen.

[0088] In certain embodiments, the VH comprises or consists of an amino acid sequence having at least 85% (i.e., 85%, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100%) identity to the amino acid sequence according to any one of SEQ ID NOs.: 1, 9-15, 23, 24, 27, 28-46, 55, 63, 79, 87, 95, 103, 105, 113-120, 129-146, 155, 172, 176-178, 194, 196, 198, 200, 202, and 239, wherein the variation 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% (i.e., 85%, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100%) identity to the amino acid sequence according to any one of SEQ ID NOs.: 5, 47-50, 59, 67, 71-72, 75, 76, 83, 91, 99, 109, 147-150, 159, 168, 182, 190, 234, and 243, wherein the variation is optionally limited to one or more framework regions and/or the variation comprises one or more substitution to a germline-encoded amino acid.

[0089] In certain embodiments, an antibody or an antigen-binding fragment of the present disclosure comprises a VH comprising or consisting of the amino acid sequence according to SEQ ID NO: 105 and a VL comprising or consisting of the amino acid sequence according to SEQ ID NO: 168. In further embodiments, an antibody or an antigen-binding fragment of the present disclosure comprises a VH comprising or consisting of the amino acid sequence according to SEQ ID NO: 105 and a VL comprising or consisting of the amino acid sequence according to SEQ ID NO: 168 and binds to SARS-CoV-2 S protein with a K_D 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, less than about 1×10^{-12} M, or less than about 5×10^{-12} M. In still further embodiments, an antibody or an antigen-binding fragment of the present disclosure comprises a VH comprising or consisting of the amino acid sequence according to SEQ ID NO: 105 and a VL comprising or consisting of the amino acid sequence according to SEQ ID NO: 168 and is capable of neutralizing a SARS-CoV-2 infection, or a virus pseudotyped with SARS-CoV-2, with an IC₅₀ of about 0.3 to about 0.4 μ g/ml.

[0090] In certain embodiments, an antibody or an antigen-binding fragment of the present disclosure comprises a VH comprising or consisting of the amino acid sequence according to SEQ ID NO: 105 and a VL comprising or consisting of the amino acid sequence according to SEQ ID NO: 168 and binds to SARS-CoV-2 protein RBD with an EC₅₀ of about 11 to about 25 ng/ml. In certain embodiments, an antibody or an antigen-binding fragment of the present disclosure comprises a VH comprising or consisting of the amino acid sequence according to SEQ ID NO: 113 and a

VL comprising or consisting of the amino acid sequence according to SEQ ID NO: 168 and binds to SARS-CoV-2 S protein RBD with an EC₅₀ of about 9 to about 23 ng/ml. In certain embodiments, an antibody or an antigen-binding fragment of the present disclosure comprises a VH comprising or consisting of the amino acid sequence according to SEQ ID NO: 129 and a VL comprising or consisting of the amino acid sequence according to SEQ ID NO: 168 and binds to SARS-CoV-2 S protein RBD with an EC₅₀ of about 8 to about 22 ng/ml. In certain embodiments, an antibody or an antigen-binding fragment of the present disclosure comprises a VH comprising or consisting of the sequence according to SEQ ID NO: 119 and a VL comprising or consisting of the sequence according to SEQ ID NO: 168 and binds to SARS-CoV-2 S protein RBD with an EC₅₀ of about 8 to about 22 ng/ml. In certain embodiments, an antibody or an antigen-binding fragment of the present disclosure comprises a VH comprising or consisting of the amino acid sequence according to SEQ ID NO: 172 and a VL comprising or consisting of the amino acid sequence according to SEQ ID NO: 168 and binds to SARS-CoV-2 S protein RBD with an EC₅₀ of about 7 to about 19 ng/ml.

[0091] In certain embodiments, an antibody or antigen-binding fragment of the present disclosure is monospecific (e.g., binds to a single epitope) or is multispecific (e.g., binds to multiple epitopes and/or target molecules). Antibodies and antigen binding fragments may be constructed in various formats. Exemplary antibody formats disclosed in Spiess et al., Mol. Immunol. 67 (2): 95 (2015), and in Brinkmann and Kontermann, mAbs 9 (2): 182-212 (2017), which formats and methods of making the same are incorporated herein by reference and include, for example, Bispecific T cell Engagers (BiTEs), DARTs, Knobs-Into-Holes (KIH) assemblies, scFv-CH3-KIH assemblies, KIH Common Light-Chain antibodies, TandAbs, Triple Bodies, TriBi Minibodies, Fab-scFv, scFv-CH-CL-scFv, F(ab')2-scFv2, tetravalent HCabs, Intrabodies, CrossMabs, Dual Action Fabs (DAFs) (two-in-one or four-in-one), Dutamabs, DT-IgG, Charge Pairs, Fab-arm Exchange, SEEDbodies, Tricomabs, LUZ-Y assemblies, Fcabs, κλ-bodies, orthogonal Fabs, DVD-Igs (e.g., U.S. Pat. No. 8,258,268, which formats are incorporated herein by reference in their entirety), IgG(H)-scFv, scFv-(H)IgG, IgG(L)-scFv, scFv-(L)IgG, IgG (L, H)-Fv, IgG(H)-V, V(H)-IgG, IgG(L)-V, V(L)-IgG, KIH IgG-scFab, 2scFv-IgG, IgG-2scFv, scFv4-Ig, Zybody, and DVI-IgG (four-in-one), as well as so-called FIT-Ig (e.g., PCT Publication No. WO 2015/103072, which formats are incorporated herein by reference in their entirety), so-called WuxiBody formats (e.g., PCT Publication No. WO 2019/057122, which formats are incorporated herein by reference in their entirety), and so-called In-Elbow-Insert Ig formats (IEI-Ig; e.g., PCT Publication Nos. WO 2019/024979 and WO 2019/025391, which formats are incorporated herein by reference in their entirety).

[0092] In certain embodiments, the antibody or antigen-binding fragment comprises two or more of VH domains, two or more VL domains, or both (i.e., two or more VH domains and two or more VL domains). In particular embodiments, an antigen-binding fragment comprises the format (N-terminal to C-terminal direction) VH-linker-VL-linker-VH-linker-VL, wherein the two VH sequences can be the same or different and the two VL sequences can be the same or different. Such linked scFvs can include any combination of VH and VL domains arranged to bind to a given

target, and in formats comprising two or more VH and/or two or more VL, one, two, or more different epitopes or antigens may be bound. It will be appreciated that formats incorporating multiple antigen-binding domains may include VH and/or VL sequences in any combination or orientation. For example, the antigen-binding fragment can comprise the format VL-linker-VH-linker-VL-linker-VH, VH-linker-VL-linker-VL-linker-VH, or VL-linker-VH-linker-VH-linker-VL.

[0093] Monospecific or multispecific antibodies or antigen-binding fragments of the present disclosure constructed comprise any combination of the VH and VL sequences and/or any combination of the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 sequences disclosed herein. In certain embodiments, an antibody or antigen-binding fragment comprises the VH sequence provided in SEQ ID NO: 105 or SEQ ID NO: 113 and the VL sequence provided in SEQ ID NO: 168. In certain embodiments, an antibody or antigen-binding fragment comprises a CDRH1 sequence as provided in SEQ ID NO: 106, a CDRH2 sequence as provided in SEQ ID NO: 107 or 121, a CDRH3 sequence as provided in SEQ ID NO: 108, a CDRL1 sequence as provided in SEQ ID NO: 169, a CDRL2 sequence as provided in SEQ ID NO: 170, and a CDRL3 sequence as provided in SEQ ID NO: 171. In certain embodiments, an antibody or antigen-binding fragment comprises the amino acid sequence as provided in SEQ ID NO: 222-225 or SEQ ID NO: 230-233. A bispecific or multispecific antibody or antigen-binding fragment may, in some embodiments, comprise one, two, or more antigen-binding domains (e.g., a VH and a VL) of the instant disclosure. Two or more binding domains may be present that bind to the same or a different SARS-CoV-2 epitope, and a bispecific or multispecific antibody or antigen-binding fragment as provided herein can, in some embodiments, comprise a further SARS-CoV-2 binding domain, and/or can comprise a binding domain that binds to a different antigen or pathogen altogether.

[0094] In any of the presently disclosed embodiments, the antibody or antigen-binding fragment can be multispecific; e.g., bispecific, trispecific, or the like.

[0095] In certain embodiments, the antibody or antigen-binding fragment comprises: (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% (i.e., 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identity to the amino acid sequence set forth in any one of SEQ ID NOS.: 1, 9-15, 23, 24, 27-46, 55, 63, 79, 87, 95, 103, 105, 113-120, 129-146, 155, 172, 176-178, 194, 196, 198, 200, 202, and 239, and wherein the first VL and the second VL are different and each independently comprise an amino acid sequence having at least 85% (i.e., 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%) identity to the amino acid sequence set forth in any one of SEQ ID NOS.: 5, 47-50, 59, 67, 71, 72, 75, 76, 83, 91, 99, 109, 147-150, 159, 168, 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.

[0096] In certain embodiments, the antibody or antigen-binding fragment comprises a Fc polypeptide, or a fragment thereof. The "Fc" fragment or Fc polypeptide comprises the carboxy-terminal portions (i.e., the CH2 and CH3 domains

of IgG) of both antibody H chains held together by disulfides. Antibody "effector functions" refer to those biological activities attributable to the Fc region (a native sequence Fc region or amino acid sequence variant Fc region) of an antibody, and vary with the antibody isotype. Examples of antibody effector functions include: C1q binding and complement dependent cytotoxicity; Fc receptor binding; antibody-dependent cell-mediated cytotoxicity (ADCC); phagocytosis; down regulation of cell surface receptors (e.g., B cell receptor); and B cell activation. As discussed herein, modifications (e.g., amino acid substitutions) may be made to an Fc domain in order to modify (e.g., improve, reduce, or ablate) one or more functionality of an Fc-containing polypeptide (e.g., an antibody of the present disclosure). Such functions include, for example, Fc receptor (FcR) binding, antibody half-life modulation (e.g., by binding to FcRn), ADCC function, protein A binding, protein G binding, and complement binding. Amino acid modifications that modify (e.g., improve, reduce, or ablate) Fc functionalities include, for example, the T250Q/M428L, M252Y/S254T/T256E, H433K/N434F, M428L/N434S, E233P/L234V/L235A/G236+A327G/A330S/P331S, E333A, S239D/A330L/I332E, P257I/Q311, K326W/E333S, S239D/I332E/G236A, N297Q, K322A, S228P, L235E+E318A/K320A/K322A, L234A/L235A/P329G mutations, which mutations are summarized and annotated in "Engineered Fc Regions", published by InvivoGen (2011) and available online at invivogen.com/PDF/review/review-Engineered-Fc-Regions-invivogen.pdf?utm_source=review&utm_medium=pdf&utm_campaign=review&utm_content=Engineered-Fc-Regions, and are incorporated herein by reference.

[0097] For example, to activate the complement cascade, the C1q protein complex can bind to at least two molecules of IgG1 or one molecule of IgM when the immunoglobulin molecule(s) is attached to the antigenic target (Ward, E. S., and Ghettie, V., *Ther. Immunol.* 2 (1995) 77-94). Burton, D. R., described (*Mol. Immunol.* 22 (1985) 161-206) that the heavy chain region comprising amino acid residues 318 to 337 is involved in complement fixation. Duncan, A. R., and Winter, G. (*Nature* 332 (1988) 738-740), using site directed mutagenesis, reported that Glu318, Lys320 and Lys322 form the binding site to C1q. The role of Glu318, Lys320 and Lys 322 residues in the binding of C1q was confirmed by the ability of a short synthetic peptide containing these residues to inhibit complement mediated lysis.

[0098] For example, FcR binding can be mediated by the interaction of the Fc moiety (of an antibody) with Fc receptors (FcRs), which are specialized cell surface receptors on cells including hematopoietic cells. Fc receptors belong to the immunoglobulin superfamily, and shown to mediate both the removal of antibody-coated pathogens by phagocytosis of immune complexes, and the lysis of erythrocytes and various other cellular targets (e.g. tumor cells) coated with the corresponding antibody, via antibody dependent cell mediated cytotoxicity (ADCC; Van de Winkel, J. G., and Anderson, C. L., *J. Leukoc. Biol.* 49 (1991) 511-524). FcRs are defined by their specificity for immunoglobulin classes; Fc receptors for IgG antibodies are referred to as FcγR, for IgE as FcεR, for IgA as FcαR and so on and neonatal Fc receptors are referred to as FcRn. Fc receptor binding is described for example in Ravetch, J. V., and Kinet, J. P., *Annu. Rev. Immunol.* 9 (1991) 457-492; Capel,

P. J., et al., *Immunomethods* 4 (1994) 25-34; de Haas, M., et al., *J Lab. Clin. Med.* 126 (1995) 330-341; and Gessner, J. E., et al., *Ann. Hematol.* 76 (1998) 231-248.

[0099] Cross-linking of receptors by the Fc domain of native IgG antibodies (Fc γ R) triggers a wide variety of effector functions including phagocytosis, antibody-dependent cellular cytotoxicity, and release of inflammatory mediators, as well as immune complex clearance and regulation of antibody production. Fc moieties providing cross-linking of receptors (e.g., Fc γ R) are contemplated herein. In humans, three classes of Fc γ R have been characterized to-date, which are: (i) Fc γ RI (CD64), which binds monomeric IgG with high affinity and is expressed on macrophages, monocytes, neutrophils and eosinophils; (ii) Fc γ RII (CD32), which binds complexed IgG with medium to low affinity, is widely expressed, in particular on leukocytes, is believed to be a central player in antibody-mediated immunity, and which can be divided into Fc γ RIIA, Fc γ RIIB and Fc γ RIIC, which perform different functions in the immune system, but bind with similar low affinity to the IgG-Fc, and the ectodomains of these receptors are highly homologous; and (iii) Fc γ RIII (CD16), which binds IgG with medium to low affinity and has been found in two forms: Fc γ RIIIA, which has been found on NK cells, macrophages, eosinophils, and some monocytes and T cells, and is believed to mediate ADCC; and Fc γ RIIIB, which is highly expressed on neutrophils.

[0100] Fc γ RIIA is found on many cells involved in killing (e.g. macrophages, monocytes, neutrophils) and seems able to activate the killing process. Fc γ RIIB seems to play a role in inhibitory processes and is found on B-cells, macrophages and on mast cells and eosinophils. Importantly, it has been shown that 75% of all Fc γ RIIB is found in the liver (Ganesan, L. P. et al., 2012: "Fc γ RIIb on liver sinusoidal endothelium clears small immune complexes," *Journal of Immunology* 189:4981-4988). Fc γ RIIB is abundantly expressed on Liver Sinusoidal Endothelium, called LSEC, and in Kupffer cells in the liver and LSEC are the major site of small immune complexes clearance (Ganesan, L. P. et al., 2012: Fc γ RIIb on liver sinusoidal endothelium clears small immune complexes. *Journal of Immunology* 189:4981-4988).

[0101] In some embodiments, the antibodies disclosed herein and the antigen-binding fragments thereof comprise an Fc polypeptide or fragment thereof for binding to Fc γ RIIb, in particular an Fc region, such as, for example IgG-type antibodies. Moreover, it is possible to engineer the Fc moiety to enhance Fc γ RIIb binding by introducing the mutations S267E and L328F as described by Chu, S. Y. et al., 2008: Inhibition of B cell receptor-mediated activation of primary human B cells by coengagement of CD19 and FcgammaRIIb with Fc-engineered antibodies. *Molecular Immunology* 45, 3926-3933. Thereby, the clearance of immune complexes can be enhanced (Chu, S., et al., 2014: Accelerated Clearance of IgE In Chimpanzees Is Mediated By Xmab7195, An Fc-Engineered Antibody With Enhanced Affinity For Inhibitory Receptor Fc γ RIIb. *Am J Respir Crit, American Thoracic Society International Conference Abstracts*). In some embodiments, the antibodies of the present disclosure, or the antigen binding fragments thereof, comprise an engineered Fc moiety with the mutations S267E and L328F, in particular as described by Chu, S. Y. et al., 2008: Inhibition of B cell receptor-mediated activation of

primary human B cells by coengagement of CD19 and FcgammaRIIb with Fc-engineered antibodies. *Molecular Immunology* 45, 3926-3933.

[0102] On B cells, Fc γ RIIb may function to suppress further immunoglobulin production and isotype switching to, for example, the IgE class. On macrophages, Fc γ RIIb is thought to inhibit phagocytosis as mediated through Fc γ RIIA. On eosinophils and mast cells, the B form may help to suppress activation of these cells through IgE binding to its separate receptor.

[0103] Regarding Fc γ RI binding, modification in native IgG of at least one of E233-G236, P238, D265, N297, A327 and P329 reduces binding to Fc γ RI. IgG2 residues at positions 233-236, substituted into corresponding positions IgG1 and IgG4, reduces binding of IgG1 and IgG4 to Fc γ RI by 10³-fold and eliminated the human monocyte response to antibody-sensitized red blood cells (Armour, K. L., et al. *Eur. J. Immunol.* 29 (1999) 2613-2624).

[0104] Regarding Fc γ RII binding, reduced binding for Fc γ RIIA is found, e.g., for IgG mutation of at least one of E233-G236, P238, D265, N297, A327, P329, D270, Q295, A327, R292 and K414.

[0105] Two allelic forms of human Fc γ RIIA are the "H131" variant, which binds to IgG1 Fc with high affinity, and the "R131" variant, which binds to IgG1 Fc with low affinity. See, e.g., Bruhns et al., *Blood* 113:3716-3725 (2009).

[0106] Regarding Fc γ RIII binding, reduced binding to Fc γ RIIIA is found, e.g., for mutation of at least one of E233-G236, P238, D265, N297, A327, P329, D270, Q295, A327, S239, E269, E293, Y296, V303, A327, K338 and D376. Mapping of the binding sites on human IgG1 for Fc receptors, the above-mentioned mutation sites, and methods for measuring binding to Fc γ RI and Fc γ RIIA, are described in Shields, R. L., et al., *J. Biol. Chem.* 276 (2001) 6591-6604.

[0107] Two allelic forms of human Fc γ RIIIA are the "F158" variant, which binds to IgG1 Fc with low affinity, and the "V158" variant, which binds to IgG1 Fc with high affinity. See, e.g., Bruhns et al., *Blood* 113:3716-3725 (2009).

[0108] Regarding binding to Fc γ RII, two regions of native IgG Fc appear to be involved in interactions between Fc γ RIIs and IgGs, namely (i) the lower hinge site of IgG Fc, in particular amino acid residues L, L, G, G (234-237, EU numbering), and (ii) the adjacent region of the CH2 domain of IgG Fc, in particular a loop and strands in the upper CH2 domain adjacent to the lower hinge region, e.g. in a region of P331 (Wines, B. D., et al., *J. Immunol.* 2000; 164:5313-5318). Moreover, Fc γ RI appears to bind to the same site on IgG Fc, whereas FcRn and Protein A bind to a different site on IgG Fc, which appears to be at the CH2-CH3 interface (Wines, B. D., et al., *J. Immunol.* 2000; 164:5313-5318).

[0109] Also contemplated are mutations that increase binding affinity of an Fc polypeptide or fragment thereof of the present disclosure to a (i.e., one or more) Fc γ receptor (e.g., as compared to a reference Fc polypeptide or fragment thereof or containing the same that does not comprise the mutation(s)). See, e.g., Delillo and Ravetch, *Cell* 161 (5): 1035-1045 (2015) and Ahmed et al., *J. Struc. Biol.* 194 (1): 78 (2016), the Fc mutations and techniques of which are incorporated herein by reference.

[0110] In any of the herein disclosed embodiments, an antibody or antigen-binding fragment can comprise a Fc

polypeptide or fragment thereof comprising a mutation selected from G236A; S239D; A330L; and I332E; or a combination comprising any two or more of the same; e.g., S239D/I332E; S239D/A330L/I332E; G236A/S239D/I332E; G236A/A330L/I332E (also referred to herein as “GAALIE”); or G236A/S239D/A330L/I332E. In some embodiments, the Fc polypeptide or fragment thereof does not comprise S239D.

[0111] In certain embodiments, the Fc polypeptide or fragment thereof may comprise or consist of at least a portion of an Fc polypeptide or fragment thereof that is involved in binding to FcRn binding. In certain embodiments, the Fc polypeptide or fragment thereof comprises one or more amino acid modifications that improve binding affinity for (e.g., enhance binding to) FcRn (e.g., at a pH of about 6.0) and, in some embodiments, thereby extend in vivo half-life of a molecule comprising the Fc polypeptide or fragment thereof (e.g., as compared to a reference Fc polypeptide or fragment thereof or antibody that is otherwise the same but does not comprise the modification(s)). In certain embodiments, the Fc polypeptide or fragment thereof comprises or is derived from a IgG Fc and a half-life-extending mutation comprises any one or more of: M428L; N434S; N434H; N434A; N434S; M252Y; S254T; T256E; T250Q; P257I Q311I; D376V; T307A; E380A (EU numbering). In certain embodiments, a half-life-extending mutation comprises M428L/N434S (also referred to herein as “MLNS”). In certain embodiments, a half-life-extending mutation comprises M252Y/S254T/T256E. In certain embodiments, a half-life-extending mutation comprises T250Q/M428L. In certain embodiments, a half-life-extending mutation comprises P257I/Q311I. In certain embodiments, a half-life-extending mutation comprises P257I/N434H. In certain embodiments, a half-life-extending mutation comprises D376V/N434H. In certain embodiments, a half-life-extending mutation comprises T307A/E380A/N434A.

[0112] In some embodiments, an antibody or antigen-binding fragment includes a Fc moiety that comprises the substitution mutations M428L/N434S. In some embodiments, an antibody or antigen-binding fragment includes a Fc polypeptide or fragment thereof that comprises the substitution mutations G236A/A330L/I332E. In certain embodiments, an antibody or antigen-binding fragment includes a (e.g., IgG) Fc moiety that comprises a G236A mutation, an A330L mutation, and a I332E mutation (GAALIE), and does not comprise a S239D mutation (e.g., comprises a native S at position 239). In particular embodiments, an antibody or antigen-binding fragment includes an Fc polypeptide or fragment thereof that comprises the substitution mutations: M428L/N434S and G236A/A330L/I332E, and optionally does not comprise S239D. In certain embodiments, an antibody or antigen-binding fragment includes a Fc polypeptide or fragment thereof that comprises the substitution mutations: M428L/N434S and G236A/S239D/A330L/I332E.

[0113] In certain embodiments, the antibody or antigen-binding fragment comprises a mutation that alters glycosylation, wherein the mutation that alters glycosylation comprises N297A, N297Q, or N297G, and/or the antibody or antigen-binding fragment is partially or fully aglycosylated and/or is partially or fully afucosylated. Host cell lines and methods of making partially or fully aglycosylated or partially or fully afucosylated antibodies and antigen-binding

fragments are known (see, e.g., PCT Publication No. WO 2016/181357; Suzuki et al. *Clin. Cancer Res.* 13 (6): 1875-82 (2007); Huang et al. *MAbs* 6:1-12 (2018)).

[0114] In certain embodiments, the antibody or antigen-binding fragment is capable of eliciting continued protection in vivo in a subject even once no detectable levels of the antibody or antigen-binding fragment can be found in the subject (i.e., when the antibody or antigen-binding fragment has been cleared from the subject following administration). Such protection is referred to herein as a vaccinal effect. Without wishing to be bound by theory, it is believed that dendritic cells can internalize complexes of antibody and antigen and thereafter induce or contribute to an endogenous immune response against antigen. In certain embodiments, an antibody or antigen-binding fragment comprises one or more modifications, such as, for example, mutations in the Fc comprising G236A, A330L, and I332E, that are capable of activating dendritic cells that may induce, e.g., T cell immunity to the antigen.

[0115] In any of the presently disclosed embodiments, the antibody or antigen-binding fragment comprises a Fc polypeptide or a fragment thereof, including a CH2 (or a fragment thereof), a CH3 (or a fragment thereof), or a CH2 and a CH3, wherein the CH2, the CH3, or both can be of any isotype and may contain amino acid substitutions or other modifications as compared to a corresponding wild-type CH2 or CH3, respectively. In certain embodiments, a Fc polypeptide of the present disclosure comprises two CH2-CH3 polypeptides that associate to form a dimer.

[0116] In any of the presently disclosed embodiments, the antibody or antigen-binding fragment can be monoclonal. The term “monoclonal antibody” (mAb) as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., individual antibodies comprising the population are identical except for possible naturally occurring mutations that may be present, in some cases in minor amounts. Monoclonal antibodies are highly specific, being directed against a single antigenic site. Furthermore, in contrast to polyclonal antibody preparations that include different antibodies directed against different epitopes, each monoclonal antibody is directed against a single epitope of the antigen. In addition to their specificity, the monoclonal antibodies are advantageous in that they may be synthesized uncontaminated by other antibodies. The term “monoclonal” is not to be construed as requiring production of the antibody by any particular method. For example, monoclonal antibodies useful in the present invention may be prepared by the hybridoma methodology first described by Kohler et al., *Nature* 256:495 (1975), or may be made using recombinant DNA methods in bacterial, eukaryotic animal, or plant cells (see, e.g., U.S. Pat. No. 4,816,567). Monoclonal antibodies may also be isolated from phage antibody libraries using the techniques described in Clackson et al., *Nature*, 352:624-628 (1991) and Marks et al., *J. Mol. Biol.*, 222:581-597 (1991), for example. Monoclonal antibodies may also be obtained using methods disclosed in PCT Publication No. WO 2004/076677A2.

[0117] Antibodies and antigen-binding fragments of the present disclosure include “chimeric antibodies” in which a portion of the heavy and/or light chain is identical with or homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular antibody class or subclass, while the remainder of the chain(s) is identical with or homologous to corresponding

sequences in antibodies derived from another species or belonging to another antibody class or subclass, as well as fragments of such antibodies, so long as they exhibit the desired biological activity (see, U.S. Pat. Nos. 4,816,567; 5,530,101 and 7,498,415; and Morrison et al., Proc. Natl. Acad. Sci. USA, 81:6851-6855 (1984)). For example, chimeric antibodies may comprise human and non-human residues. Furthermore, chimeric antibodies may comprise residues that are not found in the recipient antibody or in the donor antibody. These modifications are made to further refine antibody performance. For further details, see Jones et al., *Nature* 321:522-525 (1986); Riechmann et al., *Nature* 332:323-329 (1988); and Presta, *Curr. Op. Struct. Biol.* 2:593-596 (1992). Chimeric antibodies also include primatized and humanized antibodies.

[0118] A “humanized antibody” is generally considered to be a human antibody that has one or more amino acid residues introduced into it from a source that is non-human. These non-human amino acid residues are typically taken from a variable domain. Humanization may be performed following the method of Winter and co-workers (Jones et al., *Nature*, 321:522-525 (1986); Reichmann et al., *Nature*, 332:323-327 (1988); Verhoeyen et al., *Science*, 239:1534-1536 (1988)), by substituting non-human variable sequences for the corresponding sequences of a human antibody. Accordingly, such “humanized” antibodies are chimeric antibodies (U.S. Pat. Nos. 4,816,567; 5,530,101 and 7,498,415) wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In some instances, a “humanized” antibody is one which is produced by a non-human cell or animal and comprises human sequences, e.g., Hc domains.

[0119] A “human antibody” is an antibody containing only sequences that are present in an antibody that is produced by a human. However, as used herein, human antibodies may comprise residues or modifications not found in a naturally occurring human antibody (e.g., an antibody that is isolated from a human), including those modifications and variant sequences described herein. These are typically made to further refine or enhance antibody performance. In some instances, human antibodies are produced by transgenic animals. For example, see U.S. Pat. Nos. 5,770,429; 6,596,541 and 7,049,426. In certain embodiments, an antibody or antigen-binding fragment of the present disclosure is chimeric, humanized, or human.

[0120] Exemplary antibodies of the present disclosure include S309, sotrovimab, and VIR-7832. S309 is a human monoclonal antibody obtained from a B cell of a SARS-CoV survivor. S309 comprises the VH amino acid sequence of SEQ ID NO.: 105 and the VL amino acid sequence of SEQ ID NO.: 168. Sotrovimab (IgG1*01 G1m17; VH of SEQ ID NO.: 113, M428L and N434S Fc mutations; VL of SEQ ID NO.: 168 (kappa light chain IgKC*01 k1m3)) and VIR-7832 ((IgG1*01 G1m17; VH of SEQ ID NO.: 113, G236A, A330L, I332E, M428L, and N434S Fc mutations; VL of SEQ ID NO.: 168 (kappa light chain IgKC*01 k1m3))) are engineered human monoclonal antibodies derived from S309.

Polynucleotides, Vectors, and Host Cells

[0121] Presently disclosed antibodies and antigen-binding fragments (and portions thereof; e.g., a CDR, a VH, a VL, a heavy chain, or a light chain) can be encoded by a

polynucleotide. The polynucleotide can comprise deoxyribonucleic acid (DNA) or ribonucleic acid (RNA). RNA can comprise messenger RNA (mRNA). Polynucleotides can be codon-optimized for expression in a host cell. Once a coding sequence is known or identified, codon optimization can be performed using known techniques and tools, e.g., using the GenScript® OptimumGene™ tool; see also Scholten et al., *Clin. Immunol.* 119:135, 2006). Codon-optimized sequences include sequences that are partially codon-optimized (i.e., one or more codon is optimized for expression in the host cell) and those that are fully codon-optimized. It will also be appreciated that polynucleotides encoding antibodies and antigen-binding fragments of the present disclosure may possess different nucleotide sequences while still encoding a same antibody or antigen-binding fragment due to, for example, the degeneracy of the genetic code, splicing, and the like. It will be appreciated that a polynucleotide encoding an antibody or antigen-binding fragment can be comprised in a polynucleotide that includes other sequences and/or features for, e.g., expression of the antibody or antigen-binding fragment in a host cell. Exemplary features include a promoter sequence, a polyadenylation sequence, a sequence that encodes a signal peptide (e.g., located at the N-terminus of a expressed antibody heavy chain or light chain), or the like.

[0122] Polynucleotides can be comprised or contained in a vector. A vector can comprise any one or more of the vectors disclosed herein. A vectors can comprise, for example, a DNA plasmid construct encoding the antibody or antigen-binding fragment, or a portion thereof (e.g., so-called “DMAb”; see, e.g., Muthumani et al., *J Infect Dis.* 214 (3): 369-378 (2016); Muthumani et al., *Hum Vaccin Immunother* 9:2253-2262 (2013)); Flingai et al., *Sci Rep.* 5:12616 (2015); and Elliott et al., *NPJ Vaccines* 18 (2017), which antibody-coding DNA constructs and related methods of use, including administration of the same, are incorporated herein by reference). A DNA plasmid construct can comprise a single open reading frame encoding a heavy chain and a light chain (or a VH and a VL) of the antibody or antigen-binding fragment, wherein the sequence encoding the heavy chain and the sequence encoding the light chain are optionally separated by polynucleotide encoding a protease cleavage site and/or by a polynucleotide encoding a self-cleaving peptide. Substituent components of the antibody or antigen-binding fragment can be encoded by a polynucleotide comprised in a single plasmid. Alternatively, the substituent components of the antibody or antigen-binding fragment can be encoded by a polynucleotide comprised in two or more plasmids (e.g., a first plasmid comprises a polynucleotide encoding a heavy chain, VH, or VH+CH, and a second plasmid comprises a polynucleotide encoding the cognate light chain, VL, or VL+CL). A single plasmid can comprise a polynucleotide encoding a heavy chain and/or a light chain from two or more antibodies or antigen-binding fragments of the present disclosure. An exemplary expression vector is pVax1, available from Invitrogen®. A DNA plasmid of the present disclosure can be delivered to a subject by, for example, electroporation (e.g., intramuscular electroporation), or with an appropriate formulation (e.g., hyaluronidase). A vector can comprise a nucleotide sequence encoding a signal peptide. The signal peptide may or may not be present (e.g., can be enzymatically cleaved from) on the mature antibody or antigen-binding fragment. Nucleic acid sequence encoding a signal

peptide include the nucleotide sequence set forth in SEQ ID NO.: 252 or SEQ ID NO.: 263. A signal peptide can comprise or consist of the amino acid sequence set forth in SEQ ID NO.: 256 or SEQ ID NO.: 264. A vector can comprise a polyadenylation signal sequence. An example of a polyadenylation signal sequence comprises or consists of the nucleotide sequence as set forth in SEQ ID NO.: 253. [0123] A vector can comprise a CMV promoter (e.g., comprising or consisting of the nucleotide sequence as set forth in SEQ ID NO.: 251).

[0124] Examples of host cells that can be used to express a presently disclosed antigen or antigen-binding fragment cells include but are not limited to, eukaryotic cells, e.g., yeast cells, animal cells, insect cells, plant cells; and prokaryotic cells, including *E. coli*. In some embodiments, the cells are mammalian cells. Cells include a mammalian cell line such as CHO cells (e.g., DHFR-CHO cells (Urlaub et al., *PNAS* 77:4216 (1980)), human embryonic kidney cells (e.g., HEK293T cells), PER.C6 cells, Y0 cells, Sp2/0 cells. NS0 cells, human liver cells, e.g. Hepa RG cells, myeloma cells or hybridoma cells. Other examples of mammalian host cell lines include mouse sertoli cells (e.g., TM4 cells); monkey kidney CV1 line transformed by SV40 (COS-7); baby hamster kidney cells (BHK); African green monkey kidney cells (VERO-76); monkey kidney cells (CV1); human cervical carcinoma cells (HELA); human lung cells (W138); human liver cells (Hep G2); canine kidney cells (MDCK); buffalo rat liver cells (BRL 3A); mouse mammary tumor (MMT 060562); TRI cells; MRC 5 cells; and FS4 cells. Mammalian host cell lines suitable for antibody production also include those described in, for example, Yazaki and Wu, *Methods in Molecular Biology*, Vol. 248 (B. K. C. Lo, ed., Humana Press, Totowa, N.J.), pp. 255-268 (2003).

[0125] Host cells also include a prokaryotic cell, such as an *E. coli*. The expression of peptides in prokaryotic cells such as *E. coli* is well established (see, e.g., Pluckthun, A. *Bio/Technology* 9:545-551 (1991). For example, antibodies may be produced in bacteria, in particular when glycosylation and Fc effector function are not needed. For expression of antibody fragments and polypeptides in bacteria, see, e.g., U.S. Pat. Nos. 5,648,237; 5,789,199; and 5,840,523. A cell may be transfected with a vector according to the present description with an expression vector. The term "transfection" refers to the introduction of nucleic acid molecules, such as DNA or RNA (e.g. mRNA) molecules, into cells, such as into eukaryotic cells. In the context of the present description, the term "transfection" encompasses any method known to the skilled person for introducing nucleic acid molecules into cells, such as into eukaryotic cells, including into mammalian cells. Such methods encompass, for example, electroporation, lipofection, e.g., based on cationic lipids and/or liposomes, calcium phosphate precipitation, nanoparticle based transfection, virus based transfection, or transfection based on cationic polymers, such as DEAE-dextran or polyethylenimine, etc. In certain embodiments, the introduction is non-viral.

[0126] Moreover, host cells may be transfected stably or transiently with a vector, e.g. for expressing an antibody, or an antigen-binding fragment thereof. Cells may be stably transfected with a vector. Alternatively, cells may be transiently transfected with a vector encoding an antibody or antigen-binding fragment.

[0127] An antibody or antigen-binding fragment (or poly-nucleotide encoding the same) can be heterologous to the

host cell. For example, the cell may be of a species that is different to the species from which the antibody was fully or partially obtained (e.g., CHO cells expressing a human antibody or an engineered human antibody). The cell type of the host cell may not express the antibody or antigen-binding fragment in nature. Moreover, the host cell may impart a post-translational modification (PTM; e.g., glycosylation or fucosylation) on the antibody or antigen-binding fragment that is not present in a native state of the antibody or antigen-binding fragment (or in a native state of a parent antibody from which the antibody or antigen binding fragment was engineered or derived). Such a PTM may result in a functional difference (e.g., reduced immunogenicity). Accordingly, an antibody or antigen-binding fragment of the present disclosure that is produced by a host cell as disclosed herein may include one or more post-translational modification that is distinct from the antibody (or parent antibody) in its native state (e.g., a human antibody produced by a CHO cell can comprise one or more post-translational modification that is distinct from the antibody when isolated from the human and/or produced by the native human B cell or plasma cell).

[0128] Insect cells useful expressing a binding protein of the present disclosure are known in the art and include, for example, *Spodoptera frugiperda* Sf9 cells, *Trichoplusia ni* BTI-TN5B1-4 cells, and *Spodoptera frugiperda* SfSWT01 "MimicTM" cells. See, e.g., Palmberger et al., *J. Biotechnol.* 153 (3-4): 160-166 (2011). Numerous baculoviral strains have been identified which may be used in conjunction with insect cells, particularly for transfection of *Spodoptera frugiperda* cells.

[0129] Eukaryotic microbes such as filamentous fungi or yeast are also suitable hosts for cloning or expressing protein-encoding vectors, and include fungi and yeast strains with "humanized" glycosylation pathways, resulting in the production of an antibody with a partially or fully human glycosylation pattern. See Gerngross, *Nat. Biotech.* 22:1409-1414 (2004); Li et al., *Nat. Biotech.* 24:210-215 (2006).

[0130] Plant cells can also be utilized as hosts for expressing a binding protein of the present disclosure. For example, PLANTIBODIESTM technology (described in, for example, U.S. Pat. Nos. 5,959,177; 6,040,498; 6,420,548; 7,125,978; and 6,417,429) employs transgenic plants to produce antibodies.

[0131] Mammalian host cells include, for example, a CHO cell, a HEK293 cell, a PER.C6 cell, a Y0 cell, a Sp2/0 cell, a NS0 cell, a human liver cell, a myeloma cell, or a hybridoma cell.

[0132] Methods for producing an antibody, or antigen-binding fragment can comprise culturing a host cell under conditions and for a time sufficient to produce the antibody, or the antigen-binding fragment. Methods useful for isolating and purifying recombinantly produced antibodies, by way of example, may include obtaining supernatants from suitable host cell/vector systems that secrete the recombinant antibody into culture media and then concentrating the media using a commercially available filter. Following concentration, the concentrate may be applied to a single suitable purification matrix or to a series of suitable matrices, such as an affinity matrix or an ion exchange resin. One or more reverse phase HPLC steps may be employed to further purify a recombinant polypeptide. These purification methods may also be employed when isolating an immu-

nogen from its natural environment. Methods for large scale production of one or more of the isolated/recombinant antibody described herein include batch cell culture, which is monitored and controlled to maintain appropriate culture conditions. Purification of soluble antibodies may be performed according to methods described herein and known in the art and that comport with laws and guidelines of domestic and foreign regulatory agencies.

Pharmaceutical Compositions

[0133] Also provided herein are compositions that comprise any one or more of the presently disclosed antibodies or antigen-binding fragments and can further comprise a pharmaceutically acceptable carrier, excipient, or diluent. Carriers, excipients, and diluents are discussed in further detail herein.

[0134] In certain embodiments, a composition comprises two or more different antibodies or antigen-binding fragments according to the present disclosure. In certain embodiments, antibodies or antigen-binding fragments to be used in a combination each independently have one or more of the following characteristics: neutralize naturally occurring SARS-CoV-2 variants; do not compete with one another for Spike protein binding; bind distinct Spike protein epitopes; have a reduced formation of resistance to SARS-CoV-2; when in a combination, have a reduced formation of resistance to SARS-CoV-2; potently neutralize live SARS-CoV-2 virus; exhibit additive or synergistic effects on neutralization of live SARS-CoV-2 virus when used in combination; exhibit effector functions; are protective in relevant animal model(s) of infection; are capable of being produced in sufficient quantities for large-scale production.

[0135] In some embodiments, a composition comprises a polynucleotide or vector that encodes an antibody or antigen-binding fragment. In certain embodiments, a composition comprises a first vector comprising a first plasmid, and a second vector comprising a second plasmid, wherein the first plasmid comprises a polynucleotide encoding a heavy chain, VH, or VH+CH, and a second plasmid comprises a polynucleotide encoding the cognate light chain, VL, or VL+CL of the antibody or antigen-binding fragment thereof. In certain embodiments, a composition comprises a polynucleotide (e.g., mRNA) coupled to a suitable delivery vehicle or carrier. Exemplary vehicles or carriers for administration to a human subject include a lipid or lipid-derived delivery vehicle, such as a liposome, solid lipid nanoparticle, oily suspension, submicron lipid emulsion, lipid microbubble, inverse lipid micelle, cochlear liposome, lipid microtubule, lipid microcylinder, or lipid nanoparticle (LNP) or a nanoscale platform (see, e.g., Li et al. *Wilery Interdiscip Rev. Nanomed Nanobiotechnol.* 11(2): e1530 (2019)). Principles, reagents, and techniques for designing appropriate mRNA and formulating mRNA-LNP and delivering the same are described in, for example, Pardi et al. (*J Control Release* 217345-351 (2015)); Thess et al. (*Mol Ther* 23:1456-1464 (2015)); Thran et al. (*EMBO Mol Med* 9 (10): 1434-1448 (2017); Kose et al. (*Sci. Immunol.* 4 eaaw6647 (2019); and Sabnis et al. (*Mol. Ther.* 26:1509-1519 (2018)), which techniques, include capping, codon optimization, nucleoside modification, purification of mRNA, incorporation of the mRNA into stable lipid nanoparticles (e.g., ionizable cationic lipid/phosphatidylcholine/cholesterol/PEG-lipid; ionizable lipid:distearoyl PC:cholesterol:polyethylene glycol lipid), and subcutaneous, intramuscular,

intradermal, intravenous, intraperitoneal, and intratracheal administration of the same, are incorporated herein by reference.

Uses

[0136] Also provided herein are methods of treating a subject using an antibody or antigen-binding fragment of the present disclosure, or a composition comprising the same, wherein the subject has, is believed to have, or is at risk for having an infection by a SARS-CoV-2, optionally having, believed to have, or at risk for COVID-19.

[0137] Accordingly, in certain embodiments, methods are provided for treating a SARS-CoV-2 infection in a subject (e.g. having or at risk of contracting a SARS-CoV-2 infection or COVID-19), wherein the methods comprise administering to the subject an effective amount of an antibody, antigen-binding fragment, or composition as disclosed herein.

[0138] Subjects that can be treated by the present disclosure are, in general, human and other primate subjects, such as monkeys and apes for veterinary medicine purposes. Other model organisms, such as mice and rats, may also be treated according to the present disclosure. In any of the aforementioned embodiments, the subject may be a human subject. The subjects can be male or female and can be any suitable age, including infant, juvenile, adolescent, adult, and geriatric subjects.

[0139] Briefly, pharmaceutical compositions according to certain embodiments of the present disclosure are formulated so as to allow the active ingredients contained therein to be bioavailable upon administration of the composition to a patient. Compositions that will be administered to a subject or patient may take the form of one or more dosage units, where for example, a tablet may be a single dosage unit, and a container of a herein described an antibody or antigen-binding in aerosol form may hold a plurality of dosage units. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see Remington: The Science and Practice of Pharmacy, 20th Edition (Philadelphia College of Pharmacy and Science, 2000). The composition to be administered will, in any event, contain an effective amount of an antibody or antigen-binding fragment, polynucleotide, vector, host cell, or composition of the present disclosure, for treatment of a disease or condition of interest in accordance with teachings herein.

[0140] A composition may be in the form of a solid or liquid. In some embodiments, the carrier(s) are particulate, so that the compositions are, for example, in tablet or powder form. The carrier(s) may be liquid, with the compositions being, for example, an oral oil, injectable liquid or an aerosol, which is useful in, for example, inhalatory administration. When intended for oral administration, the pharmaceutical composition is preferably in either solid or liquid form, where semi solid, semi liquid, suspension and gel forms are included within the forms considered herein as either solid or liquid.

[0141] As a solid composition for oral administration, the pharmaceutical composition may be formulated into a powder, granule, compressed tablet, pill, capsule, chewing gum, wafer or the like. Such a solid composition will typically contain one or more inert diluents or edible carriers. In addition, one or more of the following may be present: binders such as carboxymethylcellulose, ethyl cellulose, microcrystalline cellulose, gum tragacanth or gelatin;

excipients such as starch, lactose or dextrins, disintegrating agents such as alginic acid, sodium alginate, Primogel, corn starch and the like; lubricants such as magnesium stearate or Sterotex; glidants such as colloidal silicon dioxide; sweetening agents such as sucrose or saccharin; a flavoring agent such as peppermint, methyl salicylate or orange flavoring; and a coloring agent. When the composition is in the form of a capsule, for example, a gelatin capsule, it may contain, in addition to materials of the above type, a liquid carrier such as polyethylene glycol or oil.

[0142] The composition may be in the form of a liquid, for example, an elixir, syrup, solution, emulsion or suspension. The liquid may be for oral administration or for delivery by injection, as two examples. When intended for oral administration, preferred compositions contain, in addition to the present compounds, one or more of a sweetening agent, preservatives, dye/colorant and flavor enhancer. In a composition intended to be administered by injection, one or more of a surfactant, preservative, wetting agent, dispersing agent, suspending agent, buffer, stabilizer and isotonic agent may be included.

[0143] Liquid pharmaceutical compositions, whether they be solutions, suspensions or other like form, may include one or more of the following adjuvants: sterile diluents such as water for injection, saline solution, preferably physiological saline, Ringer's solution, isotonic sodium chloride, fixed oils such as synthetic mono or diglycerides which may serve as the solvent or suspending medium, polyethylene glycols, glycerin, propylene glycol or other solvents; antibacterial agents such as benzyl alcohol or methyl paraben; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic. Physiological saline is a preferred adjuvant. An injectable pharmaceutical composition is preferably sterile.

[0144] A liquid composition intended for either parenteral or oral administration should contain an amount of an antibody or antigen-binding fragment as herein disclosed such that a suitable dosage will be obtained. Typically, this amount is at least 0.01% of the antibody or antigen-binding fragment in the composition. When intended for oral administration, this amount may be varied to be between 0.1 and about 70% of the weight of the composition. Certain oral pharmaceutical compositions contain between about 4% and about 75% of the antibody or antigen-binding fragment. In certain embodiments, pharmaceutical compositions and preparations according to the present invention are prepared so that a parenteral dosage unit contains between 0.01 to 10% by weight of antibody or antigen-binding fragment prior to dilution.

[0145] The composition may be intended for topical administration, in which case the carrier may suitably comprise a solution, emulsion, ointment or gel base. The base, for example, may comprise one or more of the following: petrolatum, lanolin, polyethylene glycols, bee wax, mineral oil, diluents such as water and alcohol, and emulsifiers and stabilizers. Thickening agents may be present in a composition for topical administration. If intended for transdermal administration, the composition may include a transdermal patch or iontophoresis device. The pharmaceutical composition may be intended for rectal administration, in the form,

for example, of a suppository, which will melt in the rectum and release the drug. The composition for rectal administration may contain an oleaginous base as a suitable nonirritating excipient. Such bases include, without limitation, lanolin, cocoa butter and polyethylene glycol.

[0146] A composition may include various materials which modify the physical form of a solid or liquid dosage unit. For example, the composition may include materials that form a coating shell around the active ingredients. The materials that form the coating shell are typically inert, and may be selected from, for example, sugar, shellac, and other enteric coating agents. Alternatively, the active ingredients may be encased in a gelatin capsule. The composition in solid or liquid form may include an agent that binds to the antibody or antigen-binding fragment of the disclosure and thereby assists in the delivery of the compound. Suitable agents that may act in this capacity include monoclonal or polyclonal antibodies, one or more proteins or a liposome. The composition may consist essentially of dosage units that can be administered as an aerosol. The term aerosol is used to denote a variety of systems ranging from those of colloidal nature to systems consisting of pressurized packages. Delivery may be by a liquefied or compressed gas or by a suitable pump system that dispenses the active ingredients. Aerosols may be delivered in single phase, bi phasic, or tri phasic systems in order to deliver the active ingredient(s). Delivery of the aerosol includes the necessary container, activators, valves, subcontainers, and the like, which together may form a kit. One of ordinary skill in the art, without undue experimentation, may determine preferred aerosols.

[0147] It will be understood that compositions of the present disclosure also encompass carrier molecules for polynucleotides, as described herein (e.g., lipid nanoparticles, nanoscale delivery platforms, and the like).

[0148] The pharmaceutical compositions may be prepared by methodology well known in the pharmaceutical art. For example, a composition intended to be administered by injection can be prepared by combining a composition that comprises an antibody, antigen-binding fragment thereof, or antibody conjugate as described herein and optionally, one or more of salts, buffers and/or stabilizers, with sterile, distilled water so as to form a solution. A surfactant may be added to facilitate the formation of a homogeneous solution or suspension. Surfactants are compounds that non-covalently interact with the peptide composition so as to facilitate dissolution or homogeneous suspension of the antibody or antigen-binding fragment thereof in the aqueous delivery system.

[0149] In general, an appropriate dose and treatment regimen provide the composition(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit (such as described herein, including an improved clinical outcome (e.g., a decrease in frequency, duration, or severity of diarrhea or associated dehydration, or inflammation, or longer disease-free and/or overall survival, or a lessening of symptom severity). For prophylactic use, a dose should be sufficient to prevent, delay the onset of, or diminish the severity of a disease associated with disease or disorder. Prophylactic benefit of the compositions administered according to the methods described herein can be determined by performing pre-clinical (including in vitro and in vivo animal studies) and clinical studies and analyzing data obtained therefrom by appropriate statistical, biological, and

clinical methods and techniques, all of which can readily be practiced by a person skilled in the art.

[0150] Compositions are administered in an effective amount (e.g., to treat a SARS-CoV-2 infection), which will vary depending upon a variety of factors including the activity of the specific compound employed; the metabolic stability and length of action of the compound; the age, body weight, general health, sex, and diet of the subject; the mode and time of administration; the rate of excretion; the drug combination; the severity of the particular disorder or condition; and the subject undergoing therapy. In certain embodiments, following administration of therapies according to the formulations and methods of this disclosure, test subjects will exhibit about a 10% up to about a 99% reduction in one or more symptoms associated with the disease or disorder being treated as compared to placebo-treated or other suitable control subjects.

[0151] Generally, a therapeutically effective daily dose of an antibody or antigen binding fragment is (for a 70 kg mammal) from about 0.001 mg/kg (i.e., 0.07 mg) to about 100 mg/kg (i.e., 7.0 g); preferably a therapeutically effective dose is (for a 70 kg mammal) from about 0.01 mg/kg (i.e., 0.7 mg) to about 50 mg/kg (i.e., 3.5 g); more preferably a therapeutically effective dose is (for a 70 kg mammal) from about 1 mg/kg (i.e., 70 mg) to about 25 mg/kg (i.e., 1.75 g). For polynucleotides, vectors, host cells, and related compositions of the present disclosure, a therapeutically effective dose may be different than for an antibody or antigen-binding fragment.

[0152] In certain embodiments, a method according to the present disclosure comprises administering to a subject a presently disclosed antibody or antigen-binding fragment at a dose of up to 100 mg, up to 150 mg, up to 200 mg, up to 250 mg, up to 300 mg, up to 350 mg, up to 400 mg, up to 450 mg, or up to 500 mg. In certain embodiments, a method comprises administering to a subject a presently disclosed antibody or antigen-binding fragment at a dose in a range from about 50 mg to about 500 mg, or in a range from about 50 mg to 100 mg, or in a range from about 100 mg to about 500 mg, or in a range from about 250 mg to about 500 mg. In some embodiments, a method comprises administering to a subject 50, 75, 100, 125, 150, 175, 200, 225, 250, 275, 300, 325, 350, 375, 400, 425, 450, 475, or 500 mg of the antibody or antigen-binding fragment. In some embodiments, a method comprises administering to a subject 50, 150, 250, or 500 mg of the antibody or antigen-binding fragment. In some embodiments, a method comprises administering to a subject 500 mg of the antibody or antigen-binding fragment.

[0153] In particular embodiments, the antibody or antigen-binding fragment comprises CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences of SEQ ID NOS.: 106, 121, 108, 169, 170, and 171, respectively. In further embodiments, the antibody or antigen-binding fragment comprises a VH comprising the amino acid sequence of SEQ ID NO.: 113 and a VL comprising the amino acid sequence of SEQ ID NO.: 168. In certain further embodiments, the antibody or antigen-binding fragment comprises M428L and N434S Fc mutations and/or G236A, A330L, and I332E Fc mutations.

[0154] A number of criteria are believed to contribute to high risk for contraction, transmission, progression of disease, and/or severe symptoms or death associated with a SARS CoV-2 infection. These include, but are not limited to,

age, occupation, general health, pre-existing health conditions, close contacts with subjects who have or are suspected to or are at risk of having a SARS-CoV-2 infection, and lifestyle habits. In some embodiments, a subject treated according to the present disclosure comprises one or more risk factors.

[0155] In certain embodiments, a human subject treated according to the present disclosure is an infant, a child, a young adult, an adult of middle age, or an elderly person. In certain embodiments, a human subject treated according to the present disclosure is less than 1 year old, or is 1 to 5 years old, or is between 5 and 125 years old (e.g., 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, or 125 years old, including any and all ages therein or therebetween). In certain embodiments, a human subject treated according to the present disclosure is 0-19 years old, 20-44 years old, 45-54 years old, 55-64 years old, 65-74 years old, 75-84 years old, or 85 years old, or older. Persons of middle, and especially of elderly age are believed to be at particular risk. In particular embodiments, the human subject is 45-54 years old, 55-64 years old, 65-74 years old, 75-84 years old, or 85 years old, or older. In some embodiments, the human subject is male. In some embodiments, the human subject is female.

[0156] In certain embodiments, a human subject (e.g., such as an at-risk subject or a high-risk subject) treated according to the present disclosure is a resident of a nursing home or a long-term care facility, is a hospice care worker, is a healthcare provider or healthcare worker, is a first responder, is a family member or other close contact of a subject diagnosed with or suspected of having a SARS-CoV-2 infection, is overweight or clinically obese, is or has been a smoker, has or had chronic obstructive pulmonary disease (COPD), is asthmatic (e.g., having moderate to severe asthma), has an autoimmune disease or condition (e.g., diabetes), and/or has a compromised or depleted immune system (e.g., due to AIDS/HIV infection, a cancer such as a blood cancer, a lymphodepleting therapy such as a chemotherapy, a bone marrow or organ transplantation, or a genetic immune condition), has chronic liver disease, has cardiovascular disease, has a pulmonary or heart defect, works or otherwise spends time in close proximity with others, such as in a factory, shipping center, hospital setting, or the like.

[0157] In some embodiments, a close contact comprises a subject that: (a) has resided with an index case in the 7 days prior to index diagnosis, and can include residence or staff in a congregate setting such as long-term care facility or nursing home; (b) is medical staff, first responder, or other care person engaging with the index case; and/or (c) is less than 3 days since last exposure (close contact with a person with SARS-CoV-2 infection) to the index case.

[0158] In certain embodiments, a subject treated according to the present disclosure has received a vaccine for SARS-CoV-2. In some embodiments, the vaccine is determined to be ineffective, e.g., by post-vaccine infection or symptoms in the subject, by clinical diagnosis or scientific or regulatory criteria. In certain embodiments, a subject treated according to the present disclosure has not received a vaccine for SARS-CoV-2. In certain embodiments, a subject treated according to the present disclosure has received convalescent plasma therapy, remdesivir, or both, for SARS-CoV-2.

[0159] In certain embodiments, treatment is administered as pre-exposure or peri-exposure prophylaxis. In certain

embodiments, treatment is administered to a subject with mild-to-moderate disease, which may be in an outpatient setting. In certain embodiments, treatment is administered to a subject with moderate-to-severe disease, such as requiring hospitalization. Sequelae of severe disease can include: respiratory failure; thromboembolic disease leading to pulmonary embolism and stroke; arrhythmia; shock; or any combination thereof. In certain embodiments, severe COVID-19 comprises (i) hypoxemia (O₂ saturation ≤93% on room air or PaO₂/FiO₂<300) requiring oxygen supplementation for more than 1 day or (ii) the subject requiring ≥4 L/min oxygen supplementation or equivalent.

[0160] In some embodiments, wherein the subject has, or is at risk for progressing to, critical COVID-19. Critical disease generally includes an increased risk of mortality as compared to severe disease. In some embodiments, critical COVID-19 comprises respiratory failure requiring at least one of the following: invasive mechanical ventilation and ECMO; shock; and multi-organ dysfunction/failure.

[0161] In certain embodiments, a subject is hospitalized with COVID-19, which can include, for example, admission or transfer to an intensive care unit (ICU).

[0162] In any of the presently disclosed embodiments, the subject having a SARS-CoV-2 infection: has mild-to-moderate COVID-19; is experiencing any one or more of: fever; cough; fatigue; shortness of breath or difficulty breathing; muscle aches; chills; sore throat; runny nose; headache; chest pain; loss of taste and/or smell; and pink eye (conjunctivitis); malaise; and abnormal imaging; has evidence of lower respiratory disease by clinical assessment or imaging and a saturation of oxygen (SaO₂) greater than (>) 93 percent (%) on room air at sea level, has a positive SARS-CoV-2 viral testing result, and/or is at high risk for progressing to severe COVID-19 and/or hospitalization, e.g., the human subject (1) is 65 years of age or older (≥65); has a body mass index (BMI) of 35 or greater (≥35); has chronic kidney disease; has diabetes; (5) has immunosuppressive disease, is receiving immunosuppressive treatment; is 55 years of age or older (≥55) and has cardiovascular disease, hypertension, chronic obstructive pulmonary disease, or other chronic respiratory disease; and/or is 12-17 years of age and has a BMI ≥85% for their age and gender, or sickle cell disease, congenital or acquired heart disease, neurodevelopmental disorders (e.g., cerebral palsy), a medical-related technological dependence (e.g., tracheostomy, gastrostomy, or positive pressure ventilation not related to COVID-19), or asthma, reactive airway or other chronic respiratory disease that requires daily medication for control; has recently been diagnosed with COVID-19 (e.g., within 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days) and/or is within 10 days of symptom onset; or has or is experiencing any combination of the foregoing. In some embodiments, a subject receiving therapy is 18 years old or older. In some embodiments, a subject receiving therapy is 55 years old or younger, provided that the subject is 18 years or older. In some embodiments, the subject has a laboratory confirmed COVID-19 infection by positive polymerase chain reaction (PCR; e.g., RT-PCR) test; e.g., on any type of respiratory tract sample). In some embodiments, a subject has peripheral capillary oxygen saturation (SpO₂) >94% room air (RA), who have experienced one or more symptoms of COVID-19 for ≤120 h (5 days). In some embodiments, a subject receiving therapy according to the present

disclosure is receiving or has received remdesivir, dexamethasone, tocilizumab, or any combination thereof. In any of the presently disclosed embodiments, the method can comprise administering a single dose of the antibody, antigen-binding fragment, or composition to the subject.

[0163] Typical routes of administering the presently disclosed compositions thus include, without limitation, oral, topical, transdermal, inhalation, parenteral, sublingual, buccal, rectal, vaginal, and intranasal. The term "parenteral", as used herein, includes subcutaneous injections, intravenous, intramuscular, intrasternal injection or infusion techniques. In certain embodiments, administering comprises administering by a route that is selected from oral, intravenous, parenteral, intragastric, intrapleural, intrapulmonary, intrarectal, intradermal, intraperitoneal, intratumoral, subcutaneous, topical, transdermal, intracisternal, intrathecal, intranasal, and intramuscular. In particular embodiments, a method comprises orally administering the antibody, antigen-binding fragment, polynucleotide, vector, host cell, or composition to the subject.

[0164] In preferred embodiments, a method comprises administering the antibody, antigen-binding fragment, or composition to the subject intravenously or intramuscularly.

[0165] In some embodiments, the subject: (i) is aged 18 to 49 years; (ii) is 18 years old or older; (iii) has mild to moderate COVID-19; (iv) has severe COVID-19; (v) has severe to critical COVID-19; (vi) has had fewer than seven days or 5 or fewer days since onset of symptoms; (vii) has had seven days or more since onset of symptoms; (viii) has had a positive reverse-transcriptase-polymerase-chain-reaction or antigen SARS-CoV-2 test result; (ix) is 55 years of age or older; (x) has one or more of: diabetes requiring medication, obesity (body-mass index >30 kg/m²), chronic kidney disease (estimated glomerular filtration rate <60 mL/min/1.73 m²), congestive heart failure (New York Heart Association class II or higher), chronic obstructive pulmonary disease (history of chronic bronchitis, chronic obstructive lung disease, or emphysema with dyspnea on physical exertion), and moderate to severe asthma (subject requires an inhaled steroid to control symptoms or has been prescribed a course of oral steroids in the past year); or (xi) any combination of (i)-(x).

[0166] As discussed further herein, administration can include, for example, intravenous administration or intramuscular administration. In some embodiments, a single dose of the antibody or antigen-binding fragment is administered to a subject intravenously over the course of 30 minutes, 60 minutes, or 90 minutes.

[0167] In certain embodiments, a method comprises administering the antibody, antigen-binding fragment, polynucleotide, vector, host cell, or composition to the subject at 2, 3, 4, 5, 6, 7, 8, 9, 10 times, or more.

[0168] In certain embodiments, a method comprises administering the antibody, antigen-binding fragment, or composition to the subject a plurality of times, wherein a second or successive administration is performed at about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 24, about 48, about 74, about 96 hours, or more, following a first or prior administration, respectively.

[0169] In certain embodiments, a method comprises administering the antibody, antigen-binding fragment, polynucleotide, vector, host cell, or composition at least one time prior to the subject being infected by the SARS-CoV-2.

[0170] In certain embodiments, the subject receiving treatment is 18 or more years of age with laboratory-confirmed (e.g., by PCR test) SARS-CoV-2 infection.

[0171] In some embodiments, the subject has a clinical status of Grade 4 (hospitalized, oxygen by mask or nasal prongs), 5 (hospitalized, on non-invasive ventilation, or high flow oxygen), 6 (hospitalized, intubation and mechanical ventilation) or 7 (ventilation and additional organ support-pressors, renal replacement therapy (RRT), extracorporeal membrane oxygenation (ECMO)), as defined by the WHO clinical severity score, 9-point ordinal scale.

[0172] In some embodiments, the subject has mild-to-moderate COVID-19. In some embodiments, the subject is at-risk of progression to severe COVID-19. In some embodiments, following administration of the antibody, antigen-binding fragment, or composition to the subject, the subject is at a reduced risk of hospitalization for COVID-19. In certain embodiments, following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 10% or more, 20% or more, 30% or more, 40% or more, 50% or more, 60% or more, 70% or more, 80% or more, or 85% or more.

[0173] In some embodiments, the subject has or is at risk for progressing to severe COVID-19, wherein, optionally, severe COVID-19 comprises (i) hypoxemia (O₂ saturation ≤93% on room air or PaO₂/FiO₂<300) requiring oxygen supplementation for more than 1 day or (ii) the subject requiring ≥4 L/min oxygen supplementation or equivalent.

[0174] In some embodiments, the subject has or is at risk for progressing to critical COVID-19, wherein, optionally, critical COVID-19 comprises respiratory failure requiring at least one of the following: invasive mechanical ventilation and ECMO; shock; and multi-organ dysfunction/failure.

[0175] In some embodiments, the subject is less than seven days since onset of symptoms. In other embodiments, the subject is seven days or more since onset of symptoms.

[0176] In some embodiments, the subject is any one or more of (i)-(iii): (i) 18 years of age or older and has a positive SARS-CoV-2 test result (by any validated test e.g. RT-PCR on any specimen type); (ii) (1) hospitalized with severe COVID-19 disease defined as requirement for supplemental oxygen or non-invasive ventilation consistent with Grade 4 or Grade 5 disease or (2) hospitalized with critical COVID-19 disease defined as those on mechanical ventilation (Grade 6 or Grade 7 disease); (iii) is male or female, wherein, optionally, (1) the woman is non-child-bearing potential (WONCBP) or (2) is a woman of child-bearing potential (WOCBP) and uses a contraceptive method.

[0177] In any of the presently disclosed embodiments, the method can comprise administering 500 mg of the antibody or antigen-binding fragment to the subject.

[0178] In any of the presently disclosed embodiments, the subject can have had or can have close contacts to a person with a confirmed SARS-CoV-2 infection.

[0179] In any of the presently disclosed embodiments, treating can comprise preventing infection by SARS-CoV-2 and/or COVID-19. In any of the presently disclosed embodiments, treating can comprise preventing progression of COVID-19 in the subject. In any of the presently disclosed embodiments, treating can comprise preventing contraction and/or transmission of symptomatic COVID-19. In any of the presently disclosed embodiments, treating can comprise

preventing contraction and/or transmission of asymptomatic COVID-19. In any of the presently disclosed embodiments, the subject can be at-risk for contracting or progressing on COVID-19.

[0180] In any of the presently disclosed embodiments, treating can comprise preventing or reducing: (1) one or more acute respiratory symptom selected from: cough; sputum production; sore throat; and shortness of breath; or (2) fever of greater than 38° C.; (3) two or more of the following symptoms: fatigue; myalgias/arthritis; chills; nausea/vomiting; diarrhea; and anosmia/dysgeusia.

[0181] In any of the presently disclosed embodiments, treating can comprise preventing or reducing one or more of the following symptoms: fever of greater than 38° C.; chills; cough; sore throat; malaise; headache; myalgia; a change in smell or taste; nasal congestion/rhinorrhea; vomiting; diarrhea; shortness of breath on exertion.

[0182] In any of the presently disclosed embodiments, the subject can be an adult. In any of the presently disclosed embodiments, the subject can be 18 or more years of age, or can be 19 or more years of age. In any of the presently disclosed embodiments, the subject can be 55 years of age or is, or is 65 years of age or is older.

[0183] In any of the presently disclosed embodiments, administering the antibody, antigen-binding fragment, or composition can comprise intravenous infusion. In any of the presently disclosed embodiments, administering the antibody, antigen-binding fragment, or composition can comprise intramuscular injection.

[0184] In any of the presently disclosed embodiments, the method can comprise administering 250 mg of the antibody or antigen-binding fragment to the subject. In any of the presently disclosed embodiments, the method can comprise administering 500 mg of the antibody or antigen-binding fragment to the subject.

[0185] In any of the presently disclosed embodiments, the subject can have a mild-to-moderate SARS-2-CoV infection (e.g., has mild-to-moderate COVID-19) and, optionally, be at risk for progression to severe disease.

[0186] In any of the presently disclosed embodiments, the subject: (i) can be 12 years old or older; and (ii) have last had contact with a person with a confirmed SARS-CoV-2 infection less than three days prior to administration of the composition.

[0187] In any of the presently disclosed embodiments, the subject has mild-to-moderate COVID-19 and the method comprises administering a single dose of the antibody, antigen-binding fragment, or composition to the subject intramuscularly.

[0188] In any of the presently disclosed embodiments, the single dose comprises 250 mg of the antibody or antigen-binding fragment. In some embodiments, a single dose according to a treatment method comprises 500 mg of the antibody or antigen-binding fragment.

[0189] In some embodiments: (i) (i)(a) the subject is 12 years of age or older and is at high risk of progression of COVID-19 or (i)(b) the subject is 65 years of age or older; and/or (ii) the subject has a positive SARS-CoV-2 test result (e.g., by PCR test), has oxygen saturation ≥94% on room air, has COVID-19 symptoms, and is less than or equal to 7 days from onset of symptoms.

[0190] In any of the presently disclosed embodiments: (i) (i)(a) the subject can be 12 years of age or older and is at high risk of progression of COVID-19 or (i)(b) the subject

can be 65 years of age or older; and (ii) the subject can have a positive SARS-CoV-2 test result (e.g., by PCR test), has oxygen saturation $\geq 94\%$ on room air, has COVID-19 symptoms, and is less than or equal to 7 days from onset of symptoms.

[0191] In any of the presently disclosed embodiments, the subject is not hospitalized and is at high-risk for (i) hospitalization and/or (ii) progression of COVID-19.

[0192] In any of the presently disclosed embodiments, the subject can be: (1) 12 or more years of age and, optionally, at high risk of progression of COVID-19; and/or (2) 65 or more years of age. In any of the presently disclosed embodiments, the subject can have had a positive SARS-CoV-2 test result, has oxygen saturation $\geq 94\%$ on room air, has COVID-19 symptoms, and is less than or equal to 7 days from onset of symptoms.

[0193] In any of the presently disclosed embodiments, the antibody or antigen-binding fragment was obtained from a non-clonal pool of cells stably transfected with a polynucleotide encoding the antibody or antigen-binding fragment. In any of the presently disclosed embodiments, the antibody or antigen-binding fragment was obtained from a clonal master cell bank. A Master Cell Bank (MCB) is produced from an original antibody/antigen-binding fragment-producing cell line. A MCB is generally cryopreserved in multiple vials to prevent genetic variation and potential contamination by eliminating the total number of times a cell line is passaged or handled during the manufacturing process. A MCB is preferably tested for contaminants such as bacteria, fungi, and mycoplasmas; these should not be present in the MCB.

[0194] In any of the presently disclosed embodiments, the subject: is a resident of a nursing home or a long-term care facility; is a hospice care worker; is a healthcare provider or healthcare worker; is a first responder; is a family member or other close contact of a subject diagnosed with or suspected of having a SARS-CoV-2 infection, is overweight or clinically obese; is or has been a smoker; has or had chronic obstructive pulmonary disease (COPD); is asthmatic (e.g., having moderate to severe asthma); has an autoimmune disease or condition (e.g., diabetes); has a compromised or depleted immune system (e.g., due to AIDS/HIV infection, a cancer such as a blood cancer, a lymphodepleting therapy such as a chemotherapy, a bone marrow or organ transplantation, or a genetic immune condition); has chronic liver disease; has cardiovascular disease; and/or has a pulmonary or heart defect; and/or works or otherwise spends time in close proximity with others, such as in a factory, shipping center, hospital setting, or the like. In any of the presently disclosed embodiments, the subject has received a vaccine for SARS-CoV-2 and the vaccine is determined to be ineffective, e.g., by post-vaccine infection or symptoms in the subject, by clinical diagnosis or scientific or regulatory criteria. In any of the presently disclosed embodiments, the subject has not received a vaccine for SARS-CoV-2.

[0195] In any of the presently disclosed embodiments, the subject has received convalescent plasma therapy, remdesivir, or both, for SARS-CoV-2. In any of the presently disclosed embodiments, treatment comprises pre-exposure or peri-exposure prophylaxis. In any of the presently disclosed embodiments, treatment is administered to the subject having mild-to-moderate disease, optionally in an outpatient setting. In any of the presently disclosed embodiments, treatment is administered to a subject with moderate-to-severe disease, such as requiring hospitaliza-

tion. In any of the presently disclosed embodiments, the subject is hospitalized with COVID-19.

[0196] In any of the presently disclosed embodiments, the subject having a SARS-CoV-2 infection: has mild-to-moderate COVID-19; is experiencing any one or more of: fever; cough; fatigue; shortness of breath or difficulty breathing; muscle aches; chills; sore throat; runny nose; headache; chest pain; loss of taste and/or smell; and pink eye (conjunctivitis); malaise; and abnormal imaging; has evidence of lower respiratory disease by clinical assessment or imaging and a saturation of oxygen (SaO_2) greater than ($>$) 93 percent (%) on room air at sea level, has a positive SARS-CoV-2 viral testing result, and/or is at high risk for progressing to severe COVID-19 and/or hospitalization, e.g., the human subject (1) is 65 years of age or older (≥ 65); has a body mass index (BMI) of 35 or greater (≥ 35); has chronic kidney disease; has diabetes; (5) has immunosuppressive disease, is receiving immunosuppressive treatment; is 55 years of age or older (≥ 55) and has cardiovascular disease, hypertension, chronic obstructive pulmonary disease, or other chronic respiratory disease; and/or is 12-17 years of age and has a BMI $\geq 85\%$ for their age and gender, or sickle cell disease, congenital or acquired heart disease, neurodevelopmental disorders (e.g., cerebral palsy), a medical-related technological dependence (e.g., tracheostomy, gastrostomy, or positive pressure ventilation not related to COVID-19), or asthma, reactive airway or other chronic respiratory disease that requires daily medication for control; has recently been diagnosed with COVID-19 (e.g., within 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days) and/or is within 10 days of symptom onset; or has or is experiencing any combination of the foregoing.

[0197] In any of the presently disclosed embodiments, the subject is (a) 18 years old or older, or (b) 55 years old or younger, provided that the subject is 18 years or older. In any of the presently disclosed embodiments, the subject has a laboratory confirmed COVID-19 infection by positive polymerase chain reaction (PCR; e.g., RT-PCR) test; e.g., on any type of respiratory tract sample). In any of the presently disclosed embodiments, the subject has peripheral capillary oxygen saturation (SpO_2) $> 94\%$ room air (RA), and has experienced one or more symptoms of COVID-19 for ≤ 120 h (5 days). In any of the presently disclosed embodiments, the subject is further receiving or has received remdesivir, supplemental oxygen, ventilation therapy, respiration therapy, dexamethasone, tocilizumab, or any combination thereof.

[0198] In some embodiments, one or more of the following does not apply to a subject receiving therapy according to the present disclosure: any condition that would prohibit receipt of intramuscular injections such as coagulation disorder, bleeding diathesis, or thrombocytopenia; known allergy or hypersensitivity to any constituent present in an antibody composition; previous anaphylaxis or hypersensitivity to a monoclonal antibody; has previously received a COVID-19 vaccine; has previously received SARS-CoV-2 hyperimmune intravenous immunoglobulin (hIgIG) from COVID-19 survivors; has previously received convalescent plasma from a recovered COVID-19 patient or an anti-SARS-CoV-2 mAb; is a pregnant or breast-feeding female; Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) > 5 times the upper limit of normal (ULN); Stage 4 severe chronic kidney disease or requiring dialysis

(i.e., estimated glomerular filtration rate <30 mL/min/1.73 m²); has symptoms consistent with severe COVID-19 as defined by shortness of breath at rest or respiratory distress or requiring supplemental oxygen; severely immunocompromised participants including but not limited to cancer patients receiving immunosuppressive chemotherapy or immunotherapy, those with a solid organ transplant or allogeneic stem cell transplant within the last 3 months, any history of heart or lung transplant or high dose long-term systemic corticosteroids (equivalent to ≥20 mg a day of prednisone or the systemic equivalent for over 2 weeks); had diabetes (requiring medication), chronic kidney disease (i.e., eGFR <60 as determined by the Modification of Diet in Renal Disease (MDRD) study), chronic liver disease (e.g., cirrhosis), congestive heart failure (New York Heart Association (NYHA) class II or more), chronic obstructive pulmonary disease (history of chronic bronchitis, chronic obstructive lung disease, or emphysema with dyspnoea on physical exertion), and moderate to severe asthma (participant requires an inhaled steroid to control symptoms or has been prescribed a course of oral steroids in the past year); previous anaphylaxis or hypersensitivity to a monoclonal antibody; end-organ dysfunction such as—a. stroke b. meningitis c. encephalitis d. myelitis e. myocardial infarction f. myocarditis g. pericarditis h. symptomatic congestive heart failure (New York Heart Association [NYHA] class III-IV) i. arterial or deep venous thrombosis or pulmonary embolism; end-organ failure category such as—a. requirement for high-flow oxygen, non-invasive ventilation, or invasive mechanical ventilation b. extracorporeal membrane oxygenation (ECMO) c. mechanical circulatory support (e.g., intra-aortic balloon pump, ventricular assist device) d. vasopressor therapy e. commencement of renal replacement therapy (RRT) during this admission (i.e. not patients on chronic RRT); stroke; meningitis; encephalitis; myelitis; myocardial ischemia; myocarditis; pericarditis; symptomatic congestive heart failure; arterial or deep venous thrombosis or pulmonary embolism; and current or imminent requirement for invasive mechanical ventilation, ECMO (extracorporeal membrane oxygenation). Mechanical circulatory support, vasopressor therapy, or commencement of renal replacement therapy at this admission (i.e. not patients on chronic renal replacement therapy).

[0199] Compositions comprising an antibody, antigen-binding fragment, polynucleotide, vector, host cell, or composition of the present disclosure may also be administered simultaneously with, prior to, or after administration of one or more other therapeutic agents. Such combination therapy may include administration of a single pharmaceutical dosage formulation which contains a compound of the invention and one or more additional active agents, as well as administration of compositions comprising an antibody or antigen-binding fragment of the disclosure and each active agent in its own separate dosage formulation. For example, an antibody or antigen-binding fragment thereof as described herein and the other active agent can be administered to the patient together in a single oral dosage composition such as a tablet or capsule, or each agent administered in separate oral dosage formulations. Similarly, an antibody or antigen-binding fragment as described herein and the other active agent can be administered to the subject together in a single parenteral dosage composition such as in a saline solution or other physiologically acceptable solution, or each agent administered in separate parenteral dosage formulations.

Where separate dosage formulations are used, the compositions comprising an antibody or antigen-binding fragment and one or more additional active agents can be administered at essentially the same time, i.e., concurrently, or at separately staggered times, i.e., sequentially and in any order; combination therapy is understood to include all these regimens.

[0200] In certain embodiments, a combination therapy is provided that comprises one or more anti-SARS-CoV-2 antibody (or one or more nucleic acid, host cell, vector, or composition) of the present disclosure and one or more anti-inflammatory agent and/or one or more anti-viral agent. In particular embodiments, the one or more anti-inflammatory agent comprises a corticosteroid such as, for example, dexamethasone, prednisone, or the like. In some embodiments, the one or more anti-inflammatory agents comprise a cytokine antagonist such as, for example, an antibody that binds to IL6 (such as siltuximab), or to IL-6R (such as tocilizumab), or to IL-1β, IL-7, IL-8, IL-9, IL-10, FGF, G-CSF, GM-CSF, IFN-γ, IP-10, MCP-1, MIP-1A, MIP1-B, PDGR, TNF-α, or VEGF. In some embodiments, anti-inflammatory agents such as ruxolitinib and/or anakinra are used. In some embodiments, the one or more anti-viral agents comprise nucleotide analogs or nucleotide analog prodrugs such as, for example, remdesivir, sofosbuvir, acyclovir, and zidovudine. In particular embodiments, an anti-viral agent comprises lopinavir, ritonavir, favipiravir, leronlimab or any combination thereof. Other anti-inflammatory agents for use in a combination therapy of the present disclosure include non-steroidal anti-inflammatory drugs (NSAIDS). It will be appreciated that in such a combination therapy, the one or more antibody (or one or more nucleic acid, host cell, vector, or composition) and the one or more anti-inflammatory agent and/or one or more antiviral agent can be administered in any order and any sequence, or together.

[0201] In some embodiments, an antibody (or one or more nucleic acid, host cell, vector, or composition) is administered to a subject who has previously received one or more anti-inflammatory agent and/or one or more antiviral agent. In some embodiments, one or more anti-inflammatory agent and/or one or more antiviral agent is administered to a subject who has previously received an antibody (or one or more nucleic acid, host cell, vector, or composition).

[0202] In certain embodiments, a combination therapy is provided that comprises two or more anti-SARS-CoV-2 antibodies of the present disclosure. A method can comprise administering a first antibody to a subject who has received a second antibody, or can comprise administering two or more antibodies together. For example, in particular embodiments, a method is provided that comprises administering to the subject (a) a first antibody or antigen-binding fragment, when the subject has received a second antibody or antigen-binding fragment; (b) the second antibody or antigen-binding fragment, when the subject has received the first antibody or antigen-binding fragment; or (c) the first antibody or antigen-binding fragment, and the second antibody or antigen-binding fragment.

[0203] In a related aspect, uses of the presently disclosed antibodies, antigen-binding fragments, vectors, host cells, and compositions are provided.

[0204] In certain embodiments, any of the presently disclosed antibodies, antigen-binding fragments, polynucleotides, vectors, host cells, or compositions is provided for

use in a method (e.g., any of the presently disclosed methods) of treating a SARS-CoV-2 infection and/or COVID-19 in a subject.

[0205] In certain embodiments, any of the presently disclosed antibodies, antigen-binding fragments, or compositions is provided for use in a method of manufacturing or preparing a medicament for treating a SARS-CoV-2 infection and/or COVID-19 in a subject.

[0206] The present disclosure also provides the following Embodiments.

[0207] Embodiment 1. 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: (i) the CDRH1 comprises or consists of the amino acid sequence according to any one of SEQ ID NOs.: 2, 56, 64, 80, 88, 96, 106, 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 according to any one of SEQ ID NOs.: 3, 16-22, 57, 65, 81, 89, 97, 107, 121-126, 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 according to any one of SEQ ID NOs.: 4, 25, 26, 58, 66, 82, 90, 98, 104, 108, 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 according to any one of SEQ ID NOs.: 6, 51-54, 60, 68, 73, 74, 84, 92, 100, 110, 160, 169, 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 according to any one of SEQ ID NOs.: 7, 61, 69, 85, 93, 101, 111, 161, 170, 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 according to any one of SEQ ID NOs.: 8, 62, 70, 77, 78, 86, 94, 102, 112, 151-154, 162, 171, 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 surface glycoprotein of a SARS-CoV-2 expressed on a cell surface of a host cell and/or on a virion.

[0208] Embodiment 2. The antibody or antigen-binding fragment of Embodiment 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.

[0209] Embodiment 3. The antibody or antigen-binding fragment of any one of Embodiments 1-2, comprising CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to SEQ ID NOs.: (i) 2-4 and 6-8 or 235-237, respectively; (ii) 2, any one of 16-22, 4, and 6-8 or 235-237, respectively; (iii) 2, 3, any one of 25-26, and 6-8 or 235-237, respectively; (iv) 2-4, 51, 7 or 236, and 8 or 237, respectively; (v) 2-4, 52, 7 or 236, and 8 or 237, respectively; (vi) 2-4, 53, 7 or 236, and 8 or 237, respectively; (vii) 2-5, 54, 7 or 236, and 8 or 237, respectively; (viii) 56-58 and 60-62, respectively; (ix) 64-66 and 68-70, respectively; (x) 64-66, 73 or 74, 69, and 70, respectively; (xi) 64-66, 68, 69, and 77 or 78, respectively; (xii) 80-82 and 84-86, respectively; (xiii) 88-90 and 92-94, respectively; (xiv) 96-98 and 101-102, respectively; (xv) 96, 97, 104, and 100-102, respectively; (xvi) 106-108 and 110-112 or 167-171, respectively; (xvii) 106, any one of 121-126, 108, and 110-112, respectively; (xviii) 106, 107, 127 or 128, and 110-112, respectively; (xix) 106-108, 110, 111, and 151, respectively; (xx) 106-108, 110, 111, and 152, respectively; (xxi) 106-108, 110, 111, and 153, respectively; (xxii) 106-108, 110, 111, and 154, respectively; (xxiii) 106-108 and 169-171, respectively; (xxiv) 156-158 and 160-162, respectively; (xxv) 106, 123, 127, and 169-171, respectively; (xxvi) 2, 17, 25, 6 or 235 or any one of 51-54, 7 or 236, and 8 or 237, respectively; (xxvii) 2, 20, 25, 6 or 235 or any one of 51-54, 7 or 236, and 8 or 237, respectively; or (xxviii) 179-181 and 183-185, respectively (xxix) 195, 180, 181 and 183-185, respectively; (xxx) 195, 197, 181 and 183-185, respectively; (xxxi) 195, 199, 181 and 183-185, respectively; (xxxii) 195, 197, 201 and 183-185, respectively; (xxxiii) 195, 197, 203 and 183-185, respectively; (xxxiv) 195, 199, 201 and 183-185, respectively; (xxxv) 195, 199, 203 and 183-185, respectively; (xxxvi) 179, 180, 181 and 183-185, respectively; (xxxvii) 179, 197, 181 and 183-185, respectively; (xxxviii) 179, 199, 181 and 183-185, respectively; (xxxix) 179, 197, 201 and 183-185, respectively; (xxxx) 179, 197, 203 and 183-185, respectively; (xxxxi) 179, 199, 201 and 183-185, respectively; (xxxxii) 179, 199, 203 and 183-185, respectively; (xxxxiii) 179, 180, 201 and 183-185, respectively; (xxxxiv) 179, 180, 203 and 183-185, respectively; and (xxxxv) 240-242 and 244-246, respectively.

[0210] Embodiment 4. The antibody or antigen-binding fragment of any one of Embodiments 1-5, wherein: (i) the VH comprises or consists of an amino acid sequence having at least 85% identity to the amino acid sequence according to any one of SEQ ID NOs.: 1, 9-15, 23, 24, 27, 28-46, 55, 63, 79, 87, 95, 103, 105, 113-120, 129-146, 155, 172, 176-178, 194, 196, 198, 200, 202, and 239, wherein the variation 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 according to any one of SEQ ID NOs.: 5, 47-50, 59, 67, 71-72, 75, 76, 83, 91, 99, 109, 147-150, 159, 168, 182, 190, 234, and 243, wherein the variation is optionally limited to one or more framework regions and/or the variation comprises one or more substitution to a germline-encoded amino acid.

[0211] Embodiment 5. The antibody or antigen-binding fragment of any one of Embodiments 1-6, wherein the VH comprises or consists of any VH amino acid sequence set forth in Table 1, and wherein the VL comprises or consists

of any VL amino acid sequence set forth in Table 1, wherein, optionally, the VH and the VL comprise or consist of the amino acid sequences according to SEQ ID NOs.: (i) 1 and 5 or 234, respectively; (ii) any one of 9-15 and 5 or 234, respectively; (iii) 23 or 24 and 5 or 234, respectively; (iv) 27 and 5 or 234, respectively; (v) any one of 28-46 and 5 or 234, respectively; (vi) 1 and any one of 47-50, respectively; (vii) any one of 9-15 and any one of 47-50, respectively; (viii) 23 or 24 and any one of 47-50, respectively; (ix) 27 and any one of 47-50, respectively; (x) any one of 28-46 and any one of 47-50, respectively; (xi) 55 and 59, respectively; (xii) 63 and 67, respectively; (xiii) 63 and 71 or 72, respectively; (xiv) 63 and 75 or 76, respectively; (xv) 79 and 83, respectively; (xvi) 87 and 91, respectively; (xvii) 95 and 99, respectively; (xviii) 103 and 99, respectively; (xix) 105 and 109 or 168, respectively; (xx) any one of 113-120 and 109 or 168, respectively; (xxi) 129 and 109 or 168, respectively; (xxii) any one of 130-146 and 109 or 168, respectively; (xxiii) 105 and any one of 147-150, respectively; (xxiv) any one of 113-120 and any one of 147-150, respectively; (xxv) any one of 130-146 and any one of 147-150, respectively; (xxvi) 155 and 159, respectively; (xxvii) 172 and 168, respectively; (xxviii) 176 or 177 and 5 or 234 or any one of 47-50, respectively; (xxix) 178 and 182 or 190, respectively; (xxx) 194 and 182, respectively; (xxxi) 196 and 182, respectively; (xxxii) 198 and 182, respectively; (xxxiii) 200 and 182, respectively; (xxxiv) 202 and 182, respectively; or (xxxv) 239 and 243, respectively.

[0212] Embodiment 6. 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 as set forth in SEQ ID NO: 79 and the VL comprises or consists of the amino acid sequence as set forth in SEQ ID NO: 83.

[0213] Embodiment 7. 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.

[0214] Embodiment 8. 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 as set forth in SEQ ID NO: 105 and the VL comprises or consists of the amino acid sequence as set forth in SEQ ID NO: 168.

[0215] Embodiment 9. 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.

[0216] Embodiment 10. 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 as set

forth in SEQ ID NO: 178 and the VL comprises or consists of the amino acid sequence as set forth in SEQ ID NO: 182 or SEQ ID NO: 190.

[0217] Embodiment 11. 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.

[0218] Embodiment 12. The antibody or antigen-binding fragment of any one of Embodiments 1-11, which: (i) recognizes an epitope in the ACE2 receptor binding motif (RBM, SEQ ID NO.: 167) of SARS-CoV-2; (ii) is capable of blocking an interaction between SARS-CoV-2 (e.g., 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; (iv) is capable of staining about 30%, about 35%, about 40%, about 50%, about 55%, about 56%, about 57%, about 58%, about 59%, about 60%, or more of target cells expressing SARS-CoV-2 surface glycoprotein in a sample comprising about 50,000 of the target cells in approximately 100 µL when the antibody or antigen-binding fragment is present at 10 µg/ml; (v) 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).

[0219] Embodiment 13. The antibody or antigen-binding fragment of any one of Embodiments 1-12, which is a IgG, IgA, IgM, IgE, or IgD isotype.

[0220] Embodiment 14. The antibody or antigen-binding fragment of any one of Embodiments 1-13, which is an IgG isotype selected from IgG1, IgG2, IgG3, and IgG4.

[0221] Embodiment 15. The antibody or antigen-binding fragment of any one of Embodiments 1-14, which is human, humanized, or chimeric.

[0222] Embodiment 16. The antibody or antigen-binding fragment of any one of Embodiments 1-15, 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.

[0223] Embodiment 17. The antibody or antigen-binding fragment of Embodiment 16, wherein the scFab comprises: (i) the amino acid sequence as set forth in any one of SEQ ID NOs: 218-219 and 226-227; (ii) a VL comprising the amino acid sequence as set forth in SEQ ID NO: 168 and a VH comprising the amino acid sequence as set forth in SEQ ID NO: 105 or SEQ ID NO: 113; or (iii) a CDRH1 comprising the amino acid sequence as set forth in SEQ ID NO: 106, a CDRH2 comprising the amino acid sequence as set forth in SEQ ID NO: 107 or 121, a CDRH3 comprising the amino acid sequence as set forth in SEQ ID NO: 108, a CDRL1 comprising the amino acid sequence as set forth in SEQ ID NO: 169, a CDRL2 comprising the amino acid sequence as set forth in SEQ ID NO: 170, and a CDRL3 comprising the amino acid sequence as set forth in SEQ ID NO: 171.

[0224] Embodiment 18. The antibody or antigen-binding fragment of Embodiment 16, wherein the scFv comprises: (i) the amino acid sequence as set forth in any one of SEQ ID NOs: 220-221 or 228-229; (ii) a VL comprising the amino acid sequence as set forth in SEQ ID NO: 168 and a VH comprising the amino acid sequence as set forth in SEQ ID NO: 105 or SEQ ID NO: 113; or (iii) a CDRH1 comprising the amino acid sequence as set forth in SEQ ID NO: 106, a CDRH2 comprising the amino acid sequence as set forth in SEQ ID NO: 107 or 121, a CDRH3 comprising the amino acid sequence as set forth in SEQ ID NO: 108, a CDRL1 comprising the amino acid sequence as set forth in SEQ ID NO: 169, a CDRL2 comprising the amino acid sequence as set forth in SEQ ID NO: 170, and a CDRL3 comprising the amino acid sequence as set forth in SEQ ID NO: 171.

[0225] Embodiment 19. The antibody or antigen-binding fragment of Embodiment 16, wherein the scFv comprises more than one VH domain and more than one VL domain.

[0226] Embodiment 20. The antibody or antigen-binding fragment of Embodiment 19, wherein the scFv comprises: (i) the amino acid sequence as set forth in any one of SEQ ID NO: 222-225 or SEQ ID NO: 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 as set forth in SEQ ID NO: 169, a CDRL2 comprising the amino acid sequence as set forth in SEQ ID NO: 170, and a CDRL3 comprising the amino acid sequence as set forth in SEQ ID NO: 171, and two VH domains, each comprising a CDRH1 comprising the amino acid sequence as set forth in SEQ ID NO: 106, a CDRH2 comprising the amino acid sequence as set forth in SEQ ID NO: 107 or 121, a CDRH3 comprising the amino acid sequence as set forth in SEQ ID NO: 108.

[0227] Embodiment 21. The antibody or antigen-binding fragment of any one of Embodiments 1-19, wherein the antibody or antigen-binding fragment is a multi-specific antibody or antigen binding fragment.

[0228] Embodiment 22. The antibody or antigen-binding fragment of Embodiment 21, wherein the antibody or antigen binding fragment is a bispecific antibody or antigen-binding fragment.

[0229] Embodiment 23. The antibody or antigen-binding fragment of Embodiment 21 or 22, 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.: 1, 9-15, 23, 24, 27-46, 55, 63, 79, 87, 95, 103, 105, 113-120, 129-146, 155, 172, 176-178, 194, 196, 198, 200, 202 and 239, and 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.: 5, 47-50, 59, 67, 71, 72, 75, 76, 83, 91, 99, 109, 147-150, 159, 168, 182, 190, 234, and 243;

[0230] 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.

[0231] Embodiment 24. The antibody or antigen-binding fragment of any one of Embodiments 1-23, wherein the antibody or antigen-binding fragment further comprises a Fc polypeptide or a fragment thereof.

[0232] Embodiment 25. The antibody or antigen-binding fragment of Embodiment 24, 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.

[0233] Embodiment 26. The antibody or antigen-binding fragment of Embodiment 25, 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.

[0234] Embodiment 27. The antibody or antigen-binding fragment of Embodiment 25 or 26, 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).

[0235] Embodiment 28. The antibody or antigen-binding fragment of any one of Embodiments 25-27, wherein the mutation that enhances binding to FcRn comprises M428L/N434S.

[0236] Embodiment 29. The antibody or antigen-binding fragment of any one of Embodiments 25-28, wherein the mutation that enhances binding to a FcγR comprises S239D; I332E; A330L; G236A; or any combination thereof.

[0237] Embodiment 30. The antibody or antigen-binding fragment of any one of Embodiments 25-29, 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.

[0238] Embodiment 31. The antibody or antigen-binding fragment of any one of Embodiments 1-30, 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.

[0239] Embodiment 32. An isolated polynucleotide encoding the antibody or antigen-binding fragment of any one of Embodiments 1-31, or encoding a VH, a heavy chain, a VL, and/or a light chain of the antibody or the antigen-binding fragment.

[0240] Embodiment 33. The polynucleotide of Embodiment 32, wherein the polynucleotide comprises deoxyribonucleic acid (DNA) or ribonucleic acid (RNA), wherein the RNA optionally comprises messenger RNA (mRNA).

[0241] Embodiment 34. The polynucleotide of Embodiment 32 or 33, which is codon-optimized for expression in a host cell.

[0242] Embodiment 35. The polynucleotide of any one of Embodiments 32-34, 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.

[0243] Embodiment 36. A recombinant vector comprising the polynucleotide of any one of Embodiments 32-35.

[0244] Embodiment 37. A host cell comprising the polynucleotide of any one of Embodiments 32-35 and/or the vector of Embodiment 36, wherein the polynucleotide is heterologous to the host cell.

[0245] Embodiment 38. A human B cell comprising the polynucleotide of any one of Embodiments 32-35, wherein the polynucleotide is heterologous to the human B cell and/or wherein the human B cell is immortalized.

[0246] Embodiment 39. A composition comprising: (i) the antibody or antigen-binding fragment of any one of Embodiments 1-31 or 49-52; (ii) the polynucleotide of any one of Embodiments 32-35; (iii) the recombinant vector of Embodiment 36; (iv) the host cell of Embodiment 37; and/or (v) the human B cell of Embodiment 38, and a pharmaceutically acceptable excipient, carrier, or diluent.

[0247] Embodiment 40. The composition of Embodiment 39, comprising two or more antibodies or antigen-binding fragments of any one of Embodiments 1-31 or 49-52.

[0248] Embodiment 41. The composition of Embodiment 40, comprising:

[0249] (i) a first antibody or antigen-binding fragment, comprising a VH comprising or consisting of the amino acid sequence as set forth in SEQ ID NO: 79 and a VL comprising or consisting of the amino acid sequence as set forth in SEQ ID NO: 83; and

[0250] (ii) a second antibody or antigen-binding fragment comprising, a VH comprising or consisting of the amino acid sequence as set forth in SEQ ID NO: 105 and a VL comprising of consisting of the amino acid sequence as set forth in SEQ ID NO: 168.

[0251] Embodiment 42. The composition of Embodiment 40, comprising:

[0252] (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.

[0253] Embodiment 43. The composition of Embodiment 40, comprising:

[0254] (i) a first antibody or antigen-binding fragment, comprising a VH comprising or consisting of the amino acid sequence as set forth in SEQ ID NO: 178 and a VL comprising or consisting of the amino acid sequence as 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 as set forth in SEQ ID NO: 105 and a VL comprising of consisting of the amino acid sequence as set forth in SEQ ID NO: 168.

[0255] Embodiment 44. The composition of Embodiment 40, comprising:

[0256] (i) a first antibody or antigen-binding fragment comprising a heavy chain variable domain (VH) com-

prising 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.

[0257] Embodiment 45. The composition of Embodiment 40, comprising:

[0258] (i) a first antibody or antigen-binding fragment, comprising a VH comprising or consisting of the amino acid sequence as set forth in SEQ ID NO: 178 and a VL comprising or consisting of the amino acid sequence as 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 as set forth in SEQ ID NO: 63 and a VL comprising or consisting of the amino acid sequence as set forth in SEQ ID NO: 67, any one of SEQ ID NO: 71-71, or any one of SEQ ID NO: 75-76.

[0259] Embodiment 46. The composition of Embodiment 40, comprising:

[0260] (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 any one of SEQ ID NO: 70, SEQ ID NO: 77, or SEQ ID NO: 78.

[0261] Embodiment 47. A composition comprising the polynucleotide of any one of Embodiments 32-35 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.

[0262] Embodiment 48. 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 Embodiments 1-31 or 51-54; (ii) the polynucleotide of any one of Embodiments 32-35; (iii) the recombinant vector of Embodiment 36; (iv) the host cell of Embodiment 37; (v) the human B cell of Embodiment 38; and/or (vi) the composition of any one of Embodiments 39-47.

[0263] Embodiment 49. The antibody or antigen-binding fragment of any one of Embodiments 1-31 or 51-54, the polynucleotide of any one of Embodiments 32-35, the recombinant vector of Embodiment 36, the host cell of Embodiment 37, the human B cell of Embodiment 38, and/or the composition of any one of Embodiments 39-47 for use in a method of treating a SARS-CoV-2 infection in a subject.

[0264] Embodiment 50. The antibody or antigen-binding fragment of any one of Embodiments 1-31 or 51-54, the polynucleotide of any one of Embodiments 32-35, the recombinant vector of Embodiment 36, the host cell of Embodiment 37, the human B cell of Embodiment 38, and/or the composition of any one of Embodiments 39-47 for use in the preparation of a medicament for the treatment of a SARS-CoV-2 infection in a subject.

[0265] Embodiment 51. The antibody or antigen-binding fragment of any one of Embodiments 24-31, wherein the Fc polypeptide comprises a L234A mutation and a L235A mutation.

[0266] Embodiment 52. The antibody or antigen-binding fragment of any one of Embodiments 1-31 or 51, wherein the antibody or antigen-binding fragment binds to SARS-CoV-2 S protein, as measured using biolayer interferometry.

[0267] Embodiment 53. The antibody or antigen-binding fragment of Embodiment 52, wherein the antibody or antigen-binding fragment binds to SARS-CoV-2 S protein with a KD of less than about 4.5×10^{-9} M.

[0268] Embodiment 54. The antibody or antigen-binding fragment of Embodiment 52 or 53, wherein the antibody or antigen-binding fragment binds to SARS-CoV-2 S protein with a K_D less than 1×10^{-12} M.

[0269] Embodiment 55. The antibody or antigen-binding fragment of any one of Embodiments 1-31 or 51-54, 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.

[0270] Embodiment 56. The antibody or antigen-binding fragment of any one of Embodiments 1-31 or 51-54, 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.

[0271] Embodiment 57. A composition comprising (i) the antibody or antigen-binding fragment of Embodiment 8 or 9 and (ii) the antibody or antigen-binding fragment of Embodiment 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.

[0272] Embodiment 58. The antibody or antigen-binding fragment of any one of Embodiments 1-31 or 51-54, 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.

[0273] Embodiment 59. A method for in vitro diagnosis of a SARS-CoV-2 infection, the method comprising:

[0274] (i) contacting a sample from a subject with an antibody or antigen-binding fragment of any one of Embodiments 1-31 or 51-54; and

[0275] (ii) detecting a complex comprising an antigen and the antibody, or comprising an antigen and the antigen binding fragment.

[0276] Embodiment 60. The method of Embodiment 59, wherein the sample comprises blood isolated from the subject.

[0277] Embodiment 61. The antibody or antigen-binding fragment of any one of Embodiments 52-56, 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.

[0278] Embodiment 62. The antibody or antigen-binding fragment of any one of Embodiments 1-31, 51-54, or 61, 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,

[0279] wherein, optionally, the neutralizing comprises neutralizing infection in an in vitro model of infection.

[0280] Embodiment 63. The antibody or antigen-binding fragment of any one of Embodiments 1-31, 51-54, 61, or 62, 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.

[0281] Embodiment 64. The antibody or antigen-binding fragment of Embodiment 58, wherein the inducing ADCC comprises activating a Natural Killer cell that comprises a V158 Fc_YRIIIa variant, a Natural Killer cell that comprises a F158 Fc_YRIIIa variant, or both.

[0282] Embodiment 65. The antibody or antigen-binding fragment of Embodiment 58 or 64, wherein the ADCP comprises engaging a Fc_YRIIa expressed on the surface of a phagocytic cell, such as a monocyte, a macrophage, or a dendritic cell.

[0283] Embodiment 66. 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 Embodiments 1-31, 51-54, or 61-65.

[0284] Embodiment 67. An antibody, or an antigen-binding fragment thereof, that competes for binding to a SARS-CoV-2 surface glycoprotein with antibody S309 and/or antibody S303.

[0285] Embodiment 68. An antibody, or an antigen-binding fragment thereof, that competes for binding to a SARS-CoV-2 surface glycoprotein with antibody S304 and/or antibody S315.

[0286] Embodiment 69. A combination or composition comprising:

[0287] (i) an antibody or antigen-binding fragment comprising

[0288] (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 QTVSSTS, a CDRL2 amino acid sequence GAS, and a CDRL3 amino acid sequence QQHDTSLT; or

[0289] (b) a VH amino acid sequence comprising or consisting of

QVQLVQSGAEVKKPGASVKVSKASGYPFTSYGISWVRQAPGQGLEWMG
WISTYNGNTNYAQKFQGRVTMTTDSTTTGYMELRRLRSDDTAVYYCAR
DYTRGAWFGESELIGGFDNWGQGTLVTSS

[0290] or comprising or consisting of

QVQLVQSGAEVKKPGASVKVSKASGYPFTSYGISWVRQAPGQGLEWMG
WISTYQGNTNYAQKFQGRVTMTTDSTTTGYMELRRLRSDDTAVYYCAR
DYTRGAWFGESELIGGFDNWGQGTLVTSS,

[0291] and a VL amino acid sequence comprising or consisting of EIVLTQSPGTLSLSPGER-ATLSCRASQTVSSTSLSAWYQQKPGQAPRLLIY-GASSR ATGIPDRFSGSGSGTDFTLISRLEPED-FAVYYCQQHDTSLTFGGGTKEIK; and

[0292] (ii) an antibody or antigen-binding fragment comprising: (a) VH and VL amino acid sequences according to SEQ ID NOS.: 79 and 83, respectively; (b) CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to SEQ ID NOS.: 80-82 and 84-86, respectively; (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 (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.

[0293] Embodiment 70. 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 Embodiment 69, 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.

[0294] Embodiment 71. 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; 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.

[0295] Embodiment 72. 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.

[0296] Embodiment 73. 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:

[0297] (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.

[0298] Embodiment 74. 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.

[0299] Embodiment 75. A method of treating a SARS-CoV-2 infection in a subject, the method comprising administering to the subject a single dose of a composition comprising the antibody or antigen-binding fragment of any one of Embodiments 1-31, 51-54, and 61-65.

[0300] Embodiment 76. The method of Embodiment 48 or 75, wherein the antibody or antigen-binding fragment comprises CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to SEQ ID NOS.: 106, 121, 108, 169, 170, and 171, respectively, and optionally further comprises a (n e.g. IgG1) Fc polypeptide comprising a M428L/N434S mutation, preferably wherein the antibody or antigen-binding fragment comprises the CH1-CH3 amino acid sequence of SEQ ID NO.: 173 and the CL amino acid sequence of SEQ ID NO.: 174.

[0301] Embodiment 77. The method of any one of Embodiments 48, 75, and 76, wherein the antibody or

antigen-binding fragment comprises a VH according to SEQ ID NO: 113 and a VL according to SEQ ID NO: 168, and optionally further comprises a (n e.g. IgG1) Fc polypeptide comprising a M428L/N434S mutation, preferably wherein the antibody or antigen-binding fragment comprises the CH1-CH3 amino acid sequence of SEQ ID NO.: 173 and the CL amino acid sequence of SEQ ID NO.: 174.

[0302] Embodiment 78. The method of any one of Embodiments 48 and 75-77, wherein the subject: (i) is aged 18 to 49 years; (ii) is 18 years old or older; (iii) has mild to moderate COVID-19; (iv) has severe COVID-19; (v) has severe to critical COVID-19; (vi) has had fewer than seven days or 5 or fewer days since onset of symptoms; (vii) has had seven days or more since onset of symptoms; (viii) has had a positive reverse-transcriptase-polymerase-chain-reaction or antigen SARS-CoV-2 test result; (ix) is 55 years of age or older;

[0303] (x) has one or more of: diabetes requiring medication, obesity (body-mass index >30 kg/m²), chronic kidney disease (estimated glomerular filtration rate <60 mL/min/1.73 m²),²³ congestive heart failure (New York Heart Association class II or higher), chronic obstructive pulmonary disease (history of chronic bronchitis, chronic obstructive lung disease, or emphysema with dyspnea on physical exertion), and moderate to severe asthma (subject requires an inhaled steroid to control symptoms or has been prescribed a course of oral steroids in the past year); or

[0304] (xi) any combination of (i)-(x).

[0305] Embodiment 79. The method of any one of Embodiments 48 or 75-78, wherein the administering comprises intravenous infusion.

[0306] Embodiment 80. A method of preventing or reducing the severity of SARS-CoV-2 infection in a subject with close contacts to a person with a confirmed SARS-CoV-2 infection, the method comprising administering to the subject a single dose of a composition comprising the antibody or antigen-binding fragment of any one of Embodiments 1-31, 51-54, and 61-65.

[0307] Embodiment 81. The method of Embodiment 80, wherein the antibody or antigen-binding fragment comprises CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to SEQ ID NOS.: 106, 121, 108, 169, 170, and 171, respectively, and optionally further comprises a (n e.g. IgG1) Fc polypeptide comprising a M428L/N434S mutation, preferably wherein the antibody or antigen-binding fragment comprises the CH1-CH3 amino acid sequence of SEQ ID NO.: 173 and the CL amino acid sequence of SEQ ID NO.: 174.

[0308] Embodiment 82. The method of Embodiment 80 or 81, wherein the antibody or antigen-binding fragment comprises a VH according to SEQ ID NO: 113 and a VL according to SEQ ID NO: 168, and optionally further comprises a (n e.g. IgG1) Fc polypeptide comprising a M428L/N434S mutation, preferably wherein the antibody or antigen-binding fragment comprises the CH1-CH3 amino acid sequence of SEQ ID NO.: 173 and the CL amino acid sequence of SEQ ID NO.: 174.

[0309] Embodiment 83. The method of any one of Embodiments 80-82, wherein the subject: (i) is 12 years old or older; and (ii) last had contact with a person with a confirmed SARS-CoV-2 infection less than three days prior to administration of the composition.

[0310] Embodiment 84. The method of any one of Embodiments 48 or 80-83, wherein the administering comprises intravenous infusion.

[0311] Embodiment 85. The method of any one of Embodiments 48 or 75-78, wherein the administering comprises intramuscular injection.

[0312] Embodiment 86. The method of any one of Embodiments 48 or 80-83, wherein the administering comprises intramuscular injection.

[0313] Embodiment 87. The method of any one of Embodiments 75-86, wherein the single dose of the composition comprises 250 mg of the antibody or antigen-binding fragment.

[0314] Embodiment 88. The method of any one of Embodiments 75-86, wherein the single dose of the composition comprises 500 mg of the antibody or antigen-binding fragment.

[0315] Embodiment 89.1. The method of any one of Embodiments 48 or 75-88, wherein the subject has a mild-to-moderate SARS-2-CoV infection (e.g., has mild-to-moderate COVID-19) and, optionally, is at risk for progression to severe disease.

[0316] Embodiment 89.2. A method of treating COVID-19 in a subject having mild-to-moderate COVID-19, the method comprising administering intramuscularly to the subject a single dose of a composition comprising an antibody that comprises a VH according to SEQ ID NO: 113 and a VL according to SEQ ID NO: 168, and optionally further comprises a (n e.g. IgG1) Fc polypeptide comprising a M428L/N434S mutation, preferably wherein the antibody comprises the CH1-CH3 amino acid sequence of SEQ ID NO.: 173 and the CL amino acid sequence of SEQ ID NO.: 174.

[0317] Embodiment 90. The method of Embodiment 89.2, wherein the single dose of the composition comprises 250 mg of the antibody.

[0318] Embodiment 91. The method of Embodiment 89.2, wherein the single dose of the composition comprises 500 mg of the antibody.

[0319] Embodiment 92. The method of any one of Embodiments 89.2-91, wherein:

[0320] (i) (i)(a) the subject is 12 years of age or older and is at high risk of progression of COVID-19 or (i)(b) the subject is 65 years of age or older; and/or

[0321] (ii) the subject has a positive SARS-CoV-2 test result (e.g., by PCR test), has oxygen saturation ≥94% on room air, has COVID-19 symptoms, and is less than or equal to 7 days from onset of symptoms.

[0322] Embodiment 93. The method of any one of Embodiments 89.2-92, wherein:

[0323] (i) (i)(a) the subject is 12 years of age or older and is at high risk of progression of COVID-19 or (i)(b) the subject is 65 years of age or older; and

[0324] (ii) the subject has a positive SARS-CoV-2 test result (e.g., by PCR test), has oxygen saturation ≥94% on room air, has COVID-19 symptoms, and is less than or equal to 7 days from onset of symptoms.

[0325] [Embodiments 94-100—reserved]

[0326] Embodiment 101. A method of treating a SARS-CoV-2 infection in a subject, the method comprising administering to the subject a single dose of a composition comprising an antibody or antigen-binding fragment that is capable of binding to a surface glycoprotein of a SARS-CoV-2 expressed on a cell surface of a host cell and/or on a

virion, wherein the antibody comprises 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 CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 comprise the amino acid sequences set forth in: (1) SEQ ID NOS.: 106, 121, 108, 169, 170, and 171, respectively; or (2) SEQ ID NOS.: 106, 107, 108, 169, 170, and 171, respectively.

[0327] Embodiment 102. A method of treating a SARS-CoV-2 infection in a subject, the method comprising administering to the subject an effective amount of (i) an antibody or antigen-binding fragment that is capable of binding to a surface glycoprotein of a SARS-CoV-2 expressed on a cell surface of a host cell and/or on a virion, or (ii) a composition comprising (ii) (a) the antibody or antigen-binding fragment and (ii) (b) a pharmaceutically acceptable excipient, carrier, or diluent, wherein the antibody comprises 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 CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 comprise the amino acid sequences set forth in: (1) SEQ ID NOS.: 106, 121, 108, 169, 170, and 171, respectively; or (2) SEQ ID NOS.: 106, 107, 108, 169, 170, and 171, respectively.

[0328] Embodiment 103. The method of Embodiment 102, wherein the method comprises administering to the subject a single dose of the antibody or antigen-binding fragment of (i) or the composition of (ii).

[0329] Embodiment 104. The method of any one of Embodiments 101-103, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO.: 113 and the VL comprises the amino acid sequence set forth in SEQ ID NO.: 168.

[0330] Embodiment 105. The method of any one of Embodiments 101-103, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO.: 105 and the VL comprises the amino acid sequence set forth in SEQ ID NO.: 168.

[0331] Embodiment 106. The method of any one of Embodiments 101-105, wherein the antibody or antigen-binding fragment further comprises an Fc polypeptide or a fragment thereof.

[0332] Embodiment 107. The method of any one of Embodiments 101-106, which is an IgG, IgA, IgM, IgE, or IgD isotype.

[0333] Embodiment 108. The method of any one of Embodiments 101-107, which is an IgG isotype selected from IgG1, IgG2, IgG3, and IgG4.

[0334] Embodiment 109. The method of any one of Embodiments 101-108, which is an IgG1 isotype.

[0335] Embodiment 110. The method of any one of Embodiments 106-109, 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.

[0336] Embodiment 111. The method of Embodiment 110, 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.

[0337] Embodiment 112. The method of Embodiment 110 or 111, 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).

[0338] Embodiment 113. The method of any one of Embodiments 110-112, wherein the mutation that enhances binding to FcRn comprises M428L/N434S.

[0339] Embodiment 114. The method of any one of Embodiments 110-113, wherein the mutation that enhances binding to a FcγR comprises S239D; I332E; A330L; G236A; or any combination thereof, and optionally does not comprise S239D.

[0340] Embodiment 115. The method of any one of Embodiments 110-114, wherein the mutation that enhances binding to a FcγR comprises:

[0341] (i) S239D/I332E;

[0342] (ii) S239D/A330L/I332E;

[0343] (iii) G236A/S239D/I332E; or

[0344] (iv) G236A/A330L/I332E.

[0345] Embodiment 116. The method of any one of Embodiments 101-115, wherein the antibody or antigen-binding fragment comprises the CH1-CH3 amino acid sequence of SEQ ID NO.: 173 or 265 and the CL amino acid sequence of SEQ ID NO.: 174.

[0346] Embodiment 117. The method of any one of Embodiments 101-115, wherein the antibody or antigen-binding fragment comprises the CH1-CH3 amino acid sequence of SEQ ID NO.: 175 or 266 and the CL amino acid sequence of SEQ ID NO.: 174.

[0347] Embodiment 118. The method of any one of Embodiments 101-117, wherein the antibody or antigen-binding fragment comprises a heavy chain polypeptide and a light chain polypeptide, wherein:

[0348] (i) the heavy chain polypeptide comprises the VH amino acid sequence set forth in SEQ ID NO.: 113 and the CH1-CH3 amino acid sequence set forth in SEQ ID NO.: 173 or 265; and

[0349] (ii) the light chain comprises the VL amino acid sequence set forth in SEQ ID NO.: 168 and the CL amino acid sequence set forth in SEQ ID NO.: 174,

[0350] and wherein, optionally, the method comprises administering a single dose of the antibody or antigen-binding fragment to the subject.

[0351] Embodiment 119. The method of any one of Embodiments 101-117, wherein the antibody or antigen-binding fragment comprises a heavy chain polypeptide and a light chain polypeptide, wherein:

[0352] (i) the heavy chain polypeptide comprises the VH amino acid sequence set forth in SEQ ID NO.: 113 and the CH1-CH3 amino acid sequence set forth in SEQ ID NO.: 175 or 266; and

[0353] (ii) the light chain comprises the VL amino acid sequence set forth in SEQ ID NO.: 168 and the CL amino acid sequence set forth in SEQ ID NO.: 174, and wherein, optionally, the method comprises administering a single dose of the antibody or antigen-binding fragment to the subject.

[0354] Embodiment 120. The method of any one of Embodiments 101-119, wherein the subject:

[0355] (i) is aged 18 to 49 years;

[0356] (ii) is 18 years old or older;

[0357] (iii) has mild to moderate COVID-19;

[0358] (iv) has severe COVID-19;

[0359] (v) has severe to critical COVID-19;

- [0360] (vi) has had fewer than seven days or 5 or fewer days since onset of symptoms;
- [0361] (vii) has had seven days or more since onset of symptoms;
- [0362] (viii) has had a positive reverse-transcriptase-polymerase-chain-reaction or antigen SARS-CoV-2 test result;
- [0363] (ix) is 55 years of age or older;
- [0364] (x) has one or more of: diabetes requiring medication, obesity (body-mass index $>30 \text{ kg/m}^2$), chronic kidney disease (estimated glomerular filtration rate $<60 \text{ mL/min}/1.73 \text{ m}^2$), congestive heart failure (New York Heart Association class II or higher), chronic obstructive pulmonary disease (history of chronic bronchitis, chronic obstructive lung disease, or emphysema with dyspnea on physical exertion), and moderate to severe asthma (subject requires an inhaled steroid to control symptoms or has been prescribed a course of oral steroids in the past year); or
- [0365] (xi) any combination of (i)-(x).
- [0366] Embodiment 121. The method of any one of Embodiments 101-120, comprising administering the antibody, antigen-binding fragment, or composition to the subject intravenously.
- [0367] Embodiment 122. The method of Embodiment 121, comprising administering the antibody, antigen-binding fragment, or composition to the subject intravenously over the course of 30 minutes, 60 minutes, or 90 minutes.
- [0368] Embodiment 123. The method of any one of Embodiments 101-122, comprising administering the antibody, antigen-binding fragment, or composition to the subject intramuscularly.
- [0369] Embodiment 124. The method of any one of Embodiments 101-123, wherein the method comprises administering the antibody or antigen-binding fragment to the subject at a dose of up to 100 mg, up to 150 mg, up to 200 mg, up to 250 mg, up to 300 mg, up to 350 mg, up to 400 mg, up to 450 mg, or up to 500 mg.
- [0370] Embodiment 125. The method of any one of Embodiments 101-124, wherein the method comprises administering the antibody or antigen-binding fragment to the subject at a dose in a range from about 50 mg to about 500 mg, or in a range from about 50 mg to about 250 mg, or in a range from about 50 mg to 100 mg, or in a range from about 100 mg to about 500 mg, or in a range from about 250 mg to about 500 mg.
- [0371] Embodiment 126. The method of any one of Embodiments 101-125, wherein the method comprises administering 50, 75, 100, 125, 150, 175, 200, 225, 250, 275, 300, 325, 350, 375, 400, 425, 450, 475, or 500 mg of the antibody or antigen-binding fragment to the subject.
- [0372] Embodiment 127. The method of any one of Embodiments 101-126, wherein the method comprises administering 50, 150, 250, or 500 mg of the antibody or antigen-binding fragment to the subject.
- [0373] Embodiment 128. The method of any one of Embodiments 101-127, wherein the method comprises administering 500 mg of the antibody or antigen-binding fragment to the subject.
- [0374] Embodiment 129. The method of any one of Embodiments 101-128, comprising administering the antibody, antigen-binding fragment, or composition to the subject 2, 3, 4, 5, 6, 7, 8, 9, or 10 times, or more.
- [0375] Embodiment 130. The method of any one of Embodiments 101-129, comprising administering the antibody, antigen-binding fragment, or composition to the subject a plurality of times, wherein a second or successive administration is performed at about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 24, about 48, about 74, about 96 hours, or more, following the first or preceding administration.
- [0376] Embodiment 131. The method of any one of Embodiments 101-130, wherein the subject is 18 or more years of age with laboratory-confirmed (e.g., by PCR test) SARS-CoV-2 infection.
- [0377] Embodiment 132. The method of any one of Embodiments 101-131, wherein the subject has a clinical status of Grade 4 (hospitalized, oxygen by mask or nasal prongs), 5 (hospitalized, on non-invasive ventilation, or high flow oxygen), 6 (hospitalized, intubation and mechanical ventilation) or 7 (ventilation and additional organ support-pressors, renal replacement therapy (RRT), extracorporeal membrane oxygenation (ECMO)), as defined by the WHO clinical severity score, 9-point ordinal scale.
- [0378] Embodiment 133. The method of any one of Embodiments 101-131, wherein the subject has mild-to-moderate COVID-19.
- [0379] Embodiment 134. The method of Embodiment 133, wherein the subject is at-risk of progression to severe COVID-19.
- [0380] Embodiment 135. The method of Embodiment 134, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the subject is at a reduced risk of hospitalization for COVID-19.
- [0381] Embodiment 136. The method of Embodiment 135, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 10% or more.
- [0382] Embodiment 137. The method of Embodiment 135, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 20% or more.
- [0383] Embodiment 138. The method of Embodiment 135, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 30% or more.
- [0384] Embodiment 139. The method of Embodiment 135, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 40% or more.
- [0385] Embodiment 140. The method of Embodiment 135, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 50% or more.
- [0386] Embodiment 141. The method of Embodiment 135, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 60% or more.
- [0387] Embodiment 142. The method of Embodiment 135, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 70% or more.
- [0388] Embodiment 143. The method of Embodiment 135, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 80% or more.

- [0389] Embodiment 144. The method of Embodiment 135, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 85% or more.
- [0390] Embodiment 145. The method of any one of Embodiments 101-144, wherein the subject has or is at risk for progressing to severe COVID-19, wherein, optionally, severe COVID-19 comprises (i) hypoxemia (O₂ saturation ≤93% on room air or PaO₂/FiO₂<300) requiring oxygen supplementation for more than 1 day or (ii) the subject requiring ≥4 L/min oxygen supplementation or equivalent.
- [0391] Embodiment 146. The method of any one of Embodiments 101-145, wherein the subject has or is at risk for progressing to critical COVID-19, wherein, optionally, critical COVID-19 comprises respiratory failure requiring at least one of the following: invasive mechanical ventilation and ECMO; shock; and multi-organ dysfunction/failure.
- [0392] Embodiment 147. The method of any one of Embodiments 101-146, wherein the subject is less than seven days since onset of symptoms.
- [0393] Embodiment 148. The method of any one of Embodiments 101-146, wherein the subject is seven days or more since onset of symptoms.
- [0394] Embodiment 149. The method of any one of Embodiments 101-148, wherein the subject is any one or more of (i)-(iii):
- [0395] (i) 18 or older and has a positive SARS-CoV-2 test result (by any validated test e.g. RT-PCR on any specimen type);
- [0396] (ii) (1) hospitalized with severe COVID-19 disease defined as requirement for supplemental oxygen or non-invasive ventilation consistent with Grade 4 or Grade 5 disease or (2) hospitalized with critical COVID-19 disease defined as those on mechanical ventilation (Grade 6 or Grade 7 disease));
- [0397] (iii) is male or female, wherein, optionally, (1) the woman is non-childbearing potential (WONCBP) or (2) is a woman of child-bearing potential (WOCBP) and uses a contraceptive method.
- [0398] Embodiment 150. The method of any one of Embodiments 101-149, wherein the method comprises administering 500 mg of the antibody or antigen-binding fragment to the subject.
- [0399] Embodiment 151. The method of any one of Embodiments 101-150, wherein the subject had or has close contacts to a person with a confirmed SARS-CoV-2 infection.
- [0400] Embodiment 152. The method of any one of Embodiments 101-151, wherein treating comprises preventing infection by SARS-CoV-2 and/or preventing COVID-19.
- [0401] Embodiment 153. The method of any one of Embodiments 101-152, wherein treating comprises preventing progression of COVID-19 in the subject.
- [0402] Embodiment 154. The method of any one of Embodiments 101-153, wherein treating comprises preventing contraction and/or transmission of symptomatic COVID-19.
- [0403] Embodiment 155. The method of any one of Embodiments 101-153, wherein treating comprises preventing contraction and/or transmission of asymptomatic COVID-19.

- [0404] Embodiment 156. The method of any one of Embodiments 101-155, wherein the subject is at-risk for contracting or progressing on COVID-19.
- [0405] Embodiment 157. The method of any one of Embodiments 101-156, wherein treating comprises preventing or reducing:
- [0406] (1) one or more acute respiratory symptom selected from: cough; sputum production; sore throat; and shortness of breath; or
- [0407] (2) fever of greater than 38° C.;
- [0408] (3) two or more of the following symptoms: fatigue; myalgias/arthritis; chills; nausea/vomiting; diarrhea; and anosmia/dysgeusia.
- [0409] Embodiment 158. The method of any one of Embodiments 101-157, wherein treating comprises preventing or reducing one or more of the following symptoms: fever of greater than 38° C.; chills; cough; sore throat; malaise; headache; myalgia; a change in smell or taste; nasal congestion/rhinorrhea; vomiting; diarrhea; shortness of breath on exertion.
- [0410] Embodiment 159. The method of any one of Embodiments 101-158, wherein the subject is an adult.
- [0411] Embodiment 160. The method of any one of Embodiments 101-159, wherein the subject is 18 or more years of age, or is 19 or more years of age.
- [0412] Embodiment 161. The method of any one of Embodiments 101-160, wherein the subject is 55 years of age or is, or is 65 years of age or is older.
- [0413] Embodiment 162. The method of any one of Embodiments 101-161, wherein the administering the antibody, antigen-binding fragment, or composition comprises intravenous infusion.
- [0414] Embodiment 163. The method of any one of Embodiments 101-162, wherein administering the antibody, antigen-binding fragment, or composition comprises intramuscular injection.
- [0415] Embodiment 164. The method of any one of Embodiments 101-163, wherein the method comprises administering 250 mg of the antibody or antigen-binding fragment to the subject.
- [0416] Embodiment 165. The method of any one of Embodiments 101-163, wherein the method comprises administering 500 mg of the antibody or antigen-binding fragment to the subject.
- [0417] Embodiment 166. The method of any one of Embodiments 101-165, wherein the subject has a mild-to-moderate SARS-CoV infection (e.g., has mild-to-moderate COVID-19) and, optionally, is at risk for progression to severe disease.
- [0418] Embodiment 167. The method of any one of Embodiments 101-166, wherein the subject:
- [0419] (i) is 12 years old or older; and
- [0420] (ii) last had contact with a person with a confirmed SARS-CoV-2 infection less than three days prior to administration of the composition.
- [0421] Embodiment 168. The method of any one of Embodiments 101-167, wherein the subject has mild-to-moderate COVID-19 and the method comprises administering a single dose of the antibody, antigen-binding fragment, or composition to the subject intramuscularly.
- [0422] Embodiment 169. The method of Embodiment 168, wherein the single dose comprises 250 mg of the antibody or antigen-binding fragment.

[0423] Embodiment 170. The method of Embodiment 168 or 169, wherein the single dose of comprises 500 mg of the antibody or antigen-binding fragment.

[0424] Embodiment 171. The method of any one of Embodiments 168-170, wherein: (i) (i)(a) the subject is 12 years of age or older and is at high risk of progression of COVID-19 or (i)(b) the subject is 65 years of age or older; and/or (ii) the subject has a positive SARS-CoV-2 test result (e.g., by PCR test), has oxygen saturation $\geq 94\%$ on room air, has COVID-19 symptoms, and is less than or equal to 7 days from onset of symptoms.

[0425] Embodiment 172. The method of any one of Embodiments 101-171, wherein: (i) (i)(a) the subject is 12 years of age or older and is at high risk of progression of COVID-19 or (i)(b) the subject is 65 years of age or older; and (ii) the subject has a positive SARS-CoV-2 test result (e.g., by PCR test), has oxygen saturation $\geq 94\%$ on room air, has COVID-19 symptoms, and is less than or equal to 7 days from onset of symptoms.

[0426] Embodiment 173. The method of any one of Embodiments 101-172, wherein the subject is not hospitalized and is at high-risk for (i) hospitalization and/or (ii) progression of COVID-19.

[0427] Embodiment 174. The method of any one of Embodiments 101-173, wherein the subject is: (1) 12 or more years of age and, optionally, is at high risk of progression of COVID-19; and/or (2) is 65 or more years of age.

[0428] Embodiment 175. The method of any one of Embodiments 101-174, wherein the subject has had a positive SARS-CoV-2 test result, has oxygen saturation $\geq 94\%$ on room air, has COVID-19 symptoms, and is less than or equal to 7 days from onset of symptoms.

[0429] Embodiment 176. The method of any one of Embodiments 101-175, wherein the antibody or antigen-binding fragment was obtained from a non-clonal pool of cells stably transfected with a polynucleotide encoding the antibody or antigen-binding fragment.

[0430] Embodiment 177. The method of any one of Embodiments 101-175, wherein the antibody or antigen-binding fragment was obtained from a clonal master cell bank.

[0431] Embodiment 178. The method of any one of Embodiments 101-177, wherein the subject: is a resident of a nursing home or a long-term care facility; is a hospice care worker; is a healthcare provider or healthcare worker; is a first responder; is a family member or other close contact of a subject diagnosed with or suspected of having a SARS-CoV-2 infection, is overweight or clinically obese; is or has been a smoker; has or had chronic obstructive pulmonary disease (COPD); is asthmatic (e.g., having moderate to severe asthma); has an autoimmune disease or condition (e.g., diabetes); has a compromised or depleted immune system (e.g., due to AIDS/HIV infection, a cancer such as a blood cancer, a lymphodepleting therapy such as a chemotherapy, a bone marrow or organ transplantation, or a genetic immune condition); has chronic liver disease; has cardiovascular disease; and/or has a pulmonary or heart defect; and/or works or otherwise spends time in close proximity with others, such as in a factory, shipping center, hospital setting, or the like.

[0432] Embodiment 179. The method of any one of Embodiments 101-178, wherein the subject has received a vaccine for SARS-CoV-2 and the vaccine is determined to

be ineffective, e.g., by post-vaccine infection or symptoms in the subject, by clinical diagnosis or scientific or regulatory criteria.

[0433] Embodiment 180. The method of any one of Embodiments 101-178, wherein the subject has not received a vaccine for SARS-CoV-2.

[0434] Embodiment 181. The method of any one of Embodiments 101-180, wherein the subject has received convalescent plasma therapy (i.e., from a convalescent COVID-19 subject), remdesivir, or both, for SARS-CoV-2.

[0435] Embodiment 182. The method of any one of Embodiments 101-181, wherein treatment comprises pre-exposure or peri-exposure prophylaxis.

[0436] Embodiment 183. The method of any one of Embodiments 101-182, wherein treatment is administered to the subject having mild-to-moderate disease, optionally in an outpatient setting.

[0437] Embodiment 184. The method of any one of Embodiments 101-183, wherein treatment is administered to a subject with moderate-to-severe disease, such as requiring hospitalization.

[0438] Embodiment 185. The method of any one of Embodiments 101-184, wherein the subject is hospitalized with COVID-19.

[0439] Embodiment 186. The method of any one of Embodiments 101-185, wherein the subject having a SARS-CoV-2 infection: has mild-to-moderate COVID-19; is experiencing any one or more of: fever; cough; fatigue; shortness of breath or difficulty breathing; muscle aches; chills; sore throat; runny nose; headache; chest pain; loss of taste and/or smell; and pink eye (conjunctivitis); malaise; and abnormal imaging; has evidence of lower respiratory disease by clinical assessment or imaging and a saturation of oxygen (SaO_2) greater than ($>$) 93 percent (%) on room air at sea level, has a positive SARS-CoV-2 viral testing result, and/or is at high risk for progressing to severe COVID-19 and/or hospitalization, e.g., the human subject (1) is 65 years of age or older (≥ 65); has a body mass index (BMI) of 35 or greater (≥ 35); has chronic kidney disease; has diabetes; (5) has immunosuppressive disease, is receiving immunosuppressive treatment; is 55 years of age or older (≥ 55) and has cardiovascular disease, hypertension, chronic obstructive pulmonary disease, or other chronic respiratory disease; and/or is 12-17 years of age and has a BMI $\geq 85\%$ for their age and gender, or sickle cell disease, congenital or acquired heart disease, neurodevelopmental disorders (e.g., cerebral palsy), a medical-related technological dependence (e.g., tracheostomy, gastrostomy, or positive pressure ventilation not related to COVID-19), or asthma, reactive airway or other chronic respiratory disease that requires daily medication for control; has recently been diagnosed with COVID-19 (e.g., within 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days) and/or is within 10 days of symptom onset; or has or is experiencing any combination of the foregoing.

[0440] Embodiment 187. The method of any one of Embodiments 101-186, wherein the subject is (a) 18 years old or older, or (b) 55 years old or younger, provided that the subject is 18 years or older.

[0441] Embodiment 188. The method of any one of Embodiments 101-187, wherein the subject has a laboratory confirmed COVID-19 infection by positive polymerase chain reaction (PCR; e.g., RT-PCR) test; e.g., on any type of respiratory tract sample).

[0442] Embodiment 189. The method of any one of Embodiments 101-187, the subject has peripheral capillary oxygen saturation (SpO_2) >94% room air (RA), and has experienced one or more symptoms of COVID-19 for ≤ 120 h (5 days).

[0443] Embodiment 190. The method of any one of Embodiments 101-189, wherein the subject is further receiving or has received remdesivir, supplemental oxygen, ventilation therapy, respiration therapy, dexamethasone, tocilizumab, or any combination thereof.

TABLE 1

Sequences			
Sequence Description	SEQ ID NO.	Sequence	
SARS-CoV-2 S300-v1 mAb VH (aa)	1	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWRQAPGQGPFWLGVVNGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v1 mAb CDRH1 (aa)	2	GYTFTDYY	
SARS-CoV-2 S300-v1 mAb CDRH2 (aa)	3	VNGYSGAT	
SARS-CoV-2 S300-v1 mAb CDRH3 (aa)	4	ARDRPSHEWAMYFFDN	
SARS-CoV-2 S300-v1 mAb VL (VK) (aa)	5	QIVLTQSPGTLSLSPGERATLSCRASQSPV SSCLAWYQQKPGQAPRLLIYGASGRATGIP DRESGSGGTDFTLTIRRLPEDFAVYYCQ QYGSSPPLTFGGGTVKEIK	
SARS-CoV-2 S300-v1 mAb CDRL1 (aa)	6	QSVPSSC	
SARS-CoV-2 S300-v1 mAb CDRL2 (aa)	7	GAS	
SARS-CoV-2 S300-v1 mAb CDRL3 (aa)	8	QQYGSSPPLT	
SARS-CoV-2 S300-v1.1 mAb VH (aa)	9	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWRQAPGQGPFWLGVVQGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v1.2 mAb VH (aa)	10	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWRQAPGQGPFWLGVVNAYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v1.3 mAb VH (aa)	11	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWRQAPGQGPFWLGVVNSYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v1.4 mAb VH (aa)	12	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWRQAPGQGPFWLGVVNPYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v1.5 mAb VH (aa)	13	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWRQAPGQGPFWLGVVNQYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	

TABLE 1-continued

Sequence Description	SEQ NO.	Sequences	
		ID	Sequence
SARS-CoV-2 S300-v1.6 mAb VH (aa)	14	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWVRQAPGGPWEWLGVWLGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v1.7 mAb VH (aa)	15	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWVRQAPGGPWEWLGVWLGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v1.1 mAb CDRH2 (aa)	16	VQGYSGAT	
SARS-CoV-2 S300-v1.2 mAb CDRH2 (aa)	17	VNAYSGAT	
SARS-CoV-2 S300-v1.3 mAb CDRH2 (aa)	18	VNSYSGAT	
SARS-CoV-2 S300-v1.4 mAb CDRH2 (aa)	19	VNPYSGAT	
SARS-CoV-2 S300-v1.5 mAb CDRH2 (aa)	20	VNQYSGAT	
SARS-CoV-2 S300-v1.6 mAb CDRH2 (aa)	21	VLGYSGAT	
SARS-CoV-2 S300-v1.7 mAb CDRH2 (aa)	22	VTGYSGAT	
SARS-CoV-2 S300-v1.8 mAb VH (aa)	23	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWVRQAPGGPWEWLGVWVGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEFAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v1.9 mAb VH (aa)	24	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWVRQAPGGPWEWLGVWNGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEYAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v1.8 mAb CDRH3 (aa)	25	ARDRPSHEFAMYFFDN	
SARS-CoV-2 S300-v1.9 mAb CDRH3 (aa)	26	ARDRPSHEYAMYFFDN	

TABLE 1-continued

		Sequences
Sequence Description	SEQ ID NO.	Sequence
SARS-CoV-2 S300-v2 mAb VH (aa)	27	QVQLVQSGAEVKKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPEWLGFVNGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS
SARS-CoV-2 S300-v2.1 mAb VH (aa)	28	QVQLVQSGAEVKKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPEWLGFVQGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS
SARS-CoV-2 S300-v2.2 mAb VH (aa)	29	QVQLVQSGAEVKKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPEWLGFVNAYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS
SARS-CoV-2 S300-v2.3 mAb VH (aa)	30	QVQLVQSGAEVKKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPEWLGFVNSYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS
SARS-CoV-2 S300-v2.4 mAb VH (aa)	31	QVQLVQSGAEVKKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPEWLGFVNQYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS
SARS-CoV-2 S300-v2.5 mAb VH (aa)	32	QVQLVQSGAEVKKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPEWLGFVNQYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS
SARS-CoV-2 S300-v2.6 mAb VH (aa)	33	QVQLVQSGAEVKKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPEWLGFVLGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS
SARS-CoV-2 S300-v2.7 mAb VH (aa)	34	QVQLVQSGAEVKKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPEWLGFVTGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS
SARS-CoV-2 S300-v2.8 mAb VH (aa)	35	QVQLVQSGAEVKKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPEWLGFVNGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEFAMYFFDNWGQGTLVT VSS
SARS-CoV-2 S300-v2.9 mAb VH (aa)	36	QVQLVQSGAEVKKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPEWLGFVNGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEYAMYFFDNWGQGTLVT VSS
SARS-CoV-2 S300-v3 mAb VH (aa)	37	QVQLVQSGAEVKKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPEWLGYVNGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS

TABLE 1-continued

Sequence Description	SEQ ID NO.	Sequences	
		Sequence	
SARS-CoV-2 S300-v3.1 mAb VH (aa)	38	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPWEWLGYVQGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v3.2 mAb VH (aa)	39	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPWEWLGYVNAYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v3.3 mAb VH (aa)	40	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPWEWLGYVNSYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v3.4 mAb VH (aa)	41	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPWEWLGYVNPySGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v3.5 mAb VH (aa)	42	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPWEWLGYVNQySGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v3.6 mAb VH (aa)	43	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPWEWLGYVLGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v3.7 mAb VH (aa)	44	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPWEWLGYVIGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEWAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v3.8 mAb VH (aa)	45	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPWEWLGYVNNGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEFAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v3.9 mAb VH (aa)	46	QVQLVQSGAEVKPGASVKVSCKASGYTFT DYYIHWVRQAPGQGPWEWLGYVNgySGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEYAMYFFDNWGQGTLVT VSS	
SARS-CoV-2 S300-v10 mAb VL (VK) (aa)	47	QIVLTQSPGTLSLSPGERATLSCRASQSVPS SSSLAWYQQKPGQAPRLLIYGASGRATGIP DRFGSGSGSGTDFTLTIRRLPEPEDFAVYYCQ QYGSSPPLTFGGTKVEIK	
SARS-CoV-2 S300-v11 mAb VL (VK) (aa)	48	QIVLTQSPGTLSLSPGERATLSCRASQSVPS SSSLAWYQQKPGQAPRLLIYGASGRATGIP DRFGSGSGSGTDFTLTIRRLPEPEDFAVYYCQ QYGSSPPLTFGGTKVEIK	
SARS-CoV-2 S300-v12 mAb VL (VK) (aa)	49	QIVLTQSPGTLSLSPGERATLSCRASQSVPS SSSLAWYQQKPGQAPRLLIYGASGRATGIP DRESGSGSGSGTDFTLTIRRLPEPEDFAVYYCQ QYGSSPPLTFGGTKVEIK	

TABLE 1-continued

Sequence Description	SEQ ID NO.	Sequences	
		Sequence	
SARS-CoV-2 S300-v13 mAb VL (aa)	50	QIVLTQSPGTLSLSPGERATLSCRASQSVP SSALAWYQQKPGQAPRLLIYGASGRATGIP DRFSGSGSGTDFLTIRRLPEPEDFAVYYCQ QYGSSPPLTFGGTKVEIK	
SARS-CoV-2 S300-v10 mAb CDRL1 (aa)	51	QSVPSSY	
SARS-CoV-2 S300-v11 mAb CDRL1 (aa)	51	QSVPSSS	
SARS-CoV-2 S300-v12 mAb CDRL1 (aa)	53	QSVPSST	
SARS-CoV-2 S300-v13 mAb CDRL1 (aa)	54	QSVPSSA	
SARS-CoV-2 S302 mAb VH (aa)	55	QVQLVESGGVVQPGRLRLSCAAS GFTFS SYGMHWVRQAPGKGLEWAVVISYDGSNKYY ADSVKGRFTISRDN SKNTLYLQMNSLRAED TAVYYCAKDISSGWDRVFDYWGQQGTLVTVS S	
SARS-CoV-2 S302 mAb CDRH1 (aa)	56	GFTFSSYG	
SARS-CoV-2 S302 mAb CDRH2 (aa)	57	ISYDGSNK	
SARS-CoV-2 S302 mAb CDRH3 (aa)	58	AKDISSGWDRVFDY	
SARS-CoV-2 S302 mAb VL (VK) (aa)	59	EILLTQSPGTLSLSPGERATLSCR TTSQVG SSALAWYQQKPGQAPRLLIYAAASSRAIGIP DRFSGSGSGTDFLTISRLEPEDFAVYYCQ QYGSSPWTFGQQGTKVEIK	
SARS-CoV-2 S302 mAb CDRL1 (aa)	60	QSVGSSY	
SARS-CoV-2 S302 mAb CDRL2 (aa)	61	AAS	
SARS-CoV-2 S302 mAb CDRL3 (aa)	62	QQYGSSPWT	
SARS-CoV-2 S303-v1 mAb VH (aa)	63	EVQLVESGGGLVKGPGSLRLSCAAS GFTFL TYSMNVWRQTPGKRLQWVSAISGSGGATYY ADSVKGRFTISRDN SKNTLYLQMNTVTADD TAIYFCAERERDDIFPMGLNAFDIWGQGAMV IVSS	
SARS-CoV-2 S303-v1 mAb CDRH1 (aa)	64	GFTFLTYS	

TABLE 1-continued

Sequence Description	SEQ ID NO.	Sequences	
		Sequence	
SARS-CoV-2 S303-v1 mAb CDRH2 (aa)	65	I S G S G A T	
SARS-CoV-2 S303-v1 mAb CDRH3 (aa)	66	A R E R D D I F P M G L N A F D I	
SARS-CoV-2 S303-v1 mAb VL (VK) (aa)	67	D I Q M T Q S P S T L S A S V G D R V T I T C R A S Q S I S N W L A W Y Q Q K P G K A P K L L I Y K A S S L E S G V P R F S G S G T E F T L T I S S L Q P D D S A T Y Y C Q Q Y D T Y S W T F G Q G T K V E I K	
SARS-CoV-2 S303-v1 mAb CDRL1 (aa)	68	Q S I S N W	
SARS-CoV-2 S303-v1 mAb CDRL2 (aa)	69	K A S	
SARS-CoV-2 S303-v1 mAb CDRL3 (aa)	70	Q Q Y D T Y S W T	
SARS-CoV-2 S303-v2 mAb VL (VK) (aa)	71	D I Q M T Q S P S T L S A S V G D R V T I T C R A S Q S I S N F L A W Y Q Q K P G K A P K L L I Y K A S S L E S G V P R F S G S G T E F T L T I S S L Q P D D S A T Y Y C Q Q Y D T Y S W T F G Q G T K V E I K	
SARS-CoV-2 S303-v3 mAb VL (VK) (aa)	72	D I Q M T Q S P S T L S A S V G D R V T I T C R A S Q S I S N Y L A W Y Q Q K P G K A P K L L I Y K A S S L E S G V P R F S G S G T E F T L T I S S L Q P D D S A T Y Y C Q Q Y D T Y S W T F G Q G T K V E I K	
SARS-CoV-2 S303-v2 mAb CDRL1 (aa)	73	Q S I S N F	
SARS-CoV-2 S303-v3 mAb CDRL1 (aa)	74	Q S I S N Y	
SARS-CoV-2 S303-v4 mAb VL (VK) (aa)	75	D I Q M T Q S P S T L S A S V G D R V T I T C R A S Q S I S N W L A W Y Q Q K P G K A P K L L I Y K A S S L E S G V P R F S G S G T E F T L T I S S L Q P D D S A T Y Y C Q Q Y D T Y S W T F G Q G T K V E I K	
SARS-CoV-2 S303-v5 mAb VL (VK) (aa)	76	D I Q M T Q S P S T L S A S V G D R V T I T C R A S Q S I S N W L A W Y Q Q K P G K A P K L L I Y K A S S L E S G V P R F S G S G T E F T L T I S S L Q P D D S A T Y Y C Q Q Y D T Y S W T F G Q G T K V E I K	
SARS-CoV-2 S303-v4 mAb CDRL3 (aa)	77	Q Q Y D T Y S F T	
SARS-CoV-2 S303-v5 mAb CDRL3 (aa)	78	Q Q Y D T Y S Y T	
SARS-CoV-2 S304 mAb VH (aa)	79	E V Q L V E G G L V Q P G G S L R L S C A S G F T F S Y D M H W V R Q T T G K G L E W V S T I G T A G D T Y P D S V K G R F T I S R E D A K N S L Y L Q M N S L R A G D A V Y C A R G D S G Y Y Y F D Y W G Q G T L L T V S	
SARS-CoV-2 S304 mAb CDRH1 (aa)	80	G F T F S S Y D	

TABLE 1-continued

Sequence Description	SEQ ID NO.	Sequences	
		Sequence	
SARS-CoV-2 S304 mAb CDRH2 (aa)	81	IGTAGDT	
SARS-CoV-2 S304 mAb CDRH3 (aa)	82	ARGDSSGGYYYYFDY	
SARS-CoV-2 S304 mAb VL (VK) (aa)	83	DIQMTQSPSSLSAAVGDRVTITCRASQSIG SYLNWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFLTISLQPEDFAIYYCQQ SYVSPTYTFGPGTKVDIK	
SARS-CoV-2 S304 mAb CDRL1 (aa)	84	QSIGSY	
SARS-CoV-2 S304 mAb CDRL2 (aa)	85	AAS	
SARS-CoV-2 S304 mAb CDRL3 (aa)	86	QQSYVSPTYT	
SARS-CoV-2 S306 mAb VH (aa)	87	QVQLVQSGAEVKKPGASVKVSCKASTYTFT SFGISWVRQAPGOGLEMGWITYSGDTNY AQKFQGRVTMTTDTSTNTAYMELRSLRSDD TAVYYCASDYFDSSGYHHSFDYWQGTLVT VSS	
SARS-CoV-2 S306 mAb CDRH1 (aa)	88	TYTFTSFG	
SARS-CoV-2 S306 mAb CDRH2 (aa)	89	ITTYSGDT	
SARS-CoV-2 S306 mAb CDRH3 (aa)	90	ASDYFDSSGYHHSFDY	
SARS-CoV-2 S306 mAb VL (VK) (aa)	91	EIVLTQSPDTLSLSPGERATLSCRASQSVS SYLAWYQQRPQAPRLLIYDASKRATGIPA RFSGSGSGTDFLTISLLEPEDFAVYYCQQ RSNWPPGCSFGQGTKVEIK	
SARS-CoV-2 S306 mAb CDRL1 (aa)	92	QSVSSY	
SARS-CoV-2 S306 mAb CDRL2 (aa)	93	DAS	
SARS-CoV-2 S306 mAb CDRL3 (aa)	94	QQRSNWPPGCS	
SARS-CoV-2 S308-v1 mAb VH (aa)	95	QVQLVESGGVVQPGRSRLSCAASRFTFS SYGMHWVRQAPGKGLEWVAVIWHDGNKKHY GDSVKGRVTISRDNSKNTLYLQMITSLRAED TAVYYCARAVTTFKGSGRARMRGMDVWGQG TTTVSS	
SARS-CoV-2 S308-v1 mAb CDRH1 (aa)	96	RFTFSSY	

TABLE 1-continued

Sequence Description	SEQ NO.	Sequences	
		ID	Sequence
SARS-CoV-2 S308-v1 mAb CDRH2 (aa)	97	IWHDGNNK	
SARS-CoV-2 S308-v1 mAb CDRH3 (aa)	98	ARAVTTFKGSGRARMRGMDV	
SARS-CoV-2 S308-v1 mAb VL (VK) (aa)	99	DIQLTQSPSFLSASVGDRVTITCRASQGIN TYLAWYQQKPGKAPKLLIYAASTLQSGVPS RFGSGSGTEFTLTISLQPEDFATYYCQH LDTYPFTFGPGTKVDIK	
SARS-CoV-2 S308-v1 mAb CDRL1 (aa)	100	QGINTY	
SARS-CoV-2 S308-v1 mAb CDRL2 (aa)	101	AAS	
SARS-CoV-2 S308-v1 mAb CDRL3 (aa)	102	QHLDTYPFT	
SARS-CoV-2 S308-v2 mAb VH (aa)	103	QVQLVESGGVVQPGRSLRLSCAASRFTFS SYGMHWVRQAPGKGLEWVAVIWHDGNNKHY GDSVKGRVTISRDNSKNTLYLQMTSLRAED TAVYYCARAVTTFKGSGRARLRGMVDVWGQG TTTVSS	
SARS-CoV-2 S308-v2 mAb CDRH3 (aa)	104	ARAVTTFKGSGRARLRGMVD	
SARS-CoV-2 S309-v1 mAb VH (aa)	105	QVOLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGWISTYNGNTNY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWFGESLIGGFDNWGQG TLTVSS	
SARS-CoV-2 S309-v1 mAb CDRH1 (aa)	106	GYPFTSYG	
SARS-CoV-2 S309-v1 mAb CDRH2 (aa)	107	ISTYNGNT	
SARS-CoV-2 S309-v1 mAb CDRH3 (aa)	108	ARDYTRGAWFGESLIGGFDN	
SARS-CoV-2 S309-v1 mAb VL (VK) (aa)	109	DIQMTQSPSSLSTSVDRTITCRASQGIN NYVAWYQQKPGKVPKLLIYGASTLQSGVPS RFRGSGSGTGTFTLTISLQPEDVASYYCRK YNSAPWTFGQGTRVEIK	
SARS-CoV-2 S309-v1 mAb CDRL1 (aa)	110	QGINNY	
SARS-CoV-2 S309-v1 mAb CDRL2 (aa)	111	GAS	
SARS-CoV-2 S309-v1 mAb CDRL3 (aa)	112	RKYNSAPWT	

TABLE 1-continued

Sequence Description	SEQ NO.	Sequences	
		ID	Sequence
SARS-CoV-2 S309-v1.1 mAb VH (aa)	113	QVQLVQSGAEVKPGASVKVSCKAS GYPFT SYG IISWVRQAPGQGLEWMGW ISTYQGNT NY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWF GESLIGGF DNWGQG TLTVVSS	
SARS-CoV-2 S309-v1.2 mAb VH (aa)	114	QVQLVQSGAEVKPGASVKVSCKAS GYPFT SYG IISWVRQAPGQGLEWMGW ISTYNSNT NY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWF GESLIGGF DNWGQG TLTVVSS	
SARS-CoV-2 S309-v1.3 mAb VH (aa)	115	QVQLVQSGAEVKPGASVKVSCKAS GYPFT SYG IISWVRQAPGQGLEWMGW ISTYNANT NY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWF GESLIGGF DNWGQG TLTVVSS	
SARS-CoV-2 S309-v1.4 mAb VH (aa)	116	QVQLVQSGAEVKPGASVKVSCKAS GYPFT SYG IISWVRQAPGQGLEWMGW ISTYNQNT NY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWF GESLIGGF DNWGQG TLTVVSS	
SARS-CoV-2 S309-v1.5 mAb VH (aa)	117	QVQLVQSGAEVKPGASVKVSCKAS GYPFT SYG IISWVRQAPGQGLEWMGW ISTYLGNT NY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWF GESLIGGF DNWGQG TLTVVSS	
SARS-CoV-2 S309-v1.6 mAb VH (aa)	118	QVQLVQSGAEVKPGASVKVSCKAS GYPFT SYG IISWVRQAPGQGLEWMGW ISTYTGNT NY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAFF GESLIGGF DNWGQG TLTVVSS	
SARS-CoV-2 S309-v1.7 mAb VH (aa)	119	QVQLVQSGAEVKPGASVKVSCKAS GYPFT SYG IISWVRQAPGQGLEWMGW ISTYNGNT NY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAFF GESLIGGF DNWGQG TLTVVSS	
SARS-CoV-2 S309-v1.8 mAb VH (aa)	120	QVQLVQSGAEVKPGASVKVSCKAS GYPFT SYG IISWVRQAPGQGLEWMGW ISTYNGNT NY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAY FGESLIGGF DNWGQG TLTVVSS	
SARS-CoV-2 S309-v1.1 mAb CDRH2 (aa)	121	ISTYQGNT	
SARS-CoV-2 S309-v1.2 mAb CDRH2 (aa)	122	ISTYNSNT	
SARS-CoV-2 S309-v1.3 mAb CDRH2 (aa)	123	ISTYNANT	
SARS-CoV-2 S309-v1.4 mAb CDRH2 (aa)	124	ISTYNQNT	

TABLE 1-continued

Sequence Description	SEQ ID NO.	Sequences	
		Sequence	
SARS-CoV-2 S309-v1.5 mAb CDRH2 (aa)	125	I STYLGNT	
SARS-CoV-2 S309-v1.6 mAb CDRH2 (aa)	126	I STYTGN	
SARS-CoV-2 S309-v1.7 mAb CDRH3 (aa)	127	A RDYTRGAFFGESLIGGEDN	
SARS-CoV-2 S309-v1.8 mAb CDRH3 (aa)	128	A RDYTRGAYFGESLIGGFDN	
SARS-CoV-2 S309-v2 mAb VH (aa)	129	Q VQLVQSGAEVKKPGASVKVSCKASGYPFT S YGISWVRQAPGQGLEWMGFISTYNGNTNY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWFGE S LIGGFDNWGQG TLTVSS	
SARS-CoV-2 S309-v2.1 mAb VH (aa)	130	Q VQLVQSGAEVKKPGASVKVSCKASGYPFT S YGISWVRQAPGQGLEWMGFISTYQGNTNY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWFGE S LIGGFDNWGQG TLTVSS	
SARS-CoV-2 S309-v2.2 mAb VH (aa)	131	Q VQLVQSGAEVKKPGASVKVSCKASGYPFT S YGISWVRQAPGQGLEWMGFISTYNSNTNY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWFGE S LIGGFDNWGQG TLTVSS	
SARS-CoV-2 S309-v2.3 mAb VH (aa)	132	Q VQLVQSGAEVKKPGASVKVSCKASGYPFT S YGISWVRQAPGQGLEWMGFISTYNA N TNY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWFGE S LIGGFDNWGQG TLTVSS	
SARS-CoV-2 S309-v2.4 mAb VH (aa)	133	Q VQLVQSGAEVKKPGASVKVSCKASGYPFT S YGISWVRQAPGQGLEWMGFISTY N QNTNY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWFGE S LIGGFDNWGQG TLTVSS	
SARS-CoV-2 S309-v2.5 mAb VH (aa)	134	Q VQLVQSGAEVKKPGASVKVSCKASGYPFT S YGISWVRQAPGQGLEWMGFISTYLGNTNY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWFGE S LIGGFDNWGQG TLTVSS	
SARS-CoV-2 S309-v2.6 mAb VH (aa)	135	Q VQLVQSGAEVKKPGASVKVSCKASGYPFT S YGISWVRQAPGQGLEWMGFISTYTGN T NY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWFGE S LIGGFDNWGQG TLTVSS	
SARS-CoV-2 S309-v2.7 mAb VH (aa)	136	Q VQLVQSGAEVKKPGASVKVSCKASGYPFT S YGISWVRQAPGQGLEWMGFISTYNGNTNY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAFFGE S LIGGFDNWGQG TLTVSS	

TABLE 1-continued

Sequence Description	SEQ ID NO.	Sequences	
		Sequence	
SARS-CoV-2 S309-v2.8 mAb VH (aa)	137	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGYISTYNGNTNY AQKFQGRVTMTTDTSTTTGYMELRRRLSDD TAVYYCARDYTRGAYFGESLIGGFDNWGQG TLTVVSS	
SARS-CoV-2 S309-v3 mAb VH (aa)	138	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGYISTYNGNTNY AQKFQGRVTMTTDTSTTTGYMELRRRLSDD TAVYYCARDYTRGAWFGESLIGGFDNWGQG TLTVVSS	
SARS-CoV-2 S309-v3.1 mAb VH (aa)	139	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGYISTYQGNTNY AQKFQGRVTMTTDTSTTTGYMELRRRLSDD TAVYYCARDYTRGAWFGESLIGGFDNWGQG TLTVVSS	
SARS-CoV-2 S309-v3.2 mAb VH (aa)	140	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGYISTYNSNTNY AQKFQGRVTMTTDTSTTTGYMELRRRLSDD TAVYYCARDYTRGAWFGESLIGGFDNWGQG TLTVVSS	
SARS-CoV-2 S309-v3.3 mAb VH (aa)	141	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGYISTYNANTNY AQKFQGRVTMTTDTSTTTGYMELRRRLSDD TAVYYCARDYTRGAWFGESLIGGFDNWGQG TLTVVSS	
SARS-CoV-2 S309-v3.4 mAb VH (aa)	142	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGYISTYNQNTNY AQKFQGRVTMTTDTSTTTGYMELRRRLSDD TAVYYCARDYTRGAWFGESLIGGFDNWGQG TLTVVSS	
SARS-CoV-2 S309-v3.5 mAb VH (aa)	143	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGYISTYLGNTNY AQKFQGRVTMTTDTSTTTGYMELRRRLSDD TAVYYCARDYTRGAWFGESLIGGFDNWGQG TLTVVSS	
SARS-CoV-2 S309-v3.6 mAb VH (aa)	144	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGYISTYTGNNTNY AQKFQGRVTMTTDTSTTTGYMELRRRLSDD TAVYYCARDYTRGAWFGESLIGGFDNWGQG TLTVVSS	
SARS-CoV-2 S309-v3.7 mAb VH (aa)	145	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGYISTYNGNTNY AQKFQGRVTMTTDTSTTTGYMELRRRLSDD TAVYYCARDYTRGAFFGESLIGGFDNWGQG TLTVVSS	
SARS-CoV-2 S309-v3.8 mAb VH (aa)	146	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGYISTYNGNTNY AQKFQGRVTMTTDTSTTTGYMELRRRLSDD TAVYYCARDYTRGAYFGESLIGGFDNWGQG TLTVVSS	
SARS-CoV-2 S309-v9 mAb VL (VK) (aa)	147	DIQMTQSPSSLSTSVDRTITCRASQGIN NYVAWYQQKPGKVPKLLIYGASTLQSGVPS RFRGSGSGTGTFTLTISLQPEDVASYYCRK YNSAPGTFGQGTRVEIK	
SARS-CoV-2 S309-v10 mAb VL (VK) (aa)	148	DIQMTQSPSSLSTSVDRTITCRASQGIN NYVAWYQQKPGKVPKLLIYGASTLQSGVPS RFRGSGSGTGTFTLTISLQPEDVASYYCRK YNSAPRTFGQGTRVEIK	

TABLE 1-continued

Sequences			
Sequence Description	SEQ NO.	ID	Sequence
SARS-CoV-2 S309-v11 mAb VL (VK) (aa)	149	DIQMTQSPSSLSTSGDRVTITCRASQGIN NYVAWYQQKPGKVPKLLIYGASTLQSGVPS RFRGSGSGTGTFTLTISSLQPEDVASYYCRK YNSAPFTFGQGTRVEIK	
SARS-CoV-2 S309-v12 mAb VL (VK) (aa)	150	DIQMTQSPSSLSTSGDRVTITCRASQGIN NYVAWYQQKPGKVPKLLIYGASTLQSGVPS RFRGSGSGTGTFTLTISSLQPEDVASYYCRK YNSAPYTFCQGTRVEIK	
SARS-CoV-2 S309-v9 mAb CDRL3 (aa)	151	RKYNSAPGT	
SARS-CoV-2 S309-v10 mAb CDRL3 (aa)	152	RKYNSAPRT	
SARS-CoV-2 S309-v11 mAb CDRL3 (aa)	153	RKYNSAPFT	
SARS-CoV-2 S309-v12 mAb CDRL3 (aa)	154	RKYNSAPYT	
SARS-CoV-2 S310 mAb VH (aa)	155	QVQLVQSGAELKKPGSSVKVSCKASGGTFN SYSFNWVRQAPGQGLEWLGGIIPVLGTSNY AQKFQGRVAVTADEFTTAYMELSSLRSED TAVYYCATRTYDSSGYRPYYYGLDVWGQGT PTVSS	
SARS-CoV-2 S310 mAb CDRHI (aa)	156	GGTFNSYS	
SARS-CoV-2 S310 mAb CDRH2 (aa)	157	IIPVLGTS	
SARS-CoV-2 S310 mAb CDRH3 (aa)	158	ATRTYDSSGYRPYYYGLDV	
SARS-CoV-2 S310 mAb VL (VK) (aa)	159	QSALTQPASVGSPGQSITISCTGTSSDVG SYNLVSWYQQRPKAPELMIFYEVTKRPSGL SNRFSGSKSGNTASLTISGLQAEDADYYC CSYAGSDTVIFGGGTKVTL	
SARS-CoV-2 S310 mAb CDRL1 (aa)	160	SSDVGSYNL	
SARS-CoV-2 S310 mAb CDRL2 (aa)	161	EVT	
SARS-CoV-2 S310 mAb CDRL3 (aa)	162	CSYAGSDTVI	

TABLE 1-continued

TABLE 1-continued

Sequence Description	Sequences	
	SEQ ID NO.	Sequence
4201	gctagcgaaa	gctttgagaa aagtgcac ac agacaattat ataaccactt accgggtca
4261	gggttaaat	ggtacactg tagaggagc aaagacatg cttaaaagt gtaaaagtgc
4321	ctttacatt	cttacatctt ctatctctaa tgagaagcaa gaaattcttg gaactgttcc
4381	ttggaatttgc	cgagaatgc ttgcacatgc agaagaacaa cgcaattaa tgcctgtctg
4441	tgtgaaact	aaagccatag tttcaactat acagegtaaa tataaggta taaaataaca
4501	agagggtgt	gttgattatg gtgcttagatt ttactttac accagtaaaa caactgtago
4561	gtca	tttacattt aacacactta acgtatctaa tgaactctt gtacaatgc cactggcta
4621	tgtacacat	ggcttaattt tgagaagac tgcctgttat atgagatctc tcaaagtgec
4681	agctacat	ttcttcttt cactgtatgc ttttacagcg tataatggtt atcttacttc
4741	ttcttctaa	acacctgaag aacatttat tggatggac ttttacatgc tcaacttgcgt gttcttataa
4801	agatggtcc	tattctggac aatctacaca actaggataa gaatttctta agagaggta
4861	taaaagtgt	tattacatac ttttacatgc ttttacatgc ttttacatgc ttttacatgc
4921	ctttagacat	ttttagttttt gagagaatgtt ggacttattt aggtgtttac
4981	aacagtagac	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5041	acagtttgtt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5101	acatgggtt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5161	tgatgttttt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5221	cactaaaaag	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5281	caactgttat	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5341	acctgtcttac	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5401	attatcttta	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5461	gcctactgt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5521	gagttacttgc	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5581	ttttagttttt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5641	agctacaaaat	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5701	tcgtatgtaa	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5761	gtgtgttcc	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5821	acttacaaat	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5881	ttttagttttt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
5941	tgaccctaa	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6001	tgatcttgc	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6061	tgataatata	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6121	aagagacatt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6181	taaacactt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6241	gcatgttac	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6301	tcttggagc	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6361	cgcgcaggga	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6421	ggaaaatccc	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6481	aggagacatt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6541	cacagatcttac	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6601	attatcttgc	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6661	tgtcccttgc	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6721	aactactaac	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6781	ttttagttttt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6841	atctatgcgc	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6901	ggcttcat	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
6961	gtttttacta	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7021	tttaatgtct	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7081	ctctactaa	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7141	tagtttttgc	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7201	atcttttaaa	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7261	tcttttact	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7321	ctattttgc	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7381	caaaatggcc	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7441	tgtatggaaa	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7501	ttacaaaatgt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7561	gtccctttat	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7621	tgttaattgt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7681	cttgcacta	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7741	tagtttata	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7801	ttatggatata	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7861	taaagggttca	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7921	atctgcaaaa	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
7981	agatcaggca	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
8041	tgcttacgtt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
8101	agttgcact	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
8161	ttttttttca	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
8221	tgaatgtctt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
8281	ctatatgtctc	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
8341	tgactgtgt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc
8401	atggaaacgtt	ttttagttttt ttttacatgc ttttacatgc ttttacatgc ttttacatgc

TABLE 1-continued

TABLE 1-continued

Sequence Description	Sequences	
	SEQ ID NO.	Sequence
12721	gtcttgtct	gccggtaact cacaactgc ttgcactgat gacaatgcgt tagttacta
12781	caacacaaca	aagggggtaa gggttgtact tgcaactgta tccgatttac aggatttgaa
12841	atgggttaga	tccctaaga gtatggaa ctgttactate tatacagaac tggaaaccacc
12901	ttgttaggtt	tttacagaca cacttaagg toctaaggta aagtatttat actttattaa
12961	aggattaaac	aaccttaataa gaggatgtgt acttgttagt tagctgcca cagtcgtct
13021	acaagctggt	aatgcacacag aagtgcctgc caattcaact gtattatctt tctgtgtctt
13081	tgctgttagat	gctgttaaaag cttaacaaaga ttatctagct aatgggggac aaccaatcac
13141	taatgtgtt	aaatgtgtgt gtacacacac ttgttactgtt cggcaataaa cagttacacc
13201	ggaaggcaat	atgtatcaag aatcccttgg tggtgcatcg tgggtctgt actgcgttg
13261	ccacatagat	catccaaatc ctaaggatt ttgtgactta aaggtaagt atgtacaaat
13321	acctacaact	tgtgtaatg accctgtggg ttttacactt aaaaacacag tctgtaccgt
13381	ctgggttagt	tggaaagggtt aaggtgttagt ttgtgatcaa ctccgcgaac ccatgcgtca
13441	gtcaagctgt	gcacaatcgt ttttaaacgg ttgtgcggg taatgtgcagc ccgtttaca
13501	ccgtggggca	caggcaactag tactgtatgc gtatacaggg cttttgacat ctacaatgt
13561	aaagtagctg	ttttgtctaa attccaaaaa actaattgtt gtcgccttcca agaaaaggac
13621	gaagatgaca	atttaattgtt ttcttactt tagttaaga gacacactt ctctaaactac
13681	caacatgtaa	aaacaatttaa taatattttt aaggattgtc cagctgttgc taaacatgtac
13741	ttctttaagt	tttagataga cggtgacatg gtaccacata tatacgtca acgttctact
13801	aaatacacaa	ttggcagaccc cgtctatgtt ttaaggcatt ttgtgtaagg taatttgac
13861	acataaaaaa	aaatattgtt ccatacataa ttgtgtgtg atgattattt caataaaaaaaag
13921	gactggtagt	atttttgtttaa aaccccgat attatccgcg tatacgccaa cttaggtgaa
13981	cgtgtacgcc	aaaggctttttt aaaaacagta caattctgtg atgcccattgc aaatgctgg
14041	attttttgtt	tactgacatt agataatcaa gatctcaatg gtaactggta tgatttcgg
14101	gatttcatac	aaaccacgcg aggttagtgg gttccctgtt tagatttta ttatttcattt
14161	ttaatgccta	tattaacccctt gaccagggtt ttaactgtcag agtcacatgt tgacactgac
14221	ttaacaaacg	tttacattaaatgtt gttggattttt ttaattatgtt atgctgtca cctgtctatg
14281	aaacttttg	accgttatttt taaatattgg gatcagacat accacccaaa ttgtgttaac
14341	tgtttggatg	acagatgtc ttcgttattt gcaaaacttta atgtttttt ctctacatgt
14401	ttcccaccta	caagttttgg accatagtg aaaaatggg ttgttgatgg ttgtccattt
14461	gtatgttcaa	ctggataccat ctttagagag cttagtgcgt tacataatca ggatgtaaac
14521	ttacatagct	cttagacttag tttaaggaa ttactgtgt atgctgtca cctgtctatg
14581	cacgtgtctt	ctgtatctt attactatg aacgcacta cgtgttttcc agtagctgc
14641	cttactaaca	atgtgtctt tttttttttt aacccggta attttaacaa agacttctat
14701	gactttgtt	tgcttaagggtt ttcttttaaag gaaggaaatgtt ttgttgatgg ttgtccattt
14761	ttctttgtctc	aggatgttaa tgctgtatc agcgattatg actactatcg ttataatcta
14821	ccaaacatgt	gtgatgtatcga aacactacta ttgtgtgtt aagtgtgtg taatgtacttt
14881	gattgttacg	atgggggtt tttttttttt tttttttttt aacccgttca tttttttttt cttttttttt
14941	tcagctgtt	ttccattttaa taatgggtt aagggttccat ttatattatgtt tttttttttt
15001	tatgaggatc	aaatgtcaat tttttttttt aacccgttca atgtcatccc tactataact
15061	caaatacatac	ttaatgttgc cttttttttt aacccgttca atgtcatccc tactataact
15121	tctatgtta	gtactatgtc catagacatg tttttttttt aacccgttca atgtcatccc
15181	gccccatag	gaggactgtt aacccgttca atgtcatccc tactataact
15241	atgtttaaaa	ttttttttttt tttttttttt aacccgttca atgtcatccc tactataact
15301	aaatgtgtaa	ttttttttttt aacccgttca atgtcatccc tactataact
15361	aaacatacatac	ttttttttttt aacccgttca atgtcatccc tactataact
15421	caatgttta	ttttttttttt aacccgttca atgtcatccc tactataact
15481	tcatcaggag	atgggggtt tttttttttt aacccgttca atgtcatccc tactataact
15541	acggccaaatg	ttttttttttt aacccgttca atgtcatccc tactataact
15601	cgcaattttt	ttttttttttt aacccgttca atgtcatccc tactataact
15661	ttttgttaatgt	ttttttttttt aacccgttca atgtcatccc tactataact
15721	gatgtgtttt	ttttttttttt aacccgttca atgtcatccc tactataact
15781	aactttaaatgt	ttttttttttt aacccgttca atgtcatccc tactataact
15841	actggagactt	ttttttttttt aacccgttca atgtcatccc tactataact
15901	aaacagggtt	ttttttttttt aacccgttca atgtcatccc tactataact
15961	ggctgttttt	ttttttttttt aacccgttca atgtcatccc tactataact
16021	tcttttagtca	ttttttttttt aacccgttca atgtcatccc tactataact
16081	ttttttttttt	ttttttttttt aacccgttca atgtcatccc tactataact
16141	gacatgttatt	ttttttttttt aacccgttca atgtcatccc tactataact
16201	tatgaggatca	ttttttttttt aacccgttca atgtcatccc tactataact
16261	aatttcacaga	ttttttttttt aacccgttca atgtcatccc tactataact
16321	tgctgttacc	ttttttttttt aacccgttca atgtcatccc tactataact
16381	gtttgtcaatg	ttttttttttt aacccgttca atgtcatccc tactataact
16441	agcttattttt	ttttttttttt aacccgttca atgtcatccc tactataact
16501	gtttttgtt	ttttttttttt aacccgttca atgtcatccc tactataact
16561	attgcaacat	ttttttttttt aacccgttca atgtcatccc tactataact
16621	agactcaacg	ttttttttttt aacccgttca atgtcatccc tactataact
16681	tatgttattt	ttttttttttt aacccgttca atgtcatccc tactataact
16741	gtttgttaac	ttttttttttt aacccgttca atgtcatccc tactataact
16801	aaaaacagta	ttttttttttt aacccgttca atgtcatccc tactataact
16861	gttttttacc	ttttttttttt aacccgttca atgtcatccc tactataact
16921	tcacatacag	ttttttttttt aacccgttca atgtcatccc tactataact

TABLE 1-continued

Sequence Description	Sequences	
	SEQ ID NO.	Sequence
16981	attactggct tatacccaa ac actcaat atc tcagatgagt tttctagcaa tg ttg caa at	
17041	tatcaaaaagg ttgttat gca aa agtatt ct ac actccagg gaccac tgg tact ggta ag	
17101	agtcat ttttgc ttatggc tac agtctctac tacccttcg ctcgcatat g tataca gct	
17161	tgctctcatg ccgttgc tgca ctat gat gagaaggcat taaaatattt gcctatagat	
17221	aatatgtat gaaattatcc tgcacgtgt ctgttagat gtttgcataa attcaaaatgt	
17281	aattcaacat tagaaacatg ta gtctttgt actgttaatg cattgctga gacgacagca	
17341	gatatagttg tctttgtat aatttcaatg gccacaaaattt atgatttgc tg tttgtcaat	
17401	gcccatttttgc tgctcaagca ctatgtgtac atggcgc acc tgcattt acctgcacca	
17461	cgcacatttc taactaaaggg cacatagaa ccagaatattt tcaattcatt gtgttagactt	
17521	atgaaaacta taggtccaga catgttcc tggaaacttgc ggcgttgc tgctgaaatt	
17581	gttgcacatg tgagtgc ttttgcataa aataagctt aagcacat taa agcaatca agacaatca	
17641	gtcataatgtt taaaatgtt aat aagggtt cgc atgatgtt ac tgcatttcaatt	
17701	aacaggccac aaataggcgt gtaaagagaa ttcccttacat gcaaccctgc ttggagaaaa	
17761	gctgtctta ttccac ttaatttccatc aatgtgttag cttcaat gat tttggacta	
17821	ccaactcaaa ctgttgc atcacaggc tca gat atatgatcat attcactca	
17881	accactgaaa cagcttca ttttgcataa aacatgtt aatgtgttat taccagagca	
17941	aaatgttgc ttttgcataa aatgtgttgc atgatgttgc atgatgttgc atgatgttgc	
18001	agtcttgc aatgtgttgc gatgtggca actttaacatg ctgaaatgtt aacaggactc	
18061	ttttaaagatt gtagaaggtt aatctactggg ttatcatcttta cacaggcacc tacacac ctc	
18121	agtgttgcata ctaatccatc aatgtgttgc ttatgtgttgc atacatcttgc cataccta	
18181	gacatgactt atagaagactt catcttcatg attttttttta aatgtat tcaatgtt	
18241	ggtttac ttttgcataa atcatgttgc ctttttttgcataa gacatgttgc ttttgcataa	
18301	ggcttcgtat ttttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa	
18361	cagcttgc ttttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa	
18421	cctaataatc ctttttttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa	
18481	caccttacatc ctttttttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa	
18541	caa atgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
18601	catgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
18661	tgtcttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
18721	catcttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
18781	ggtttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
18841	catgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
18901	aaggcttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
18961	gcttttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19021	gttcttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19081	tggaaatgcata atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19141	tatttttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19201	aatgttgcataa atcatgttgc ttttgcataa ttttgcataa ttttgcataa ttttgcataa	
19261	aaccttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19321	acaccaatgcata atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19381	tctgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19441	ctaaatgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19501	gcta atgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19561	tttgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19621	agtttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19681	gaatgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19741	gaatgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19801	cgcaatgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19861	gcta atgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19921	tttgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
19981	gttcttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20041	gttcttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20101	agtttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20161	aaatgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20221	caagaatgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20281	ttcatttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20341	agtttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20401	tcacccatgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20461	acatgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20521	gatgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20581	actatgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20641	tttgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20701	tacaaatgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20761	acatgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20821	aaacatgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20881	gataaaggatgcata atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
20941	tttgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
21001	tgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	
21061	aagactaaaa atgttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa	
21121	gggttatac aacaaatgcata atcatgttgc atgatgttgc ttttgcataa ttttgcataa	
21181	tcttttgcataa atcatgttgc atgatgttgc ttttgcataa ttttgcataa ttttgcataa	

TABLE 1-continued

TABLE 1-continued

Sequence Description	SEQ NO.	Sequences	
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	25561	cagagcgctt caaaatcat aaccctcaa aagagatggc aacttagact ctccaagggt	
	25621	gttcaacttgc ttgcaactt gctgtgttg ttgttaacag ttactcaca cctttgttc	
	25681	gttgcgtcg gcctgaage ctatccatc tatctttatc tttagtcta ctcttgcag	
	25741	agtataaact ttgttgaagaat aataatgagg ctttggctt gotgaaatg cogttccaa	
	25801	aaccattac ttatgatgc caactatccc ctttgcgttgc atactaattt ttacgactat	
	25861	tgtataccctt acaatagtgt aacttcttca attgtcatta cttcagggtga tggcacaaca	
	25921	agtcttattt ctgaacatgt ctaccaggatt ggtgggtt ctgaaaaatg ggaatcttgg	
	25981	gttggact gtgttggat acacagttac ttcaacttcg actattacca gctgtactca	
	26041	actcaattgtg acatcagacac tgggtttgaa catgttaccc ttttcatctca caataaaatt	
	26101	gttgcgttgc ctgaaagaaca tgccttcaattt cacacaatcg acgggtcata cggagttgtt	
	26161	aatccatgtt tggaaacat ttatgatgaa cggacgacga ctactagcgt gccttggtaa	
	26221	gcacaaatgtt atgatgtcgtt acttgcgttcc tttttttttt cttttttttt	
	26281	atagtaataa gctgtacttct tttttttttt ttgttggat ttgttgcgtt tacactagcc	
	26341	atccctactgt cgcttcgttgc ttgttgcgttgc tgctgtcaata ttgtttaacgtt gatgtttgtt	
	26401	aaaccttctt ttacgtttt ccctcgttgc ttgttgcgtt aatccatgtt atccatgtt agtccctgtat	
	26461	cttcttgcgttgc ttgttgcgtt aatccatgtt atccatgtt agtccctgtat ttatccatgtt	
	26521	ccatggcaga ttccaaatgtt acttccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	26581	ggaaatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	26641	ccaaatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	26701	taatccatgtt ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	26761	ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt ttatccatgtt	
	26821	tcagactgtt tgcgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	26881	tcaacatgttgc tttttttttt tttttttttt tttttttttt tttttttttt	
	26941	tcggagatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	27001	acatcaatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	27061	aatccatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	27121	ggatgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt ttatccatgtt	
	27181	ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt ttatccatgtt	
	27241	atccatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	27301	aatccatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	27361	gaagatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	27421	ataacatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	27481	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	27541	gtctgtatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	27601	ggcgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt ttatccatgtt	
	27661	caatccatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	27721	ataacatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	27781	tctatccatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	27841	gggttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt ttatccatgtt	
	27901	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	27961	agtcgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt ttatccatgtt	
	28021	ctaaatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	28081	atggatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	28141	gttccatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	28201	cggttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt ttatccatgtt	
	28261	cgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt ttatccatgtt	
	28321	gtttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	28381	atccatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	28441	cgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt ttatccatgtt	
	28501	caatccatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	28561	gtttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	28621	ggatgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt ttatccatgtt	
	28681	ggatgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt ttatccatgtt	
	28741	atccatgttgc ttgttgcgtt aatccatgtt ttgttgcgtt aatccatgtt ttatccatgtt	
	28801	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	28861	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	28921	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	28981	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	29041	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	29101	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	29161	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	29221	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	29281	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	29341	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	29401	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	29461	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	29521	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	29581	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	29641	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	
	29701	ttttttttttt tttttttttt tttttttttt tttttttttt tttttttttt	

TABLE 1-continued

Sequence Description	SEQ ID NO.	Sequences	
		Sequence	
		29761 acagtgaaca atgctaggga gagctgccta tatggaaagag ccctaattgtg taaaattaat 29821 tttagtagtg ctatccccat gtgattttaa tagttctta ggagaatgac aaaaaaaaaaa 29881 aaaaaaaaaa aaaaaaaaaa aaa	
Wuhan seafood market pneumonia virus isolate	164	MESLVPFGNEKTHVQLSLPVLVQVRDVLRVG FGDSVEEVILSEARQHLKDGTGCLVEKEKG LPQLEQPYVFIKRSDARTAPIHGHVMVELVA ELEGIQYGRSGETLGVLVPHGEIPVAYRK VLLRKNGNKGAGGHSYGAIDLKSFDLGEDLG TDPYEDFQENWNTKHSSGVTRELMRELNGG AYTRYVDNNFCGPDGYPLECIKDLLARAGK ASCTLSEQLDFIDTCKRGVYCRCREHEHEIAW YTERSEKSYELQTPFEIPLAKKKPDTFNNGEC PNFVFPLNSIIKTIQPRVEKKLDGFMGRI RSVYPVASPNECNQMCILSTLMKCDHCGETS WQTGDFVKATCEFCGTENLTKEGATTGYL PQNAVVKLYCPACHNSEVGPEHSLAEYHNE SGLKTILRKGGRTIAFGGCVFSYVGCHNKC AYWVPRASANIIGCNHTGVVGESEGELNDNL LEILQKEKVNNINIVGDFKLNEEIAIILASF SASTSAFVETVKGLDYKAFKQIVESCENFK VTKGAKKGAWNIGEQKSILSPLYAFASEA ARVURSISFRSLTAQNSVRVLQKAAITIL DGISQYSRLRIDAMMFTSDELATMNLVVMAY ITGGVVQLTSQWLTNIFCTVYKEKLKPVLDW LEEKFKEGVEFLRDGEWEIVKFISTCACEIV GGQIVTCAKEIKEVSQTFKLVNKFLALCA DSI II GGAKLKA LNLGETFVTHSKGLYRK VKSREETGLLMPPLKAPKEIIIFLEGETLPT VLTEEVVLKTGDLQPLQOPTSEAVEAPLVG TPVCINGLMLIEIKDTEKYCALAPNMVTN NTFTLKGAPTKVTFQDDTVIEVQGYKSVN ITFELDERIDKVLNEKCSAYTVELGTEVNE FACVVADAVIKTQLQPVSELLTPLGIDLDEW SMATYYLFDESGEFKFLASHMYCSFYPPDED EEECDCEEEEFPESTQYEYGTEDDYQGKPL EFGATSAALQPEEEQEEDWLDDDSQQTVCQ QDGSEDNQTTIQTIVTVEQPOLEMELTPVV QTEEVNSFSGYLKLTDNVYIKNADIVEEAK KVKPTVVVNAANVYLNKHGGVAGALNKATN NAMQVESDDYIATNGPLKVGGSCLSGHNL AKHCLHVGPVNKGEDIQLLK SAYENFNQ HEVLLAPLLSSAGIFGADPIHSLRVCVDTQ TNVLA VFDK NLYDKL VSSF LEMK S EK QVE QKIAEIPKEEVKPFITESKPSV EQRK QDDK KIKACVEEVTTL EETKPLTENLL YIDIN GNLHPDSATLVDSDIDITFLKDAPYIVGDV VQBGVLTA VVIPTKKA GGTTEMLAKALRKV PTDNYITTPGQGLNGYTVEAKTVLKKC SAFYI LPSI ISNEKQ EILGTVWSNLREMLA HAEETRKLMPCV C ETKA VSTIQRKYKG IK IQ EGVVDY GARF YFY TS KTTV ASL INTL ND LNETL VTMPLGVV THGLN LEA ARY MRS LK VPATV SVSSPD AVTAY NGY LTSS SKT PEEH FIETISLAGSYK DW SY SG QST QL GIEFL KR GD KS VYY TS NPT FHD GEV IT FDN LK TLL SLREV RTIKVFTTVDN INL HTQV VDMS MTY GQ QFG P T YLDG AD VT K1 KPH NS HEG KTF YV LPN DDT LR VEA F EY YHT TDPS FL GR YM SAL NHTKKW K YPQ VN GL TS I KWAD NN CYL AT AL L TLQ QI ELK FN PPA LQ DAY YR A RAGE A ANF CAL I LAY CN KTV GEL DV RET M S YL F QH AN LD SCK RV LN VV C K TCG Q Q QT TL KG V EA VM Y MGT LS YEQ FK KG V QIP CT CG K QAT K YL V Q Q ESP FV MM S A P P A QY E LK HG GT F T C A S E Y T G N Y QCG HY K H I T SK E T LY C I D G ALL L T K S S E Y K GPI T D V F Y K E N S Y T T T I K P V T Y K L D G V V C T EIDPKL D NYK K D N S Y F T E Q P I D L V P N Q P Y P N A S F D N F K F V C D N I K F A D D L N Q L T G Y K K P A S R E L K V T F F P D L N G D V V A I D Y K H Y T P S F K KGAKL LH KPI VVWHVNNATN KAT YK P N T W C I	
Wuhan-Hu-1 genomic sequence (GenBank: MN908947.3; Jan. 23, 2020) - amino acid translation			

TABLE 1-continued

		Sequences
Sequence Description	SEQ ID NO.	Sequence
		RCLWSTKPVETNSNSFDVLSKSEDAQGMDNLA CEDLKPVSEEVENPTIQLKDVLCECNVKTTE VVGDIIILKPAANSLKITEEVGHTDLMAYAV DNSSLTIKKPNELSRLVGLKTLATHGLAAV NSVPWDITIANYAKPFLNKVSTTTNIVTRC LNRVCNTNYMPYFFTLLLQLCTFTRSTNSRI KASMPPTIAKNTVKSVGKFCLEASFNYNLKS PNFSKLINIIIWFLLLSVCLGSLIYSTAAL GVLMSNLGMPSYCTGYREGYLNSTNVTIAT YCTGSIPCSVCLSGLDSDLTYPSETIQIT IISPFKWDLTAFGLVAEWFPLAYILFTRFYV LGLAAIMQLFFSYFAVHFISNSWLMWLIIIN LVQMAPISAMVRMYIFFASFYVYWWKSYVHV VDGCNSSTCMCMYKRNRATRVECTTIVNGV RRSFYVYANGKGKFCKLHNWNCVNCDTFCA GSTFIISDEARDLQLQFKRPINPTDQSSYI VDSTVTKNGSIHLYFDKAGQKTYERHSLSH FVNLDNLRANNTKGSLPINIVFVDGSKKCE ESSAKSASVYYSQLMCQPILLLDQALVSDV GDSAEVAVKMFDAYVNTFSSTPNVPMEKLK TLVATAEELAKNSLDNVLSTFISAARQG FVDSVETKDVVECLKLSHQSDIEVTGDS NNYMLTYNKVENMTPRDLGACIDCSARHIN AQVAKSHNIALIWNVKDFMSLSEQLRKQIR SAAKKNNLPFKLTCATTRQVNVVTTKIAL KGKIVNNWKLQOLIKVTLVFLVAAIFYLI TPVHVMKSHTDFSSEIIIGYKAIDGGVTRDI ASTDTCFANKHADFDTWFSQRGGSYTNDKA CPLIAAVITREVGFVVPGPLPGTILRTTNGD FLHFLPRVFSAVGNICYTPSKLIEYTDFA SACVLAECTIFKDASGKPVPYCYDTNVLE GSVAYESLRPDTRYVLMGSIQFPNTYLE GSVRVTTFDSEYCRHGTCEAGVCVST SGRWVLNNDDYRSLPGVFCGVDAVNLLTNM FTPLIQPICALDISASIVAGGIVAIIVTCL AYYFMFRRAFGHEYSHVVAFTNLLFLMSFT VLCITPVYSFLPGVYSVIYLTFYLTNDV SFLAHIOWMVMTPLVFWITIAYIICIST KHFYWFFSNYLKRRVVFNGVSFSTFEEAAL CTFLLNKEMYLKLRSDFVLLPLTQYNRYLAL YNKYKYFSGAMDTTSYREAACCHLAKALND FSNSGSDVLYQPQQTTSITSAVLQSGFRKMA FPSPGKVEGCMVQVTCGTTLNGWLDDVVY CPRHVICTEDMLNPNEYEDLLIRKSNNHNFL VQAGNVQLRVIGHSMQNCVLUKLKVDTANPK TPKYKFVRIQPGOTFSVLACYNGSPGCVYQ CAMRPNFTIKGSFLNGSCGSVGFNIDYDCV SFCYMHMELPTGVHAGTDLEGNFYGFVFD RQTAQAAGTDTITTVNVLAWLYAAVINGDR WFNLRFTTTLDNFNLVAMKYYEPLTQDHV DILGPLSLAQTGIAVLDMCASLKEQQNGMN GRTILGSALLEDEFTPFDVVRQCSGGVTFQS AVKRTIKGTHWLLLTILTSLLVLVQSTQW SLFFFPLYENAFLPFAMGI IAMSAFAMMFVK HKHAFLCLFLPLPSLATVAYFNMVYMPASWV MRIMTWDMDVDTSLSGFKLKDVCVMYASAVV LLILMARTVYDDGARRVWTLMNVTLVYK VYYGNALDQAIISMWALIISVTSNYSGVVT VMPFLARGIVFMCEYCPIFFITGNTLQCIM LVYCFLGYFCTCYFGLFCLLNRYFRLLTGLV YDYLVSTQEFRYMNNSQGLLPPKNSIDAFKL NIKLLGVGGKPCIKVATQSKMSDVKCTSV VLLSVLQLRVESSSKLWAQCVQLHNDILL AKDTTEAFEKMSLSSVLLSMQAVDINKL CEMLDNRATLQAIASEFSSLPSYAAPATA QEAYEQAVANGDSEVVVLKKLKKSLNVAKSE FRDAAMQRKLEKMAQDMQMTQMYKQARSED KRAKVTSAQMQLFTMLRKLDNDALNNIIN NARDGCVPLNIIPLTTAAKLMVVIPDYNTY KNTCDGTTFTYASALWEIQQVVDADSKIVQ LSEISMDNSPNLAWPLIVTALRANSAVKLQ

TABLE 1-continued

Sequence Description	Sequences	
	SEQ ID NO.	Sequence
		NNELSPVALRQMSCAAGTTQACTDDNALA YYNTTKGGRFVLALLSDLQDLKWARFPKSD GTGTIYTELEPPCRFVTDTPKGPKVLYF IKGLNNLNRMVGLGSLAATVRLQAGNATEV PANSTVLSFCAFAVDAAKAYKDYLASGGQP ITNCVVKMLCTHTGTGQAI TVTPEANMDQES FGGASCLLYCRCHIDHNPNGKFCDLKGKYV QIPTTCANDPVGFTLKNTVCTVCGMWKGY CSCDQLREPMQSLADAQSFLNRVCVGSAAR LTPCGTGTSTDVVYRAFDIYNDKVAGFAKF LKTNCRCRQEKDDEDDNLIDSYPFVVKRHTFS NYQHEETIYNLLKDCPAVAKHDFFKFRIDG DMVPHISRQLRTKYMADLVYALRHFDEN CDTLKEILVTYNCDDDFNKKDWYDFVEN PDILRVYANLGERVRQALLKTQFCDAMRN AGIVGVLTLDNQDLNGNWYDFGDFIQTTPG SGVPVVDSYSSLLMPILTLTRALTAESHVD TDLTKPYIKWDLKYDFTTEERLKLFDRYFK YWDQTYHPNCVNCNLCDDRCILHCANFNVLFS TVFPPTSFGPLVRKIFVGDGVPPVVSTGYHF RELGVVHNQDVNLHSSRLSFKEELVYAADP AMHAASGNLLLDKRTTCSVAALTNNVAFQ TVKPGNFNKDFYDFAVSKGFFKEGSSVELK HFFFAQDGNAASI DYDYYRYNLPTMCDIRQ LLFVVEVVDKYFDCYDGCCINANQVIVNNL DKSAGFPFNWKGKARLYYDMSYEDQDALF AYTKRNVIPITITQMNLYKAISAKNRARTVA GVSICSTMTRQFHQKLKSIATRGRATVV IGTSKFKYGGWHNMLKTIVSDVNPFLMGWD YPKCDRAMPNMLRIMASLVLARKHTTCSSL SHRFYRLANECAQLSEMVCMCGGSLYVKPG GTS SGDATTAYANSVFNIQCQAVTANVNALL STDGNKIADKYVRNLQHRLYECLYRNRDVD TDFVNEFYAYLKRHKFSMILSCLDAVVCFNS TYASQGLVASICNFKSVLYQQNNVFMSEAK CWTFETDLTKGPHEFCSQHTMLVHQGDYYV LPYDPDSRILGACCFVDDIVKTDTLMIER FVSLAIDAYPLTKHPNQFYADVFHLYLQYI RKLHDELTGHMLDMYSVMLINDNTSRYWEP EFEYEAAMYTPHTVLQAVGACVLCNSQTSLRC GACIRRPLCCKCYDHVISTSHKLVL SVN PYVCNAPGCDVTDVTQLYLGGMYYCKSHK PPISFPLCANGQVFGLYKNTCVGSDNVTFD NAIATCDWTNAQDYIILANTCTERLKLFAAE TLKATEETFKLSSYGIATVREVLSDRELHLS WEVGKPRPPLNRNYVFTGYRVTKNSKVQIG EYT FEKGDYGDAVVYRGTTTYKLNVDYFV LTSHTVMPLSAFTLVPQEHYVRITGLYPTL NISDEFSSNVANYQKVGQMOKYSTLQGPPGT GKSHFAIGLALYPPSARI VYTACSHAADVDA LCEKALKYLPIDKCSR II PARARVECDFK KVNSTLEQYVFCTVNALPETTADIVVDEI SMATNYDLSVNRRLRAKHVVYI GDPAQLP APRTLLTKTGLEPEYFNSVCRMLMKTIGDM FLGTCRRCPAEIVDTV SALVYDNKLKAHD KSAQCFKMFYKGVI THDVS SAINRPQIGVV REFLTRNPWARKAVFISPYNQNAVASKIL GLPTQTVDSQQSEYDVIFTQTTEAHSC NVNRFNVAITRAKVGILCIMS DRDLYDKLQ FTSLEIPRRNVA TLQAENVTGLFKDCSKVI TGLHPTQAPTHLSVDTKF KTEGLCVDIPGI PKDMTYRRLISMMGFKM NYQVN GPNMFIT REEAIRHVRRAWIGFDVEGCHATREAVGTLN PLQLGFSTGVNLVAVPTGYVDTPNNTDFSR VSAKPPPQDFQKHLIPLMYKGLPWNVVR IVQMLS DTLKNLSDR VVFLWAHG FEL TSM KYFVKIGPERTCLCDRRATC FSTASDTYA CW HHSIGFDYVYNP FMIDVQ QWGFTGNLQS NH DLYCQVHGNAHVAS CDAIMTRCLAVHEC FVKRVDWTIEYPII GDELKINAACRKVQHM VVKA ALLADKF PVLDIGNPKAIKCVPQAD

TABLE 1-continued

		Sequences	
Sequence Description	SEQ ID NO.	Sequence	
		VEWKFYDAQPCSDKAYKIEELFYSYATHSD KFTDGVCFLFWNCNVDRYPANSIVCRFDTRV LSNLNLPGCDGGSLYVNKHAFHTPAFDKSA FVNVLKQLPFFYYSDSPCCESSHGKQVVSDIDY VPLKSATCITRCNLGGAVCRHHANEYRLYL DAYNMMISAGFSLWVYKQFDTYNLWNNTFTR LQSLENVAFNVVNKGHFDGQQGEVPVSIIN NTVYTKVDGVDFVELFENKTTLPVNVAFELW AKRNIKPVEVKILNNNLGVDIAANTVIWDY KRDAPAHISTIGCSMTDIACKPTETICAP LTVFFDGRVGDQVDFRNARNGVILTEGSV KGLQPSVGPQKQASLNGVTLIGEAVKTQFNY YKKVVGVVQQLPETYFTQSRNLQEFEKPRSQ MEIDFLELAMDEFIERYKLEGYAFEHIVG DFSHSQLGGLHLLIGLAKRFKESPFELED IPMDSTVKNYFITDAQTGSSKCVCSVIDL LDDFVEIIKSQDLSVSVSKVVKVTIDYTEIS FMLWCKDGHVETFYPKLQSSQAWQPGVAMP NLYKMQRMLLEKCDLQNYGDSATLPKGIMM NVAKYTQLCQYLNTLTLAVPYNMNRVIHFGA GSDKGVAPGTAVLRQWLPTGTLVVDSDLND FVSDADSTLIGDCATVHTANKWDLIISDMY DPKTKNVTKENDSKEGFETYICGFIQQKLA LGGSVAIKITEHSWNADLYKLMGHFAWWTA FVTNVNASSSEAFLIGCNYLGKPREQIDGY VMHANYIIFWRNTNPIIQLSSYSLFDMSKFPL KLRGTAVMSLKEQOINDMILSLLSKGRLLI RENNRVRVISSDVLVNN	
surface glycoprotein [Wuhan seafood market pneumonia virus]; GenBank: QHD43416.1; Jan. 23, 2020	165	mfvflvllpl vssqcvnltt rtqlppaytn sftrgvyydp kvfrssvlhs tqdlflpffs 61 nvtwfhaihv sgtngtkrfd npvlpfndgv yfasteksn iргwifgttl dsktqsliv 121 nnatnvvkv cefqfondpf lgvyvhnnk swmesefrvy ssannctfey vsqpfldmle 181 gkgnfnknlr efvfknidgy fkiyshktpi nlvrdrlpqgf saleplvldp iginitrfqt 241 lalahrstytl pgdsssgwta gaaayyvgyl qprtfllykn engtitdavd caldplsetk 301 ctksftvek giyqtsnfrv qptesivrfp ntitnlcpfge vfnatrfasv yawnrkrisn 361 cvadsvlyn sasfstfkcy gvsptklndl cftnvyadef virgdevrqi apgqtgkia 421 ynyklpddft gcviawnsnn ldkvqggyn ylyrlfrksn lkpferdist eiylqagstpc 481 ngvegfncfy plqsygfpqpt ngvgyqpyrv vvlsfellha patvcgpkks tnlvknkcvn 541 fnfnlgltg vltessnkf1 pfqqfqgrdia dttdavrdpq tleilditpc sfggvsvitp 601 gtntsnnqvav lyqdvntev pvalihadqtl ptwrvystgs nvfqtrac1 igaehvnnsy 661 ecdipigagi casyqtqtns prrarsvasq siiaytmssl aensvaysnn siaiptnfti 721 svtceilps mtktsvdctm yicgdstece nlllqygsc tqlnraltgi aveqdktqe 781 vfaqvkqiyk tppikdfggf nfsqilpdps kpskrsfied llfnkvttlad agfikqygdc 841 lgdiaardli caqkfngltv lppltdemi aqytsallag titsgwtfga gaalqipfan 901 qmayrfngig vtqnvllyenq klianqfnsa igkiqdslls tasalgklqd vvnqnaqln 961 tlvkqlssnf gaissvlni lsrldkveae vqidrlitgr lqslqtyvtq qliraaeira 1021 sanlaatkms ecvlqggskrv dfcgkgylml stpqsapnvg vflhvtyvpq qeknftapa 1081 ichdgkahfp regvftvsnfy hwftvqrnfy epqittdnt fvsgncdvv1 givnntvydp 1141 lqpeledsfk eldkyfknht spfdlgdis ginavvniq keidrlneva knlneslid1 1201 qelgkyeqyi kpwyiwlgf iagliaivmv timlccmtsc csclkGCCSC gscckfde 1261 sepvlkgvkl hyt	
surface glycoprotein RBD [Wuhan seafood market pneumonia virus]; GenBank: QHD43416.1; Jan. 23, 2020	166	nitnlcpfgevfnatrfasvyawnrkrisn cvadsvlynsasfstfkcygvsptklndl cftnvyadsfvirgdevrqiapgqtgkia ynyklpddftgcviawnsnnldskvqggyn ylyrlfrksnlpferdisteiylqagstpc ngvegfncfyplqsygfpqtnvgvgyqpyrv vvlsfellhapatvcgpkstnlvknkcvn fnfnlgltg	

TABLE 1-continued

Sequence Description	SEQ NO.	Sequences	
		ID	Sequence
Receptor Binding Motif (RBM) in surface glycoprotein RBD [Wuhan seafood market pneumonia virus]; GenBank: QHD43416.1; Jan. 23, 2020	167		Nsmnldskvggnynylyrlfrksnlkpfer disteiyqagstpcngvegfncyfplqsyg fqptngvgyqpy
SARS-CoV-2 S309-v13 mAb VL (VK) (aa)	168	EIVLTQSPGTLSSLPGGERATLSCRASQTVS STSLAWYQQKPGQAPRLLIYGASSRATGIP DRFSGSGSGTDFLTISRLEPEDFAVYYCQ QHDTSLTFGGGTKEIK	
SARS-CoV-2 S309-v13 mAb CDRL1 (aa)	169	QTVSSTS	
SARS-CoV-2 S309-v13 mAb CDRL2 (aa)	170	GAS	
SARS-CoV-2 S309-v13 mAb CDRL3 (aa)	171	QQHDTSLT	
SARS-CoV-2 S309-v2.9 mAb VH (aa)	172	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGFISTYNANTNY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAFFGESLIGGFDNWGQG TLTVSS	
SARS-CoV-2 CH1-CH3 G1m17; IgG1*01 LS (aa)	173	ASTKGPSVFPLAPSSKSTSGGTAALGCLVK DYFPEPVTVWSNSGALTSGVHTFPAVLQSS GLYSLSVVTPVSSSLGTQTYICNVNHHKPS NTKVDDKKVEPKSCDKTHTCPCCPAPELLGG PSVFLFPKPKDLMISRTPEVTCVVVDVS HEDPEVKENWYWDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKA LPAPIEKTIASKAKGQPREPQVTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVLHEALTHSHYTQKSLSLSPGK	
SARS-CoV-2 mAb CL (Ck) IgG1*01 klm3 (aa)	174	RTVAAPSVFIFPPSDEQLKSGTASVVCNN NFYPREAKWQWKVDNALQSGNSQESVTEQD SKDSTYSLSSTTLSKADYEKHKVYACEVT HQGLSSPVTKSFNRGEC	
SARS-CoV-2 CH1-CH3 G1m17; IgG1*01 LS GAALIE (aa)	175	ASTKGPSVFPLAPSSKSTSGGTAALGCLV KDYFPEPVTVWSNSGALTSGVHTFPAVLQSS SGLYSLSSVTVPPSSSLGTQTYICNVNHHKPS SNTKVDDKKVEPKSCDKTHTCPCCPAPELLGG GPSVFLFPKPKDLMISRTPEVTCVVVDVS SHEDPEVKENWYWDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA ALPLPEEKTIASKAKGQPREPQVYTLPPSRDE ELTKNQVSLTCLVKGFYPSDIAVEWESNGQP QPNENYKTPPVLDSDGSFFLYSKLTVDKSRW RWQQGNVFSCSVLHEALTHSHYTQKSLSLSP GK	

TABLE 1-continued

Sequence Description	SEQ NO.	Sequences	
		ID	Sequence
SARS-CoV-2 S300-v2.10 mAb VH (aa)	176	QVQLVQSGAEVKPGASVKVSCKAS GYTFT DYYIHWVRQAPGQPGEWLGFVNAYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEFAMYFFDNWGQGLVTVSS	
SARS-CoV-2 S300-v2.11 mAb VH (aa)	177	QVQLVQSGAEVKPGASVKVSCKAS GYTFT DYYIHWVRQAPGQPGEWLGFVQGYSGATRY AQKYQGRVTMTRDTSISTAYMQLSRLRPDD TAVYYCARDRPSHEFAMYFFDNWGQGLVTVSS	
SARS-CoV-2 S315-v1 mAb VH (aa)	178	EVQLVESGGGLVQPGGSLRLSCAAS GFTFS NYWMWTWVQAPGKLEWVANIKQDGSEKYY VDSVKGRTISRDNAKNSLYLQMNSLRAED TAVYYCARDLWWND QAHYYGMDVWQGQTTV TVSS	
SARS-CoV-2 S315-v1 mAb CDRH1 (aa)	179	GPTFSNYW	
SARS-CoV-2 S315-v1 mAb CDRH2 (aa)	180	IKQDGSEK	
SARS-CoV-2 S315-v1 mAb CDRH3 (aa)	181	ARDLWWND QAHYYGMDV	
SARS-CoV-2 S315-v1 mAb VL (aa)	182	SYELTQPPSVSPGQTARITCSGDAPPNQ YAYWYQQ KPGQAPVMLIYKDSE RGPSGIPER FFGSSSGTIVTTLTIRGVQA EADYYCQSA DSSGTVPFGGTKLTVL	
SARS-CoV-2 S315-v1 mAb CDRL1 (aa)	183	AFPNQY	
SARS-CoV-2 S315-v1 mAb CDRL2 (aa)	184	KDS	
SARS-CoV-2 S315-v1 mAb CDRL3 (aa)	185	QSADSSGT	
SARS-CoV-2 S315-v1 mAb VH (nt-wt)	186	gagggtcagctggggagttctgggggg ttggtcacgcctgggggtccctgggggg tcctgtcagccctgg gatccac tttagt aattattggat gacctgggtccggccaggct ccagggaagggggtggggatggggggccaaac ataaagcaagatggaaagtgaga aatactat gtggactctgtgaaggccgattcaccatc tccagagacaacgccaagaactcaactgtat ctgcacaaatgaaacagcctgagagccggagac acggctgttattactgt cgagagat tt tgttggaacgac agggtcactactacggt atggacgtct ggggccaagggaccacggtc accgtctccatcg	
SARS-CoV-2 S315-v1 mAb VL (nt-wt)	187	tccttatgagctgacacagccaccctcggt tcagtgtcccaggacagacggccaggatc acctgctctggagat cat ttccaaaccaa tat gttattggtaccagcagaagccaggc caggccctgtatgtat aaagac agt gagaggccctcaggatccctgagcga ttctttggctccagctcaggacaacagtc acgttgaccatcagaggatccaggcagaa gacagggtgactattactgt eaat cagca	

TABLE 1-continued

Sequence Description	SEQ ID NO.	Sequences	
		Sequence	
		gacagcagtggtaccgtgttccggcgagggg	
		accaagctgaccgtccctag	
SARS-CoV-2 S315-v1 mAb VH (nt-codon optimized)	188	GAAGTCAGCTTGTGAGAGCGGGAGGC CTCGTTAGCCAGGTGGGAGTCCTCGTCTT TCATGCGCCGCTTCAGGATTACGTTCTCC AACTACTGGATGACATGGGTGAGGCAGGCA CCTGGGAAGGGGCTGGAGTGGGTGGCTAAC ATCAAGCAGGACGGATCTGAAAAAATTAT GTAGATTCTGTGAAGGGCGGTTACCATC TCAAAGGGATAATGCCAAAACCTTTGTAT TTACAGATGAACTCTCTCGAGCCGAGGAC ACGCCGTTACTACTGTGCCAGAGCTA TGGTGGAAATGACCAGGCTCACTATTATGGA ATGGACGTGGGGCCAGGGTACTACCGTT ACCGTCTCCTCA	
SARS-CoV-2 S315-v1 mAb VL (nt-codon optimized)	189	TCTTACGAGCTCACCCAGCCACCCCTCAGTG TCAGTGAGCCCTGGCCAAACAGCTCGCATC ACCTGTTAGGTGACGCCCTTCCAAATCAG TACGCCCTACTGGTATCAGCAGAAACCCGGC CAGGCACCCGTTATGCTCATCTACAAAGAT TCTGAGCGGCCATCGGTATCCCGAACGC TTTTTCGGAAGCTCAGTGGGACTACAGTT ACACTTACTATCCGGGAGTGAAGCTGAA GATGAGGCCGACTATTATGCCAGAGGGCA GACTCCTCAGGCACAGTGTGTTGGGGCGGG ACTAAACTAACTGTGCTG	
SARS-CoV-2 S315-v2 mAb VL (aa)	190	SYELTOPPSVSVPQQTARIICSGDAFPNQ YAWYQOKPGQAPVMLIYKDSERPSGIPER FFGSSSGTTVTLTISGVQAEDADYYCQSA DSSGTVFGGGTKLTVL	
SARS-CoV-2 S315-v2 mAb VL (nt-wt)	191	tctatgagctgacacagccaccctcggt tcagtgtcccaggacacaggccaggatc acctgctctggagat gcattccaaaccaa tatgcattttggtagccacggcagaaggcaggc caggccctgtatgtctgatctataaagac agttagaggccctcaggatccctgagcga ttcttgctccaggctcaggagacaacgatc acgttgaccatcgtggatccaggcagaa gacgggtgactattactgt caatcagca gacagcagtggtaccgtgttccggcgagggg accaagctgaccgtccctag	
SARS-CoV-2 S315-v2 mAb VL (nt-codon optimized)	192	TCCTACGAGCTCACCCAGCCCCCTCAGTC TCTGTGTCCTCGACAGACAGCCAGAATC ACCTGCTCGGGAGATGCTTTTCCCAACCAA TACGCCCTACTGGTACCAACAGAAACCAAGGT CAGGCCTGTCATGCTGATTATA AAAGAC TCAGAGCGGCCCTCAGGAATTCCGAAAGA TTCTCGGGAGTTCAAGGGAAACTACCGTG ACCTTAACCATAAAGCGGGGTGCAGGCCGAA GATGAAGCAGACTATTATGCCAGAGTGCC GATAGTAGTGGCACAGTCTTGGGGGGGG ACAAAGCTGACAGTACTC	
SARS-CoV-2 mAb CL IgLC*01	193	GQPKAAPSVTLFPPSSEELQANKATLVCLI SDPYPGAVTVAWKADSSPVKAGVETTPSK QSNNKYAASSYLSLTPEQWKSHRSYSQCVT HEGSTVEKTVAPTECS	
SARS-CoV-2 S315-v3 mAb VH (aa)	194	EVQLVESGGGLVQPGGSLRLSCAASGFTFS NYFMTWVRQAPKGLEWVANIKDGSKEYY VDSVKGRFTISRDNAKNSLYLQMNSLRAED TAVYYCARIDLWWND QAHYYGMDVWGQGTTV TVSS	

TABLE 1-continued

Sequence Description	SEQ NO.	Sequences	
		ID	Sequence
SARS-CoV-2 S315-v3 mAb CDRH1 (aa)	195	GFTFSNYF	
SARS-CoV-2 S315-v4 mAb VH (aa)	196	EVQLVESGGGLVQPGGSLRLSCAASGFTFS NYWMTWVRQAPGKGLEWVANIKQDASEKYY VDSVKGRFTISRDNAKNSLYLQMNSLRAED TAVYYCARDLWWNDQAHYYGMDVWGQGTTV TVSS	
SARS-CoV-2 S315-v4 mAb CDRH2 (aa)	197	IKQDASEK	
SARS-CoV-2 S315-v5 mAb VH (aa)	198	EVQLVESGGGLVQPGGSLRLSCAASGFTFS NYWMTWVRQAPGKGLEWVANIKQEGSEKYY VDSVKGRFTISRDNAKNSLYLQMNSLRAED TAVYYCARDLFWNDQAHYYGMDVWGQGTTV TVSS	
SARS-CoV-2 S315-v5 mAb CDRH2 (aa)	199	IKQEGSEK	
SARS-CoV-2 S315-v6 mAb VH (aa)	200	EVQLVESGGGLVQPGGSLRLSCAASGFTFS NYWMTWVRQAPGKGLEWVANIKQDGSEKYY VDSVKGRFTISRDNAKNSLYLQMNSLRAED TAVYYCARDLFWNDQAHYYGMDVWGQGTTV TVSS	
SARS-CoV-2 S315-v6 mAb CDRH3 (aa)	201	ARDLFWNDQAHYYGMDV	
SARS-CoV-2 S315-v7 mAb VH (aa)	202	EVQLVESGGGLVQPGGSLRLSCAASGFTFS NYWMTWVRQAPGKGLEWVANIKQDGSEKYY VDSVKGRFTISRDNAKNSLYLQMNSLRAED TAVYYCARDLFWNDQAHYYGMDVWGQGTTV TVSS	
SARS-CoV-2 S315-v7 mAb CDRH3 (aa)	203	ARDLWFNDQAHYYGMDV	
SARS-CoV-2 Heavy Chain IgHG1*01 Fd (aa)	204	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGWISTYNGNTNY AQKFQGRVTMTTDSTTTGYMELRRRLRSDD TAVYYCARDYTRGAWFGEESLIGGFDNWGQG TLTVVSSASTKGPSVFP LAPSSKSTSGGTA ALGCLVKDYYFPEPVTVWSNSGALTSGVHTF PAVLQSSGLYSLSSVVTPSSSLGTQTYIC NWNHKPSNTKVDKRVEPKSC	
SARS-CoV-2 Light Chain IgKC*01 (aa)	205	EIVLTQSPGTLSSLPGGERATLSCRASQTVS STS LAWYQOKPGQAPRLLIYGASSRATGIP DRFSGSGSGTDFTLTISRLEPEDFAVYYCQ QHDTSLT PFGGGTKVEIKRTVAAPS VFI FPP SDEQLKSGTASVVC LNNFYPREAKVQWKV DNA LQSGNSQESVTEQDSKDST YSL S STL LSKAD YEKHKVYACEVTHQGLSSPVT KSFN RGE C	
Linker (aa)	206	GSTSGSGKPGS GEG STKG	
Linker (aa)	207	GSGKPGS GEG	
Linker (aa)	208	GKPGS GEG	
Linker (aa)	209	SGKPGS GE	

TABLE 1-continued

TABLE 1-continued

Sequence Description	SEQ NO.	Sequences	
		ID	Sequence
			FTSYGISWVRQAPGQGLEWMGWISTYNGNTNYA AQKFQGRVTMTTDSTTTGYMELRRRLRSDD DDTAVYYCARDYTRGAWFGESELIGGFDNWGQ QGTLVTVSS
SARS-CoV-2 S309-scFv (VH-VL) - (VH-VL) (aa)	222		QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGWISTYNGNTNYA AQKFQGRVTMTTDSTTTGYMELRRRLRSDD DDTAVYYCARDYTRGAWFGESELIGGFDNWGQ TAVYYCARDYTRGAWFGESELIGGFDNWGQG TLTVVSSGGGGSGGGGGGGGGSEIVLTQSP GTLSLSPGERATLSCRAS QTVSSTS LAWYQ QKPGQAPRLLIY GASSRATGIP DRFSGSGS GTDFTLTISRLEPEDFAVYYC QOHDTS LTF GGGTKVEIKGGGGSGGGGGGGGGGGGGGGGGGG VQLVQSGAEVKPGASVKVSCKASGYPFT YGLISWVRQAPGQGLEWMGWISTYNGNTNYA QKPGQAPRLLIY GASSRATGIP DRFSGSGS GTDFTLTISRLEPEDFAVYYC QOHDTS LTF AVYYCARDYTRGAWFGESELIGGFDNWGQG TLTVVSSGGGGSGGGGGGGGGGGSEIVLTQSP GTLSLSPGERATLSCRAS QTVSSTS LAWYQ KPGQAPRLLIY GASSRATGIP DRFSGSGS GTDFTLTISRLEPEDFAVYYC QOHDTS LTF GGTKVEIK
SARS-CoV-2 S309-scFv- (VH-VL) - (VL-VH) (aa)	223		QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGWISTYNGNTNYA AQKFQGRVTMTTDSTTTGYMELRRRLRSDD DDTAVYYCARDYTRGAWFGESELIGGFDNWGQ TAVYYCARDYTRGAWFGESELIGGFDNWGQG TLTVVSSGGGGSGGGGGGGGGGGSEIVLTQSP GTLSLSPGERATLSCRAS QTVSSTS LAWYQ QKPGQAPRLLIY GASSRATGIP DRFSGSGS GTDFTLTISRLEPEDFAVYYC QOHDTS LTF GGGTKVEIKGGGGSGGGGGGGGGGGGGGG IVLTQSPGTLSLSPGERATLSCRAS QTVS TSLAWYQQKPGQAPRLLIY GASSRATGIP RFSGSGSGTDFLTISRLEPEDFAVYYC QO HDTSLTPGGCTKVEIKGGGGSGGGGGGGGG SQVQLVQSGAEVKPGASVKVSCKASGYPFT TSYGISWVRQAPGQGLEWMGWISTYNGNTNYA AQKFQGRVTMTTDSTTTGYMELRRRLRSDD DTAVYYCARDYTRGAWFGESELIGGFDNWGQ GTLSLSPGERATLSCRAS QTVSSTS LAWYQ
SARS-CoV-2 S309-scFv- (VL-VH) - (VH-VL) (aa)	224		EIVLTQSPGTLSLSPGERATLSCRAS QTVS STS LAWYQQKPGQAPRLLIY GASSRATGIP DRFSGSGSGTDFLTISRLEPEDFAVYYC Q QHDTSLTFGGTKVEIKGGGGSGGGGGGG GSQVQLVQSGAEVKPGASVKVSCKASGYPFT FTSYGISWVRQAPGQGLEWMGWISTYNGNTNYA AQKFQGRVTMTTDSTTTGYMELRRRLRSDD DDTAVYYCARDYTRGAWFGESELIGGFDNWGQ QGTLVTVSSGGGGSGGGGGGGGGGGGGGG QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGWISTYNGNTNYA AQKFQGRVTMTTDSTTTGYMELRRRLRSDD DDTAVYYCARDYTRGAWFGESELIGGFDNWGQ TAVYYCARDYTRGAWFGESELIGGFDNWGQG TLTVVSSGGGGSGGGGGGGGGGGSEIVLTQSP GTLSLSPGERATLSCRAS QTVSSTS LAWYQ QKPGQAPRLLIY GASSRATGIP DRFSGSGS GTDFTLTISRLEPEDFAVYYC QOHDTS LTF GGGTKVEIK
SARS-CoV-2 S309-scFv- (VL-VH) - (VL-VH) (aa)	225		EIVLTQSPGTLSLSPGERATLSCRAS QTVS STS LAWYQQKPGQAPRLLIY GASSRATGIP DRFSGSGSGTDFLTISRLEPEDFAVYYC Q QHDTSLTFGGTKVEIKGGGGSGGGGGGG GSQVQLVQSGAEVKPGASVKVSCKASGYPFT FTSYGISWVRQAPGQGLEWMGWISTYNGNTNYA AQKFQGRVTMTTDSTTTGYMELRRRLRSDD DDTAVYYCARDYTRGAWFGESELIGGFDNWG QGTLVTVSSGGGGSGGGGGGGGGGGGGGGGG

TABLE 1-continued

		Sequences
Sequence Description	SEQ ID NO.	Sequence
		EIVLTQSPGTLSLSPGERATLSCRASQTVS STS LAWYQQKPGQAPRLLIYGASSRATGIP DRFSGSGSGTDFLTISRLEPEDFAVYYCQ QHDTSLTFGGTKVEIKGGGSGGGGGGG GSVQLVQSGAEVKPGASVKVSCKASGYP FTSYG ISWVRQAPGQGLEWMGWISTYNGNT NYAQKFQGRVTMTTDSTTTGYMELRRRLRS DDTAVYYCARDYTRGAWFGESELIGGF DNWG QGTLVTVSS
SARS-CoV-2 S309-scFab- (H-L) v1.1 (aa)	226	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYG ISWVRQAPGQGLEWMGWISTYQGNTNY AQKFQGRVTMTTDSTTTGYMELRRRLRSDD TAVYYCARDYTRGAWFGESELIGGF DNWGQGD TLTVVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYPPEPVTVWSNSGALTSGVHTF PAVLQSSGLYSLSSVVTVPSSSLGTQTYIC NVNHPNSNTKVDKRVEPKSCGGGGGGGG GGGGSGGGGGGGGGGGGGGGGGGGGGGGGG GGGGSGGGGGSEIVLTQSPGTLSLSPGERAT LSCRASQTVSSTS LAWYQQKPGQAPRLLIY GASSRATGIPDRFSGSGSGTDFLTISRLE PEDFAVYYCQQHDTSLTFGGTKVEIKRTV AAPSVFIFPPSDEQLKSGTASVVCNNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKD STYSLSSLTLSKADYEHKVKVACEVTHQG LSSPVTKSFNRGEC
SARS-CoV-2 S309-scFab- (L-H) v1.1 (aa)	227	EIVLTQSPGTLSLSPGERATLSCRASQTVS STS LAWYQQKPGQAPRLLIYGASSRATGIP DRFSGSGSGTDFLTISRLEPEDFAVYYCQ QHDTSLTFGGTKVEIKRTVAAPS VFI FPP SDEQLKSGTASVVCNNFYPREAKVQWKV DNALQSGNSQESVTEQDSKD STYSLSSLT LSKADYEHKVKVACEVTHQGLSSPVTKSFN RGECGGGGGGGGGGGGGGGGGGGGGGGGGG GGGGGGGGGGGGGGGGGGGGGGGGGGGG GAEVKPGASVKVSCKASGYPFTSYG ISWV RQAPGQGLEWMGWISTYQGNTNYAQKFQGR VTMTTDSTTTGYMELRRRLRSDDTAVYYCA RDYTRGAWFGESELIGGF DNWGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVK DYFPEPVTVWSNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPS NTKVDKRVEPKSC
SARS-CoV-2 S309-scFv- (VH-VL) v1.1 (aa)	228	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYG ISWVRQAPGQGLEWMGWISTYQGNTNY AQKFQGRVTMTTDSTTTGYMELRRRLRSDD TAVYYCARDYTRGAWFGESELIGGF DNWGQGD TLTVVSSGGGGGGGGGGGGGGSEIVLTQSP GTLSLSPGERATLSCRASQTVSSTS LAWYQ QKPGQAPRLLIYGASSRATGIPDRFSGSGS GTDFTLTISRLEPEDFAVYYCQQHDTSLTF GGGT KVEIK
SARS-CoV-2 S309-scFv- (VL-VH) v1.1 (aa)	229	EIVLTQSPGTLSLSPGERATLSCRASQTVS STS LAWYQQKPGQAPRLLIYGASSRATGIP DRFSGSGSGTDFLTISRLEPEDFAVYYCQ QHDTSLTFGGTKVEIKGGGSGGGGGGG GSVQLVQSGAEVKPGASVKVSCKASGYP FTSYG ISWVRQAPGQGLEWMGWISTYQGNT NYAQKFQGRVTMTTDSTTTGYMELRRRLRS DDTAVYYCARDYTRGAWFGESELIGGF DNWG QGTLVTVSS

TABLE 1-continued

Sequences			
Sequence Description	SEQ ID NO.	Sequence	
SARS-CoV-2 S309-scFv- (VH-VL) - (VH-VL) v1.1 (aa)	230	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYG1SWVRQAPGQGLEWMGWISTYQGNTNY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWFGESLIGGFDNWGQG TLTVTSSGGGSGGGGGGGSEIVLTQSP GTLSLSPGERATLSCRASQTVSSTSLAWYQ QKPGQAPRLLIYGASSRATGIPDRFSGSGS GTDFTLTISRLEPEDFAVYYCQOHDTSLTF GGGTKEIKGGGGSGGGGGGGGGGGGGGG VQLVQSGAEVKPGASVKVSCKASGYPFTS YGI1SWVRQAPGQGLEWMGWISTYQGNTNYA QKFQGRVTMTTDSTTTGYMELRRLRSDDT AVYYCARDYTRGAWFGESLIGGFDNWGQGT LTVTSSGGGSGGGGGGGSEIVLTQSPG TLSLSPGERATLSCRASQTVSSTSLAWYQQ KPGQAPRLLIYGASSRATGIPDRFSGSGSG TDFTLTISRLEPEDFAVYYCQOHDTSLTFG GGTKVEIK	
SARS-CoV-2 S309-scFv- (VH-VL) - (VL-VH) v1.1 (aa)	231	QVQLVQSGAEVKPGASVKVSCKASGYPFT SYG1SWVRQAPGQGLEWMGWISTYQGNTNY AQKFQGRVTMTTDSTTTGYMELRRLRSDD TAVYYCARDYTRGAWFGESLIGGFDNWGQG TLTVTSSGGGSGGGGGGGSEIVLTQSP GTLSLSPGERATLSCRASQTVSSTSLAWYQ QKPGQAPRLLIYGASSRATGIPDRFSGSGS GTDFTLTISRLEPEDFAVYYCQOHDTSLTF GGGTKEIKGGGGSGGGGGGGGGGGGGSE IVLTQSPGTLSLSPGERATLSCRASQTVS TSLAWYQQKPGQAPRLLIYGASSRATGIPD RFSGSGSTDFLTISRLEPEDFAVYYCQQ HDTSLTFGGGTKEIKGGGGSGGGGGGG SQVQLVQSGAEVKPGASVKVSCKASGYPF TSYGI1SWVRQAPGQGLEWMGWISTYQGNT YAQKFQGRVTMTTDSTTTGYMELRRLRS DATAVYYCARDYTRGAWFGESLIGGFDNWGQ GTLVTVSS	
SARS-CoV-2 S309-scFv- (VL-VH) - (VH-VL) v1.1 (aa)	232	EIVLTQSPGTLSLSPGERATLSCRASQTVS STS LAWYQQKPGQAPRLLIYGASSRATGIP DRFSGSGSTDFLTISRLEPEDFAVYYCQ QHDTSLTFGGGTKEIKGGGGSGGGGGGG GSQVQLVQSGAEVKPGASVKVSCKASGYP FTSYGI1SWVRQAPGQGLEWMGWISTYQGNT NYAQKFQGRVTMTTDSTTTGYMELRRLRS DDTAVYYCARDYTRGAWFGESLIGGFDNWG QGT1LVTVSSGGGGSGGGGGGGGGGGGG VQLVQSGAEVKPGASVKVSCKASGYPFTS YGI1SWVRQAPGQGLEWMGWISTYQGNTNYA QKFQGRVTMTTDSTTTGYMELRRLRSDDT AVYYCARDYTRGAWFGESLIGGFDNWGQGT LTVTSSGGGSGGGGGGGSEIVLTQSPG TLSLSPGERATLSCRASQTVSSTSLAWYQQ KPGQAPRLLIYGASSRATGIPDRFSGSGSG TDFTLTISRLEPEDFAVYYCQOHDTSLTFG GGTKVEIK	
SARS-CoV-2 S309-scFv- (VL-VH) - (VL-VH) v1.1 (aa)	233	EIVLTQSPGTLSLSPGERATLSCRASQTVS STS LAWYQQKPGQAPRLLIYGASSRATGIP DRFSGSGSTDFLTISRLEPEDFAVYYCQ QHDTSLTFGGGTKEIKGGGGSGGGGGGG GSQVQLVQSGAEVKPGASVKVSCKASGYP FTSYGI1SWVRQAPGQGLEWMGWISTYQGNT NYAQKFQGRVTMTTDSTTTGYMELRRLRS DDTAVYYCARDYTRGAWFGESLIGGFDNWG QGT1LVTVSSGGGGSGGGGGGGGGGGSE IVLTQSPGTLSLSPGERATLSCRASQTVS TSLAWYQQKPGQAPRLLIYGASSRATGIPD RFSGSGSTDFLTISRLEPEDFAVYYCQQ HDTSLTFGGGTKEIKGGGGGGGGGGGG	

TABLE 1-continued

Sequence Description	SEQ NO.	Sequences	
		ID	Sequence
			QVQLVQSGAEVKPGASVKVSCKASGYPFT SYGISWVRQAPGQGLEWMGWISTYQGNTNY AQKFQGRVTMTTDSTTTGYMELRRRLRSDD TAVYYCARDYTRGAWFGESLIGGFDNWGQG TLTVTSS
SARS-CoV-2 S300-v14 mAb VL (VK) (aa)	234	DIVMTQSPDSLAVSLGERATINCKSSQSVL YSSNNKNYLAWYQQKPGQPPKLLISWASTR ESGPVPDRFSGSGSGTDFLTISLQAEDVA VYYCQQYYSAAPGITFGQGTRLEIK	
SARS-CoV-2 S300-v14 mAb CDRL1 (aa)	235	QSVLYSSNNKNY	
SARS-CoV-2 S300-v14 mAb CDRL2 (aa)	236	WAS	
SARS-CoV-2 S300-v14 mAb CDRL3 (aa)	237	QQYYSAAPGIT	
SARS-CoV2 S300-v14 mAb VL (VK) (nt)	238	GACATCGTGATGACCCAGTCCTCCAGACTCA CTGGCTGTGTCCTGGGGAGAGGGCCACC ATCAACTGTAAGTCCAGCCAGAGTGTTTA TACAGCTCCAAACAATAAGAACACTTAGCT TGGTACACAGCAGAACCCAGGACAGCCTCCT AAGCTGCTCATTTCTGGCTTCTACCCGG GAATCCGGGGTCCCTGACCGATTCACTCTCACC AGCGGGCTGGGACAGATTCACTCTCACC ATCAGCAGCCTGCAGGCTGAAGATGTGGCA GTTTATTACTGTCAACAAATATTATAGTGCT CCCCGGATCACCTTCGGCCAGGGGACACGA CTGGAGATTAAAC	
SARS-CoV2 S307 mAb VH (aa)	239	QVQLQESGPGLVKPSETLSLTCTVSGGSVT SGSYYWSWIRQPPGKGLEWIGYMYSGSTN YNPSLKSRTVISVDTSKNQFSLKLSVTAA DTAVYYCARAGCTGITCLRYDYYYGLDVWG QGTTVTVSS	
SARS-CoV2 S307 mAb CDRH1 (aa)	240	GGSVTSGSYY	
SARS-CoV2 S307 mAb CDRH2 (aa)	241	MYYSGST	
SARS-CoV2 S307 mAb CDRH3 (aa)	242	ARAGCTGITCLRYDYYYGLDV	
SARS-CoV2 S307 mAb VL (VK) (aa)	243	EIVLTQSPGTLSSLSPGKRATLSCRASQSVS SSYLAWSYQORPGQAPRLLIYGASSRAAGIP DRESGSGSGTDFLTISRLEPEDFAVYYCQ QYGSSSWTFGQGTKVEIK	
SARS-CoV2 S307 mAb CDRL1 (aa)	244	QSVSSSY	
SARS-CoV2 S307 mAb CDRL2 (aa)	245	GAS	

TABLE 1-continued

Sequence Description	SEQ ID NO.	Sequences	
		Sequence	
SARS-CoV2 S307 mAb CDRL3 (aa)	246	QQYGSSSWT	
SARS-CoV2 S307 mAb VH (nt)	247	CAGGTGCAGCTGCAGGAGTCGGGCCAGGA CTGGTGAAGCCTTCGGAGACCTGTCCCTC ACCTGCACTGTCTCGGTGGCTCCGTACC ATGGTAGTTACTACTGGAGCTGGATCGG CAGCCCCAGGAAAGGGACTGGAGTGGATT GGGTATAATGTATTACAGTGGAGACCAAT TACAACCCCTCCCTCAAGAGTCGAGTCACC ATATCAGTAGACACGTCCAAGAACCGAGTC TCCCTGAAGCTGAGCTCTGTGACCGTGCG GACACGGCCGTGATTACTGTGCGAGGGCA GGTTGACTGGTATCACCTGCTTACGGTAC GACTACTACTACGGTCTGGACGTCTGGGC CAAGGGACCACGGTCACCGTCTCCTCA	
SARS-CoV2 S307 mAb VL (VK) (nt)	248	GAAATTGTGTTGACGCAGTCCTCAGGCACC CTGTCTTGTCTCCAGGGAAAAGAGCCACC CTCTCCTGCAGGGCCAGTCAGAGTGTAGC AGCAGCTACTTACGCTGGTACCCAGCAGAGA CCTGGCCAGGCTCCAGGCTCCTCATCTAT GGTGCATCCAGCAGGGCCCTGGCATCCCA GACAGGTTCACTGGCAGTGGTCTGGGAC GACTTCACTCTACCATCAGCAGACTGGAG CCTGAAGATTTGCACTGTATTACTGTICAG CACTATGGTAGCTCATCGTGACGTTCGGC CAAGGGACCAAGGTGAAATCAAAC	
SARS-CoV-2 S309-v1 mAb VH (nt)	249	CAGGTTCACTGGTCACTCTGGAGCTGAG GTGAAGAAGCCTGGGGCTCAGTGAAGGTG TCTGCAAGGCTCTGGTTACCCCTTAC AGTTATGGTATCAGCTGGTGGCAGACAGGC CCTGGACAAGGGCTTGAAGTGGATGGATGG ATCAGCACTTACATGGTAACACAATTAT GCACAGAACTTCAAGGGCAGACTCACCATG ACCACAGACACATCCACGACACAGGCTAC ATGGAGCTGAGGAGGCTGAGATCTGACGAC ACGGCCGTGATTACTGTGCGAGAGATTAT ATCGTGGTGCCTGGTCCGGGGAGTCATTG ATAGGGGCTTGACAACGTGGGCCAGGG ACCCTGGTACCCGTCCTCTCA	
SAES-CoV-2 S309-v13 mAb VL (VK) (nt)	250	GAAATTGTGTTGACGCAGTCCTCAGGCACC CTGTCTTGTCTCCAGGGAAAAGAGCCACC CTCTCCTGCAGGGCCAGTCAGACTGTAGC AGCACCTCTTACGCTGGTACCCAGCAGAAA CCTGGCCAGGCTCCAGGCTCCTCATCTAT GGTGCATCCAGCAGGGCCACTGGCATCCCA GACAGGTTCACTGGCAGTGGGCTGGGACA GACTTCACTCTACCATCAGCAGACTGGAG CCTGAAGATTTGCACTGTATTACTGTICAG CAGCATGATACTCACTACTTCGGCGGA GGGACCAAGGTGGAGATCAAAC	
CMV promoter (nt)	251	GACATTGATTATTGACTAGTTATAATAGT AATCAATTACGGGGTATTAGTCATAGCC CATATATGGAGTCCCGCGTTACATAACTTA CGGTAAATGGCCCGCCCTGGCTGACCGCCCA ACGACCCCCGCCATGAGTCATAATGAC GTATGTTCCATAGTAACGCCAATAGGGAC TTTCATTGACGTCAATGGGTGGAGTATT ACGGTAAACTGCCACTTGGCAGTACATCA AGTGTATCATATGCCAAGTACGCCCTTAT TGACGTCAATGACGGTAATGGCCGCGCTG GCATTATGCCAGTACATGACCTTATGGGA CTTCCCTACTTGGCAGTACATCTACGTATT AGTCATCGCTATTACCATGGTATGCGGTT TTGGCAGTACATCAATGGCGTGGATAGCG	

TABLE 1-continued

Sequence Description	SEQ ID NO.	Sequences	
		Sequence	
		GTTTGACTCACGGGGATTCACAAGTCTCCA CCCCATTGACGTCAATGGGAGTTGTTTG GCACCAAATCAACGGACTTCCAAAATG TCGTAACAACCTCGCCCCATTGACGCAAAT GGCCGGTAGGGTGTACGGTGGGAGGTCA TATAAAGCAGAGCTCGTTAGTGAACCGTCA GATCGCTTGGAGACGCCATCAGCTGTTT TGACCTCCATAGAAGACACCGGGACCGATC CAGCCTCCGGCGGGAAACGGTGCATTGG AACCGGATTCCCCGTGCCAAGAGTACGT AAAGTACCCCTATAGAGTCTATAGGCCAC CCCCTGGCTCGTTAG	
Signal peptide (nt)	252	ATGGGATGGTCATGTATCATCCTTTCTA GTAGCAACTGCAACCGGTGT	
Poly-adenylation signal sequence (nt)	253	AACTTGTATTGAGCTTATAATGGTAC AAATAAAGCAATAGCATTACAAATTTACA AAATAAAGCATTTTTTCACTGCATTCTAGT TGTGTTTGTCCAACACTCATCAATGTATCT TATCATGTCTGGATC	
SARS-CoV-2 Light Chain IgKC*01 (nt)	254	GTACGGTGGCTGCACCCTCTGCTTCATCT TCCCGCCATCTGATGAGCAGTTGAAATCTG GAAGTCCTCTGTTGTGCTGCTGTA ACTCTATCCAGAGAGGCCAAAGTACAGT GGAGGTTGGATAACGCCCTCAATGGGTA ACTCCAGAGAGTGTACAGAGCAGGACA GAAGGAGAGCACCTACAGCCTCAGCAGCA CCCTGACGCTGAGCAAAGCAGACTACGAGA AACACAAAGTCTACGCTGGAAAGTCACCC ATCAGGGCTTGAGCTCGCCCCTCACAAAGA GCTTCAACAGGGAGAGTGTAG	
SARS-CoV-2 CH1-CH3 G1m1 ⁷ ; IgG1*01 (nt)	255	GCGTCGACCAAGGGCCATCGTCTTCCC CTGGCACCCCTCTCCAAGAGCACCTCTGGG GGCACAGCGCCCTGGGCTGCCCTGGTCAAG GAECTACTCCCGAACCTGTGACGGCTCG TGGAACTCAGGCCCTGACCAGCGCGTGT CACACCTTCCCGCTGTCTACAGTCTCA GGACTCTACTCCCTCAGCAGCGTGGTGA GTGCCCTCAGCAGCTGGGCACCCAGACC TACATCTGCAACGTGAATCACAGCCCAGC AACACCAAGGTGGACAAGAGAGTTGAGCCC AAATCTTGACAAAACCTCACACATGCCA CCGTGCCAGCACCTGAACCTCTGGGGGA CCGTCACTTCTCTTCCCCCAAAACCC AAGGACACCCCTCATGATCTCCCGACCC GAGGTACATGCGTGGTGGACGTGAGC CACGAAGACCTGAGGTCAAGGTCAACTGG TACGTGGACGGCTGGAGGTGCTATAATGCC AAGACAAAGCCGGGGAGGAGCAGTACAAC AGCACGTACCGTGTGGTCAGGTCCTCACC GTCTGCACCAAGGACTGGCTGAATGGCAAG GAGTACAAGTGAAGGTCTCAACAAAGCC CTCCAGCCCCATCGAGAAAACCATCTCC AAAGCCAAGGGCAGCCCCGAGAACACAG GTGTACACCTGCCCTATCCCGGAGGAG ATGACCAAGAACCAAGGTCAAGGTGAC CTGGTCAAGGCTTCTATCCACCGACATC GCCGTGGAGTGGGAGAGCAATGGCAGCCG GAGAACAACTACAAGAACACGCCCTCCCGT CTGGACTCCGACGGCTCTTCTCTCTAT AGCAAGCTCACCGTGGACAAGAGCAGGTGG CAGCAGGGAAAGTCTCTCATGCTCCCGT ATGCATGAGGCTCTGCACAACCAACTACACG CAGAAGAGCCTCTCCCTGTCCCCGGTAAA TGA	

TABLE 1-continued

TABLE 1-continued

Sequence Description	SEQ NO.	Sequences	
		ID	Sequence
	ggcgccctgacaagcggcgtcacacattc ccagctgtgtgcagagcagcggcctgtat agcctgagcagcgtggtacacctgcccagc agcagcctggaaacacagacactacatctgc aacgtgaaccacaaggcttctaataccaag gtggataagaagggtggaaaccttaagagctgc gacaaaacacacacatgccctccatgttct gctccagagctgtggcgggcccagegtt tttcgtcccccccaaacctaagacacc ctgatgatcagcagaacccctgaggtgacc tgtgtgtgtggacgtgtccacgaaagat cctgagggtgaagttaactgttacgttgat ggagtggaaatgcacaacgcacaagaccaa cctagagaagagcagtacaacacgcacat agagtctgttccgtgtttacagtgtgcac caggactggcttaatggaaaggaaatacaag tgcaagggttccaacaaggccctgcctctg cctgaggagaagacaatcttctaagccaa ggccaacactcgggaaacctcagggttacaca ctgccccccaggcgggacgagctgaccaag aaccagggttccctgtacccgttggtaag ggtttccatccctctgtatccgcgtggaa tgggagagcaacggccaaaccttggaaaca tacaagaccacccctccagggttggacagc gacggcagcttccctgtacccgttac accctgtacaaggccatgttccgttgcac aacgttccatcttactacacccagaagagc gcctgcatttccatccctgttac ctgtccctcagccctggcaagtga		
SARS-CoV-2 S309-v1.1 mAb CH1- CH3 G1m17; IgGHG1*01 LS; signal peptide (nt- CO)	259	atggggctgttccctgttatcatccctgttccctg gtcgccacaggccaccggagggtgcacaggccaa gtgcagctgttccagagcggccgcggagggtg aagaaggccggcgctacgtgttggatgtcc tgtaaaggccagoggatatcccttaccagc tacggcatctccctgggttgcggcaggccc ggcaggggcttggaatggatgggttggatc agcacctaccaggaaataccactacgcc cagaagttccaggaaagagtgtacaatgacc acagatacatctacaaccacccgcttacatg gaacttggggcggttgcggcggcggc gcccgttactactgcggccaggatattacc agaggcgcttgggttgcggcggaggctgt ggcggttgcacaacttggggccagggaacc ctgggtgacatgtttagcgttccatccaaa ggcccttctgtttcccttgcggcccttct agcaagtctacaaggccggggcc ctgggtgttgcgttgcggcggaggacttcc gagccctgtgaccgttgcgttgcggatagggc gcccgttgcacaaggccggccgttgcac gtgtgtgttgcggcggaggccgttatagc cttgcggcggcgttgcggcggaggcc agccctggaaacacagacactacatctgc gtgaaccacaaggcccttataatccaagggt gataagaagggtggaaaccttaagagctgt aaaacacacacatgcggccatgttccct ccagagctgtggccggcccaaggctt ctgttcccccccaaccttaagacacccctg atgtatcagcagaacccctgagggtgac gtgggtgtggacgtgtcccacgaagatcc gagggtgaagtcaactgttacgttgc gtggaaatgttgcacaacgcacaaggcc agagaaggcgttacaacacgcacatata gtcgtgtccgtgttacagtgtgc gactgggtgaatggaaaggaaatacaagtgc aagggttccacaaggccctgttgc atcgagaagacaatcttcaaaaggcc caacccctggaaacctcagggttac cccccccaaggccggacgtgttgc cagggttccctgttgcacgttgc ttctaccctctgtatccgcgttgc atgttgc	

TABLE 1-continued

Sequence Description	SEQ NO.	Sequences	
		ID	Sequence
			gagagcaacggccaacctgagaacaactac aagaccacccctccagtgtctggacagcgac ggcagcttcttcgtacagcaagctgacc gttgacaagtccagatggcagcagggaac gtgttcagctgttagcgtctgcacgaggcc ctgcattctcaactacacccagaagagcctg tccctcagccctggcaagtga
SARS-CoV-2 S309-v1.1 mAb CH1- CH3 G1m17; IgGHG1*01 LS (nt-CO)	260	caagtgcagctggtccagagcggcgccgag gtgaaaagccggcgctagcgtgaagggt tctctgtaaaggccagcggatatacttttacc agetacgccatctcctgggtgeggcaggcc cctggccaggccctggaaatggatgggtgg atcagcacctaccaggaaataccaactac gcccagaagttccagggaaagagtgacaatg accacagatatacttacaaccacccggctac atggaaactgaggccggctgagaagcgcac accgcgcgtgtactactgcgcacagattac accaggaggccgttggtcggcgagagcctg atcggccggcttcgacaactggggccaggga acccctggtgcacgtgtctagcgttttacc aaaggcccttctgtcttcctctggccccct tctagcaagtctacaagccggaggaccgc gccttgggctgcttggtaaggactacttc cccgagccgtgaccgtgagctggaaatagc ggcccccgtacaacgcggcgtcacacccct ccagctgtgtcagacgcggccgttatgtat agcctgagcagcgtggtacccgtgcccac agcagcctggaaacacagacactatctgc aacgtgaaccacaacgccttataatccaag gtggataagaagggtggaaacctaaagagctc gaaaaacacacatgcctccatgttcc gtcccaagatgtgtggggccggccaggctt tttctgtcccccccaaaaccttataagacacc ctgtatgtacgcagaaccccttgcagggtacc tgtgtgtgtggacgtgtcccacgaaat cttgagggtgaagtcaactggtacgtggat ggagtgaaatgcacaacgcacaacaaa cctagagaagaggcgtacaacagcacat agagtctgtccgtgttacagtgtgcac caggactggcgtaatggaaaggaaatacaag tgcagggtgtccaaacaacgcctgcctgcc cctatcgagaagacaatcttaagccaag ggccaaacctccggaaacctcagggttacaca ctgccccccacgcgggacgagctgaccaag aaccagggtgtccctgacccgtgtccat gggttctaccctctgtatatcgccgtggaa tgggagagacaacgcacaaccttgcagaacaac tacaagagaccacccctccagggtgtccac gacggcagcttccctgtacagcagctg accgtgtacgttacactacccagaagagc gcctgcattctcaactacacccagaagagc ctgtccctcagccctggcaagtga	
S309-v13 Light chain k1m3; IgKC*01; signal peptide (nt-CO)	261	tgggctggtccgtcatcatctgtttctgg tggccacagccacccggcgtgcacagcgaga tctgtccctgacacagagccccggcacactga gcctctcccccaggccgagccggctacactgt cttgcgttagcttcgtacaggctgtccagca ccagcctgcgtggatcagccatccggc gccaggcccctagactgtgtatctacggcg ccacgcacgcggccatccctgtata gattcagccgcacggatctggaaaccgact tcaccctgtacccatcagccggctggaaaccgg aggactttgcgtgtactactgcgcac acgacaccaggccgtacccctccggccggaa caaagggtggaaatcaagagaaccgtggcc cccctagcgtgttcatcttcccccccaagcg acgagcagctgaagagcggtaagctgt tgggtgtccctgtgaacaacttctaccgc	

TABLE 1-continued

Sequences			
Sequence Description	SEQ ID NO.	Sequence	
		gggaaggccaaagggtgcagtggaaagggtggaca acgcccctgcagagcggcaacagccaggaga gcgtgacagacaggacaggcaaggacacgca cctacacgcctgagcagcacccctgaccctga gcaaggccgactacgagaagcacaagggtgt acgcctgtgaagtgcaccacaggccctgt ctagccctgtgaccaagtctttAACAGAG gcgagtgtga	
S309-v13 Light chain k1m3; IgKC*01; (nt- CO)	262	Gagatcgtcctgacacagagccccggcaca ctgagccctcccccaggcgagccggctaca ctgtcttgcagcttcagaccgtgtcc agcaccctgcctggctgttatcagcagaaa cctggccaggcccctagactgtgtatctac ggcgcacagcagcagccacccggcatccct gatagattcagccgcagccgtatggaaacc gacttcacccgtaccatcagccggctggaa cccgaggacttgcctgtactactgcacag caacacgcacccgcctgacccctggggc ggaacaaaagggtggaaatcaagagaaccgtg gcccgccttaegegtgttcatctccccccc agegcacgcacgtgaagagccgttacagct tctgtggtgtgcctgtcataacttac cccgccggaaaggcaagggtgcagtggagggt gacaacgcctgcagagccgcacacgc gagagcgtgcacagacaggacacgc agcacctacgcctgacccctgacc ctgagacaggccgactacgagaagcacaag gtgtacgcctgtgaagtgcaccacccaggc ctgtctagccctgtgaccaagtctttAAC agaggcgagtgtga	
Signal peptide (nt-CO)	263	Atgggctggcctgcacatcctgttccctg gtggccacagccacccggcgtgcacagc	
Signal peptide (aa)	264	MGWSCIILFLVATATGVHS	
SARS-CoV-2 CH1-CH3 G1m17; IgG1*01 LS no C-term Lys (aa)	265	ASTKGPSVFPLAPSSKSTSGGTAALGCLVK DYFPEPVTVWSNSGALTSGVHTFPALVLQSS GLYSLSVVTVPSLGTQTYICNVNHNKPS NTKVDKKVEPKSCDKTHTCPGPCPAPELLGG PSVFLFPKPKDLMISRTPEVTCVVVDVS HEDPEVKFNWYWDGVEVHNAKTKPREEQYN STYRVSVLTVLHQDWLNGKEYKCKVSNKA LPAPIEKTIASKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVLHEALHSHYTQKSLSLSPG	
SARS-CoV-2 CH1-CH3 G1m17; IgG1*01 LS GAALIE no C-term Lys (aa)	266	ASTKGPSVFPLAPSSKSTSGGTAALGCLVK DYFPEPVTVWSNSGALTSGVHTFPALVLQSS GLYSLSVVTVPSLGTQTYICNVNHNKPS NTKVDKKVEPKSCDKTHTCPGPCPAPELLAG PSVFLFPKPKDLMISRTPEVTCVVVDVS HEDPEVKFNWYWDGVEVHNAKTKPREEQYN STYRVSVLTVLHQDWLNGKEYKCKVSNKA LPLPEEKTIASKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVLHEALHSHYTQKSLSLSPG	

EXAMPLES

Example 1

Human Monoclonal Antibodies that Bind Spike Protein of SARS-CoV-2

[0444] B cells from a donor with previous SARS-CoV infection were sorted and immortalized with EBV and screened in 384-well plates, as described in European patent EP1597280B1.

[0445] Two weeks after immortalization, supernatants of immortalized B cells were tested for antibodies binding to SARS-CoV-2 Spike protein using a flow cytometry-based method. ExpiCHO cells were transfected with S protein of SARS-CoV-2 (strain BetaCoV/Wuhan-Hu-1/2019), or with an empty plasmid as a negative control. Fourteen monoclonal antibodies were identified that bind SARS-CoV-2 S, and were termed SARS-CoV-2 S300 through SARS-CoV-2 S312 and SARS-CoV-2 S315.

Example 2

Binding of Human Monoclonal Antibodies to RBD of SARS-CoV-2 Using Octet

[0446] Streptavidin biosensors (Pall ForteBio) were used to immobilize anti-Strep Tag II antibody at 3 µg/ml (clone 5A9F9, Biotin, LabForce AG, Muttenz CH), after a hydration step for 10 min with Kinetics Buffer (KB; 0.01% endotoxin-free BSA, 0.002% Tween-20, 0.005% NaN₃ in PBS). SARS-CoV-2 RBD with a Strep Tag II (produced in-house) was then loaded for 6 min at a concentration of 4 µg/ml in KB. Antibodies from B cell supernatant were allowed to associate for a period of time. To observe dissociation, sensors were moved from the antibody solution into KB and antibody dissociation was monitored.

[0447] The S309 mAb comprises the S309-v1 VH and S309-v13 VL amino acid sequences provided in Table 1 (SEQ ID Nos.: 105 and 168, respectively). Comparison of the binding curves for S303 and S309 indicates that S303 has both a faster on-rate and a faster off-rate than S309, suggesting that S309 may bind with higher affinity.

Example 3

Binding of Human Monoclonal Antibodies to RBD of SARS-CoV-2 and SARS-CoV-1 Using Octet

[0448] The affinity of three cross-reactive recombinant antibodies (S303 rIgG1, S304 rIgG1, S309 rIgG1) and two SARS-CoV-1 specific antibodies was tested using Octet. The affinity was measured by immobilizing the antibody on sensors and dipping the sensors into wells with different concentrations of RBD.

[0449] The kinetics of antibody binding to RBD was recorded during the association phase, after which the sensors were dipped into buffer without antibody to observe the kinetics of antibody detaching from the RBD during the dissociation phase. Briefly, protein A biosensors (Pall ForteBio) were used to immobilize recombinant antibodies at 2.7 µg/ml for 1 minute, after a hydration step for 10 minutes with Kinetics Buffer (KB; 0.01% endotoxin-free BSA, 0.002% Tween-20, 0.005% NaN₃ in PBS). Association curves were recorded for 5 minutes by incubating the antibody-coated sensors with different concentration of

SARS-CoV-1 RBD (Sino Biological) or SARS-CoV-2 RBD (produced in house in Expi-CHO cells; residues 331-550 of spike from BetaCoV/Wuhan-Hu-1/2019, accession number MN908947). The highest RBD concentration tested was 10 µg/ml, then 1:2.5 serially diluted. Dissociation was recorded for 9 minutes by moving the sensors to wells containing KB. Affinities, represented by KD values, were calculated using a global fit model (Octet). Octet Red96 (ForteBio) equipment was used.

[0450] Three cross-reactive antibodies (S303 rIgG1, S304 rIgG1, S309 rIgG1) and two SARS-CoV-1 specific antibodies (S230 and S109) were tested. All antibodies showed strong binding to SARS-CoV-1 RBD. S230 and S109 did not bind to SARS-CoV-2 RBD. Binding of S303 rIgG1, S304 rIgG1, and S309 rIgG1 to SARS-CoV-2 RBD was in the nanomolar range, with S309 rIgG1 showing the strongest affinity. KD values are indicated below the graphs. KD values are only estimates ($KD = <1.0 \times 10^{-12} M$) if the antibody binding is very strong and dissociation is slow. An exact KD for S309 rIgG1 could not be measured by this assay since the dissociation was too slow.

Example 4

Neutralization of SARS-CoV-2 by Human Monoclonal Antibodies

[0451] Replication-incompetent viruses pseudotyped with the SARS-CoV-2 S gene (isolate BetaCoV/Wuhan-Hu-1/2019; accession number MN908947) were produced using methods as previously described (Temperton NJ, et al. (2005) Longitudinally profiling neutralizing antibody response to SARS coronavirus with pseudotypes. Emerg Infect Dis 11 (3): 411-416.). Briefly, HEK293T/17 was cotransfected with a SARS-CoV-2 S-expressing plasmid (phCMV1, Genlantis) and with a complementing viral-genome reporter gene vector, pNL4-3. Luc+ E-R+. A single-cycle infectivity assay was used to measure the neutralization of luciferase-encoding virions pseudotyped with the SARS-CoV-2 S protein, as previously described (Temperton NJ, et al. (2007) A sensitive retroviral pseudotype assay for influenza H5N1-neutralizing antibodies. Influenza Other Respi Viruses 1(3): 105-112.). Briefly, appropriate dilutions of the virion-containing culture supernatants were preincubated at 37° C. for 1 h with antibodies at various concentrations and the virus-mAb mixtures was then added to Vero E6 cells that were seeded the day before infection. The cells were then lysed with Steady-Glo reagent (Promega, E2520), and the relative luminescence units (RLU) in the cell lysates was determined on a luminometer microplate reader (Synergy H1 Hybrid Multi-Mode Reader; Biotek). The reduction of infectivity was determined by comparing the RLU in the presence and absence of antibody and expressed as percentage of neutralization.

[0452] Antibodies SARS-CoV-2 S300-v1, S301, S302, S303-v1, S304, S306, S307, S308-v1, S309 (comprising the S309-v1 VH sequence and the S309-v13 VL (VK) sequence), and S310 were tested for neutralization capacity. Antibodies SARS-CoV-2 S300-v1 and SARS-CoV-2 S309 were shown to neutralize SARS-CoV-2.

[0453] Further neutralization assays were carried out using SARS donor plasma and antibodies SARS-CoV-2 S309, S311, S312, S303-v1 (rIgG1), S304 (rIgG1), S306

(rIgG1), S310 (rIgG1), and S315. Using this assay, antibodies S309, S311, S312, and S315 were shown to neutralize SARS-CoV-2.

[0454] Additional neutralization assays were carried out using monoclonal antibodies S303, S304, S306, S309, S310, and S315.

Example 5

Neutralization of SARS-CoV-2 by Recombinant Human Monoclonal Antibodies

[0455] The neutralizing activity of two recombinant SARS-CoV-1 and SARS-CoV-2 cross-neutralizing antibodies, S304 rIgG1 and S309 rIgG1, against SARS-CoV-2 pseudotyped viruses (SARS-CoV-2pp) was determined.

[0456] Murine leukemia virus (MLV) pseudotyped with SARS-CoV-2 Spike protein (SARS-CoV-2pp) were used. DBT cells stably transfected with ACE2 (DBT-ACE2) were used as target cells. SARS-CoV-2pp was activated with trypsin TPCK at 10 ug/ml. Activated SARS-CoV-2pp was added to a dilution series of antibodies (starting with 50 ug/ml final concentration per antibody, 3-fold dilution). Antibodies were tested at concentrations between 50 ug/ml and 0.02 ug/ml. for the combination of S304 rIgG1 and S309 rIgG1, starting concentrations were 50 ug/ml for each antibody, i.e. the total starting antibody amount was 100 ug/ml. DBT-ACE2 cells were added to the antibody-virus mixtures and incubated for 48 hours. Luminescence was measured after aspirating cell culture supernatant and adding steady-GLO substrate (Promega). S309 rIgG1 showed an IC50 of 0.37 ug/ml, and S304 rIgG1 showed an IC50 of approximately 17 ug/ml. A combination of both antibodies was strongly neutralizing, with an IC50 of 0.077 ug/ml. Further neutralization assays were carried out using the same procedure for recombinant monoclonal antibodies S309 and S315, singly and in combination. S309 showed an IC50 of 1.091 ug/ml, and S315 showed an IC50 of 25.1 ug/ml. The combination of both antibodies showed an IC50 of 0.3047 ug/ml.

Example 6

Reactivity of Human Monoclonal Antibodies to SARS-CoV and SARS-CoV-2

[0457] Reactivity of additional human mAbs S311 and S312 with the spike S1 subunit protein and the RBD of SARS-CoV and SARS-CoV-2 protein was determined by enzyme-linked immunosorbent assays (ELISA).

[0458] 96-well plates were coated with recombinant SARS-CoV-2 Spike S1 Subunit Protein (Sino Biological), SARS-CoV-2 RBD (Sino Biological or produced in house; residues 331-550 of spike from BetaCoV/Wuhan-Hu-1/2019, accession number MN908947), recombinant SARS-CoV Spike S1 Subunit Protein (Sino Biological), or SARS-CoV RBD (Sino Biological).

[0459] Wells were washed and blocked with PBS+1% BSA for 1 hour at room temperature and were then incubated with serially diluted mAbs for 1 hour at room temperature. Bound mAbs were detected by incubating alkaline phosphatase-conjugated goat anti-human IgG (Southern Biotechnology: 2040-04) for 1 hour at room temperature and were developed by 1 mg/ml p-nitrophenylphosphate substrate in 0.1 M glycine buffer (pH 10.4) for 30 min at room temperature. The optical density (OD) values were measured at

a wavelength of 405 nm in an ELISA reader (Powerwave 340/96 spectrophotometer, BioTek).

[0460] Further assays were carried out to determine reactivity of human monoclonal antibodies S300, S307, and S309 to RBD of SARS-CoV-2 and SARS-CoV-1 using the same procedure.

Example 7

Neutralization of SARS-CoV-2 by Recombinant Human Monoclonal Antibodies S309 and S315

[0461] Neutralizing activity of recombinant antibodies S309 rIgG1-LS and S315 rIgG1-LS against SARS-CoV-2 pseudotyped viruses (SARS-CoV-2pp) was determined.

[0462] Murine leukemia virus (MLV) pseudotyped with SARS-CoV-2 Spike protein (SARS-CoV-2pp) were used. DBT cells stably transfected with ACE2 (DBT-ACE2) were used as target cells. SARS-CoV-2pp was activated with trypsin TPCK at 10 ug/ml. Activated SARS-CoV-2pp was added to a dilution series of antibodies. DBT-ACE2 cells were added to the antibody-virus mixtures and incubated for 48 hours. Luminescence was measured after aspirating cell culture supernatant and adding steady-GLO substrate (Promega). Luciferase signal of infected cells was used to calculate the percentage of neutralization relative to a no-antibody control.

[0463] S309 rIgG1-LS showed an IC50 of approximately 3.9 nM, and S315 rIgG1-LS showed an IC50 of approximately 111.7 mM.

[0464] The neutralizing activity of S309-rFab was compared to that of full length S309 rIgG1-LS. Full length S309 rIgG-LS showed an IC50 of 3.821 nM, while S309-rFab showed in IC50 of 3.532 nM.

Example 8

Reactivity of Human Monoclonal Antibodies to RBD of SARS-CoV-1, RBD of SARS-CoV-2, and Ectodomains of Various Coronaviruses

[0465] The reactivity of monoclonal antibodies with the RBD of SARS-CoV-1 and SARS-CoV-2 and the Spike protein of SARS-CoV-1, SARS-CoV-2, OC43, and MERS was determined by enzyme-linked immunosorbent assays (ELISA).

[0466] 384-well shallow ELISA plates were coated with stabilized prefusion Spike protein trimer of SARS-CoV-1, SARS-CoV-2, OC43, or MERS at 1 µg/ml, or with SARS-CoV-2 RBD (produced in house; residues 331-550 of spike from BetaCoV/Wuhan-Hu-1/2019, accession number MN908947) at 10 µg/ml, or SARS-CoV-1 RBD (Sino Biological) at 1 µg/ml.

[0467] Wells were washed and blocked with PBS+1% BSA for 1 hour at room temperature and were then incubated with serially diluted antibodies for 1-2 hours at room temperature. Antibodies were tested at a concentration range of 5 to 0.00028 µg/ml. Plates were washed and bound antibodies were detected by incubating alkaline phosphatase-conjugated goat anti-human IgG (Southern Biotechnology: 2040-04) for 1 hour at room temperature followed by color development using 1 mg/ml p-nitrophenylphosphate substrate (Sigma-Aldrich 71768) in 0.1 M glycine buffer (pH 10.4) for 30 min at room temperature. The optical density

(OD) values were measured at a wavelength of 405 nm in an ELISA reader (Powerwave 340/96 spectrophotometer, BioTek).

Example 9

Binding of Monoclonal Antibodies to SARS-CoV-1 and SARS-CoV-2 Spike Protein

[0468] ExpiCHO cells were transfected with phCMV1-SARS-CoV-2-S, SARS-spike_pcDNA.3 (strain SARS), or empty phCMV1 using Expifectamine CHO Enhancer. Two days after transfection, cells were collected for immunostaining with antibody. An Alexa647-labelled secondary antibody anti-human IgG Fc was used for detection. Binding of monoclonal antibody to transfected cells was analyzed by flow cytometry using a ZE5 Cell Analyzer (Biorad) and FlowJo software (TreeStar). Positive binding was defined by differential staining of CoV-S transfectants versus mock transfectants. Monoclonal antibody S309 was tested by flow-cytometry at 10 µg/ml for the ability to stain ExpiCHO cells expressing the S protein of SARS-CoV-1 or SARS-CoV-2.

[0469] Binding to SARS-CoV-1 S protein or SARS-CoV-2 S protein was measured by flow cytometry for monoclonal antibodies S303, S304, S306, S309, S310, S315, S110, S124, S230, and S109, and the EC₅₀ values were calculated. Eight of these antibodies were calculated to have EC₅₀ values ranging between 1.4 ng/ml and 6,100 ng/ml for SARS-CoV-2 S protein binding and between 0.8 ng/ml and 254 ng/ml for SARS-CoV-1 S protein binding.

[0470] Further binding assays using the same procedure were carried out on recombinant monoclonal antibody S309 and four S309 variants. The EC₅₀ values for each antibody are shown in Table 2. The VH and VL amino acid SEQ ID NOs.: are summarized in Example 17.

TABLE 2

Antibody	EC ₅₀ (ng/ml) - Exp. 1	EC ₅₀ (ng/ml) - Exp. 2
S309-11 ("11")	23.1	11.5
S309-12 ("12")	22.3	9.6
S309-13 ("13")	21.8	8.9
S309-14 ("14")	21.4	8.4
S309-15 ("15")	18.8	7.8

[0471] Additional assays using the same procedure were carried out using monoclonal antibodies S303, S304, S306, S309, S310, S315, and comparator antibodies S109, S110, S124, and S230.

[0472] Assays using the same procedure were also carried out using recombinant monoclonal antibodies S300 and S307.

Example 10

Binding of Human Monoclonal Antibodies S309, S303, S304, and S315 to RBD of SARS-CoV-2 and SARS-CoV-1 Using Octet

[0473] Affinity of recombinant monoclonal antibodies S309, S303, S304, and S315 was tested using Octet.

[0474] His-tagged RBD of SARS-CoV-1 or SARS-CoV-2 were loaded at 3 µg/ml in kinetics buffer (KB) for 15 minutes onto anti-HIS (HIS2) biosensors (Molecular Devices, ForteBio). Association of full-length antibodies

was performed in KB at 15 µg/ml for 5 minutes. Association of Fab fragments was performed in KB at 5 µg/ml for 5 minutes. Dissociation in KB was measured for 10 minutes.

[0475] Affinities, represented by KD values, were calculated using a global fit model (Octet). Octet Red96 (ForteBio) equipment was used.

[0476] Each of these antibodies bound SARS-CoV-2 and SARS-CoV-1 RBD with nanomolar to sub-picomolar affinity.

Example 11

Binding of Human Monoclonal Antibody S309 IGG and S309 FAB to SARS-CoV-2 S Protein Ectodomain Trimer and RBD

[0477] Affinity and avidity determination of IgG1 compared to Fab fragment: biotinylated RBD of SARS-CoV-2 (produced in house; residues 331-550 of spike protein from BetaCoV/Wuhan-Hu-1/2019, accession number MN908947, biotinylated with EZ-Link NHS-PEG4-Biotin from ThermoFisher) and biotinylated SARS-CoV-2 2P S avi-tagged were loaded at 7.5 µg/ml in Kinetics Buffer (KB; 0.01% endotoxin-free BSA, 0.002% Tween-20, 0.005% NaN₃ in PBS) for 8 minutes onto Streptavidin biosensors (Molecular Devices, ForteBio). Association of IgG1 and Fab was performed in KB at 100, 33, 11, 3.6, 1.2 nM for 5 minutes. Dissociation in KB was measured for 10 minutes. KD values were calculated using a 1:1 global fit model (Octet). S309 IgG bound to the SARS-CoV-2 RBD and to the S ectodomain trimer with sub-picomolar and picomolar avidities, respectively. S309 Fab bound to both the SARS-CoV-2 RBD and the S ectodomain trimer with nanomolar to sub-nanomolar affinities.

Example 12

Competitive Binding of Human Monoclonal Antibodies to RBD of SARS-CoV-1 OR SARS-CoV-2

[0478] Competitive binding of pairs of monoclonal antibodies to SARS-CoV-1 RBD or SARS-CoV-2 RBD was measured to define the binding sites of the antibodies.

[0479] Strepavidin biosensors (Pall ForteBio) were used to immobilize anti-Strep Tag II antibody at 3 µg/ml (clone 5A9F9, Biotin, LabForce AG, Muttenz CH), after a hydration step for 10 min with Kinetics Buffer (KB; 0.01% endotoxin-free BSA, 0.002% Tween-20, 0.005% NaN₃ in PBS). Either SARS-CoV-1 or SARS-CoV-2 RBD with a Strep Tag II (produced in-house) was then loaded for 6 min at a concentration of 4 µg/ml in KB. The first antibody was allowed to associate for a period of time, then the second antibody was allowed to associate for a period of time.

Example 13

Competitive Binding of Human Monoclonal Antibody S309 and RBD to Human ACE2

[0480] Competitive binding of monoclonal antibodies and RBD to human ACE2 was measured. ACE2-His (Biotechne AG) was loaded for 30 minutes at 5 µg/ml in kinetics buffer (KB) onto anti-HIS (HIS2) biosensors (molecular Devices-ForteBio) SARS-CoV-1 RBD-rabbit Fc or SARS-CoV-2 RBD-mouse Fc (Sino Biological Europe GmbH) at 1

$\mu\text{g}/\text{ml}$ was associated for 15 minutes, after a preincubation with or without antibody at $30 \mu\text{g}/\text{ml}$ for 30 minutes. Dissociation was monitored for 5 minutes.

Example 14

Antibody-Dependent Cytotoxicity and Antibody-Dependent Cellular Phagocytosis of Human Monoclonal Antibodies

[0481] Natural killer (NK)-mediated antibody-dependent cell cytotoxicity (ADCC) can contribute to viral control by killing infected cells displaying viral protein on their surface. To investigate the ability of the Abs isolated to leverage this function, ADCC was investigated in vitro using freshly isolated human NK cells as effector cells and SARS-CoV-2 S-transfected ExpiCHO cells as target cells. Target cells were incubated with different amounts of antibody and after 10 minutes were incubated with primary human NK cells as effector cells at a target:effector ratio of 9:1. NK cells were isolated from fresh blood of healthy donors using the MACSxpress NK Isolation Kit (Miltenyi Biotec, Cat. Nr.: 130-098-185). Antibody-dependent cell killing was measured using an LDH release assay (Cytotoxicity Detection Kit (LDH) (Roche; Cat. Nr.: 11644793001) after 4 hours of incubation at 37°C .

[0482] Macrophage or dendritic cell-mediated antibody-dependent cellular phagocytosis (ADCP) can also contribute to viral control by clearing infected cells and by potentially stimulating T cell response with viral antigen presentation. ADCP was tested with peripheral blood mononuclear cells as phagocytes and ExpiCHO transfected with SARS-CoV-2 S fluorescently labeled with PKH67 Fluorescent Cell Linker Kits (Sigma Aldrich, Cat. Nr.: MINI67) as target cells. Target cells were incubated with different amounts of antibody for 10 minutes, followed by incubation with human PBMCs isolated from healthy donors that were fluorescently labeled with Cell Trace Violet (Invitrogen, Cat. Nr.: C34557) at an effector:target ratio of 20:1. After an overnight incubation at 37°C , cells were stained with anti-human CD14-APC antibody (BD Pharmingen, Cat. Nr.: 561708, Clone M5E2) to stain phagocytic cells. Antibody-mediated phagocytosis was determined by flow cytometry, measuring the % of monocytes that were positive for PKH67 fluorescence.

[0483] Human monoclonal antibodies S309, S304, S306, S315, S230, and the combination of S309 and S304 were assayed for antibody-dependent cell-mediated cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).

[0484] Fc variants of monoclonal antibody S309 were tested for ADCC. S309-LS includes the MLNS Fc mutation. S309-GRLR includes the G236R/L328R Fc mutation, which exhibits minimal binding to Fc γ Rs. S309-LS-GAALIE includes both the MLNS and GAALIE Fc mutations.

[0485] Human monoclonal antibodies S303, S304, S306, S309, S315, and the combination of S309 and S315 were assayed for ADCC and ADCP. At least the non-GRLR S309 antibodies (alone or in combination with S304) demonstrated ADCC and ADCP.

Example 15

Reactivity of Monoclonal Antibodies to Cell Lysate of SARS-CoV-2-Infected Cells

[0486] Reactivity of monoclonal antibodies S304, S306, S309, and S310 to cell lysate of SARS-CoV-2-infected VeroE6 cells was measured.

Example 16

Neutralization of SARS-CoV-2 Infection by Monoclonal Antibodies S304 and S309, Alone and in Combination

[0487] Neutralization of SARS-CoV-2 infection by monoclonal antibodies S304 and S309 was assessed using a SARS-CoV-2 live virus assay. The live virus neutralization assay quantifies the number of infected cells by staining for viral nucleoprotein (NP) with an NP-specific polyclonal rabbit serum. Inhibition was assessed by measuring NP expression at 24 and 45 hours post infection. Enzyme immunoassay (EIA) was used to quantify the level of infection for each antibody dilution tested.

[0488] Neutralization was carried out for one hour at room temperature at the indicated antibody concentrations using Vero E6 cells in monolayer in 96-well plates. Wells were infected with 100 TCID50 of virus. After 24 or 45 hours, monolayers were fixed and stained for inhibition of NP expression. Monoclonal antibodies S304 and S309 show a synergistic enhancement of neutralization.

Example 17

Production of S309 rIgG Variants

[0489] Recombinant IgG1 antibodies were produced using the VH and VL sequences of monoclonal antibody S309. S309-11 comprises the wild-type VH sequence (SEQ ID NO: 105) and wild-type VL sequence (SEQ ID NO: 168) of S309. S309-12 comprises an N55Q VH variant sequence (SEQ ID NO: 113) and the wild-type VL sequence (SEQ ID NO: 168) of S309. S309-13 comprises a W50F variant sequence (SEQ ID NO: 129) and the wild-type VL sequence (SEQ ID NO: 168) of S309. S309-14 comprises a W105F variant sequence (SEQ ID NO: 119) and the wild-type VL sequence (SEQ ID NO: 168) of S309. S309-15 comprises a W50F/G56A/W105F VH variant sequence (SEQ ID NO: 172) and the wild-type VL sequence of S309. S309 recombinant antibody and each of the four variants were produced by transient transfection and expression of a plasmid vector encoding the recombinant antibody in HD 293F cells (GenScript). Cells were harvested on day 4 and IgG expression was validated by Western blot and protein A titer analysis.

Example 18

Binding of S309 RIGG and Variants to SARS-CoV-2 RBD Measured by SPR

[0490] Binding of recombinant monoclonal antibody S309 and four variants (see Example 17) to RBD was measured using surface plasmon resonance (SPR). SPR experiments were carried out with a Biacore T200 instrument using a single-cycle kinetics approach. S309 IgG was captured on the surface and increasing concentrations of purified SARS-CoV-2 RBD, either glycosylated or deglycosylated, were

injected. SPR was conducted using a sensor chip with anti-human Fc covalently immobilized (GE). Buffer used was 10 mM HEPES pH 7.4, 150 mM NaCl, 3 mM EDTA, and 0.05% P20 detergent. Assays were conducted at 25° C. Recombinant antibodies were diluted from supernatant to approximately 2 µg/ml. RBD concentrations were 0.8 nM, 3.1 nM, 12.5 nM, 50 nM, and 200 nM. Glycosylated RBD was obtained by expression in HEK293 cells and purified using one-step Ni affinity purification. Deglycosylated RBD

was obtained by expression in-house in Expi293 cells grown in the presence of kifunensine, purification using one-step Ni affinity purification, and treatment with endoglycosidase H. Single-cycle kinetics assays were carried out with 3 minute injections and 20 minute dissociation periods. Association and dissociation kinetics were monitored and fit to a binding model to determine affinity. The results are summarized in Table 3.

TABLE 3

S309 variant	Glycosylated RBD			Deglycosylated RBD		
	K _D	K _a (1/Ms)	K _d (1/s)	K _D	K _a (1/Ms)	K _d (1/s)
S309-11 (WT)	0.50 nM	10.0e4	5.0e-5	0.91 nM	3.0e5	2.8e-4
S309-11 (WT) replicate	0.68 nM	9.5e4	6.5e-5	0.98 nM	2.9e5	2.9e-4
S309-12 (N55Q)	0.46 nM	9.2e4	4.2e-5	1.3 nM	2.7e5	3.6e-4
S309-13 (W50F)	0.51 nM	9.9e4	5.0e-5	1.8 nM	3.0e5	5.3e-4
S309-14 (W105F)	0.38 nM	1.0e5	3.9e-5	7.9 nM	9.8e5	7.7e-3
S309-15 (W50F/G56A/W105F)	1.7 nM	9.9e4	1.6e-4	>10 nM	estimate Kd with steady-state fit	

[0491] Binding to deglycosylated RBD was measured in two different SPR assays using different parameters. Experiment 1 used 10 minute injections and an RBD concentration series of 4-fold dilutions from 100 nM. Experiment 2 used 3 minute injections and a concentration series of 4-fold dilutions from 200 nM, as described 5 above. Results are shown in Table 4.

TABLE 4

S309 variant	Experiment 1			Experiment 2		
	K _D	K _a (1/Ms)	K _d (1/s)	K _D	K _a (1/Ms)	K _d (1/s)
S309-11 (WT)	0.83 nM	3.0e5	2.5e-4	0.91 nM	3.0e5	2.8e-4
S309-11 (WT) replicate	0.91 nM	3.0e5	2.7e-4	0.98 nM	2.9e5	2.9e-4
S309-12 (N55Q)	1.2 nM	2.7e5	3.2e-4	1.3 nM	2.7e5	3.6e-4
S309-13 (W50F)	1.7 nM	2.8e5	4.6e-4	1.8 nM	3.0e5	5.3e-4
S309-14 (W105F)	14 nM	Fit to steady state		7.9 nM	9.8e5	7.7e-3
S309-15 (W50F/G56A/W105F)	37 nM	Fit to steady state		Steady-state fit not possible		

[0492] Binding of recombinant monoclonal antibody S309 and five variants to RBD was measured by surface plasmon resonance (SPR) using the same procedure described above, except using purified recombinant antibodies rather than cell culture supernatant. Results are shown in Table 5.

TABLE 5

S309 variant	Glycosylated RBD			Deglycosylated RBD		
	K _D	K _a (1/Ms)	K _d (1/s)	K _D	K _a (1/Ms)	K _d (1/s)
S309 WT	0.26 nM	9.3e4	2.4e-5	0.67 nM	3.4e5	2.3e-4
S309 N55Q	0.39 nM	8.5e4	3.3e-5	1.1 nM	3.1e5	3.2e-4
S309 W50F	0.39 nM	9.2e4	3.6e-5	1.4 nM	3.5e5	4.9e-4
S309 W105F	0.35 nM	9.6e5	3.4e-5	5.1 nM	1.5e6	7.9e-3
S309 W50F/G56A/W105F	1.6 nM	9.4e4	1.5e-4	>10 nM	estimate Kd with steady-state fit	
S306 G56A	0.54 nM	9.3e4	5.1e-5	0.70 nM	3.4e5	2.4e-4

Example 19

Neutralization of SARS-CoV-2 by Recombinant Monoclonal Antibody S309 and Four Variants

[0493] Neutralizing activity of recombinant monoclonal antibody S309 and four variants (Example 17) was determined using a VSV-based luciferase reporter pseudotyping system (Kerafast). VSV pseudoparticles and antibody are mixed in DMEM and allowed to incubate for 30 minutes at 37C. The infection mixture is then allowed to incubate with Vero E6 cells for 1 h at 37C, followed by the addition of DMEM with Pen-Strep and 10% FBS (infection mixture is not removed). The cells are incubated at 37 C for 18-24 hours. Luciferase is measured using an Envision Plate Reader (Perkin Elmer) after the addition of Bio-Glo reagent (Promega). Calculated EC50 values based on this experiment are shown in Table 6.

TABLE 6

Recombinant Antibody	EC50
S309-11 (WT)	109
S309-12 (N55Q)	103
S309-13 (W50F)	97
S309-14 (W105F)	65
S309-15 (W50F/G56A/W105F)	53

Example 20

Determination of Antibody-Dependent Activation of Human FcγRIIIa OR FcγRIIa

[0494] Determination of antibody-dependent activation of human FcγRIIIa or FcγRIIa was performed using ExpiCHO cells transiently transfected with SARS-CoV-2 S (BetaCoV/Wuhan-Hu-1/2019), incubated with titrated concentrations of antibody for 10 minutes. ExpiCHO cells then were incubated with Jurkat cells expressing FcγRIIIa receptor or FcγRIIa on their surface and stably transfected with NFAT-driven luciferase gene (Promega, Cat. Nr.: G9798 and G7018) at an effector to target ratio of 6:1 for FcγRIIIa and 5:1 for FcγRIIa. Activation of human FcγRs in this bioassay results in the NFAT-mediated expression of the luciferase reporter gene. Luminescence was measured after 21 hours of incubation at 37° C. with 5% CO₂, using the Bio-Glo-TM Luciferase Assay Reagent according to the manufacturer's instructions. Monoclonal antibodies S303, S304, S306, S309, S315, and a combination of S309 and S315 were assayed, along with comparator antibody S320. S309, alone or in combination with S315, activated FcγRIIIa (V158) and FcγRIIa (H131)

Example 21

Analysis of SARS-CoV-2 S Glycoprotein Sequences

[0495] Analysis of the S glycoprotein sequences of 2,229 SARS-CoV-2 isolates was carried out, and indicates that several mutations have occurred with variable frequency on the SARS-CoV-2 S ectodomain.

[0496] Further analysis of the S glycoprotein sequences was carried out using 11,839 SARS-CoV-2 isolates. The epitope bound by S309 is conserved in all but four isolates,

and those isolates contained N354D or S359N substitutions that are not expected to affect S309 recognition.

Example 22

Competition of Antibody S309 with Antibodies Isolated from SARS-CoV-2 Patients

[0497] Human monoclonal antibodies isolated from patients who recovered from SARS-CoV-2 infection were tested for overlapping RBD binding sites with monoclonal antibody S309. Competition assays were performed using Octet (instrument: Octet Red96, ForteBio). Anti-His sensors (BIOSENSOR ANTI-PENTA-HIS (HIS1K) 1*1ST) were used to immobilize in house produced HIS-tagged RBD of SARS-CoV-2 (residues 331-550 of Spike protein from Beta-CoV/Wuhan-Hu-1/2019, accession number MN908947) at a concentration of 3 µg/ml. Antibodies were associated for 6 min at 15 µg/ml. All proteins were diluted in kinetics buffer (KB). Competing antibodies were then associated at the same concentration for additional 6 mins. Two antibodies were shown to compete with S309 for binding to RBD but, unlike S309, they were not neutralizing for SARS-CoV-2. Data not shown.

Example 23

Resistance Selection of SARS-CoV-2 Against Monoclonal Antibody S309-12-MLNS

[0498] To examine resistance selection, SARS CoV-2 was passaged for over one month in the presence of Vero E6 cells and fixed concentrations of monoclonal antibody S309-12-MLNS (i.e. S309 N55Q (VH) with MLNS mutations in Fc). Cytopathogenic effect (CPE) was evaluated by visual inspection of plates. Even when no CPE was observed, viral titers were evaluated by focus-forming assay with a methylcellulose overlay. No evidence of viral breakthrough in antibody-treated wells was observed, even at the minimum antibody concentration tested. Data are representative of wells in triplicate.

Example 24

Neutralization of SARS-CoV-2 Infection of CALU-3 Human Lung Cells by Monoclonal Antibody S309

[0499] Monoclonal antibody S309 was tested for its ability to neutralize live SARS-CoV-2 virus infection of Calu-3 human lung cells (which are positive for the transmembrane protease TMPRSS2) and VeroE6 cells using a nano luciferase assay. In this assay, S309 had an IC50 in Calu-3 cells of 97.70 µg/mL and in VeroE6 cells of 158.5 µg/mL

Example 25

Neutralization of SARS-CoV-2 Infection by Monoclonal Antibody S309

[0500] Monoclonal antibody S309 was tested neutralization of live SARS-CoV-2 virus infection using both a nano luciferase assay and IFA assay. Briefly, model cells were infected with live SARS-CoV-2 luciferase virus for six hours. Data were collected using three different antibody concentrations: 1, 0.1, and 0.01 MOI.

[0501] Results from the nano-luciferase assay were as follows: at 1 MOI, S309 IC₅₀ was 240.6 µg/mL; at 0.1 MOI, S309 IC₅₀ was 235.3 µg/mL, and at 0.01 MOI, S309 IC₅₀ was 206.6 µg/mL.

[0502] Results from the IFA assay were as follows: at 1 MOI, S309 IC₅₀ was 233.0 µg/mL; at 0.1 MOI, S309 IC₅₀ was 156.5 µg/mL, and at 0.01 MOI, S309 IC₅₀ was 142.8 µg/mL. Notably, no clusters of infection (or foci) were observed in this infection format.

Example 26

Neutralization of SARS-CoV-2 Infection by Monoclonal Antibodies S309 N55Q LS and S309 N55Q LS GAALIE

[0503] Monoclonal antibodies S309 N55Q LS (also referred to herein as S309 N55Q MLNS, comprising M428L/N434S Fc mutations) and S309 N55Q LS GAALIE (also referred to herein as S309 N55Q MLNS GAALIE, comprising G236A, A330L, I332E, M428L, and N434S Fc mutations) were assayed for ability to neutralize live SARS-CoV-2 virus infection. Each of S309 N55Q LS and S309 N55Q LS GAALIE comprises a VH having the sequence set forth in SEQ ID NO.: 113 and a VL having the sequence set forth in SEQ ID NO.: 168. The calculated EC₅₀ for S309 N55Q LS was 100.1 ng/ml. The calculated EC₅₀ for S309 N55Q LS GAALIE was 78.3 ng/ml.

Example 27

Neutralization of SARS-CoV-2 Pseudotyped Virus by Monoclonal Antibodies S309 N55Q LS and S309 N55Q LS GAALIE

[0504] Neutralization of SARS-CoV-2 pseudotyped virus by monoclonal antibodies S309 N55Q LS and S309 N55Q LS GAALIE was tested. The pseudotyped virus was VSV pseudotyped with SARS-CoV-2 Spike protein. The calculated EC₅₀ value for S309 N55Q LS was 24.06 ng/ml. The calculated EC₅₀ value for S309 N55Q LS GAALIE was 22.09 ng/ml.

Example 28

Binding of Monoclonal Antibodies S309 N55Q LS and S309 N55Q LS GAALIE to SARS-CoV-2 RBD

[0505] Binding of monoclonal antibodies S309 N55Q LS and S309 N55Q LS GAALIE to SARS-CoV-2 RBD was measured by surface plasmon resonance (SPR). Both antibodies exhibited strong binding.

Example 29

Binding of Monoclonal Antibodies S309 N55Q LS and S309 N55Q LS GAALIE to SARS-CoV-2 Spike Protein

[0506] Binding of monoclonal antibodies S309 N55Q LS and S309 N55Q LS GAALIE to SARS-CoV-2 to SARS-CoV-2 Spike protein was measured by flow cytometry. Both antibodies bound to Spike protein at concentrations as low as approximately 10 ng/mL, and binding to more than 60% of cells at 10,000 ng/ml antibody.

Example 30

Binding of Monoclonal Antibodies S309 N55Q LS and S309 N55Q LS GAALIE to Human Fc_γ Receptors

[0507] Binding of monoclonal antibodies S309 N55Q LS and S309 N55Q LS GAALIE to human Fc_γ receptors was assayed using SPR. Binding to Fc_γRIIa (both low affinity R131 and high affinity H131 alleles), Fc_γRIIIa (both low affinity F158 and high affinity V158 alleles), and FC_γRIIb was measured. Biotin CAPture Reagent (modified streptavidin) was injected across all flow cells of a CAP sensor chip docked in a Biacore T200 (Cytiva). Biotinylated Fc receptors at 1 µg/mL were injected across a single flow cell at 10 µL/min for 60 seconds (one receptor per flow cell), with one flow cell reserved as a reference surface. Antibody at 100 µg/mL (diluted in HBS-EP+) was injected across all flow cells for 200 seconds using a flow rate of 30 µL/min and association was monitored. Dissociation was monitored for another 200 seconds after injection. Data was collected at 10 Hz. After each binding measurement, CAP Regeneration reagent was injected to prepare the surface for a new cycle. Experiments were performed at 25° C., with the samples held at 15° C. in the instrument prior to injection. Both antibodies had at least measurable binding to all Fc_γ receptors tested. S309 N55Q LS GAALIE had increased binding (as compared to S309 N55Q LS) to all Fc_γ receptors except for Fc_γRIIb.

Example 31

Binding of Monoclonal Antibodies S309 LS, S309 N55Q LS, and S309 N55Q LS GAALIE to Complement Component C1q

[0508] Binding of monoclonal antibodies S309 LS, S309 N55Q LS, and S309 N55Q LS GAALIE to complement component C1q was measured by biolayer interferometry (BLI) on an Octet instrument. Anti-human Fab (CH1-specific) sensors were used to capture antibody at 10 µg/ml for 10 minutes. The IgG-loaded sensors were then exposed to kinetics buffer containing 3 µg/ml of purified human C1q for 4 minutes, followed by a dissociation step in the same buffer for additional 4 minutes. Association and dissociation profiles were measured in real time as changes in the interference pattern. S309 LS and S309 N55Q LS, but not S309 N55Q LS GAALIE, bound strongly to C1q.

Example 32

In Vitro Activation of Human Fc Gamma Receptors by Monoclonal Antibodies S309 LS, S309 N55Q LS, and S309 N55Q LS GAALIE

[0509] The ability of monoclonal antibodies S309 LS, S309 N55Q LS, and S309 N55Q LS GAALIE to elicit antibody-dependent activation of human Fc_γ receptors was assayed in vitro. Each of S309 LS, S309 N55Q LS, S309 N55Q LS GAALIE, and negative control antibody S309-GRLR was serially diluted 6-fold in assay buffer from 10,000 ng/ml to 0.006 ng/ml. Nine point serial dilutions of antibody were incubated with 12,500 (for Fc_γRIIIa and Fc_γRIIb) or 10,000 (for Fc_γRIIa) CHO-CoV-2-Spike cells per 96-well plate in a white, flat-bottom plate for 15 minutes at room temperature. Jurkat effector cells expressing the

indicated Fc γ Rs and stably transfected with an NFAT-driven luciferase gene were thawed, diluted in assay buffer, and added to the plate at an effector to target cell ratio of 6:1 for FcR γ IIIa and Fc γ RIIb or 5:1 for Fc γ RIIa. Control wells were included to measure antibody-independent activation (containing target cells and effector cells but no antibody) and background luminescence of the plate (wells containing assay buffer only). Plates were incubated for 18 hours at 37° C. with 5% CO₂. Activation of human Fc γ Rs in this bioassay results in the NFAT-mediated expression of the luciferase reporter gene. Luminescence was measured with a luminometer after adding the Bio-Glo™ Luciferase Assay Reagent according to the manufacturer's instructions. The negative control showed low-level activation of Fc γ RIIb and did not activate any of the other Fc γ Rs. S309 N55Q LS GAALIE was the only antibody to strongly activate Fc γ RIIa (F158). All non-GRLR S309 antibodies activated Fc γ RIIa, Fc γ RIIb, and Fc γ RIIIa (V158),

Example 33

Effector Function of Human Monoclonal Antibodies S309 LS, S309 N55Q LS, and S309 N55Q LS GAALIE

[0510] Human monoclonal antibodies S309 LS, S309 N55Q LS, and S309 N55Q LS GAALIE were assayed for their ability to promote NK-cell mediated antibody-dependent cell-mediated cytotoxicity (ADCC) and monocyte-mediated antibody-dependent cellular phagocytosis (ADCP) against cells expressing CoV2-spike protein.

[0511] ADCC was measured in vitro by exposing freshly isolated human NK cells from two genotyped donors expressing homozygous low-affinity (F/F158) or high-affinity (V/V158) Fc γ RIIIa to antibody pre-incubated with CHO-CoV-2-Spike cells and measuring LDH release as a readout according to the manufacturer's instructions (Cytotoxicity Detection Kit (LDH), Roche) after 4 hours of incubation at 37° C. In brief, plates were centrifuged for 4 minutes at 400× g, and 35 µl of supernatant was transferred to a flat 384-well plate. LDH reagent was prepared and 35 µl were added to each well. Using a kinetic protocol, the absorbance at 490 nm and 650 nm was measured once every 2 minutes for 8 minutes, and the slope of the kinetics curve was used as result. The percent specific lysis was determined by applying the following formula: (specific release-spontaneous release)/(maximum release-spontaneous release)×100. S309 GRLR was used as a negative control. All non-GRLR S309 antibodies elicited ADCC.

[0512] The ability of monoclonal antibodies S309 LS, S309 N55Q LS, S309 N55Q LS GAALIE, and control antibody S309-GRLR to promote ADCP by primary CD14+ monocytes was measured in vitro by exposing freshly isolated human PBMCs (labeled with cell trace violet) to CHO-CoV-2-Spike expressing cells (labeled with PKH67 Fluorescent Cell Linker Kit (Sigma Aldrich)) that were pre-incubated with antibody. Serial dilutions of mAbs (serially diluted 5-fold from 5,000 ng/ml to 0.32 ng/ml in

RPMI-1640+L-glutamine supplemented with 10% Hyclone FBS+2× anti-anti (antibiotic-antimycotic)) were incubated with 10'000 CHO-CoV-2-Spike cells per well of a 96 well polypropylene plate for 10 minutes. Primary PBMCs were fluorescently labeled with Cell Trace Violet according to the manufacturer's instructions. Target cell and antibody mixtures were then incubated with labeled PBMCs at an effector-to-target ratio of 16:1. ADCP activity was measured after overnight incubation by labeling the monocyte population for CD14, and measuring the percentage of cell trace violet+ PKH67+ cells amongst CD14+ monocytes by flow cytometry.

Example 34

[0513] Effect of Monoclonal Antibody S309 on SARS-CoV-2 Spike Protein-Mediated Cell Fusion

[0514] The effect of monoclonal antibody S309 on SARS-CoV-2 Spike protein-mediated fusion was tested using cells engineered to over-express Spike protein on the cell surface. The addition of S309 to these cell cultures inhibited S protein-mediated cell-cell fusion.

Example 35

Effect of Monoclonal Antibodies S309 N55Q LS and S309 N55Q LS GAALIE on SARS-CoV-2 Replication

[0515] The effect of monoclonal antibodies S309 N55Q LS and S309 N55Q LS GAALIE on SARS-CoV-2 replication was tested in VeroE6 cells, PBMCs, and dendritic cells. SARS-CoV-2 virus was incubated for one hour with antibody S309 N55Q LS or S309 N55Q LS GAALIE. The virus/antibody mixture was then added to plated VeroE6, PBMC, or monocyte-derived dendritic (MoDC) cells. After incubating the cells with the virus/antibody mixture for one hour at 37° C., the cells were washed and incubated for a further 72 hours in fresh medium. The supernatant from the cultured cells then assayed for focus-forming units (FFU). The supernatant was diluted 1:5 and added to VeroE6 cells. After one hour at 37° C., the VeroE6 cells were overlaid with methylcellulose. After 24 hours' further incubation, the VeroE6 cell cultures were stained for SARS-CoV-2 nucleoprotein. The results showed that S309 variant antibodies do not cause antibody-mediated enhancement of SARS-CoV-2 replication in human donor-derived PBMCs or dendritic cells.

Example 36

RBD Epitope-Specific Antibodies in Sera of Individuals Who Recovered from SARS-CoV-2 Infection

[0516] Sera from hospitalized, symptomatic, and asymptomatic individuals diagnosed with COVID-19 were tested for competition for binding with monoclonal antibodies that bind identified antigenic sites of SARS-CoV-2 Spike protein RBD.

[0517] Six antibodies (S2H13, S2H14, S2A4, S2X35, S304 and S309), whose antigenic binding sites were iden-

tified on RBD molecule by X-crystallography or Cryo-EM, were produced, purified and biotinylated using EZ-Link™ NHS-PEO solid phase biotinylation kit (Thermo Scientific #21450) according to manufacturer's instructions. Binding to RBD was measured by ELISA. Briefly, 96-well half-area plates (corning, cat.3690) were coated with 1 µg/ml RBD (mouse Fc Tag, Sino Biological Europa GmbH, cat. no 40592-V05H) and blocked with Blocker buffer (Casein 1%, Thermo Fisher Scientific, cat. no 37528, +0.05% Tween 20). Biotinylated monoclonal antibodies were titrated and added to the plate, followed by incubation with streptavidin-AP and pNPP substrate (Sigma N2765-100TAB). Plates were read by spectrophotometer at 405 nm to determine optical densities (OD). Concentration of biotinylated antibody that determines 80% of binding to RBD (EC80) was calculated by non-linear regression analysis using Graph Prism software. Most sera (58-62%) contained antibodies to RBD Site Ia, which is one of the main portions of the receptor binding motif that interacts with ACE2 receptor. This portion is accessible only in the open conformation of RBD. A smaller fraction of sera (25-41%) contained antibodies recognizing the other RBD sites.

[0518] To determine the amount of RBD antigenic site-specific antibodies, titrated sera were tested by ELISA as described above with the additional step whereby a 2× BC80 concentration of biotinylated antibody was added on top of the sera after 20 min of incubation. ODs reflecting residual binding of biotinylated antibodies were measured and percentage of inhibition of binding was measured compared to control wells (100% in wells without sera and biotinylated antibodies and 0% in wells without sera). Dilution of sera that determine 80% of blocking of binding (BD80) was calculated by non-linear regression analysis using Graph Prism software. Similarly, 80% of self-blocking of binding of the 6 monoclonal antibodies was determined (BC80) by testing titrations of purified monoclonal antibodies instead of sera. The estimated amount of RBD antigenic site-specific antibodies was determined for each serum as concentration equivalents (µg/ml) sample with the following formula: BD80×BC80. The antibody response to the six RBD sites varied among individuals, with some individuals showing a poor antibody response.

Example 37

Materials and Methods

Flow-Cytometry Based Screening for Binding to CoV S Protein Expressed on Mammalian Cells

[0519] ExpiCHO cells were transfected with S protein of SARS-CoV-2, SARS-CoV and MERS-CoV, or with an empty plasmid as a negative control. The monoclonal antibodies were then tested by flow-cytometry at 10 µg/ml for their ability to stain ExpiCHO cells expressing the S protein of 2019-nCoV, SARS-CoV, MERS-CoV or Mock cell transfectants.

Transient Expression of Recombinant SARS-CoV-2 Protein

[0520] The full-length S gene of SARS-CoV-2 strain (2019-nCoV-S) isolate BetaCoV/Wuhan-Hu-1/2019 (acces-

sion number MN908947) was codon optimized for human cell expression and cloned into the phCMV1 expression vector (Genlantis). Expi-CHO cells were transiently transfected with phCMV1-SARS-CoV-2-S, phCMV1-MERS-CoV-S (London1/2012), SARS-spike_pcDNA.3 (strain SARS) or the empty phCMV1 (Mock) using Expifectamine CHO Enhancer. Two days after transfection, cells were collected, fixed, or fixed and permeabilized with saponin for immunostaining with a panel of monoclonal antibodies reactive to SARS-CoV Receptor Binding Domain (RBD). An Alexa647-labelled secondary antibody anti-human IgG Fc was used for detection. Binding of antibodies to transfected cells was analyzed by flow-cytometry using a ZE5 Cell Analyzer (Biorad) and FlowJo software (TreeStar). Positive binding was defined by differential staining of CoV-S-transflectants versus mock-transflectants.

Competition Experiments Using Octet (BLI, Biolayer Interferometry)

[0521] Unless otherwise indicated herein, anti-His sensors (BIOSENSOR ANTI-PENTA-HIS (HIS1K)) were used to immobilize the S1 subunit protein of SARS-CoV (Sino Biological Europe GmbH). Sensors were hydrated for 10 min with Kinetics Buffer (KB; 0.01% endotoxin-free BSA, 0.002%Tween-20, 0.005% NaN3 in PBS). SARS-CoV S1 subunit protein was then loaded for 8 min at a concentration of 10 µg/ml in KB. Antibodies were associated for 6 min at 15 µg/ml for full length mAbs nCOV-10 and nCov-6 mAbs or 5 µg/ml for Fab nCOV-4, and in a subsequent experiment comprising nCoV-1 all at 10 µg/ml. Competing antibodies were then associated at the same concentration for additional 6 mins.

Competition Experiments Using Octet (BLI, Biolayer Interferometry)

[0522] For ACE2 competition experiments, ACE2-His (Bio-Techne AG) was loaded for 30 minutes at 5 g/ml in KB onto anti-HIS (HIS2) biosensors (Molecular Devices-ForteBio). SARS-CoV-1 RBD-rabbitFc or SARS-CoV-2 RBD-mouseFc (Sino Biological Europe GmbH) at 1 µg/ml was associated for 15 minutes, after a preincubation with or without antibody (30 µg/ml, 30 minutes). Dissociation was monitored for 5 minutes.

Affinity Determination Using Octet (BLI, Biolayer Interferometry)

[0523] For K_D determination of full-length antibodies, protein A biosensors (Pall ForteBio) were used to immobilize recombinant antibodies at 2.7 µg/ml for 1 minute, after a hydration step for 10 minutes with Kinetics Buffer. Association curves were recorded for 5 min by incubating the antibody-coated sensors with different concentration of SARS-CoV-1 RBD (Sino Biological) or SARS-CoV-2 RBD (produced in house; residues 331-550 of spike from Beta-CoV/Wuhan-Hu-1/2019, accession number MN908947). Highest RBD concentration tested was 10 µg/ml, then 1:2.5 serially diluted. Dissociation was recorded for 9 min by moving the sensors to wells containing KB. K_D values were calculated using a global fit model (Octet). Octet Red96 (ForteBio) equipment was used.

[0524] For K_D determination of full-length antibodies compared to Fab fragments, His-tagged RBD of SARS-CoV-1 or SARS-CoV-2 were loaded at 3 $\mu\text{g}/\text{ml}$ in KB for 15 minutes onto anti-HIS (HIS2) biosensors (Molecular Devices, ForteBio). Association of full-length antibody and Fab was performed in KB at 15 $\mu\text{g}/\text{ml}$ and 5 $\mu\text{g}/\text{ml}$ respectively for 5 minutes. Dissociation in KB was measured for 10 min.

ELISA Binding

[0525] The reactivities of mAbs with SARS-CoV Spike S1 Subunit Protein (strain WH20) protein were determined by enzyme-linked immunosorbent assays (ELISA). Briefly, 96-well plates were coated with 3 $\mu\text{g}/\text{ml}$ of recombinant SARS-CoV Spike S1 Subunit Protein (Sino Biological). Wells were washed and blocked with PBS+1% BSA for 1 h at room temperature and were then incubated with serially diluted mAbs for 1 h at room temperature. Bound mAbs were detected by incubating alkaline phosphatase-conjugated goat anti-human IgG (Southern Biotechnology: 2040-04) for 1 h at room temperature and were developed by 1 mg/ml p-nitrophenylphosphate substrate in 0.1 M glycine buffer (pH 10.4) for 30 min at room temperature. The optical density (OD) values were measured at a wavelength of 405 nm in an ELISA reader (Powerwave 340/96 spectrophotometer, BioTek).

Neutralization Assay

[0526] Unless otherwise indicated, Murine leukemia virus (MLV) pseudotyped with SARS-CoV-2 Spike protein (SARS-CoV-2pp) or SARS-CoV-1 Spike protein (SARS-CoV-1pp) were used. DBT cells stably transfected with ACE2 (DBT-ACE2) were used as target cells. SARS-CoV-2pp or SARS-CoV-1pp was activated with trypsin TPCK at 10 $\mu\text{g}/\text{ml}$. Activated SARS-CoV-2pp or SARS-CoV-1pp was added to a dilution series of antibodies (starting 50 $\mu\text{g}/\text{ml}$ final concentration per antibody, 3-fold dilution). DBT-ACE2 cells were added to the antibody-virus mixtures and incubated for 48 h. Luminescence was measured after aspirating cell culture supernatant and adding steady-GLO substrate (Promega).

[0527] Unless otherwise indicated, pseudoparticle neutralization assays use a VSV-based luciferase reporter pseudotyping system (Kerafast). VSV pseudoparticles and antibody are mixed in DMEM and allowed to incubate for 30 minutes at 37C. The infection mixture is then allowed to incubate with Vero E6 cells for 1 h at 37C, followed by the addition of DMEM with Pen-Strep and 10% FBS (infection mixture is not removed). The cells are incubated at 37 C for 18-24 hours. Luciferase is measured using an Envision Plate Reader (Perkin Elmer) after the addition of Bio-Glo reagent (Promega).

SPR Single-Cycle Kinetics

[0528] SPR experiments were carried out with a Biacore T200 instrument using a single-cycle kinetics approach. S309 IgG was captured on the surface and increasing concentrations of purified SARS-CoV-2 RBD, either glycosylated or deglycosylated, were injected. Association and dissociation kinetics were monitored and fit to a binding model to determine affinity.

Expression of Recombinant Antibodies

[0529] Recombinant antibodies were expressed in ExpiCHO cells transiently cotransfected with plasmids expressing the heavy and light chain as previously described. (Stettler et al. (2016) Specificity, cross-reactivity, and function of antibodies elicited by Zika virus infection. *Science*, 353 (6301), 823-826) Monoclonal antibodies S303, S304, S306, S309, S310, and S315 were expressed as rIgG-LS antibodies. The LS mutation confers a longer half-life in vivo. (Zalevsky et al. (2010) Enhanced antibody half-life improves in vivo activity. *Nature Biotechnology*, 28 (2), 157-159)

Sequence Alignment

[0530] SARS-CoV-2 genomics sequences were downloaded from GISAID on Mar. 29, 2020, using the “complete (>29,000 bp)” and “low coverage exclusion” filters. Bat and pangolin sequences were removed to yield human-only sequences. The spike ORF was localized by performing reference protein (YP_009724390.1)-genome alignments with GeneWise2. Incomplete matches and indel-containing ORFs were rescued and included in downstream analysis. Nucleotide sequences were translated in silico using seqkit. Sequences with more than 10% undetermined aminoacids (due to N basecalls) were removed. Multiple sequence alignment was performed using MAFFT. Variants were determined by comparison of aligned sequences (n=2,229) to the reference sequence using the R/Bioconductor package Biostrings. A similar strategy was used to extract and translate spike protein sequences from SARS-CoV genomes sourced from ViPR (search criteria: SARS-related coronavirus, full-length genomes, human host, deposited before December 2019 to exclude SARS-CoV-2, n=53). Sourced SARS-CoV genome sequences comprised all the major published strains, such as Urbani, Tor2, TW1, P2, Frankfurt1, among others. Pangolin sequences as shown by Tsang-Yuk Lam et al were sourced from GISAID. Bat sequences from the three clades of Sarbecoviruses as shown by Lu et al (Lancet 2020) were sourced from Genbank. Civet and raccoon dog sequences were similarly sourced from Genbank.

Example 38

Phase 1/2 Clinical Study of Sotrovimab (S309 N55Q LS) and VIR-7832 (S309 N55Q LS GAALIE) for Treatment of Mild to Moderate COVID-19 Disease

[0531] In one arm of a multi-center, multi-arm, multi-dose, multi-stage open-label, adaptive, seamless phase I/II Bayesian randomised platform trial (600 patients) to determine the optimal dose, activity and safety of multiple candidate agents for the treatment of COVID-19, sotrovimab (S309 N55Q LS; in more detail, sotrovimab is an engineered monoclonal antibody (IgG1*01 G1m17; VH of SEQ ID NO.: 113, M428L and N434S Fc mutations; VL of SEQ ID NO.: 168 (kappa light chain IgKC*01 k1m3)) and VIR-7832 ((IgG1*01 G1m17; VH of SEQ ID NO.: 113,

G236A, A330L, I332E, M428L, and N434S Fc mutations; VL of SEQ ID NO.: 168 (kappa light chain IgKC*01 k1m3)) are evaluated, randomizing between candidate and control with 2:1 allocation in favor of the candidate. Each dose is assessed for safety sequentially in cohorts of 6 patients. This arm comprises 3:1 randomised, blinded, placebo-controlled phase I of VIR-7832, followed by a 2:2:1 blinded, parallel group Phase II trial of VIR-7832 versus sotrovimab versus placebo. Single doses of VIR-7832 are administered by intravenous (IV) infusion. The starting dose is 50 mg, and dose escalations of 150 and 500 mg may be used. The active comparator is sotrovimab (500 mg by i.v. infusion over 1 hour). Placebo is given by i.v. infusion over 1 hour.

Primary Outcome Measures:

- [0532] 1 Dose-finding/Phase I [Time Frame: 29 days from randomisation]
- [0533] Determination of a dose(s) for efficacy evaluation. Dose limiting toxicities (Safety and Tolerability of drug under study—CTCAE v5 Grade ≥ 3 adverse events)
- [0534] 2. Efficacy evaluation/Phase II-Severe patients (Group A) [Time Frame: 29 days from randomisation]
- [0535] Determination of activity and safety.
- [0536] In severe patients (Group A): time to clinical improvement. Improvement will be determined according to the WHO Clinical Progression Scale; improvement is defined as a minimum 2-step change from randomisation in the scale up to day 29 post-randomisation.
- [0537] 3. Efficacy evaluation/Phase II-Mild to moderate patients (Group B) [Time Frame: 15 days from randomisation]
- [0538] Determination of activity and safety.
- [0539] In mild to moderate patients (Group B): pharmacodynamics of drug under study, defined as time to negative viral titres in nose and/or throat swab, measured up to 15 days post-randomisation.

Secondary Outcome Measures:

- [0540] 1. Safety assessed by rate of adverse events [Time Frame: Up to 29 days from randomisation]
- [0541] Adverse event rate according to CTCAE v5
- [0542] 2. To evaluate clinical improvement [Time Frame: From randomisation to day 29]
- [0543] Proportion of patients with clinical improvement (as defined above) at day 8, 15 and day 29.
- [0544] 3. To evaluate clinical improvement using WHO clinical progression scale [Time Frame: From randomisation to day 15]
- [0545] Change at day 8 and 15 from randomisation in the WHO Clinical Progression Scale
- [0546] 4. To evaluate clinical improvement using WHO clinical progression scale [Time Frame: From randomisation to day 29]
- [0547] Time to a one point change on the WHO Clinical Progression Scale
- [0548] 5. To evaluate clinical improvement using SpO₂/FiO₂ [Time Frame: From randomisation to day 29]
- [0549] The ratio of the oxygen saturation to fractional inspired oxygen concentration (SpO₂/FiO₂)
- [0550] 6. To evaluate discharge [Time Frame: From randomisation to day 29]

- [0551] Proportion of patient discharged at days 8, 15 and 29
- [0552] 7. To evaluate admission to ICU [Time Frame: From randomisation to day 29]
- [0553] Admission rate to ICU
- [0554] 8. To evaluate safety further (WCC) [Time Frame: From randomisation to day 29]
- [0555] White cell count on day 1, 3, 5, 8, 11 (while hospitalised); and Day 15 and 29
- [0556] 9. To evaluate safety further (Hg) [Time Frame: From randomisation to day 29]
- [0557] Haemoglobin on day 1, 3, 5, 8, 11 (while hospitalised); and Day 15 and 29
- [0558] 10. To evaluate safety further (platelets) [Time Frame: From randomisation to day 29]
- [0559] Platelets on day 1, 3, 5, 8, 11 (while hospitalised); and Day 15 and 29
- [0560] 11. To evaluate safety further (creatinine) [Time Frame: From randomisation to day 29]
- [0561] Creatinine on day 1, 3, 5, 8, 11 (while hospitalised); and Day 15 and 29
- [0562] 12. To evaluate safety further (ALT) [Time Frame: From randomisation to day 29]
- [0563] ALT on day 1, 3, 5, 8, 11 (while hospitalised); and Day 15 and 29
- [0564] 13. To evaluate overall mortality [Time Frame: From randomisation to day 29]
- [0565] Mortality at Days 8, 15 and 29. Time to death from randomisation
- [0566] 14. To evaluate the number of oxygen-free days [Time Frame: From randomisation to day 29]
- [0567] Duration (days) of oxygen use and oxygen-free days
- [0568] 15. To evaluate ventilator-free days [Time Frame: From randomisation to day 29]
- [0569] Duration (days) of mechanical ventilation and mechanical ventilation-free days
- [0570] 16. To evaluate incidence of new mechanical ventilation use [Time Frame: From randomisation to day 29]
- [0571] Incidence of new mechanical ventilation use
- [0572] 17. To evaluate National Early Warning Score (NEWS) 2/qSOFA [Time Frame: From randomisation to day 29]
- [0573] NEWS2/qSOFA assessed daily while hospitalised
- [0574] 18. To evaluate translational outcomes (Viral Load) [Time Frame: From randomisation to day 29]
- [0575] Change in viral load over time
- [0576] 19. To evaluate translational outcomes (Baseline SARS-CoV-2) [Time Frame: From randomisation to day 29]
- [0577] Change in viral load over time

Eligibility

- [0578] Ages Eligible for Study: 18 Years and older (Adult, Older Adult)
- [0579] Sexes Eligible for Study: A11
- [0580] Accepts Healthy Volunteers: No

Inclusion Criteria

- [0581] 1. Adults (≥ 18 years) with laboratory-confirmed SARS-CoV-2 infection (PCR)

- [0582] 2. Ability to provide informed consent signed by study patient or legally acceptable representative
- [0583] 3. Women of childbearing potential (WOCBP) and male patients who are sexually active with WOCBP agree to use a highly effective method of contraception (as outlined in the protocol) from the first administration of trial treatment, throughout trial treatment and for the duration outlined in the candidate-specific trial protocol after the last dose of trial treatment

Additional Criteria May be Applied:

- [0584] Group A (severe disease) 4a. Patients with clinical status of Grades 4 (hospitalised, oxygen by mask or nasal prongs), 5 (hospitalised, on non-invasive ventilation, or high flow oxygen), 6 (hospitalised, intubation and mechanical ventilation) or 7 (ventilation and additional organ support-pressors, renal replacement therapy (RRT), extracorporeal membrane oxygenation (ECMO)), as defined by the WHO clinical severity score, 9-point ordinal scale.
- [0585] Group B (mild-moderate disease) 4b. Ambulant or hospitalised patients with the following characteristics peripheral capillary oxygen saturation (SpO_2) >94% RA N.B.

[0586] The main trial exclusion criteria are outlined in the master protocol as:

- [0587] 1. *
- [0588] 2. *
- [0589] 3. Pregnant or breast feeding
- [0590] 4. *
- [0591] 5. Allergy to any study medication
- [0592] 6. Patients taking other prohibited drugs (as outline in CST protocol) within 30 days or 5 times the half-life (whichever is longer) of enrolment
- [0593] 7. Patients participating in another clinical trial of an investigational medicinal product (CTIMP)
- [0594] *The master protocol stipulates the following for '1', '2' and '4':
- [0595] 1. Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) >5 times the upper limit of normal (ULN)
- [0596] 2. Stage 4 severe chronic kidney disease or requiring dialysis (i.e., estimated glomerular filtration rate <30 mL/min/1.73 m²)
- [0597] 4. 'anticipated transfer to another hospital which is not a study site within 72 hours'
- [0598] Those criteria are not applicable to this protocol as the IMP is a monoclonal antibody, which is not cleared from the body by the liver or kidneys (1 and 2) and patients who are hospitalised are excluded from the study.
- [0599] For the purpose of the VIR-7832 and sotrovimab candidate-specific trial the following exclusion criteria also apply:
- [0600] 8. Currently hospitalised or judged by the investigator as likely to require hospitalisation for acute medical care in the next 24 hours
- [0601] 9. Symptoms consistent with severe COVID-19 as defined by shortness of breath at rest or respiratory distress or requiring supplemental oxygen.
- [0602] 10. Participants who, in the judgement of the investigator are likely to die in the next 7 days
- [0603] 11. Severely immunocompromised participants including but not limited to cancer patients receiving

immunosuppressive chemotherapy or immunotherapy, those with a solid organ transplant or allogeneic stem cell transplant within the last 3 months, any history of heart or lung transplant or high dose long-term systemic corticosteroids (equivalent to ≥ 20 mg a day of prednisone or the systemic equivalent for over 2 weeks)

- [0604] 12. Phase I only: Diabetes (requiring medication), chronic kidney disease (i.e., eGFR <60 as determined by the Modification of Diet in Renal Disease (MDRD) study), chronic liver disease (e.g., cirrhosis), congestive heart failure (New York Heart Association (NYHA) class II or more), chronic obstructive pulmonary disease (history of chronic bronchitis, chronic obstructive lung disease, or emphysema with dyspnoea on physical exertion), and moderate to severe asthma (participant requires an inhaled steroid to control symptoms or has been prescribed a course of oral steroids in the past year).

- [0605] 13. Any current medical condition that, in the Investigator's judgment, precludes the participant's safe participation in and completion of the study.

- [0606] 14. Known hypersensitivity to any constituent present in the investigational product

- [0607] 15. Previous anaphylaxis or hypersensitivity to a monoclonal antibody

- [0608] 16. Have ever received a vaccine for SARS-CoV-2, as part of clinical trial or otherwise.

- [0609] 17. Receipt of any vaccine within 48 hours prior to enrolment. Vaccination will not be allowed for 4 weeks after dosing.

- [0610] 18. Receipt of convalescent plasma from a recovered COVID-19 patient or anti SARS-CoV-2 mAb within the last 3 months.

- [0611] 19. Participants who, in the judgment of the investigator, will be unlikely or unable to comply with the requirements of the protocol

Example 39

Phase 2/3 Clinical Study of Sotrovimab for Treatment of Mild to Moderate COVID-19 Disease

- [0612] A randomized, multi-center, double-blind, placebo-controlled study is performed to assess safety and efficacy of sotrovimab (S309 N55Q LS) for the early treatment of COVID-19 in outpatients. Sotrovimab is an engineered monoclonal antibody (IgG1*01 G1m¹⁷; VH of SEQ ID NO.: 113, M428L and N434S Fc mutations; VL of SEQ ID NO.: 168 (kappa light chain IgKC*01 k1m3)).

- [0613] A primary objective is to evaluate efficacy of sotrovimab versus placebo in preventing the progression of mild/moderate to severe or critical COVID-19 disease. Primary endpoints are the proportion of participants to develop severe disease, critical disease, or death, with a primary analysis up to Day 29.

- [0614] Key secondary objectives are to determine safety and tolerability of sotrovimab compared to placebo, evaluate efficacy of sotrovimab versus placebo in preventing COVID-19 disease progression by days 8, 15, and 22, evaluate efficacy of sotrovimab versus placebo in preventing mortality, evaluate efficacy of sotrovimab versus placebo in shortening ventilator days, ICU length of stay (LOS), and total hospital LOS, evaluate efficacy of sotrovimab versus placebo in shortening the duration and decreasing the severity of COVID-19 clinical signs and symptoms, evaluate

efficacy of sotrovimab versus placebo in preventing non-respiratory complications of COVID-19, evaluate efficacy of sotrovimab versus placebo in reducing duration of SARS-CoV-2 viral shedding, evaluate efficacy of sotrovimab versus placebo in inducing an anti-viral response, evaluate efficacy of sotrovimab versus placebo in facilitating a return to normal living, assess pharmacokinetics (PK) of sotrovimab in serum, and assess immunogenicity of sotrovimab.

[0615] Exploratory objectives are to evaluate efficacy of sotrovimab against versus placebo in preventing COVID-19 disease progression by days 8, 15, and 22, monitor on-treatment emergence of SARS-CoV-2 resistant mutants against sotrovimab, evaluate efficacy of sotrovimab versus placebo in reducing SARS-CoV-2 viral load, evaluate effect of sotrovimab versus placebo on potential biomarkers of host response to SARS-CoV-2, evaluate potential relationships between subject genetic polymorphisms and sotrovimab mechanisms of action and/or PK, and measure impact of sotrovimab treatment on time away from work and work productivity due to COVID-19 illness.

[0616] Further study details are shown in FIG. 6.

Details of Criteria for Evaluation

Primary Endpoints of this Study are as Follows:

[0617] Proportion of subjects who progress to severe or critical COVID-19 or die through Day 29 as defined by:

[0618] 1. Severe disease: hypoxemia (O₂ saturation ≤93% on room air or PaO₂/FiO₂<300) requiring oxygen supplementation >1 day OR subject requires ≥4 L/min oxygen supplementation or equivalent AND the investigator or designee determine that the measurement of O₂ saturation on room air is medically unsafe.

[0619] OR

[0620] 2. Critical disease: Respiratory failure requiring at least one of the following: invasive mechanical ventilation, ECMO; OR shock; OR multi-organ dysfunction/failure

[0621] OR

[0622] 3. Death

Secondary Endpoints of this Study are as Follows:

[0623] 1. Occurrence of adverse events (AEs)

[0624] 2. Occurrence of serious adverse events (SAEs)

[0625] 3. Occurrence of adverse events of special interest (AESI)

[0626] 4. Proportion of subjects who progress to develop severe or critical COVID-19 at Day 8, Day 15, or Day 22

[0627] 5. 29-day, 60-day, and 90-day all-cause mortality

[0628] 6. Total number of ventilator days from randomization through 29 days

[0629] 7. Total intensive care length of stay (LOS)

[0630] 8. Total hospital LOS

[0631] 9. Severity and duration of subject reported signs and symptoms of COVID-19 related illness using the Flu-PRO patient-reported outcome measurement instrument

[0632] 10. Occurrence of cardiac, thromboembolic, renal, neurologic events

[0633] 11. Detection of SARS-CoV-2 in nasal secretions by PCR at baseline and during follow-up period through Day 29

[0634] 12. Sotrovimab pharmacokinetics (PK) in serum

[0635] 13. Incidence and titers (if applicable) of serum ADA to Sotrovimab Exploratory endpoints of this study are as follows:

[0636] 1. Proportion of subjects at Day 8, Day 15, Day 22, and Day 29 in each category of the ordinal scale for clinical improvement (see below)

[0637] 2. Emergence of viral resistance mutants to mAb by SARS-CoV-2

[0638] 3. Viral load in nasal secretions and blood by qRT-PCR

[0639] 4. Host transcriptome and immunophenotyping analysis

[0640] 5. FcγR polymorphisms as determined by genotyping

[0641] 6. IgG1 allotypes as determined by genotyping

[0642] 7. Change from baseline in Work Productivity and Activity Impairment (WPAI)

[0643] 8. Change from baseline in health-related quality of life according to EQ-5D-5L

The Ordinal Scale for Use in Categorizing Clinical Improvement is as Follows:

[0644] 1. Uninfected: No clinical or virologic evidence of infection

[0645] 2. Non-hospitalized, no limitation of activity (if using oxygen at home, report as category 4)

[0646] 3. Non-hospitalized, limitation of activity

[0647] 4. Hospitalized, no oxygen therapy

[0648] 5. Hospitalized, low-flow oxygen by mask or nasal prongs

[0649] 6. Hospitalized, high-flow oxygen, Continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP), non-invasive ventilation

[0650] 7. Hospitalized, intubation and mechanical ventilation

[0651] 8. Hospitalized, mechanical ventilation plus organ support (vasopressors, RRT, ECMO)

[0652] 9. Death

Number of Subjects

[0653] This study is comprised of two parts. The lead-in phase enrolls approximately 20 subjects with early, mild to moderate COVID-19 who are at high risk for progression of disease. The expansion phase enrolls approximately 850 subjects with early, mild to moderate COVID-19 who are at high risk for progression of disease.

Diagnosis and Main Criteria for Inclusion

Inclusion Criteria Include:

Age:

[0654] 1. Subjects aged 18 years and older at high risk of complications from COVID-19 disease including diabetes, obesity (BMI>30), chronic kidney disease, congestive heart failure, chronic obstructive pulmonary disease, and moderate to severe asthma

[0655] AND

[0656] 2. Subjects ≥55 years old, irrespective of comorbidities

Disease Characteristics:

- [0657] 1. Subjects who have a positive SARS-CoV-2 test result (by any validated test e.g. RT-PCR on any specimen type)
- [0658] AND
- [0659] 2. Have an oxygen saturation $\geq 94\%$ on room air
- [0660] AND
- [0661] 1. Have mild to moderate or moderate uncomplicated COVID-19 illness defined by one or more of the following symptoms:
- [0662] fever, chills, cough, sore throat, malaise, headache, joint or muscle pain, change in smell or taste, vomiting, diarrhea, shortness of breath on exertion
- [0663] AND
- [0664] 3. Are less than or equal to 4 days from onset of symptoms

Sex:

- [0665] 1. No gender restriction
- [0666] 2. Female subjects must meet and agree to abide by the following contraceptive criteria. Contraception use by women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.
- [0667] 3. A female subject is eligible to participate if she is not pregnant or breastfeeding, and one of the following conditions applies:
- [0668] Is a woman of non-childbearing potential (WONCBP)
- [0669] OR
- [0670] Is a woman of child-bearing potential (WOCBP) and using a contraceptive method that is highly effective, with a failure rate of $<1\%$ during the study intervention period and for up to one year after the last dose of study intervention. The investigator should evaluate potential for contraceptive method failure (e.g., noncompliance, recently initiated) in relationship to the first dose of study intervention.
- [0671] 4. A WOCBP must have a negative highly sensitive pregnancy test (urine or serum as required by local regulations) at hospital admission or before the first dose of study intervention. If a urine test cannot be confirmed as negative (e.g., an ambiguous result), a serum pregnancy test is required. In such cases, the subject must be excluded from participation if the serum pregnancy result is positive.

Informed Consent:

- [0672] 5. Willing to comply with the study requirements and capable of giving signed informed consent or, if not able to give signed informed consent, if alternative consent procedures are able to be followed.

Exclusion Criteria:

Medical Conditions

- [0673] Currently hospitalized or judged by the investigator as likely to require hospitalization in the next 24 hours
- [0674] Symptoms consistent with severe Covid-19 as defined by shortness of breath at rest or respiratory distress or requiring supplemental oxygen

[0675] Patients who, in the judgment of the investigator, are likely to die in the next 7 days

[0676] Severely immunocompromised patients, including but not limited to cancer patients actively receiving immunosuppressive chemotherapy or immunotherapy, those with a solid organ transplant or allogeneic stem cell transplant within the last 3 months, or those having conditions requiring the use of systemic corticosteroids equivalent to ≥ 0.5 mg/kg of body weight per day of prednisone within 6 weeks of randomization

[0677] Known hypersensitivity to any constituent present in the investigational product

[0678] Previous anaphylaxis or hypersensitivity to a monoclonal antibody

Prior/Concurrent Clinical Study Experience

[0679] Enrollment in any investigational vaccine study within the last 180 days or any other investigational drug study within 30 days prior to day 1 or within five half-lives of the investigational compound, whichever is longer

[0680] Enrollment in any trial of an investigational vaccine for SARS-CoV-2

Other Exclusions

[0681] Receipt of any vaccine within 48 hours prior to enrollment. Receipt of a SARS-CoV-2 vaccine prior to randomization at any time point. Vaccination (including vaccination for SARS-CoV-2) will not be allowed for 4 weeks after dosing

[0682] Receipt of convalescent plasma from a recovered Covid-19 patient or anti-SARS-CoV-2 monoclonal antibody within the last 3 months

[0683] Patients who, in the judgment of the investigator, will be unlikely or unable to comply with the requirements of the protocol through day 29

Duration of Study Participation and Follow Up

[0684] The duration of study drug treatment is a single dose. The estimated total time on study, inclusive of screening and follow-up, for each subject is approximately nine months. All subjects are monitored through at least two hours post-dose prior to discharge from the study unit. Subjects enrolled in the lead-in portion of the study are monitored in an in-patient setting for a minimum of seven days. Subjects are subsequently actively monitored on an outpatient basis with in-person study visits at Weeks 1, 2, 3, and 4 and daily telephone calls on non-study visit days through Day 14. After Day 29, patients are monitored monthly via remote telehealth or phone call for a total of nine months from dosing.

Study Design

[0685] An Independent Data Monitoring Committee (IDMC) actively monitors interim unblinded safety data (Lead-in Phase) and interim unblinded safety and efficacy data (Expansion Phase) to make recommendations regarding ongoing study conduct. The IDMC members include physicians with relevant medical specialist training and one statistician. The IDMC reviews unblinded safety data from the Lead-in Phase of the study prior to initiation of the Expansion Phase. In addition, the IDMC performs regular safety reviews during the Expansion Phase. The first safety

review includes available safety and tolerability data through Day 14 from a total of 60 patients (30 per arm). If there are no safety or tolerability concerns according to pre-specified criteria, the IDMC recommends initiation of a separate study in hospitalized patients with severe to critical COVID-19. If necessary, additional safety reviews are conducted after each additional approximately 100 patients are enrolled (50 per arm). Finally, two interim analyses are conducted at approximately 33% of subjects enrolled (145 per arm) and approximately 67% of subjects enrolled (290 per arm) to evaluate safety, futility, and efficacy. A Joint Safety Review Team (JSRT) determines if a safety concern identified during the instream blinded data review needs to be escalated to the IDMC.

[0686] This study is a randomized, double-blind, multi-center, placebo-controlled trial of sotrovimab, a monoclonal antibody (mAb) against SARS-CoV-2 for the prevention of progression of mild to moderate COVID-19 disease in high-risk subjects, with interim monitoring to allow early stopping for futility, efficacy, or safety. Subjects with early, mild to moderate COVID-19 who are at high-risk for progression of disease are randomized 1:1 to receive a single, intravenous infusion of either sotrovimab or equal volume saline placebo. Comparisons of safety and efficacy are based on data from concurrently randomized participants.

[0687] The study is comprised of 2 parts. The lead-in phase enrolls 20 subjects who have early, mild to moderate COVID-19 and are at high risk of disease progression. Following a safety assessment of unblinded data by an independent data monitoring committee (IDMC), the expansion phase progresses, where additional subjects with early, mild to moderate COVID-19 and who are at high risk of disease progression are enrolled.

Lead-In Phase:

[0688] The Lead-In Phase of the study evaluates the safety and tolerability of sotrovimab in subjects with early, mild to moderate COVID-19 who are at high-risk of progression to severe disease. Subjects are monitored in an in-patient setting for seven days including assessments of respiratory status, oxygenation and other vital signs and laboratory evaluations. A single dose level is studied and is delivered via intravenous infusion. Subjects are admitted to a study unit and monitored closely for adverse events, changes in laboratory parameters and progression or improvement in disease signs and symptoms.

[0689] The first two eligible subjects enrolled are randomized 1:1 to sotrovimab or placebo. These sentinel subjects are dosed and monitored for at least 48 hours in an in-patient setting. During dose administration, vital signs are monitored every 15 minutes over the one hour IV infusion. Vital signs are also monitored every one hour after infusion for two hours. Vital signs, ECG, symptom-directed physical examinations(s), and adverse events (AEs) are reviewed by the investigator. If the investigator has no immediate safety concerns, the remainder of the subjects in the Lead-In phase is dosed (total of ten per arm inclusive of the sentinel subjects).

[0690] All 20 subjects enrolled in the Lead-In (N=10 per arm; sotrovimab or placebo) are assigned to an intensive PK and immunogenicity substudy. Sparse samples are collected from all participants not enrolled in the substudy. Serum PK and anti-drug antibodies (ADA) samples are collected.

Expansion Phase:

[0691] The Expansion Phase of the study follows the Lead-in Phase (N=10 per arm through 14 days of follow-up) by an IDMC. The purpose of the Expansion Phase is to evaluate the safety and efficacy of sotrovimab in comparison to the placebo control arm. Subjects with early mild to moderate COVID-19 who are at risk for progression to severe disease are randomized in a 1:1 ratio (435 per arm) to receive a single, IV infusion of sotrovimab or placebo.

[0692] Subjects are monitored through at least 2 hours post-dose prior to discharge from the study unit. Subjects are subsequently actively monitored on an outpatient basis with in-person study visits at Weeks 1, 2, 3, and 4 and daily telephone calls on non-study visit days through Day 14 for AEs and worsening of illness. In addition, the subjects are provided a device to monitor for hypoxemia.

[0693] After Day 29, patients are monitored monthly via remote telehealth or phone call to assess for the incidence and of severity of subsequent COVID-19 illness, if any, for a total of 9 months from dosing.

[0694] Two interim analyses at approximately 33% of subjects enrolled (145 per arm) and approximately 67% of subjects enrolled (290 per arm) are conducted to evaluate futility, efficacy, and safety, as well as allow for sample size reestimation if the overall disease progression rate is lower than expected.

[0695] A placebo control distinguishes safety and tolerability of sotrovimab from the background signs and symptoms of COVID-19 and evaluates its potential benefit on clinical outcomes. The use of a placebo arm allows for a valid evaluation of any changes in efficacy and safety attributable to sotrovimab versus those attributable to background supportive care given during the study.

[0696] A primary endpoint to assess efficacy of treatment is progression to severe disease defined as hypoxia requiring oxygen supplementation, or the development of critical disease (respiratory failure requiring at least one of the following: invasive mechanical ventilation, ECMO; OR shock; OR multi-organ dysfunction/failure), or death within 29 days of randomization. The transition from outpatient status without hypoxia or oxygen requirement to hypoxia with a need for oxygen therapy or higher levels of respiratory/organ support is a clinically significant milestone.

[0697] A significant secondary endpoints is all-cause mortality at Day 29. Other secondary efficacy endpoints related to hospital stay-length of hospital stay, ICU stay, time ventilated and the severity and duration of subject-reported signs and symptoms of COVID-19 are also clinically relevant.

Immunology Assessment Substudy:

[0698] To explore the host immune response and potential biomarkers of infection, subjects may consent to an optional sub-study in which peripheral blood mononuclear cells (PBMCs) are collected at specified timepoints. This optional sub-study is performed at selected sites. Approximately 20-50 participants per arm are enrolled in the optional sub-study. Subjects from both the Lead-In and Expansion Phases of the study may be included in the Immunology Assessment Substudy.

Study Intervention Groups and Duration

[0699] Screening assessments are performed within 24 hours before the first dose. Eligible subjects are treated in a blinded manner with a single IV dose on Day 1 and followed up to 9 months (36 weeks).

[0700] In the Lead-In Phase, 20 subjects with mild to moderate COVID-19 are randomized 1:1 to receive a single IV dose of sotrovimab or placebo. Subjects enrolled in the Lead-in Phase of the study are closely monitored in an in-patient setting for a minimum of 7 days. At the end of 7 days they are either discharged to home, remain in the inpatient unit or are formally hospitalized based on investigator assessment of clinical status.

[0701] In the Expansion Phase, subjects with mild to moderate COVID-19 are randomized 1:1 to receive a single IV dose of sotrovimab or placebo.

[0702] Participants in the Expansion phase are stratified by the following criteria:

- [0703] 1. Duration of symptoms: ≤2 days vs. 3-4 days
- [0704] 2. Age: ≤70 vs. >70 years old

Study Interventions

[0705] Study interventions and dosing instructions are as follows in Table 7:

TABLE 7

Dose Formulation	Solution in single-use vial (25 mg/mL)	Sterile 0.9% (w/v) sodium chloride solution
Unit Dose Strength(s)	250 mg/vial (250 mg/10 mL)	Not applicable
Dosage Level(s)	nn mg once	Once
Route of Administration	IV infusion	IV infusion
Dosing instructions	Withdraw 10.0 mL from the vial into a 10-20 mL small syringe and transfer to a 150 mL or 250 mL IV empty saline bag by an unblinded pharmacist. Repeat this procedure until the required dose is reached and administer over 1 hour.	Dose per IV infusion instructions
Special instructions	Gently mix sotrovimab and saline prior to IV infusion.	None
Packaging and Labelling	Study intervention is provided in a single-use vial in an individual carton and labelled as required per country requirement.	Labelled as required per country requirement

[0706] Dose selection is guided by live virus neutralization data, resistance data, human PK projections informed by non-human primate PK and the no observed adverse effect level (NOAEL) in a cynomolgus monkey.

[0707] Further study details are shown in FIGS. 1-2D.

Example 40

Sotrovimab Monotherapy Reduces Hospitalization and Risk of Death in Early Treatment of Adults with COVID-19

[0708] In the Phase 3 portion of the clinical trial described in Example 39, safety and efficacy of a single intravenous infusion of sotrovimab (500 mg) or placebo was assessed in 583 non-hospitalized participants globally (291 patients in the treatment arm and 292 patients in the placebo arm). The primary efficacy endpoint is the proportion of patients who

have progression of COVID-19 as defined by the need for hospitalization for at least 24 hours or death within 29 days of randomization. Among those studied, 63% were Hispanic or Latinx and 7% were Black or African-American. According to the Centers for Disease Control and Prevention, these populations are approximately three times more likely to be hospitalized and approximately two times more likely to die of COVID-19 (Data source: COVID-NET (www.cdc.gov/coronavirus/2019-ncov/covid-data/covid-net/purpose-methods.html, accessed Mar. 1, 2020, through Jan. 30, 2021); Numbers are ratios of age-adjusted rates standardized to the 2019 US standard COVID-NET catchment population; Data source: NCHS provisional death counts (data.cdc.gov/NCHS/Deaths-involving-coronavirus-disease-2019-COVID-19/ks3g-spdg, data through Jan. 30, 2021). Numbers are ratios of age-adjusted rates standardized to the 2019 US intercensal population estimate).

[0709] Interim analysis of data from the 583 patients enrolled in the trial demonstrated an 85% (p=0.002) reduction in hospitalization or death in patients sotrovimab as monotherapy compared to placebo, the primary endpoint of the trial. Sotrovimab was well tolerated. The trial remains ongoing and blinded with patients continuing to be followed for 24 weeks; additional results, including epidemiology and virology data, are collected.

[0710] This study and results are described in further detail:

[0711] Methods: In a multicenter, double-blind, phase 3 trial, nonhospitalized patients with symptomatic Covid-19 and at least one risk factor for disease progression were randomized (1:1) to an intravenous infusion of sotrovimab 500 mg or placebo. The primary efficacy endpoint was the proportion of patients with Covid-19 progression, defined as hospitalization longer than 24 hours or death, through day 29.

[0712] Results: In this preplanned interim analysis, which included an intent-to-treat population of 583 patients (sotrovimab, 291; placebo, 292), the primary efficacy endpoint was met. The risk of Covid-19 progression was significantly reduced by 85% (97.24% confidence interval, 44% to 96%; P=0.002) with a total of three (1%) patients progressing to the primary end-

point in the sotrovimab group versus 21 (7%) patients in the placebo group. All five patients admitted to intensive care, including one who died by day 29, received placebo. Safety was assessed in 868 patients (sotrovimab, 430; placebo, 438). Adverse events were reported by 17% and 19% of patients receiving sotrovimab and placebo, respectively; serious adverse events were less common with sotrovimab (2%) versus placebo (6%).

In the intention-to-treat analysis (N=1057, full dataset), the adjusted relative risk reduction of hospitalization (all causes) was 79% (95% CI, 9% to

50%; p<0.001) through Day 29 in recipients of sotrovimab (n=523) vs. placebo (n=526). Treatment with sotrovimab (ITT) resulted in a numerical reduction in the need for ER visits for illness management, hospitalisation for acute illness management (any duration) or death (any cause) compared to placebo. No participants on sotrovimab required ICU admission, compared to 9 participants on placebo, of whom 4 participants required mechanical ventilation. No participants who received sotrovimab died, compared to 4 participants on placebo. The incidence of adverse events was similar between treatment arms and SAEs were numerically more common in the placebo arm.

Conclusion: Sotrovimab reduced progression of Covid-19 in patients with mild/moderate disease, was well tolerated, and no safety signals were identified.

Methods

Trial Objectives and Oversight

[0713] This phase 3, randomized, double-blind, multi-center, placebo-controlled study evaluates a single intravenous infusion of sotrovimab 500 mg for the prevention of progression of mild/moderate Covid-19 in high-risk, non-hospitalized patients. For this preplanned interim analysis, patients were recruited beginning on Aug. 27, 2020 and followed through Mar. 4, 2021 at 37 study sites in four countries (United States, Canada, Brazil, and Spain). Any changes made to the protocol and statistical analysis plan after the trial started are summarized in the Supplementary Appendix of this Example.

[0714] This study is conducted in accordance with the principles of the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, applicable International Council for Harmonisation Good Clinical Practice guidelines, and applicable laws and regulations. All patients provided written informed consent.

Patients and Procedures

[0715] Adult patients 18 years of age or older with a positive reverse-transcriptase-polymerase-chain-reaction or antigen SARS-CoV-2 test result and onset of symptoms within the prior 5 days were screened for eligibility; screening was performed within 24 hours before study drug administration. Patients were required to be at high risk for Covid-19 progression, defined as older adults (age ≥ 55 years) or adults with at least one of the following risk factors: diabetes requiring medication, obesity (body-mass index $>30 \text{ kg/m}^2$), chronic kidney disease (estimated glomerular filtration rate $<60 \text{ mL/min/1.73 m}^2$),²³ congestive

heart failure (New York Heart Association class II or higher), chronic obstructive pulmonary disease, and moderate to severe asthma.²⁴

[0716] Patients with already severe Covid-19, defined by shortness of breath at rest, respiratory distress, or requiring supplemental oxygen, were excluded. Inclusion criteria are described in the Supplementary Appendix of this Example.

[0717] Eligible patients were randomized 1:1 using an interactive web response system to receive either a single 500-mg, 1-hour infusion of sotrovimab or equal volume saline placebo on day 1 (FIG. 69).

Efficacy Assessments

[0718] The primary endpoint was the proportion of patients with hospitalization for more than 24 hours or death, due to any cause, through day 29. Secondary efficacy endpoints included the proportion of patients with an emergency room visit, hospitalization, or death; mortality; patient-reported outcomes; changes in viral load; and the proportion of patients who progressed to require supplemental oxygen.

Safety Assessments

[0719] Safety endpoints included adverse events, serious adverse events, and adverse events of special interest, defined as infusion-related reactions (including hypersensitivity reactions), immunogenicity testing for anti-drug antibodies, and evaluation of antibody-dependent enhancement. All hospitalizations, including those due to Covid-19, were counted as serious adverse events.

Statistical Analyses

[0720] A preplanned interim analysis for safety, futility, and profound efficacy was triggered when approximately 41% of the required number of study patients reached day 29. Sample size calculations were based on a group sequential design with two interim analyses to assess both futility due to lack of efficacy or profound efficacy. A Lan-DeMets alpha spending function to control type I error was used, employing a Pocock analog rule for futility and a Hwang-Shih-DeCanis (with parameter $\gamma=1$) analog for efficacy.²⁵ The overall sample size of 1360 would have provided approximately 90% power to detect a 37.5% relative efficacy in reducing progression of Covid-19 through day 29 at the overall two-sided 5% significance level, with an assumed progression rate of 16% in the placebo group.

[0721] The interim analysis intent-to-treat (ITT) population included all randomized patients through the prespecified interim analysis cutoff date of Jan. 19, 2021, irrespective of whether they received study drug. The interim analysis safety analysis population included all patients who received study medication and were randomized through Feb. 17, 2021; patients were grouped according to the actual treatment received. The primary endpoint was analyzed in the ITT population using a Poisson regression model with robust sandwich estimators adjusting for treatment, duration of symptoms, age, and gender. Missing progression status was imputed under a missing at random assumption, using multiple imputation. Based on this analysis model, the statistical significance testing, the relative risk of progression, and its appropriate confidence interval (CI) are provided using the adjusted significance level for this interim analysis.

[0722] As a result of the observed efficacy, an independent data monitoring committee recommended that enrollment in the study be stopped on Mar. 10, 2021, at which time 1057 patients had been randomized. Analyses of all secondary and exploratory endpoints is conducted when all patients have completed day 29.

Results

Patients

[0723] Of 795 patients screened, 583 were randomized through Jan. 19, 2021 to sotrovimab (291 patients) or placebo (292 patients); these patients comprise the interim analysis ITT population (Scheme 1, in the Supplementary Appendix of this Example). In this ITT population, similar disposition was observed across treatment groups. Overall, four patients each in the sotrovimab and placebo groups withdrew from the study. Three patients in the sotrovimab group withdrew prior to dosing, with a fourth patient withdrawing consent on day 5 for personal reasons. One patient in the placebo group withdrew consent prior to dosing, and three patients withdrew after dosing for personal reasons (days 16, 25, and 85). The median duration of follow-up in the ITT population was 72 days (range, 5 to 190) for the sotrovimab group and 72 days (range, 16 to 190) for the placebo group.

[0724] Overall, 868 patients (sotrovimab, 430 patients; placebo, 438 patients) were randomized and received study drug through Feb. 17, 2021; these patients comprise the interim analysis safety analysis population. The median duration of follow-up in this population was 56 days (range, 5 to 190) for the sotrovimab group and 55 days (range, 2 to 190) for the placebo group.

[0725] Treatment groups in the ITT population were well balanced for baseline demographic and disease characteristics (Table 8). Overall, 22% of patients were greater than 65 years of age, 7% were Black or African American, 63% were Hispanic or Latino, and 42% had two or more conditions considered to be risk factors for Covid-19 progression. The most common risk factors were obesity, age 55 years or older, and diabetes requiring medication. The most common presenting symptoms (>60% of all patients) were cough, muscle aches/myalgia, headache, and fatigue (Table 11, in the Supplementary Appendix of this Example). Baseline demographic and disease characteristics in the safety analysis population were similar across treatment groups and are reported in Table 12, in the Supplementary Appendix of this Example.

Efficacy Outcomes

[0726] Treatment with sotrovimab resulted in an 85% reduction in the need for hospitalization over 24 hours or death, due to any cause, compared with placebo (relative risk, 0.15 [97.24% CI, 0.04 to 0.56]). Three (1%) patients progressed to the primary endpoint in the sotrovimab group versus 21 (7%) patients in the placebo group ($P=0.002$) (Table 9). The primary reasons for the 24 hospitalizations of more than 24 hours were consistent with progressive Covid-19 (Table 13, in the Supplementary Appendix of this Example), with one likely exception: a patient in the sotrovimab group, with a notable past medical history of small intestinal obstruction, presented 22 days after infusion with a small intestinal obstruction. Regarding the severity of

these hospitalizations, all five patients who required admission to intensive care were in the placebo group; two of these five patients required invasive mechanical ventilation and a third declined intubation and subsequently died by day 29. Emergency room visits or hospitalizations for less than 24 hours were observed in fewer patients in the sotrovimab group compared with the placebo group (Table 9).

Safety

[0727] The proportion of patients in the safety analysis population who reported an adverse event was 17% (73 of 430 patients) in the sotrovimab group and 19% (85 of 438 patients) in the placebo group (Table 10). A lower proportion of patients reported grade 3 or 4 adverse events in the sotrovimab group (2%) compared with the placebo group (6%). Overall, the only adverse event occurring in at least 1% of patients receiving sotrovimab was diarrhea, which occurred infrequently—six (1%) patients in the sotrovimab group versus three (<1%) patients in the placebo group. Among patients in the sotrovimab group, all cases of diarrhea were mild (five patients) or moderate (one patient) in severity.

[0728] Infusion-related reactions were observed in a similar proportion of patients receiving sotrovimab (1%) compared with placebo (1%). One patient receiving sotrovimab had an infusion-related reaction that was considered related to study treatment: moderate (grade 2) dyspnea.

[0729] Serious adverse events occurred in 2% of patients receiving sotrovimab and 6% of patients receiving placebo. Most of these events were hospitalizations due to Covid-19-related causes. No serious adverse events were considered related to sotrovimab.

[0730] One patient in the placebo group died after day 29; this patient died due to Covid-19 pneumonia on day 37.

[0731] No trends were observed in hematologic, liver, or chemistry laboratory data. Overall, laboratory results were similar in the sotrovimab and placebo groups.

DISCUSSION

[0732] In this preplanned interim analysis of the COMET-ICE study, a single 500-mg dose of sotrovimab reduced the risk of hospitalization (>24 hours) or death in high-risk adults with symptomatic Covid-19 by 85% compared with placebo ($P=0.002$). For every 17 high-risk patients with symptomatic Covid-19, sotrovimab prevented one hospitalization. Among those who were hospitalized, no patient who received sotrovimab required admission to intensive care compared with five patients who received placebo, suggesting that sotrovimab may also prevent more severe complications of Covid-19 in addition to preventing the need for hospitalization itself. The full analysis provided similar results. Furthermore, as a result of investigator site selection, over 60% of the study population consisted of patients self-identifying as Hispanic or Latino; thus, this trial is one of the first to demonstrate efficacy in a population that has been largely underrepresented in Covid-19 clinical trials, despite the disproportionately negative impact the pandemic has had in this ethnic group. Overall, sotrovimab was well tolerated, and no safety signals were identified in this study. There was also no evidence of antibody-dependent enhancement with sotrovimab, which could have manifested as worsening of disease compared with placebo.²⁶

[0733] Treatments for Covid-19 will need to retain activity in the face of an evolving virus. To that end, sotrovimab may have an intrinsically high barrier to resistance as a result of targeting a pan-sarbecovirus epitope.¹⁴ In one analysis, among more than 584,000 sequences in the Global Influenza Surveillance and Response System database (Global Initiative on Sharing All Influenza Data), amino acid positions comprising the sotrovimab epitope were at least 99.96% conserved in naturally occurring viruses.¹⁴ Moreover, when necessary to further enhance breadth and barrier to resistance, sotrovimab can likely be combined with currently authorized receptor-binding motif-targeted antibodies due to its nonoverlapping resistance profile.

[0734] These results also indicate that a non-receptor-binding motif binding antibody, which does not directly block the ACE2 receptor interaction, can be clinically therapeutic, and suggests a role for other receptors.²⁷ Moreover, as sotrovimab has potent effector function, the absence of safety signals and observed efficacy strongly suggest that effector function is neither detrimental nor associated with antibody-dependent enhancement.²⁶ In fact, preclinical models of Covid-19 suggest that its potent effector function may be beneficial.^{13,14}

[0735] Results from this interim analysis (as well as from the full intent-to-treat analysis) of the COMET-ICE trial support that sotrovimab can be an important therapeutic for the outpatient treatment of Covid-19. Notably, a 500-mg dose may be administered intramuscularly, increasing the convenience of and access to antibody therapeutics for patients with Covid-19. Studies are currently underway to evaluate this route of administration.

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TABLE 8

	Baseline Demographic and Disease Characteristics (ITT Population)		
	Sotrovimab (N = 291)	Placebo (N = 292)	Total (N = 583)
Characteristic			
Age - yr, median (range)	53.0 (18-96)	52.5 (18-88)	53.0 (18-96)
≥65 yr - no. (%)	63 (22)	65 (22)	128 (22)
>70 yr - no. (%)	33 (11)	32 (11)	65 (11)
Male gender - no. (%)	135 (46)	131 (45)	266 (46)
Race* - no. (%)			
White	254 (88)	252 (87)	506 (87)
Black or African American	16 (6)	22 (8)	38 (7)
Asian	17 (6)	17 (6)	34 (6)
Mixed race	2 (<1)	0	2 (<1)
American Indian or Alaska Native	1 (<1)	0	1 (<1)
Hispanic or Latino ethnic group - no. (%)	190 (65)	178 (61)	368 (63)
Body-mass index† - mean (SD)	32.0 (6.4)	32.1 (6.3)	32.1 (6.3)
Duration of symptoms‡ - no. (%)			
≤3 days	167 (57)	171 (59)	338 (58)
4-5 days	123 (42)	121 (41)	244 (42)
Any risk factor for Covid-19 progression - no. (%)	291 (100)	290 (>99)	581 (>99)
Age ≥55 yr	135 (46)	141 (48)	276 (47)
Diabetes requiring medication	66 (23)	66 (23)	132 (23)
Obesity (body-mass index >30†)	182 (63)	187 (64)	369 (63)
Chronic kidney disease (eGFR <60 by MDRD)	1 (<1)	4 (1)	5 (<1)
Congestive heart failure (NYHA class II or more)	1 (<1)	3 (1)	4 (<1)
Chronic obstructive pulmonary disease	14 (5)	10 (3)	24 (4)
Moderate to severe asthma	46 (16)	46 (16)	92 (16)
Number of concurrent risk factors for Covid-19 progression - no. (%)			
0	0	2 (<1)	2 (<1)
1	170 (58)	168 (58)	338 (58)
2	91 (31)	86 (29)	177 (30)
≥3	30 (10)	36 (12)	66 (11)

ITT denotes intent-to-treat, SD standard deviation, eGFR estimated glomerular filtration rate, MDRD Modification of Diet in Renal Disease, NYHA New York Heart Association.

*Race data were not available for one patient in the sotrovimab group and one patient in the placebo group.

†Body-mass index is the weight in kilograms divided by the square of the height in meters.

‡One patient in the sotrovimab group had a symptom duration of 6 days.

TABLE 9

Summary of Efficacy Outcomes Through Day 29 (ITT Population)		
	Sotrovimab (N = 291)	Placebo (N = 292)
Primary outcome		
Hospitalized >24 hours or death for any cause - no. (%)	3 (1)	21 (7)
Hospitalized >24 hours for any cause	3 (1)	21 (7)
Death by any cause	0	1 (<1)
Alive and not hospitalized - no. (%)	284 (98)	270 (92)
Missing - no. (%)	4 (1)	1 (<1)
Withdrew consent prior to dosing - no. (%)	3 (1)	1 (<1)
Percent reduction (97.24% CI), P value	85% (44% to 96%); P = 0.002	
Other clinical outcomes*		
Emergency room visit, hospitalization, or death for any cause - no. (%)	6 (2)	28 (10)
Emergency room visit for any cause	2 (<1)	8 (3)
Hospitalized for any cause	4 (1)†	21 (7)
Death by any cause	0	1 (<1)
Emergency room visit without hospitalization or hospitalized for <24 hours for any cause - no. (%)	3 (1)	7 (2)
Severe or critical progression‡ - no. (%)	2 (<1)	19 (7)
Low-flow nasal cannula or face mask	2 (<1)	11 (4)
Non-rebreather mask, high-flow nasal cannula, or noninvasive ventilation	0	5 (2)
Invasive mechanical ventilation	0	2 (<1)
Death by any cause	0	1 (<1)
Admission to intensive care for any cause - no. (%)	0	5 (2)

ITT denotes intent-to-treat; CI, confidence interval.

*Inferential testing of secondary endpoints has not been performed at this interim analysis.

†One patient was hospitalized for less than 24 hours for diabetes management.

‡Severe or critical progression as manifested by supplemental oxygen use.

TABLE 10

Summary of Adverse Events (Safety Analysis Population)		
	Sotrovimab (N = 430)	Placebo (N = 438)
Any adverse event - no. (%)	73 (17)	85 (19)
Related to study treatment*	8 (2)	8 (2)
Leading to permanent discontinuation of study treatment†	0	0
Leading to dose interruption/delay	2 (<1)*	0
Occurring in ≥1% of patients receiving sotrovimab by preferred term		
Diarrhea	6 (1)	3 (<1)
Any infusion-related reaction§ - no. (%)	6 (1)	5 (1)
Related to study treatment*	1 (<1)	2 (<1)
Leading to permanent discontinuation of study treatment†	0	0
Leading to dose interruption/delay	0	0
Any grade 3 or 4 adverse event - no. (%)	7 (2)	27 (6)
Any serious adverse event - no. (%)	7 (2)	26 (6)
Related to study treatment*	0	1 (<1)
Fatal	0	2 (<1)¶
Related to study treatment*	0	0

*Relatedness was determined by individual study investigators while blinded to study treatment.

†A patient was permanently discontinued from the completion of drug infusion if they experienced life-threatening infusion-related reactions, including severe allergic or hypersensitivity reactions during the intravenous infusion.

‡For both patients, the adverse event was infusion extravasation; both infusions were completed.

§Infusion-related reactions were defined as adverse events with preferred terms of pyrexia, chills, dizziness, dyspnea, pruritus, rash, and infusion-related reaction within 24 hours of study drug administration.

¶In addition to the patient in the placebo group who died by day 29, another patient in the placebo group died due to Covid-19 pneumonia on day 37; this patient was admitted to the hospital prior to day 29 and was thus considered to have met the primary endpoint definition of Covid-19 progression.

SUPPLEMENTARY APPENDIX

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- [0763] Supplementary methods
- [0764] Changes to protocol/SAP
- [0765] Table 11. Presenting symptoms (ITT population)
- [0766] Table 12. Baseline demographic and disease characteristics (safety analysis population)
- [0767] Table 13. Primary reasons for hospitalizations of more than 24 hours (ITT population)
- [0768] Scheme 1. Patient disposition (ITT population)

Supplementary Methods

Inclusion Criteria

- [0769] Patients are eligible to be included in the study only if all of the following criteria apply:

Age and Risk Factors

- [0770] 6. Patient must be 18 years of age or older AND at high risk of progression of Covid-19 based on presence of one or more of the following risk factors:
 - [0771] 1. Diabetes (requiring medication)
 - [0772] 2. Obesity (body-mass index >35 kg/m²)
- [0773] 1. Change: body-mass index threshold was >30 kg/m² in the original protocol. See “Changes to Protocol/SAP” section for more information

[0774] 3. Chronic kidney disease (i.e., estimated glomerular filtration rate <60 mL/min/1.73 m² according to the Modification of Diet in Renal Disease study equation)

[0775] 4. Congestive heart failure (New York Heart Association class II or more)

[0776] 5. Chronic obstructive pulmonary disease (history of chronic bronchitis, chronic obstructive lung disease, or emphysema with dyspnea on physical exertion) and moderate to severe asthma (patient requires an inhaled steroid to control symptoms or has been prescribed a course of oral steroids in the past year)

or

7. Patient 55 years of age or older, irrespective of comorbidities

Note: target enrollment of ~15% of patients over 70 years of age

Change: target enrollment criterion was not in the original protocol. See "Changes to Protocol/SAP" section for more information

Type of Patient and Disease Characteristics

[0777] 8. Patients who have a positive SARS-CoV-2 test result (by any validated diagnostic test [e.g. RT-PCR, antigen-based testing on any specimen type])

[0778] and

[0779] 9. Oxygen saturation ≥94% on room air

[0780] and

[0781] 10. Have Covid-19 defined by one or more of the following symptoms: fever, chills, cough, sore throat, malaise, headache, joint or muscle pain, change in smell or taste, vomiting, diarrhea, shortness of breath on exertion

[0782] and

[0783] 11. Less than or equal to 5 days from onset of symptoms

Sex and Contraceptive/Barrier Requirements

[0784] 12. No gender restrictions

[0785] 13. Female patients must meet and agree to abide by the following contraceptive criteria:

[0786] 1. Contraception use by women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies

[0787] 2. A female patient is eligible to participate if she is not pregnant or breastfeeding and one of the following conditions applies:

[0788] 14. Is a woman of nonchildbearing potential

[0789] 15. Is a woman of childbearing potential and is using a contraceptive method that is highly effective, with a failure rate of <1%, during the study intervention period and for up to 24 weeks after the last dose of study intervention. The investigator should evaluate potential for contraceptive method failure (e.g., non-compliance, recently initiated) in relationship to the first dose of study intervention

[0790] 16. A woman of childbearing potential must have a negative highly sensitive pregnancy test (urine or serum as required by local regulations) before the first dose of study intervention. If a urine test cannot be confirmed as negative (e.g., an ambiguous result), a

serum pregnancy test is required. In such cases, the patient must be excluded from participation if the serum pregnancy result is positive

[0791] 17. The investigator is responsible for the review of medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy

Informed Consent

[0792] 18. Capable of giving signed informed consent, which includes compliance with the requirements and restrictions listed in the informed consent form and in this protocol

[0793] or

[0794] 19. If patients are not capable of giving written informed consent, alternative consent procedures will be followed

Prior/Concurrent Clinical Study Experience

[0795] 20. Enrollment in any investigational vaccine study within the last 180 days or any other investigational drug study within 30 days prior to day 1 or within five half-lives of the investigational compound, whichever is longer

[0796] 21. Enrollment in any trial of an investigational vaccine for SARS-CoV-2

Procedures

[0797] In-person study visits occurred on days 5, 8, 11, 15, 22, and 29, as well as daily telephone calls through day 15 (except on in-person visit days) to assess for adverse events and worsening of Covid-19. Starting at week 8, patients were monitored monthly via alternating telephone calls (weeks 8 and 16) and in-person visits (weeks 12, 20, and 24) for Covid-19 illness for a total of 24 weeks from dosing. Blood samples were collected for laboratory assessments at days 1, 15, 22, and 29 and for anti-drug antibodies on days 1 and 29. Patient-reported outcome assessments are administered through week 24.

Changes to Protocol/SAP

[0798] 22. Local safety laboratory assessments at screening were modified to specify that only ABO typing was required per protocol

[0799] 23. Rationale:

[0800] 24. While certain screening assessments to confirm study patient eligibility must be performed or documented locally (e.g., pregnancy test for women of childbearing potential and SARS-CoV-2 infection via a validated diagnostic test), ABO typing is the only required local laboratory assessment at screening for safety purposes

[0801] 25. All other local safety laboratory assessments during the screening visit (hematology, clinical chemistry, and coagulation parameters) may or may not be performed according to the clinical discretion of the study investigator or as required by local regulations

[0802] 26 Considering the time to randomization and requirement for central laboratory testing on day 1 (randomization), the amount of sample collection was overly cumbersome for sites

[0803] 27 Study objectives and endpoints (secondary and exploratory endpoints) were modified, including

the introduction of an additional secondary endpoint (i.e., evaluation of the proportion of patients who have progression of Covid-19 through day 29 as defined by a visit to a hospital emergency room for management of illness, hospitalization for acute management of illness, or death), amendment to existing patient-reported outcome and virology endpoints, and introduction of additional exploratory endpoints

[0804] 1. Rationale:

[0805] 2. Preliminary clinical trial data generated for other monoclonal antibodies targeting Covid-19 suggest that the rate of progression of Covid-19 leading to the requirement for hospitalization may be lower than originally estimated and the efficacy of anti-spoke protein monoclonal antibodies in the treatment of Covid-19 in the outpatient population is greater than a 50% decrease in the proportion of medically attended visits through day 29

[0806] 3. In light of new data from recent clinical trials of anti-SARS-CoV-2 mAbs, the secondary and exploratory endpoints were modified to reflect the clinical outcomes that are most relevant in the outpatient populations who receive Covid-19 monoclonal antibodies

[0807] 28 Modified the “Age and Risk Factors” eligibility criteria (inclusion criteria #3 and #4) to enrich high-risk populations with the highest unmet medical need

[0808] 1. Rationale:

[0809] 2. The “Age and Risk Factors” eligibility criteria has been modified to increase the body-mass index requirement defining obesity and introduce a targeted minimum number of patients (approximately 15%) >70 years of age

[0810] 3. In light of emerging clinical data on the progression of Covid-19 in the outpatient setting, eligibility criteria were amended to enrich for populations at high risk for progression to severe Covid-19

[0811] 4. Modified the “Medical Conditions” eligibility criteria (exclusion criteria #10) to enrich high-risk populations with the highest unmet medical need

[0812] 5. Rationale:

[0813] 6. The “Medical Conditions” eligibility criteria have been modified to clarify the definition of “severely immunocompromised”

[0814] 7. In light of emerging clinical data on the progression of Covid-19 in the outpatient setting, eligibility criteria were modified to enrich for immunosuppressed populations at high risk for progression to severe Covid-19

[0815] 29 Modified the “Other Exclusions” eligibility criteria and “Medication Not Permitted During the Study” to clarify restrictions around dosing with a SARS-CoV-2 vaccine

[0816] 1. Rationale:

[0817] 1. Considering the recent data published on SARS-CoV-2 vaccines, the protocol was amended to clarify restrictions surrounding administration of an experimental or approved SARS-CoV-2 vaccine

[0818] 2. Clarified guidance for infusion-related reactions

[0819] 1. Rationale:

[0820] 1. Protocol language was amended to clarify that sites should follow local or institutional guidelines for the treatment of infusion-related reactions

[0821] 2. Statistical analysis plan (interim analysis #1, interim analysis #2, and statistical approach) were modified

[0822] 1. Rationale:

[0823] 1. Preliminary clinical trial data generated for other monoclonal antibodies targeting Covid-19 suggest that the rate of progression of Covid-19 to requirement for hospitalization may be lower than originally estimated and the efficacy of antispike protein monoclonal antibodies in the treatment of Covid-19 in the outpatient population is greater than a 50% decrease in the proportion of medically attended visits through day 29

[0824] 2. In light of this emerging data, the interim analyses were modified to more accurately reflect the most recent data on progression of Covid-19 and the potential efficacy of monoclonal antibodies against SARS-CoV-2

[0825] 3. Specified an intention to conduct a “non-Covid-19” safety analysis

[0826] 1. Rationale:

[0827] 1. Since it is not be possible to delineate in a single patient whether the hospitalization is directly related to Covid-19 complications or could be related to sotrovimab causing more severe disease due to antibody-dependent enhancement, all hospitalizations regardless of cause are included in the primary endpoint and are counted as serious adverse events

[0828] 2. To inform on the number and nature of non-Covid-19 adverse events and serious adverse events, additional safety analyses are performed in which select, prespecified terms consistent with known progression of Covid-19 disease are excluded.

TABLE 11

Presenting Symptoms (ITT Population)			
Symptom - no. (%)	Sotrovimab (N = 291)	Placebo (N = 292)	Total (N = 538)
Cough	240 (82)	247 (85)	487 (84)
Muscle aches/myalgia	215 (74)	215 (74)	430 (74)
Headache	202 (69)	216 (74)	418 (72)
Fatigue	180 (62)	183 (63)	363 (62)
Malaise	172 (59)	172 (59)	344 (59)
Sore throat	171 (59)	172 (59)	343 (59)
Fever	164 (56)	168 (58)	332 (57)
Loss of taste	171 (59)	159 (54)	330 (57)
Loss of smell	175 (60)	152 (52)	327 (56)
Chills	164 (56)	158 (54)	322 (55)
Joint pain/arthritis	153 (53)	153 (52)	306 (52)
Shortness of breath	131 (45)	131 (45)	262 (45)
Diarrhea	87 (30)	101 (35)	188 (32)
Nausea	85 (29)	91 (31)	176 (30)
Vomiting	34 (12)	37 (13)	71 (12)

ITT denotes intent-to-treat.

TABLE 12

Baseline Demographic and Disease Characteristics (Safety Analysis Population)			
	Sotrovimab (N = 430)	Placebo (N = 438)	Total (N = 868)
<u>Characteristic</u>			
Age - yr, median (range)	53.0 (18-96)	52.0 (17-88)	53.0 (17-96)
≥65 yr - no. (%)	84 (20)	88 (20)	172 (20)
>70 yr - no. (%)	42 (10)	42 (10)	84 (10)
Male gender - no. (%)	194 (45)	212 (48)	406 (47)
Race* - no. (%)			
White	374 (87)	384 (88)	758 (88)
Black or African American	27 (6)	33 (8)	60 (7)
Asian	21 (5)	19 (4)	40 (5)
Mixed race	6 (1)	0	6 (<1)
American Indian or Alaska Native	1 (<1)	1 (<1)	2 (<1)
Hispanic or Latino ethnic group - no. (%)	280 (65)	280 (64)	560 (65)
Body-mass index† - mean (SD)	32.1 (6.4)	32.5 (6.7)	32.3 (6.5)
Duration of symptoms‡ - no. (%)			
≤3 days	254 (59)	260 (59)	514 (59)
4-5 days	173 (40)	178 (41)	351 (40)
Any risk factor for Covid-19 progression - no. (%)	427 (>99)	434 (>99)	861 (>99)
Age ≥55 yr	195 (45)	205 (47)	400 (46)
Diabetes requiring medication	93 (22)	88 (20)	181 (21)
Obesity (body-mass index >30†)	267 (62)	292 (67)	559 (64)
Chronic kidney disease (eGFR <60 by MDRD)	2 (<1)	5 (1)	7 (<1)
Congestive heart failure (NYHA class II or more)	4 (<1)	3 (<1)	7 (<1)
Chronic obstructive pulmonary disease	24 (6)	18 (4)	42 (5)
Moderate to severe asthma	69 (16)	72 (16)	141 (16)
Number of concurrent risk factors for Covid-19 progression - no. (%)			
0	3 (<1)	4 (<1)	7 (<1)
1	251 (58)	250 (57)	501 (58)
2	132 (31)	130 (30)	262 (30)
≥3	44 (10)	54 (13)	98 (11)

SD denotes standard deviation, eGFR estimated glomerular filtration rate, MDRD Modification of Diet in Renal Disease, NYHA New York Heart Association.

*Race data were not available for one patient in the sotrovimab group and one patient in the placebo group.

†Body-mass index is the weight in kilograms divided by the square of the height in meters.

‡One patient in the sotrovimab group had a symptom duration of 6 days. For two other patients in the sotrovimab group, symptom duration data were not available at the time of this interim analysis.

TABLE 13

Primary Reasons for Hospitalizations of More Than 24 Hours (ITT Population)						
Patient	Age (yr)	Sex	Hospitalization day	Primary reason	Intensive care unit admission	Invasive mechanical ventilation
<u>Sotrovimab-treated patients</u>						
A	96	M	19	Covid-19	N	N
B	65	F	22	Small intestinal obstruction	N	N
C	71	F	2	Covid-pneumonia	N	N
<u>Placebo-treated patients</u>						
D	52	F	4	Covid-pneumonia	N	N
E	50	F	4*	Covid-pneumonia	N	N
F	66	F	6	Covid-pneumonia	N	N

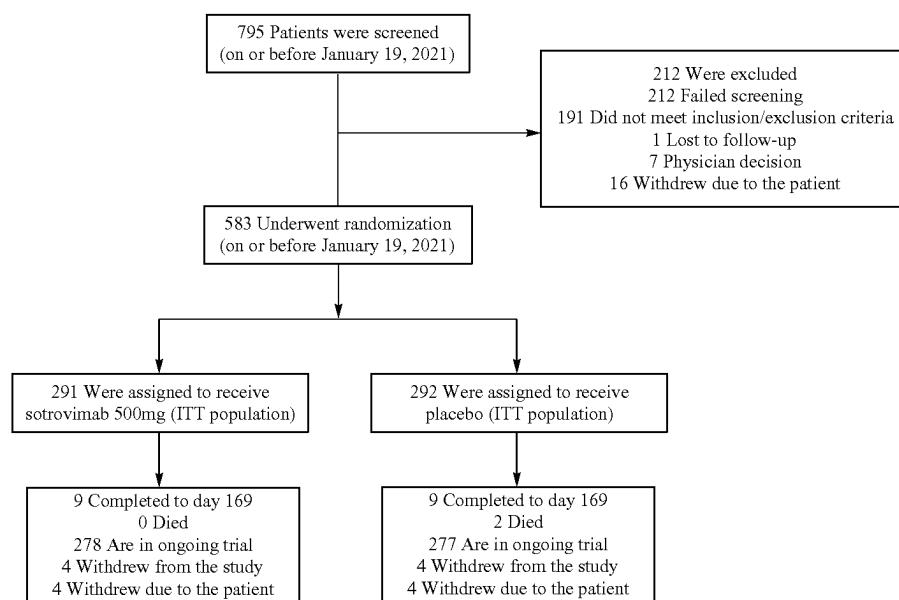
TABLE 13-continued

Primary Reasons for Hospitalizations of More Than 24 Hours (ITT Population)							
Patient	Age (yr)	Sex	Hospitalization day	Primary reason	Intensive care unit admission	Invasive mechanical ventilation	Fatal
G	38	M	9*	Covid-pneumonia	N	N	N
H	50	F	4*	Covid-pneumonia	Y	N	N
I	82	F	7	Acute respiratory failure	N	N	N
J	70	M	12	Respiratory distress	Y	Y	N
K	70	M	5	Pneumonia	Y	N	Y
L	65	M	6	Dehydration	N	N	N
M	52	F	5	Covid-pneumonia	N	N	N
N	62	M	7	Covid-pneumonia	N	N	N
O	57	M	6	Pneumonia	N	N	N
P	65	M	12	Pneumonia	N	N	N
Q	68	M	7	Covid-pneumonia	N	N	N
R	55	F	7	Pulmonary embolism	N	N	N
S	60	M	10	Covid-pneumonia	N	N	N
T	71	F	10	Covid-pneumonia	Y	Y	Y
U	37	F	6*	Covid-pneumonia	N	N	N
V	83	M	8	Dyspnea	N	N	N
W	56	M	2	Covid-pneumonia	Y	N	N
X	55	M	7	Covid-pneumonia	N	N	N

ITT denotes intent-to-treat, M male, F female, N no, Y yes.

*The adverse event associated with the hospitalization started the day before the patient was admitted to the hospital.

Scheme 1. Patient disposition (ITT population).



ITT denotes intent-to-treat.

Example 41

Phase 2/3 Clinical Study of Sotrovimab for
Treatment of Hospitalized Subjects with Severe to
Critical COVID-19 Disease

[0829] A randomized, multi-center, double-blind, placebo-controlled study is performed to assess safety and efficacy of monoclonal antibody sotrovimab in patients with severe or critical COVID-19 disease.

[0830] A primary objective is to compare efficacy of sotrovimab versus placebo. Secondary objectives are to compare efficacy of sotrovimab versus placebo on viral shedding in upper and lower respiratory samples, to compare safety and tolerability of sotrovimab versus placebo, to determine efficacy of sotrovimab versus placebo for induction of an anti-viral response, to determine efficacy of sotrovimab versus placebo for increasing ICU- and hospital-free days, and to determine serum pharmacokinetics (PK) of sotrovimab.

[0831] Exploratory objectives are to compare efficacy of sotrovimab against versus placebo in preventing non-respiratory complications of COVID-19 disease, to compare effect of sotrovimab versus placebo on viral shedding in upper and lower respiratory samples and blood samples, to assess emergence of resistance to sotrovimab, to evaluate effect of sotrovimab on potential biomarkers of host response, and to assess correlations between efficacy, safety, PK, viral shedding, and immunogenicity.

Details of Criteria for Evaluation

[0832] Primary endpoints of this study are as follows:

[0833] 1. Proportion of subjects who progress to severe or critical COVID-19 or die through Day 29 as defined by:

[0834] 1. Severe disease: hypoxemia (O₂ saturation ≤93% on room air or PaO₂/FiO₂<300) requiring oxygen supplementation >1 day OR subject requires ≥4 L/min oxygen supplementation or equivalent AND the investigator or designee determine that the measurement of O₂ saturation on room air is medically unsafe

[0835] OR

[0836] 2. Critical disease: Respiratory failure requiring at least one of the following: invasive mechanical ventilation, ECMO; OR shock; OR multi-organ dysfunction/failure

[0837] OR

[0838] 3. Death

[0839] 2 Time to clinical response, defined as being alive and independent of oxygen supplementation through Day 29, as compared to standard of care (SOC).

[0840] Secondary endpoints of this study are as follows:

[0841] 3. Occurrence of adverse events (AEs)

[0842] 4. Occurrence of serious adverse events (SAEs)

[0843] 5. Occurrence of adverse events of special interest (AESI)

[0844] 6. Proportion of subjects who progress to develop severe or critical COVID-19 at Day 8, Day 15, or Day 22

[0845] 7. 29-day, 60-day, and 90-day all-cause mortality

[0846] 8. Total number of ventilator days from randomization through 29 days

[0847] 9. Total number of days requiring supplemental oxygen through 29 days

[0848] 10. Total intensive care length of stay (LOS)

[0849] 11 Total hospital LOS

[0850] 12. Severity and duration of subject reported signs and symptoms of COVID-19 related illness using the Flu-PRO patient-reported outcome measurement instrument

[0851] 13. Occurrence of cardiac, thromboembolic, renal, neurologic events

[0852] 14. Detection of SARS-CoV-2 in nasal secretions by PCR at baseline and during follow-up period through Day 29

[0853] 15. Time to no detectable viral RNA (<LLOQ) by quantitative RT-PCR from nasopharyngeal samples

[0854] 16. Sotrovimab pharmacokinetics (PK) in serum

[0855] 17. Incidence and titers (if applicable) of serum ADA to Sotrovimab

[0856] Exploratory endpoints of this study are as follows:

[0857] 30. Proportion of subjects at Day 8, Day 15, Day 22, and Day 29 in each category of the ordinal scale for clinical improvement (see below)

[0858] 31. Emergence of viral resistance mutants to mAb by SARS-CoV-2

[0859] 32. Viral load in nasal secretions and blood by qRT-PCR

[0860] 33. Host transcriptome and immunophenotyping analysis

[0861] 34. FcγR polymorphisms as determined by genotyping

[0862] 35. IgG1 allotypes as determined by genotyping

[0863] 36. Change from baseline in Work Productivity and Activity Impairment (WPAI)

[0864] 37. Change from baseline in health-related quality of life according to EQ-5D-5L

[0865] The ordinal scale to be used for categorization of clinical improvement is as follows:

[0866] 1. Uninfected: No clinical or virologic evidence of infection

[0867] 2. Non-hospitalized, no limitation of activity (if using oxygen at home, report as category 4)

[0868] 3. Non-hospitalized, limitation of activity

[0869] 4. Hospitalized, no oxygen therapy

[0870] 5. Hospitalized, low-flow oxygen by mask or nasal prongs

[0871] 6. Hospitalized, high-flow oxygen, Continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP), non-invasive ventilation

[0872] 7. Hospitalized, intubation and mechanical ventilation

[0873] 8 Hospitalized, mechanical ventilation plus organ support (vasopressors, RRT, ECMO)

[0874] 9 Death

Number of Subjects Planned

[0875] This study is comprised of two parts. Part 1 enrolls approximately 20 subjects with severe COVID-19 disease. Part 2 enrolls approximately 500 subjects with severe to critical COVID-19 disease; approximately 250 subjects per treatment arm.

Randomization and Stratification

[0876] Subjects are randomized in a 1:1 ratio to receive a single IV dose of sotrovimab plus standard of care (SoC) or equal volume saline placebo plus SoC.

[0877] For Part 1, the first 20 subjects enrolled in the study (ten per arm) are in the severe COVID-19 disease population (Grade 4 or 5). These subjects are stratified by time from onset of symptoms, either 1) less than seven days or 2) seven days or more. All subjects enrolled in Part 1 are assigned to intensive PK sampling. Serum PK samples are collected from these subjects.

[0878] For Part 2, the clinical status of the subjects are stratified by disease status (severe or critical) and time from onset of symptoms, as follows:

[0879] 1. Severe (Grade 4 or 5) and less than seven days since onset of symptoms

[0880] 2. Severe (Grade 4 or 5) and seven days or more since onset of symptoms

[0881] 3. Critical (Grade 6 or 7) and less than seven days since onset of symptoms

[0882] 4. Critical (Grade 6 or 7) and seven days or more since onset of symptoms. Sparse PK samples are collected from subjects enrolled in Part 2.

Diagnosis and Main Criteria for Inclusion

Inclusion Criteria Include:

Age:

[0883] 10. Subjects aged 18 years and older

Disease Characteristics:

[0884] 11. Subjects who have a positive SARS-CoV-2 test result (by any validated test e.g. RT-PCR on any specimen type)

[0885] AND

[0886] 12. Hospitalized with severe COVID-19 disease defined as requirement for supplemental oxygen or non-invasive ventilation consistent with Grade 4 or Grade 5 disease

[0887] OR

[0888] 13. Hospitalized with critical COVID-19 disease defined as those on mechanical ventilation (Grade 6 or Grade 7 disease)

[0889] AND

[0890] 14. Onset of COVID-19 symptoms within 14 days of Day 14

[0891] AND

[0892] 15. Randomized within 48 hours of admission to hospital

Sex:

[0893] 16. No gender restriction

[0894] 17. Female subjects must meet and agree to abide by the following contraceptive criteria. Contraception use by women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.

[0895] 18. A female subject is eligible to participate if she is not pregnant or breastfeeding, and one of the following conditions applies:

[0896] Is a woman of non-childbearing potential (WONCBP)

[0897] OR

[0898] Is a woman of child-bearing potential (WOCBP) and using a contraceptive method that is highly effective, with a failure rate of <1% during the study intervention period and for up to one year after the last dose of study intervention. The investigator should evaluate potential for contraceptive method failure (e.g., noncompliance, recently initiated) in relationship to the first dose of study intervention.

[0899] 19. A WOCBP must have a negative highly sensitive pregnancy test (urine or serum as required by local regulations) at hospital admission or before the first dose of study intervention. If a urine test cannot be confirmed as negative (e.g., an ambiguous result), a serum pregnancy test is required. In such cases, the subject is excluded from participation if the serum pregnancy result is positive.

Informed Consent:

[0900] 20. Willing to comply with the study requirements and capable of giving signed informed consent or legally acceptable representative is willing and able to give written informed consent on behalf of the subject to participate in the study for unconscious adults and those incapable of consenting themselves due to their medical condition.

Exclusion Criteria:

[0901] in the opinion of the responsible investigator, any condition for which participation would not be in the best interest of the participant, or that could limit protocol-specified assessments; expected inability to participate in study procedures; participants who, in the opinion of the investigator, are not likely to survive beyond 48 hours at the time of randomization; planned or anticipated discharge or transfer to another hospital within 72 hours at the time of randomization; history of hypersensitivity to other mAbs or any of the excipients present in the investigational product;

[0902] For the lead-in phase: participants with end organ failure or dysfunction are not eligible for Lead-in phase but are eligible for Expansion-Phase.

[0903] End-organ dysfunction categories are: a. stroke b. meningitis c. encephalitis d. myelitis e. myocardial infarction f. myocarditis g. pericarditis h. symptomatic congestive heart failure (New York Heart Association [NYHA] class III-IV) i. arterial or deep venous thrombosis or pulmonary embolism

[0904] End-organ failure categories are: a. requirement for high-flow oxygen, non-invasive ventilation, or invasive mechanical ventilation b. extracorporeal membrane oxygenation (ECMO) c. mechanical circulatory support (e.g., intra-aortic balloon pump, ventricular assist device) d. vasopressor therapy e. commencement of renal replacement therapy (RRT) during this admission (i.e. not patients on chronic RRT).

[0905] Prior receipt of

[0906] any SARS-CoV-2 hyperimmune intravenous immunoglobulin (hIVIG) from COVID-19 survivors

[0907] convalescent plasma from a person who recovered from COVID-19 or

[0908] SARS-CoV-2 neutralizing mAbs at any time.

[0909] Participating in other clinical trials involving an investigational study intervention, including for COVID-19

[0910] Pregnant or breast-feeding females

Duration of Study Participation and Follow Up

[0911] The duration of study drug treatment is a single dose. The estimated total time of study, inclusive of screening and follow-up, for each subject is approximately 36 weeks. Screening assessments are performed up to 48 hours before the first dose. After completion of screening assessments, eligible subjects are treated with a single IV dose of sotrovimab or placebo. Subjects are assessed daily up to the day of hospital discharge. Following discharge from hospital, assessments occur on Day 15 and Day 29 and follow up continues to Week 36 after randomization.

Study Design

[0912] An Independent Data Monitoring Committee (IDMC) actively monitors interim unblinded safety data (Part 1) and interim unblinded safety and efficacy data (Part 2) to make recommendations regarding ongoing study conduct. The IDMC members include 3-4 physicians with relevant medical specialist training and one statistician. A Joint Safety Review Team (JSRT) determines if a safety concern based on instream blinded data review needs to be escalated to the IDMC.

[0913] This study is a randomized, double-blind, multi-center, placebo-controlled trial of sotrovimab, a monoclonal antibody (mAb) against SARS-CoV-2, to assess efficacy and safety of a single IV dose of sotrovimab versus placebo on top of investigator-defined standard of care (SoC) as treatment in adult participants hospitalized with COVID-19 disease. The study population consists of hospitalized subjects with COVID-19 disease with a positive SARS-CoV-2 test result. These participants can have either critical (Grade 6 or 7) or severe (Grade 4 or 5) disease. All subjects receive SoC as per institutional protocols, in addition to study treatment.

[0914] The study comprises 2 parts. Part 1 enrolls 20 participants who have severe COVID-19 disease. Following an initial safety assessment of unblinded data at Day 14 by the IDMC, Part 2 (the main cohort) progresses, where participants with both severe and critical COVID-19 disease are enrolled. Only severe participants are enrolled in Part 2 without pausing the study until the IDMC recommend recruiting critical participants as well.

[0915] To explore the host immune response and potential biomarkers of infection, subjects may consent to an optional sub-study in which peripheral blood mononuclear cells (PBMCs) are collected at specified timepoints. This optional substudy is performed at selected sites. Approximately 50-100 participants per arm are enrolled into the optional sub-study.

[0916] During this study, an unblinded safety data review conducted by an IDMC determines whether it is safe to expand from Part 1, which includes subjects with severe (Grade 4 or 5) COVID-19 disease to Part 2, which additionally includes subjects with critical (Grade 6 or 7) COVID-19 disease.

[0917] A placebo control distinguishes the safety and tolerability of sotrovimab from the background signs and symptoms of COVID-19 and evaluates its potential benefit on clinical outcomes. The use of a placebo arm allows for a valid evaluation of any changes in efficacy and safety attributable to sotrovimab versus those attributable to SoC and other treatments given during the study.

[0918] The primary endpoint to assess efficacy of treatment is time to clinical response defined as subjects being alive and independent of supplementary oxygen or return to pre-morbid oxygen requirement (for subjects with chronic oxygen use) for at least 24 hours within 29 days of randomization. The transition from requiring oxygen therapy or higher levels of respiratory/organ support is a clinically significant milestone.

[0919] A significant secondary endpoints is all-cause mortality at Day 29. Other secondary efficacy endpoints related to hospital stay-length of hospital stay, ICU stay, time ventilated and the severity and duration of subject-reported signs and symptoms of COVID-19 are also clinically relevant.

Study Intervention Groups and Duration

[0920] Screening assessments are performed up to 48 hours before the first dose. Screening procedures include taking a medical and disease history; testing for SARS-CoV-2 infection by nasal, nasopharyngeal, or endotracheal swab for subjects without a prior confirmed positive test; a full physical examination including measurement of height and weight; measurement of vital signs including blood pressure, pulse, respiratory rate, and temperature; oxygen saturation (SpO₂) for subjects not on invasive mechanical ventilation; oxygen delivery and ventilation status; 12-lead ECG (triplicate); urine or serum pregnancy test for all female subjects of childbearing potential; laboratory assessments including hematology, clinical chemistry profile, coagulation parameters, CRP, D-dimer, urinalysis, and cardiac troponin; chest radiography (chest x-ray or computed tomography scan taken after hospitalization per SoC); and review of prior or concomitant medication.

[0921] Eligible subjects are treated with a single IV dose (sotrovimab or placebo) plus SoC on Day 1. They are assessed daily up to the day of hospital discharge. Following discharge from hospital, assessments occur on Day 15 and Day 29 and follow up continues to Week 36 after randomization.

[0922] In Part 1, subjects with severe COVID-19 disease (Grade 4 or 5) are randomized 1:1 by interactive response technology (IRT) in a blinded manner to receive a single IV dose of sotrovimab or placebo. In Part 2 (the main cohort), subjects with severe (Grade 4 or 5) or critical (Grade 6 or 7) COVID-19 disease are randomized 1:1 to receive a single IV dose of sotrovimab or placebo. All participants receive SoC as per institutional protocols, in addition to study treatment.

[0923] The randomization is stratified based on the disease severity (severe or critical) and time from onset of symptoms (less than seven days or seven days or more) at randomization.

Study Interventions

[0924] Study interventions and dosing instructions are as follows:

TABLE 14

Dose Formulation	Solution in single-use vial (25 mg/mL)	Sterile 0.9% (w/v) sodium chloride solution
Unit Dose Strength(s)	250 mg/vial (250 mg/10 mL)	Not applicable
Dosage Level(s)	(tbc) mg once	Once
Route of Administration	IV infusion	IV infusion
Dosing instructions	Withdraw 10.0 mL from the vial into a 10-20 mL small syringe and transfer to a 150 mL or 250 mL IV empty saline bag by an unblinded pharmacist. Repeat this procedure until the required dose is reached and administer over 1 hour.	Dose per IV infusion instructions
Special instructions	Gently mix sotrovimab and saline prior to IV infusion.	None
Packaging and Labelling	Study intervention are provided in a single-use vial in an individual carton and labelled as required per country requirement.	Labelled as required per country requirement

[0925] Further study details are shown in FIG. 3.

Example 42

Phase 3 Clinical Study of Sotrovimab in Patients Who have been Hospitalized with COVID-19

[0926] A Phase 3 clinical study is performed evaluate safety and effectiveness of different drugs in treating COVID-19 in people who have been hospitalized with the infection. Participants in the study are treated with either a study drug (e.g., sotrovimab) plus current standard of care (SOC), or with placebo plus current SOC.

[0927] The protocol is for a randomized, blinded, controlled platform study that allows investigational drugs to be added and dropped during the course of the study. This allows for efficient testing of drugs against placebo and standard of care (SOC) treatment within the same study. When more than one drug is tested at the same time, participants are randomly allocated to treatments or placebo.

[0928] Randomization are stratified by study site pharmacy and disease severity. There are 2 disease severity strata: Participants without organ failure (severity stratum 1); and participants with organ failure (severity stratum 2).

[0929] An independent Data and Safety Monitoring Board (DSMB) regularly reviews interim analyses and summarizes safety and efficacy outcomes. For investigational drugs with minimal pre-existing safety knowledge, the pace of enrollment is initially restricted, and there is an early review of safety data by the DSMB. For the study of each agent, at the outset of the trial, only participants in disease severity stratum 1 are enrolled. This continues until approximately 300 participants are enrolled and followed for 5 days. The exact number can vary according to the speed of enrollment and the timing of DSMB meetings. Prior to expanding enrollment to also include patients in disease severity stra-

tum 2, safety is evaluated and a pre-specified futility assessment by the DSMB is carried out using 2 ordinal outcomes assessed at Day 5.

[0930] Both ordinal outcomes are used to assess futility because it is unclear whether the investigational agents under study will primarily influence non-pulmonary outcomes, for which risk is increased with SARS-CoV-2 infection, in part, through mechanisms that may be different from those that influence pulmonary outcomes.

[0931] For investigational agents passing this futility assessment, enrollment of participants is expanded, seamlessly and without any data unblinding, to include participants in disease severity stratum 2 as well as those in disease severity stratum 1. Future interim analyses are based on the primary endpoint of sustained recovery and use pre-specified guidelines to determine early evidence of benefit, harm or futility for the investigational agent. Participants are followed for 18 months following randomization.

[0932] The international trials within this protocol are conducted in several hundred clinical sites. Participating sites are affiliated with networks funded by the United States National Institutes of Health (NIH) and the US Department of Veterans Affairs.

[0933] Approximately 10,000 participants are enrolled. The allocation is randomized. The intervention model is parallel assignment. Masking is triple (Participant, Care Provider, Investigator). The primary purpose is treatment. In one arm, participants are randomized to receive drug (e.g. sotrovimab) plus SOC or placebo plus SOC. Subsequently, participants are no longer randomized to sotrovimab. In a placebo arm, placebo (commercially available 0.9% sodium chloride solution administered by IV infusion) plus remdesivir is provided absent contraindication.

Primary Outcome Measures

[0934] 1. Time from randomization to sustained recovery [Time Frame: Up to Day 90]. Sustained recovery defined as being discharged from the index hospitalization, followed by being alive and home for 14 consecutive days prior to Day 90.

Secondary Outcome Measures

- [0935] 1. All-cause mortality [Time Frame: Thru Day 90]
- [0936] 2. Composite of time to sustained recovery and mortality [Time Frame: Thru Day 90]
- [0937] 3. Days alive outside short-term acute care hospital [Time Frame: Up to Day 90]
- [0938] 4. Pulmonary ordinal outcome [Time Frame: Days 1-7, 14 and 28]
- [0939] Oxygen requirements measured by 7 categories (1=least severe, 7=most severe). The participant's highest (i.e. most severe) observed score is used.
- [0940] 5. Pulmonary+ ordinal outcome [Time Frame: Days 1-7]
- [0941] Extrapulmonary complications and respiratory dysfunction measured by 7 categories (1=least severe, 7=most severe). The participant's highest (i.e. most severe) observed score is used.
- [0942] 6. Incidence of clinical organ failure [Time Frame: Thru Day 28]
- [0943] 7. Composite of death or serious clinical COVID-19 related events
- [0944] [Time Frame: Thru Day 90]
- [0945] 8. Composite of cardiovascular events and thromboembolic events
- [0946] [Time Frame: Thru Day 90]
- [0947] 9. Composite of grade 3 and 4 clinical adverse events, serious adverse events (SAEs) or death [Time Frame: Thru Days 5 and 28]
- [0948] 10. Incidence of infusion reactions [Time Frame: Thru Day 0]
- [0949] 11. Composite of SAEs or death [Time Frame: Thru 18 months]
- [0950] 12. Change in SARS-CoV-2 neutralizing antibody levels [Time Frame: Baseline to Days 1, 3, 5, 28 and 90]
- [0951] 13. Change in overall titers of antibodies [Time Frame: Baseline to Days 1, 3, 5, 28 and 90]
- [0952] 14. Change in neutralizing antibody levels [Time Frame: Baseline to Days 1, 3, 5, 28 and 90]
- [0953] 15. Incidence of home use of supplemental oxygen above pre-morbid oxygen use [Time Frame: 18 months]
- [0954] Measured as: Alive at home and no use of continuous supplemental oxygen for an uninterrupted 14 day period
- [0955] 16. Incidence of no home use of supplemental oxygen above pre-morbid oxygen use [Time Frame: 14 days]
- [0956] Measured as: alive at home for an uninterrupted 14 day period and no use of continuous supplemental oxygen at end of 14 day time period.
- [0957] Adults aged 18 years and older (adults and older adults) of all sexes are eligible. Inclusion criteria are: signing of informed consent; positive test for COVID-19 and progressive disease suggestive of ongoing COVID-19 infection; symptoms of COVID-19 for ≤12 days; and require admission to hospital for acute medical care (not for purely public health or quarantine purposes). Exclusion criteria are:
- [0958] Patients who have received plasma from a person who recovered from COVID-19 or who have received neutralizing monoclonal antibodies at any time prior to hospitalization.

- [0959] Patients not willing to abstain from participation in other COVID-19 treatment trials until after Day 5 of the study. Co-enrollment in certain trials that compare recommended Standard of Care treatments may be allowed, based on the opinion of the study leadership team.
- [0960] Any condition which, in the opinion of the responsible investigator, participation would not be in the best interest of the participant or that could prevent, limit, or confound the protocol-specified assessments.
- [0961] Patients considered unable to participate in study procedures.
- [0962] Women of child-bearing potential who are not already pregnant at study entry and who are unwilling to acknowledge strong advice to abstain from sexual intercourse with men or practice appropriate contraception through 18 months of the study.
- [0963] Men who are unwilling to acknowledge the strong advice to abstain from sexual intercourse with women of child-bearing potential or to use barrier contraception through 18 months of the study.
- [0964] Pregnant women
- [0965] Nursing mothers
- [0966] Presence at study enrollment of any of the following:
 - [0967] 1. stroke
 - [0968] 2. meningitis
 - [0969] 3. encephalitis
 - [0970] 4. myelitis
 - [0971] 5. myocardial ischemia
 - [0972] 6. myocarditis
 - [0973] 7. pericarditis
 - [0974] 8. symptomatic congestive heart failure
 - [0975] 9. arterial or deep venous thrombosis or pulmonary embolism
- [0976] Current or imminent requirement for any of the following:
 - [0977] 1. invasive mechanical ventilation
 - [0978] 2. ECMO (extracorporeal membrane oxygenation)
 - [0979] 3. Mechanical circulatory support
 - [0980] 4. vasopressor therapy
 - [0981] 5. commencement of renal replacement therapy at this admission (i.e. not patients on chronic renal replacement therapy).
- [0982] In addition, prior to the initial futility assessment which is performed when approximately 150 participants have been enrolled on sotrovimab and 150 on placebo, patients on high-flow oxygen or non-invasive ventilation (category 5 of the pulmonary ordinal outcome) will be excluded. These patients may be eligible for the trial if the initial futility assessment is passed by this agent.
- [0983] A single dose of 500 mg sotrovimab is administered. The dose is selected based on in vitro neutralization data, in vitro resistance data, expected human PK extrapolated from a study in cynomolgus monkeys, and results of a GLP monkey toxicology study. Sotrovimab neutralized SARS-CoV-2 live virus with an average EC90 value of 186.3 ng/ml (range: 125.8-329.5 ng/mL). In resistance analyses, no viral breakthrough was observed through 10 passages at fixed concentrations of antibody even at the lowest dose tested (~10× EC50), indicating the potential for sotrovimab to have a high barrier to resistance.

[0984] Using an increasing concentration selection method to force resistance emergence, modest fold changes in EC50 were observed during viral selection (5- to 6-fold change in EC50) for some passages. Sequencing and testing of spike variants from these passages using a pseudotyped virus system did not identify causal variants for this modest shift in potency. One passage of virus did demonstrate a >10-fold shift in EC50 which correlated with an E340A mutation. Further assessment has identified E340A to be a monoclonal antibody-resistant mutant (MARM) that confers a >100-fold reduction in susceptibility to sotrovimab. Notably, E340 is 100% conserved among available SARS-CoV-2 sequences. Due to the binary nature of the resistance selection results, a specific inhibitory quotient (IQ) was not informed by the resistance profiling. However, as very few strains are available to directly assess breadth of coverage, a conservative IQ (>10) is appropriate in this case. The cynomolgus monkey PK study (single IV dose, 5 mg/kg) was fit to a 2 compartment PK model. Human PK parameters were scaled from the cynomolgus monkey using an allometric scaling approach for fully human IgGs (allometric coefficient of 0.85 and 1 for CL and V, respectively; 10). The predicted serum clearance of sotrovimab in humans is estimated to be 141 mL/day and estimated volume of distribution is 6500 mL (~93 mL/kg) assuming human weight of 70 kg. The projected human terminal elimination half-life is approximately 32 days.

[0985] In order to reduce risk to patients (treatment failure, emergence of viral resistance), a single therapeutic dose was selected that ensures sotrovimab concentrations in the lung are maintained far above levels anticipated to be protective for SARS-CoV-2 infection for the duration of the 28-day treatment window and beyond. A dose of 500 mg is expected to maintain serum levels at or above 38.5 µg/mL for the duration of the 28-day treatment period. Based on a conservative EC90 (0.33 µg/mL) from the highest end of the EC90 range, and accounting for the lung: serum ratio for IgG (assumed conservative value of 0.25; reported range 0.25-0.68 for whole lung and interstitial fluid, respectively; the serum trough concentration following a 500 mg dose is expected to result in lung concentrations associated with maximal (>99%) antiviral activity; >29× tissue-adjusted EC90 for the duration of the 28 day treatment period. This conservative inhibitory quotient (29-fold) in lung is believed to be appropriate to increase potential for treatment success and reduce risk for resistance.

[0986] Additionally, a 500 mg dose is anticipated to result in protective levels of sotrovimab in nasopharyngeal secretions (>5× tissue adjusted EC90 assuming NPS: serum ratio of 0.05, 12) which could potentially reduce transmission.

[0987] The NOAEL for sotrovimab was 500 mg/kg, the highest dose tested, when sotrovimab was administered via IV infusion once a week for 2 weeks in cynomolgus monkeys. At this NOAEL, preliminary Cmax and area-under-the-curve (AUC)0-t (AUC from time 0 to 168 hr post-end of infusion following the 2nd dose) were 13500 µg/mL and 48200 µg·day/mL, respectively. The human equivalent dose (HED) (HED calculated via direct mg/kg conversion according to FDA guidance on proteins administered intravascularly with Mr >100,000 daltons; is 500 mg/kg or a 30,000 mg fixed dose (using human body weight of 60 kg). Using a safety factor of 10, the maximum recommended starting dose in humans is approximately 50 mg/kg or a 3,000 mg fixed dose. Based on the proposed 500 mg human dose, the

margins based on the HED, Cmax, and AUC (conservative AUC margin based on partial AUC0-t from TX-7831-0102 and expected AUCinf in humans) are 60-, 87-, and 13.6-fold, respectively, supporting the proposed clinical dose of 500 mg.

[0988] In addition to the inclusion and exclusion criteria outlined in the master protocol, the following patients will be excluded: 1) pregnant women; and 2) nursing mothers. In addition, prior to the initial futility assessment which is performed when approximately 150 participants have been enrolled on sotrovimab and 150 on placebo, patients on high-flow oxygen or non-invasive ventilation (category 5 of the pulmonary ordinal outcome) are excluded. These patients may be eligible for the trial if the initial futility assessment is passed by this agent.

[0989] A single infusion is administered over a one-hour period. Study participants are monitored closely, and, per discretion of the physician supervising the infusion, adjustments in the infusion rate is made and/or the infusion paused or stopped.

[0990] Physician supervising the infusion may use supportive measures per local practice, if indicated. Sotrovimab is provided in vials of 10 ml solution containing 250 mg antibody each. Sotrovimab must be stored between 2° C. and 8° C. A total of 2 vials are required for dosing of the agent at 500 mg. The agent is administered at a concentration of 1 mg/ml to 10 mg/ml. Placebo is normal saline from local supply. If an infusion reaction occurs during administration or if the participant has a medical history suggesting a potential benefit from premedication, the study investigator(s) should determine the appropriate premedication. If the frequency of infusion reactions among participants warrants it, premedication may be recommended. If minor infusion reactions are observed, administration of acetaminophen, 500 mg to 1000 mg, antihistamines and/or other appropriately indicated medications may be given prior to the start of infusions for subsequent participants. The decision to implement premedication for infusions in subsequent participants is made by the investigator and sponsor and recorded in the study documentation. Any pre-medications given are documented as a concomitant therapy.

[0991] At Days 0, 28, and 90, venous blood samples are collected to determine antibody production against sotrovimab. Immunogenicity may be assessed by a validated assay designed to detect ADAs in the presence of sotrovimab. Antibodies may be further characterized for their ability to neutralize the activity of sotrovimab. Remaining volume from the PK sample may also be used for immunogenicity assessments as needed.

[0992] At Days 0, 1, 5, 28, and 90, venous blood samples are collected to determine sotrovimab serum concentration for pharmacokinetic assessment. The PK/Immunogenicity assessment requires 2 mL of the serum collected. PK samples may be assessed by a validated assay at a bioanalytical lab. The PK assessment uses the same 2 ml serum. Analysis of samples from placebo-treated subjects is not planned. Remaining sample used for PK may be pooled and used for exploratory metabolism or bioanalytical method experiments as deemed appropriate. Samples may be shipped to the lab for analyses in batches as the substudy is unfolding. Results from such analyses are returned to the trial central database. This data and all other data on the participants remain in the trial central database until the trial is unblinded. All participants should be monitored closely

for 2 hours after the infusion, as there is a risk of infusion reaction and hypersensitivity (including anaphylaxis) with any biological agent.

[0993] Symptoms and signs that may occur as part of an infusion reaction, include, but are not limited to, fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, and dizziness.

[0994] The clinical site should have necessary equipment, medications, adequately qualified and experienced staff with appropriate medical cover for the management of any infusion reaction, which may include, but is not limited to, oxygen, IV fluid, epinephrine (/adrenaline), acetaminophen (/paracetamol) and antihistamine.

[0995] If the participant experiences an infusion reaction, then supportive care should be used in accordance with the signs and symptoms. If a severe and potentially life-threatening infusion reaction occurs with sotrovimab/placebo, its use should be permanently discontinued. The following are AESIs for the agent sotrovimab or placebo for sotrovimab: infusion-related reactions; allergic/hypersensitivity reactions.

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Example 43

Phase 3 Clinical Study of Sotrovimab for Prevention of COVID-19 Among Adult and Adolescent Subjects Exposed to SARS-CoV-2

- [1013] A randomized, multi-center, double-blind, placebo-controlled Phase 3 study is performed to assess safety and efficacy of monoclonal antibody sotrovimab in preventing COVID-19 in adult and adolescent subject exposed to SARS-CoV-2.
- [1014] A primary objective is to evaluate efficacy of sotrovimab versus placebo for prevention of symptomatic COVID-19 among close contacts of persons with SARS-CoV-2 infection and to determine safety and tolerability of sotrovimab compared to placebo.
- [1015] Secondary objectives are:
 - [1016] Evaluate efficacy of sotrovimab in the prevention of asymptomatic SARS-CoV-2 infection compared to placebo among close contacts of persons with SARS-CoV-2 infection
 - [1017] Evaluate efficacy of sotrovimab in reducing duration of viral shedding among those with SARS-CoV-2 infection
 - [1018] Evaluate efficacy of sotrovimab in reducing the incidence, severity, and duration of clinical signs and symptoms of COVID-19 among those with SARS-CoV-2 infection
 - [1019] Evaluate efficacy of sotrovimab on the time to alleviation of clinical symptoms among those with SARS-CoV-2 infection
 - [1020] Evaluate efficacy of sotrovimab in reducing progression to severe disease among those with SARS-CoV-2 infection as assessed by rate of hospitalization, ICU admission, or death due to COVID-19.
 - [1021] Evaluate the serum pharmacokinetics (PK) of sotrovimab
 - [1022] Evaluate potential immunogenicity (induction of ADA) response to sotrovimab

- [1023] The exploratory objectives include:
- [1024] Evaluate efficacy of sotrovimab in reducing viral load among those with SARS-CoV-2 infection
- [1025] Evaluate association of SARS-CoV-2 viral load with treatment and with severity of disease
- [1026] Monitor emergence of viral resistance to sotrovimab in subjects with confirmed SARS-CoV-2.
- [1027] Evaluate potential relationships between subject genetic polymorphisms and sotrovimab mechanisms of action and/or PK
- [1028] Measure impact of sotrovimab on time away from work and work productivity due to COVID-19
- [1029] Evaluate effects of sotrovimab on potential biomarkers of host response

Criteria for Evaluation

- [1030] A primary efficacy endpoint of this study is as follows:
- [1031] Proportion of subjects with laboratory confirmed (RT-PCR) COVID-19 defined as one or more the following through Week 2 (Day 15±1):
- [1032] 1 Acute respiratory symptoms (cough, sputum production, sore throat or shortness of breath);
- [1033] OR
- [1034] 2. Fever >38° C.;
- [1035] OR
- [1036] 3. 2 or more of the following symptoms (fatigue, myalgias/arthritis, chills, nausea/vomiting, diarrhea, anosmia/dysgeusia)
- [1037] The primary safety endpoints of this study are as follows:
- [1038] The proportion of subjects with treatment emergent adverse events (AEs) and serious AEs (SAEs) following administration of sotrovimab
- [1039] Clinical assessments including but not limited to laboratory test results
- [1040] Secondary endpoints of this study are as follows:
- [1041] Incidence of laboratory confirmed (RT-PCR) asymptomatic SARS-CoV-2 infection through Week 2 (Day 15±1) in subjects with a negative baseline test
- [1042] The difference in duration of viral shedding between sotrovimab and placebo treatment groups as assessed by RT-PCR from nasal swabs
- [1043] The incidence, severity, and duration of clinical signs and symptoms of COVID-19.
- [1044] Percentage of participants requiring hospitalization due COVID-19.
- [1045] Percentage of participants requiring ICU care.
- [1046] Percentage of participants requiring mechanical ventilation or ECMO.
- [1047] Percentage of participants with COVID-19 related death.
- [1048] Concentrations of sotrovimab in serum.
- [1049] Incidence and titers (if applicable) of serum ADA to sotrovimab
- [1050] The exploratory endpoints of this study include:
- [1051] The difference in viral load at the time of illness onset between sotrovimab and placebo treatment groups as assessed by qRT-PCR from nasal swabs
- [1052] Relationship between viral load (qRT-PCR) and severity of COVID-19
- [1053] Incidence of laboratory confirmed SARS-CoV-2 infection by serology at Week 4 in subjects with a negative baseline test

- [1054] FcR polymorphisms as determined by genotyping
- [1055] Immunoglobulin G1 (IgG1) allotypes as determined by genotyping
- [1056] Change from baseline in Work Productivity and Activity Impairment (WPAI)
- [1057] Change from baseline in health-related quality of life according to EQ-5D-5L
- [1058] Impact of sotrovimab administration on biomarkers of host response as assessed by host transcriptome and immunophenotyping analysis

Number of Subjects

- [1059] Approximately 1350 subjects (450 per treatment arm) are enrolled.

Diagnosis and Main Eligibility Criteria

- [1060] 1. Male and female subjects aged 12 years or older
- [1061] 2. Close contact of a person (index) with known PCR-confirmed SARS-CoV-2 infection

Close contact defined as:

- [1062] a. Residing with the index case in the 7 days prior to index diagnosis, including residence or staff in a congregate setting such as long-term care facility or nursing home
- [1063] b. Medical staff, first responders, or other care persons
- [1064] c. Less than 3 days since last exposure (close contact with a person with SARS-CoV-2 infection) to the index case
- [1065] 4 Female subjects must have a negative pregnancy test or confirmation of post-menopausal status
- [1066] 5. Negative rapid test for SARS-CoV-2 infection within 4 hours prior to dosing

Duration of Study Participation

- [1067] The estimated total time on study for each subject, inclusive of screening, is up to 36 weeks. Subjects are screened within 24 hours prior to randomization. Following study drug administration, subjects are evaluated for up to Week 6 (D43±3) for endpoint assessments and up to 36 weeks for safety follow-up.

Study Design

- [1068] This is a randomized, double-blind, placebo-controlled study of 2 dose levels of sotrovimab for the prevention of symptomatic SARS-CoV-2 infection in adults exposed to the virus. The study is designed to evaluate efficacy of a low and a high dose sotrovimab compared to placebo in prevention of symptomatic SARS-CoV-2 infection.

- [1069] This study enrolls approximately 1350 asymptomatic male and female subjects 12 years of age or older, including those with comorbidities, who are close contacts (i.e. household members or healthcare providers) of persons with reverse transcriptase-polymerase chain reaction (RT-PCR)-confirmed SARS-CoV-2 infection. A rapid diagnostic test is used at screening to enrich for subjects without established infection. Eligible subjects are randomized to receive either sotrovimab low dose, sotrovimab high dose, or placebo in a 1:1:1 ratio as a single administration on Day 1.

[1070] An independent data monitoring committee (DMC) consisting of members with relevant expertise convenes to review study data. The purpose of the DMC is to monitor safety, efficacy, and futility and determine the need for sample size readjustment based on observed infection rate in the placebo arm. Two interim analyses are conducted. The first interim analysis is conducted after approximately 20% of subjects have been enrolled (~90 per arm) to assess safety and tolerability of each dose level of S309 N55Q LS.

[1071] The second interim analysis is conducted after approximately 50% of subjects have been enrolled (~225 per arm) to assess safety, futility, and efficacy. A dose level may be discontinued due to safety concerns or lack of efficacy.

[1072] If data emerges on effective agents for SARS-CoV-2 prophylaxis, the protocol may be modified to include new standard of care agents in the control arm.

[1073] The study includes a PK sub-study in approximately 75 subjects (25 per arm) for intensive PK and ADA sample collections. All other subjects have sparse PK and ADA sample collections. If a new lot of sotrovimab is introduced into the study, additional subjects may be included into an intensive PK and immunogenicity sub-study.

Study Procedures

Screening:

[1074] Screening is performed within 24 hours prior to randomization and includes written informed consent, determination of eligibility, collection of demographics, past and current medical conditions (including known pregnancy and/or lactation status), concomitant medications and information regarding exposure to the Index Case.

Dosing (Day 1):

[1075] Following collection of a baseline nasal swab for RT-PCR on Day 1, eligible subjects are randomized to receive either sotrovimab or placebo. Subjects remain in the clinic for a minimum of 4 hours post-dose to assess safety and local tolerability of sotrovimab and complete assessments.

Follow-Up Period:

[1076] Subjects complete a daily diary from Day 1 through Week 2 visit. This survey includes documentation of clinical signs and symptoms of infection and concomitant medication review. In addition, all subjects collect a nasal swab at home on Days 4, 7, and 10 to monitor for asymptomatic SARS-CoV-2 infection. A study team member contacts subjects via telephone to evaluate adverse events and provide support for completion of study procedures. Subjects have an in-clinic visit at Week 2 (Day 15±1) and Week 6 (Day 42±3) and complete assessments.

[1077] Subjects are followed per the COVID-19 Monitoring Schedule if they experience symptom onset defined as acute onset of respiratory symptoms (dry cough, shortness of breath, sore throat, or sputum production); OR fever of >38.0° C.; OR ≥2 of the following symptoms: myalgias/arthralgias, chills, nausea/vomiting, diarrhea, anosmia/dysgeusia.

[1078] Subjects meeting criteria for potential symptomatic COVID-19 complete an in-clinic evaluation for SARS-CoV-2 infection, including nasal swab for confirmation of infection. Subjects continue to complete a daily diary for 21 days following symptom onset. Additional nasal swabs are collected to assess viral load and duration of viral shedding. In these subjects, nasal swabs are collected every other day for the first week following a positive test and then every 3 days during the second- and third-week post infection.

[1079] Subjects are followed for up to 36 weeks following dosing for assessment of safety, PK and immunogenicity. The duration of follow up is informed by the predicted human t_{1/2} of sotrovimab based on allometric scaling of NHP PK. The final follow up period is specified in the protocol. Between Week 6 visit and the last follow-up visit, subjects are contacted by phone for adverse event monitoring.

Product, Dosage, and Mode of Administration

[1080] Sotrovimab is an engineered human IgG monoclonal antibody directed against SARS-CoV-2 spike protein with modifications to increase half-life. Sotrovimab is administered in a single dose IV or IM at either a low or high dose level. Subjects randomized to placebo are administered sterile, preservative-free normal saline 0.9% solution by IM injection.

Statistical Methods

[1081] Not all individuals exposed to SARS-CoV-2 will become infected or develop symptoms, and early estimates place family members at a 3% to 15% risk of infection after likely exposure. For the purpose of sample size calculation an estimated 10% attack rate was used. Sample size was chosen to achieve 80% power with 0.05 two-sided Type 1 error for the endpoint of laboratory confirmed symptomatic COVID-19, an attack rate of 10% and 50% efficacy of sotrovimab in reducing symptomatic COVID-19. Based on these assumptions, approximately 450 subjects are enrolled per treatment arm (total of 1350).

[1082] Two interim analysis are conducted for this study. The first interim analysis is conducted after approximately 20% of subjects have been enrolled (90 per arm) to assess safety and tolerability of each dose level of sotrovimab. A dose level may be discontinued due to safety concerns. The second interim analysis is conducted after approximately 50% of subjects have been enrolled (225 per arm) to assess safety, futility, and efficacy. A dose level may be discontinued due to safety concerns or lack of efficacy. Based on the attack rate observed at the interim analysis, sample size may be adjusted in order to increase the likelihood of achieving the overall expected number of cases to meet the primary endpoint. In order to properly control the overall type 1 error rate (the ‘alpha’) at the 0.05 level, O’Brien-Fleming method is used to allocate alpha between the second interim analysis (0.0052) and the final analysis (0.048).

[1083] All efficacy analyses are performed using the ITT population (all randomized subjects). Incidence of symptomatic and asymptomatic SARS-CoV-2 infection is also evaluated in the mITT population (subjects who are SARS-

CoV-2 negative at the baseline visit). Safety is assessed in all subjects who received any amount of study drug.

[1084] Further details of the study are shown in FIG. 4.

Example 44

Phase 3 Clinical Study of Sotrovimab for Prevention of COVID-19 Among Adult and Adolescent Subjects Exposed to SARS-CoV-2

[1085] A randomized, double-blind, placebo-controlled Phase 3 study is conducted to evaluate safety and efficacy of sotrovimab for prophylaxis of COVID-19. Approximately 3150 participants are randomized in a 2:1 ratio to receive either sotrovimab or placebo respectively to evaluate the safety and efficacy of sotrovimab for the prevention of COVID-19.

[1086] The primary objective is to evaluate safety and efficacy versus placebo in preventing COVID-19. The primary endpoint is incidence rate of protocol-defined COVID-19 through Week 13 (3 months) as defined by:

[1087] A positive SARS-CoV-2 reverse transcriptase polymerase chain reaction (RT-PCR) from a nasopharyngeal swab

[1088] AND

[1089] New onset (or exacerbation) of at least one or more of the following symptoms that persist or reoccur after a period of at least 24 hours:

[1090] Fever >38° C., chills, cough, sore throat, malaise, headache, myalgia, change in smell or taste, nasal congestion/rhinorrhea, vomiting, diarrhea, shortness of breath on exertion

[1091] This is a clinically meaningful endpoint to both clinicians and participants as prevention of symptomatic COVID-19 may lead to decreased morbidity and mortality from this disease as well as potentially lead to decreased transmission. In addition, a statistical testing hierarchy approach is employed to control the overall type I error to determine the efficacy of sotrovimab in the prevention of protocol-defined symptomatic COVID-19 at additional timepoints (up to Weeks 17, 21 and 26).

[1092] Other secondary efficacy endpoints including prevention of CDC-defined symptomatic COVID-19, and prevention of asymptomatic SARS-CoV-2 infection (as assessed by seroconversion at Weeks 13 and 26) are also clinically relevant.

[1093] A participant is considered to have completed the study if he/she has completed the study through to Week 26.

[1094] Participants 18 years or older at the time of giving informed consent (except for in South Korea, where participants are 19 years or older) and of any gender are eligible. Female participants must meet and agree to abide by the contraceptive criteria listed below. Contraception use by women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies.

[1095] A female participant is eligible to participate if she is not pregnant or breastfeeding, and one of the following conditions applies:

[1096] a. Is a woman of non-childbearing potential (WONCBP), or

[1097] OR

[1098] b. Is a woman of childbearing potential (WOCBP) and using a contraceptive method that is highly effective, with a failure rate of <1%, during the study intervention

[1099] period and for up to 26 weeks after the last dose of study intervention. The investigator should evaluate potential for contraceptive method failure (e.g., noncompliance, recently initiated) in relationship to the first dose of study intervention.

[1100] A WOCBP must have a negative highly sensitive pregnancy test (urine or serum as required by local regulations) before the first dose of study intervention.

[1101] a. If a urine test cannot be confirmed as negative (e.g., an ambiguous result), a serum pregnancy test is required. In such cases, the participant must be excluded from participation if the serum pregnancy result is positive.

[1102] b. Additional requirements for pregnancy testing during and after the study intervention may be in-place.

[1103] The investigator reviews medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy.

[1104] Participants are capable of giving informed consent. Participants agree to study procedures including the collection of nasopharyngeal swabs, self-collected nasal mid-turbinate swabs and venous blood as specified in the schedule of activities. Participants are able and willing to complete study surveillance questionnaires and activities.

[1105] Participants have an anti-spike SARS-CoV-2 antibody test during screening for enrollment. Participants with a positive anti-spike SARS-CoV-2 antibody test are not enrolled. Participants have a nasopharyngeal SARS-CoV-2 RT-PCR and an anti-N SARS-CoV-2 antibody test at Day 1 prior to dosing. Participants found to have a positive SARS-CoV-2 RT-PCR test or a positive anti-N SARS-CoV-2 antibody test at Day 1 are excluded from the primary analysis (mITT) population.

Exclusion Criteria

[1106] Participants are excluded from the study if any of the following criteria apply:

Medical Conditions

[1107] 1. History of prior positive SARS-CoV-2 RT-PCR or antigen test or history of positive SARS-CoV-2 serology test including during screening.

[1108] 2. Febrile illness with or without respiratory symptoms (e.g., cough, nasal congestion) within 7 days prior to randomization

[1109] 3. Unstable medical condition and not expected to survive for the duration of study participation as judged by the investigator

[1110] 4. Participant has any condition that would prohibit receipt of intramuscular injections in the investigator's opinion such as coagulation disorder, bleeding diathesis, or thrombocytopenia

[1111] 5. Known hypersensitivity to any constituent present in the investigational product

[1112] 6. Previous anaphylaxis or hypersensitivity to a monoclonal antibody

[1113] 7. Participants who, in the judgment of the investigator, will be unlikely or unable to comply with the requirements of the protocol through Week 26

Prior Medications

[1114] 8. Receipt of a COVID-19 vaccine at any time prior to enrollment, or planned receipt of a COVID-19 vaccine during the first 13 weeks of the study

[1115] 9. Receipt of any vaccine within 48 hours prior to enrollment. Vaccination will not be allowed for 2 weeks after dosing

[1116] 10. Receipt of any SARS-CoV-2 hyperimmune intravenous immunoglobulin (hIVIG) from COVID-19 survivors

[1117] 11. Receipt of convalescent plasma from a recovered COVID-19 patient or an anti-SARS-CoV-2 mAb within 3 months or 5 half-lives, whichever is longer, prior to screening and/or during the study

Prior/Concurrent Clinical Study Experience

[1118] 12. Enrolment in any investigational drug or device study for SARS-CoV-2/COVID-19 within 90 days prior to Day 1 or within 5 half-lives of the investigational compound, whichever is longer.

Other Exclusions

[1119] 13. Pregnant or breast-feeding females.

[1120] (all female participants regardless of childbearing potential status must have a negative pregnancy test at screening/pre-dosing)

BRIEF SUMMARY

Lead-In Phase

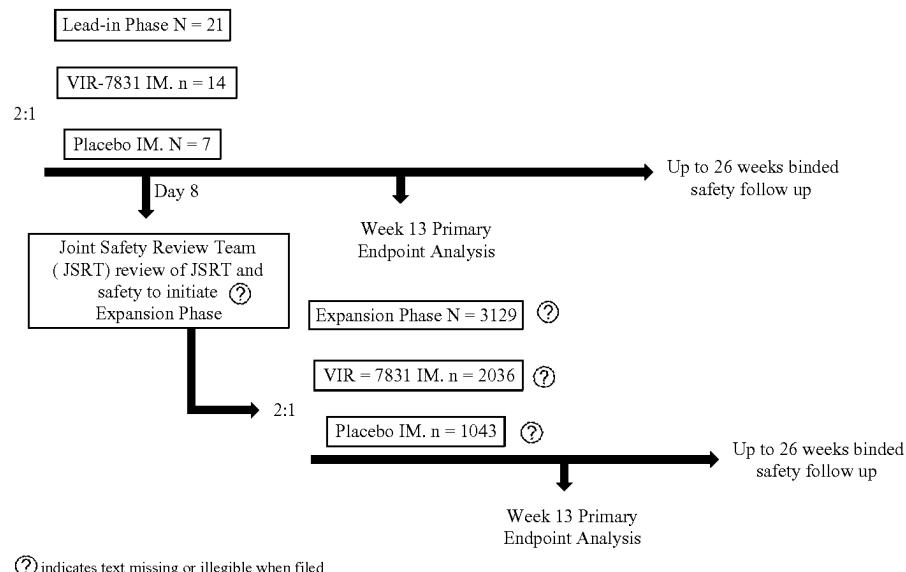
[1122] The Lead-in phase of the study is intended to evaluate the safety, tolerability, and pharmacokinetics (PK) of sotrovimab with frequent assessments of injection site reactions (ISRs) and intensive blood sampling for PK analysis. These participants are pooled with the Expansion phase participants for efficacy evaluations. Approximately 21 participants are enrolled and randomized 2:1 to receive VIR-7831 (N=14) or equal volume saline placebo (N=7). Participants are monitored for 6 hours after dosing for safety monitoring and local injection site tolerability assessments. At the end of 6 hours, they are discharged. Randomization is paused upon enrollment of the Lead-in phase, until Day 8 safety assessment by the Joint Safety Review Team (JSRT) recommends continuing. If the JSRT requires escalation to the IDMC, then randomization pauses pending a recommendation to proceed by the IDMC.

Intensive PK Sampling and Immunogenicity

[1123] All participants enrolled in the Lead-In phase have additional timepoints for PK blood sampling. Serum PK and anti-drug antibodies (ADA) samples are collected.

[1124] The lead-in phase of the study is summarized in Scheme 2, wherein sotrovimab is identified as VIR-7831.

Scheme 2. Lead-in Phase



② indicates text missing or illegible when filed

[1121] Sotrovimab is formulated in solution in a single use vial (62.5 mg/mL). the unit dose strength is 500 mg/vial (500 mg/8 mL). Sotrovimab is administered in a single dose (500 mg, once) by intramuscular injection. Placebo is locally sourced sterile 0.9% (w/v) sodium chloride solution, administered in a single dose by intramuscular injection.

Expansion Phase

[1125] The Expansion phase of the study is gated to a safe to proceed recommendation from the JSRT. Specifically, randomization into the Expansion phase starts following blinded assessment of local injection site tolerability assess-

ment data (ISRs) and other safety data from the Lead-in phase through Day 8 of follow-up by the JSRT.

[1126] Approximately 3129 additional participants are enrolled and randomized in a 2:1 ratio to receive sotrovimab or equal volume saline placebo via IM administration respectively.

[1127] Participants in the Expansion phase are monitored through 1 or 2 hours post-dose prior to discharge from the clinic/study unit. The duration of monitoring (1 or 2 hours) is based on assessment of ISRs from the Lead-in phase. The decision regarding the duration of monitoring is communicated as part of the JSRT recommendations to sites, and as a protocol file note.

[1128] Participants from both the Lead-in and Expansion phases are monitored for COVID-19 throughout the study via two mechanisms, as follows:

[1129] 1. Participants are provided with a printed guide of COVID-19 signs and symptoms to look out for, and a study site phone number to call within 24 hours of experiencing any of those symptoms, or if they have any other reason to suspect they may be infected with SARS-CoV-2.

[1130] 2. In addition, the site makes a regular once-weekly phone call to the participant, from Day 1 through Week 13 (every two weeks from Week 13 to Week 26), to capture adverse events (AEs), serious adverse events (SAEs) and to review the COVID-19 symptoms checklist with the participant.

[1131] All participants are provided with a nasal (mid-turbinate) swab self-test kit and return envelope for central lab testing, at the start of the study. Any participant who experiences COVID-19 symptoms during the 26-weeks study follow-up period, are instructed to use the self-test kit immediately, and to follow any additional local guidance for managing suspected COVID-19. Those that test positive complete weekly self-reported COVID-19 symptom surveillance and weekly Work Productivity and Activity Impairment (WPAI) questionnaires and are followed per a COVID-19 Illness Monitoring Schedule for 4 weeks after symptom onset. If a participant tests negative and is still experiencing symptoms, a second self-collection kit is sent to the participant for repeat testing.

[1132] All participants have regular follow-up phone calls and attend specific follow-up visits for assessments of efficacy, safety, and PK (sparse).

Number of Participants:

[1133] Approximately 3150 participants are randomly assigned to the study intervention in a 2:1 ratio to sotrovimab or placebo. Any participant who receives the study intervention are considered evaluable.

Study Screening, Randomization, and Duration

[1134] Screening assessments are performed during the 14 days prior to Day 1. Eligible participants are treated in a blinded manner with an IM dose on Day 1 and followed up to End of Study (EOS)-26 weeks (6 months). Participants remain blinded through EOS. Participants who develop COVID-19 (hospitalized or not hospitalized) are followed through 4 weeks post-symptomatic infection or EOS, whichever is earlier.

[1135] Randomization of participants in both the Lead-in and Expansion phases are stratified based on the following:

[1136] Age strata (<65 years of age, ≥65 years of age)
Increased risk exposure group

[1137] Presence of an immunocompromising condition

[1138] Block randomization occurs by country.

Independent Data Monitoring Committee

[1139] An unblinded Independent Data Monitoring Committee (IDMC) evaluates the overall safety profile of sotrovimab including evaluation of the incidence and severity of COVID-19 cases in participants randomized to sotrovimab compared to those randomized to placebo throughout the conduct of the study. The roles and responsibilities of the IDMC, including membership, scope, frequency of meetings and communication plan are defined in the IDMC charter. IDMC meetings occur regularly throughout the study as outlined by the IDMC charter.

Joint Safety Review Team

[1140] A Joint Safety Review Team (JSRT) comprised of team members from clinical research, pharmacovigilance, and statistics from study sponsors determines if a safety concern identified during instream blinded data review needs to be escalated to the IDMC. The JSRT is responsible for blinded safety review of the Lead-in phase as described above, with escalation to the IDMC if needed. The IDMC acts in accordance with the process defined in the IDMC Charter. Initiation of the Expansion phase is contingent on a safe to proceed recommendation from the JSRT. The responsibilities of the JSRT and frequency of assessments are available in relevant safety review team (SRT) documents.

[1141] The incidence rate of protocol-defined COVID-19 through Week 13 (3 months) and is analyzed using a Poisson regression model to estimate the relative risk. The model includes terms for treatment group, age strata, exposure risk group, immunocompromised group and country. However, for countries with no events, countries may be collapsed into regions for the model. The relative risk, 95% confidence interval and corresponding p-value are presented for the comparison of sotrovimab with placebo.

Example 45

Intramuscular Sotrovimab for Mild/Moderate COVID-19

[1142] A Phase 3 randomized, multi-center, open label study is conducted to assess the efficacy, safety, and tolerability of sotrovimab given intramuscularly versus intravenously for the treatment of mild/moderate COVID-19 in high-risk non-hospitalized patients. Arms and interventions are as in Table 15.

TABLE 15

Arms and Interventions	
Arms	Assigned Interventions
Active Comparator: Sotrovimab 500 mg IV	Sotrovimab
Sotrovimab given by intravenous infusion	500 mg IV
Experimental: Sotrovimab 500 mg IM	Sotrovimab
Sotrovimab given by intramuscular injection	500 mg IM
Experimental: Sotrovimab 250 mg IM	Sotrovimab
Sotrovimab given by intramuscular injection	250 mg IM

Outcome Measures

Primary Outcome Measure:

- [1143] 1. Progression of COVID-19
 [1144] [Time Frame: Up to Day 29]

Secondary Outcome Measure:

- [1145] 2. Occurrence of adverse events (AEs)
 [1146] [Time Frame: Up to 24 weeks]
 [1147] 3. Occurrence of serious adverse events (SAEs)
 [1148] [Time Frame: Up to 24 weeks]
 [1149] 4. Occurrence of adverse events of special interest (AESI)
 [1150] [Time Frame: Up to 24 weeks]
 [1151] 5. Incidence and titers (if applicable) of serum anti-drug antibody (ADA) to sotrovimab
 [1152] [Time Frame: Up to 24 weeks]
 [1153] 6. Mean area under the curve of SARS-CoV-2 viral load in nasal secretions as measured by qRT-PCR
 [1154] [Time Frame: Up to Day 8]
 [1155] 7. Change from baseline in viral load by qRT-PCR
 [1156] [Time Frame: Up to Day 8]
 [1157] 8. Proportion of participants with a persistently high SARS-CoV-2 viral load at Day 8 by qRT-PCR
 [1158] [Time Frame: Up to Day 8]
 [1159] 9. Development of severe and/or critical respiratory COVID-19
 [1160] [Time Frame: Up to Day 29]
 [1161] 10. IV and IM sotrovimab pharmacokinetics (PK) in serum
 [1162] [Time Frame: Up to Week 24]

Eligibility

- [1163] Minimum Age: 12 Years
 [1164] Maximum Age:
 [1165] Sex: All
 [1166] Gender Based: No
 [1167] Accepts Healthy Volunteers: No
 [1168] Criteria: Inclusion Criteria:
 [1169] Participant must be aged 12 years or older at time of consent AND at high risk of progression of COVID-19 or ≥ 65 years old
 [1170] Participants must have a positive SARS-CoV-2 test result and oxygen saturation $\geq 94\%$ on room air and have COVID-19 symptoms and be less than or equal to 7 days from onset of symptoms

Exclusion Criteria:

- [1172] Currently hospitalized or judged by the investigator as likely to require hospitalization in the next 24 hours
 [1173] Symptoms consistent with severe COVID-19
 [1174] Participants who, in the judgement of the investigator are likely to die in the next 7 days
 [1175] Known hypersensitivity to any constituent present in the investigational product

Example 46

Phase II Study of a Second Generation Sotrovimab Material in Non-Hospitalized Participants with Mild-to-Moderate Coronavirus Disease 2019 (COVID-19)

[1176] Sotrovimab drug material used in the studies described in Examples 39-40 was produced using a non-clonal pool of stably transfected cells. This is referred to as “Gen1” drug material. “Gen2” drug material is made using a clonal master cell bank derived from the original pool of transfectants. A multicenter, randomized, double-blind, parallel group phase II study is performed to evaluate safety, tolerability and pharmacokinetics of Gen2 drug materials in non-hospitalized participants with mild to moderate COVID-19.

[1177] The primary objective is to evaluate safety and tolerability of Gen2 and Gen1 sotrovimab drug material. Endpoints are: occurrence of adverse events (AEs) through Day 29; occurrence of serious adverse events (SAEs) through Day 29; occurrence of adverse events of special interest (AESIs) through Day 29; occurrence of clinically significant abnormalities on 12-lead electrocardiogram (ECG) readings through Day 29; and occurrence of disease progression events (not classified as AEs) through Day 29.

[1178] Secondary objectives are:

[1179] (1) To assess the pharmacokinetics (PK) of sotrovimab Gen2 and Gen1 in serum

[1180] Endpoints: C_{max} , C_{last} , T_{max} , T_{last} , AUC_{D0-28} , AUC_{inf} , AUC_{last} , % AUC_{exp} , $t_{1/2}$, λ_z , V_z , V_{ss} , CL;

[1181] (2) To evaluate safety and tolerability profile of sotrovimab Gen2 and Gen1

[1182] Endpoints: occurrence of SAEs through Week 24; occurrence of AESIs through Week 24; occurrence of clinically significant abnormalities on 12-lead ECG readings through Week 24; occurrence of disease progression events (not classified as AEs) through Week 24.

[1183] Exploratory endpoints are:

[1184] (1) To assess potential immunogenicity of sotrovimab Gen2 and Gen1

[1185] Endpoint: Incidence and titers (if applicable) of serum antidrug antibodies (ADA) to sotrovimab

[1186] (2) To characterize the effect of sotrovimab Gen2 and Gen1 on the viral shedding profile in upper respiratory samples.

[1187] Endpoint: Change from baseline in viral load at all visits through Day 29 as measured by quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) from saliva samples.

[1188] This study is a randomized, double-blind, multicenter, parallel group phase II trial of sotrovimab, a monoclonal antibody (mAb) against SARS-CoV-2 for the prevention of progression of mild to moderate COVID-19 in non-hospitalized patients. Participants with early mild to moderate COVID-19 are randomized 3:1 to receive a single, 500 mg intravenous infusion of either Gen2 or Gen1 study material. Safety, tolerability and PK are evaluated.

[1189] Screening assessments are performed within 24 hours before the start of infusion. Eligible participants are treated in a blinded manner with a single IV dose on Day 1 and followed up to 24 weeks. Participants are monitored for approximately 9 hours on Day 1 for safety assessments and intensive PK sampling.

[1190] The study includes nonhospitalized patients with mild to moderate SARS-CoV-2 infection as confirmed by local laboratory tests and/or point of care tests. A single dose level of Gen1 or equal volume Gen2 material is studied and delivered via IV infusion. Participants receive the infusion in a clinic/study unit where they are monitored closely for adverse events in the post-infusion period. Subsequent visits for study activities and clinical monitoring are conducted via clinic or home nursing visits (except for Week 16). A double-blind design is a standard methodology for randomized, controlled studies to minimize bias. A Gen1 study arm is included to maintain blinding of Gen1 versus Gen2 sotrovimab study material receipt during the conduct of the study. This blinding is critical for minimizing bias that may occur during study assessments, including during evaluation of AEs and disease-related safety outcomes.

[1191] Blinded safety data are reviewed regularly by the JSRT through Week 24. There is no placebo in this study because the primary aim is to evaluate safety and tolerability of Gen2 material. All participants receive standard of care for COVID-19 disease during this study, including admission to a hospital if deemed necessary by the responsible investigator.

[1192] Analytical comparability studies support the use of Gen2 in clinical studies.

Example 47

ACE2-Independent Mechanism of SARS-CoV2 Neutralization by S309 Antibody

[1193] In the following experiments, S309 antibody (VH of SEQ ID NO.: 105, VL of SEQ ID NO.: 168) was expressed as recombinant IgG1 with M428L and N434S Fc mutations. The effect of ACE2 overexpression on S309 antibody neutralization of infection was investigated. Vero E6 or Vero E6-TMPRSS2 cells were infected with SARS-CoV-2 (isolate USA-WA1/2020) at MOI 0.01 in the presence of S309 (10 µg/ml). Cells were fixed 24 h post infection, viral nucleocapsid protein was immunostained and quantified. Nucleocapsid staining was effectively absent in antibody-treated cells. S309 had an IC₅₀ (ng/ml) in Vero E6 cells of 65 and in Vero E6-TMPRSS2 of 91 (data not shown).

[1194] A panel of 7 cell lines (HeLa, 293T (wt), Vero E6, Huh7, 293T ACE2, MRC 5-ACE2-TMPRSS2, A549-ACE2-TMPRSS2 clone 5, A549-ACE2-TMPRSS2 clone 10) were infected with SARS-CoV-2-Nluc or VSV pseudotyped with the SARS-CoV-2 spike protein in the presence of S309. Luciferase signal was quantified 24 h post infection. S309 maximum neutralization values were as shown in Table 16.

TABLE 16

Cell Type	Maximum Neutralization Values of S309	
	Virus/Pseudotype	
	SARS-CoV-2-Nluc	VSV Pseudotype
Vero E6	>99%	>99%
Vero E6-TMPRSS2	>99%	96%
Huh7	98%	78%
293T ACE2	26%	34%

TABLE 16-continued

Cell Type	Maximum Neutralization Values of S309	
	Virus/Pseudotype	
	SARS-CoV-2-Nluc	VSV Pseudotype
MRC5-ACE2-TMPRSS2	87%	45%
A549-ACE2-TMPRSS2 clone 5	89%	65%
A549-ACE2-TMPRSS2 clone 10	81%	42%

[1195] Binding of purified, fluorescently-labeled SARS-CoV-2 spike protein binding to these cell lines was quantified by flow cytometry. HeLa and 239T WT cells had the lowest MFIs, followed by Huh7 and VeroE6 cells. 293T ACE2 cells (highest), MRC 5-ACE2-TMPRSS2 (third-highest), A549-ACE2-TMPRSS2 clone 5 (fourth-highest), and A549-ACE2-TMPRSS2 clone 10 (second-highest) had higher MFIs. Correlation analysis between spike binding maximum neutralization potential of S309 was determined; S309 Spearman correlation values were: $r=-0.94$ for both viral models. $p=0.017$.

[1196] To further characterize SARS-CoV-2-susceptible cell lines, the seven cell lines described above were incubated with purified, fluorescently-labeled SARS-CoV-2 spike protein or RBD protein and protein binding was quantified by flow cytometry. In descending order of MFI, the cell lines were: A549-ACE2-TMPRSS2 clone 10; 293T ACE2; MRC 5-ACE2-TMPRSS2; A549-ACE2-TMPRSS2 clone 5; Vero E6; Huh7; 293T (wt); and HeLa.

[1197] Selected lectins and published receptor candidates were screened using HEK293T cells infected with SARS-CoV-2 VSV pseudoviruses. ACE2, DC-SIGN, L-SIGN, and SIGLEC-1 gave the highest signals. ACE2 provided a signal of approximately 10^5 relative luminescence units (RLUs), and DC-SIGN, SIGLEC-1, and L-SIGN had signals of approximately 10^4 RLUs. All other lectins/candidates tested gave signals of approximately 10^2 - 10^3 RLUs.

[1198] HEK 293T, HeLa and MRC5 cells were transiently transduced to overexpress DC-SIGN, L-SIGN, SIGLEC1 or ACE2 and infected with SARS-CoV-2 VSV pseudoviruses. Uninfected cells and untransduced cells were included as controls. In HEK293T cells, ACE2, DC-SIGN, SIGLEC-1, and L-SIGN all provided substantial increases in infection. In HeLa and MRC5 cells, only ACE2 increased infection.

[1199] Stable HEK293T cell lines overexpressing DC-SIGN, L-SIGN, SIGLEC-1 or ACE2 were infected with authentic SARS-CoV-2 (MOI 0.1), fixed and immunostained at 24 hours for the SARS-CoV-2 nucleoprotein. Wild-type cells (infected and uninfected) were used as controls. Increased staining was observed in cells overexpressing DC-SIGN, L-SIGN, or SIGLEC-1, and staining was significantly increased in cells overexpressing ACE2.

[1200] Stable cell lines were infected with SARS-CoV-2-Nluc and luciferase levels were quantified at 24 hours. In ascending order of RLUs: uninfected (approx. 10^2 - 10^3 RLUs); parental 293T (approx. 10^4 RLUs); DC-SIGN (approx. 10^5 RLUs); L-SIGN (approx. 10^5 RLUs); SIGLEC-1 (approx. 10^5 - 10^6 RLUs); ACE2 ($>10^7$ RLUs).

[1201] Stable cell lines were incubated with different concentration of anti-SIGLEC1 mAb (clone 7-239) and infected with SARS-CoV-2-Nluc. Infection as a percentage of untreated cells remained near to exceeded 100% in 293T cells expressing DC-SIGN, L-SIGN, or ACE2, but dropped

to below 50% (0.2 µg/mL anti-SIGLEC) to close to 0 (1 µg/mL or 5 µg/mL anti-SIGLEC) in 293T cells expressing SIGLEC-1.

[1202] Single cell expression levels of selected potential SARS-CoV-2 (co) receptor candidates were determined in different lung cell types derived from the Human Lung Cell Atlas (nature.com/articles/s41586-020-2922-4). DC-SIGN, L-SIGN and SIGLEC-1 are expressed in a variety of cell types in the lung at levels similar to or even higher than ACE2.

[1203] Binding of antibodies targeting DC-/L-SIGN, DC-SIGN, SIGLEC1 or ACE2 on HEK293T cells stably over-expressing the respective attachment receptor was analyzed by flow cytometry and immunofluorescence analysis. HEK 293T cells over-expressing the respective attachment receptors were infected with VSV pseudotyped with SARS-CoV-2 wildtype spike or spike bearing mutations of the B1.1.7 lineage. Luminescence was analyzed one day post infection. Infection was increased in cells expressing the attachment receptors. Infection by VSV pseudotyped with either spike was similar for each test group. Cells expressing ACE2 gave the highest luminescence signal.

[1204] Vero E6 cells, *in vitro* differentiated moDCs or PBMCs were infected with SARS-CoV-2 at MOI 0.01. At 24 h post infection, cells were fixed, immunostained for viral nucleocapsid protein and infected cells were quantified. Only VeroE6 cells showed infection (approximately 7% of cells). Supernatant of the infected cells was taken at 24, 48 and 72 h and infectious viral titer was quantified by FFU assay on Vero E6 cells.

[1205] Major cell types with detectable SARS-CoV-2 genome in bronchoalveolar lavage fluid (BALF) and sputum of severe COVID-19 patients were assessed. A t-SNE plot was generated, and the count of each SARS-CoV-2+ cell type was determined (total n=3,085 cells from 8 subjects in Ren et al. *Cell* 2021). Cell types were T, NK, plasma, neutrophil, macrophage, ciliated, squamous, and secretory. Expression of ACE2, DC-SIGN, L-SIGN, SIGLEC-1, and combinations of these was assessed for each cell type.

[1206] ACE2, DC-SIGN (CD209), L-SIGN (CLEC4M), SIGLEC1 transcript counts were correlated with SARS-CoV-2 RNA counts in macrophages and in secretory cells. Correlation was based on counts (before log transformation), from Ren et al. *Cell* 2021.

[1207] Cell lines were generated to overexpress DC-SIGN, L-SIGN or ACE2 by transducing HEK293T cells with lentivirus encoding the transgene, and immunofluorescence assays were performed to assess transgene expression.

[1208] Expression of DC-SIGN or L-SIGN increased pseudovirus infection levels by over 10-fold compared to infection of WT HEK293T cells, and expression of ACE2 increased pseudovirus infection levels by over 100-fold compared to infection of WT HEK293T cells.

[1209] Neutralizing activity of exemplary mAb S309 against the VSV pseudovirus was assessed in the engineered HEK293T cells. S309 fully neutralized infection via DC-SIGN and L-SIGN, and to a lesser extent, ACE2.

[1210] The ability of live SARS-CoV-2 with luciferase reporter to infect the HEK293T cells was examined using a luminescence assay. Expression of DC-SIGN or L-SIGN increased live virus infection levels by over 3-fold compared to infection of WT HEK293T cells, and expression of ACE2 increased live virus infection levels by over 100-fold compared to infection of WT HEK293T cells.

[1211] Neutralizing activity of mAb S309 against the VSV pseudovirus was assessed in the engineered HEK293T cells. S309 fully neutralized infection via DC-SIGN and L-SIGN, and neutralized infection via ACE2 to a lesser extent.

[1212] Experiments were performed to investigate whether S309 antibody can neutralize entry of SARS-CoV-2 via SIGLEC-1. Briefly, stable cell HEK293T lines were generated as described above to overexpress DC-SIGN/L-SIGN, DC-SIGN, SIGLEC-1, or ACE2. Expression of DC-SIGN, L-SIGN, or SIGLEC increased live virus infection levels by over 10-fold compared to infection of WT HEK293T cells, and expression of ACE2 increased pseudovirus infection levels by over 100-fold compared to infection of WT HEK293T cells. S309 fully neutralized infection via DC-SIGN, L-SIGN, and SIGLEC-1.

[1213] Expression of DC-SIGN (CD209) and other cell surface receptor proteins including SIGLEC-1 and other SIGLECs was determined on a variety of cell types.

[1214] Further experiments were performed to investigate the function(s) of DC-SIGN, L-SIGN, and SIGLEC-1 in SARS-CoV-2 infection. In one set of experiments, HEK293T cells stably expressing DC-SIGN, L-SIGN, SIGLEC-1 or ACE2 were infected with live SARS-CoV-2 Nluc at three different multiplicities of infection (MOI): 0.01, 0.1, and 1). Infection was determined using relative luminescence units and compared to infection in HEK293T cells (parental). At the lowest MOI tested, an increase of infection in cells expressing DC-SIGN, L-SIGN, or SIGLEC was observed. At the highest MOI tested, infection was not further increased versus parental by expression of DC-SIGN, L-SIGN, or SIGLEC. These data indicate that the parental 293T cells are susceptible to infection by SARS-CoV-2 and L-SIGN, DC-SIGN, and SIGLEC-1 enhance infection levels but do not function as primary receptors for infection.

[1215] In another set of experiments, 293T cells, HeLa cells, and MRC5 cells were transiently transduced with lentivirus encoding DC-SIGN, L-SIGN, SIGLEC-1 or ACE2 and infected with VSV pseudovirus three days after transduction. While the 293T cells showed a low level of susceptibility (compare uninfected with untransduced), HeLa and MRC5 cells were completely refractory to the virus. The low level of infection in 293T cells can be increased by expression of L-SIGN, DC-SIGN, or SIGLEC-1, consistent with a role for these proteins as attachment factors. The HeLa and MRC5 cells remained refractory to infection even after expression of L-SIGN, DC-SIGN, or SIGLEC-1, and only become susceptible after expression of ACE2. These data indicate that L-SIGN, DC-SIGN, and SIGLEC-1 are not primary receptors for SARS-CoV-2.

Example 48

In Vivo Efficacy of S309 Antibody in an Animal Model of Infection

[1216] The efficacy of S309 was investigated in Syrian hamsters. This animal model represents to-date the most relevant model of SARS-CoV-2 infection that did not require *in vivo* over-expression of ACE2 to support productive infection and disease. Prophylactic administration of S309 induced dose-dependent protection against SARS-CoV-2 infection and tissue damage in hamsters, as demonstrated by the viral RNA levels, the viral load as well as the histopathological score in the lungs. These data indicate that

poor and incomplete neutralization of entry by S309 in vitro when using ACE2 over-expressing cells did not compromise in vivo efficacy of non-RBM mAbs.

[1217] S309 carrying the N297A mutation has a reduced capacity to trigger effector functions as a consequence of

mined by sequence reads. Antibodies REGN10933 and REGN10987 (Hansen et al., *Science* 369 (6506): 1010-1014; eabd0827-0810 (2020) and PDB 6XDG (rcsb.org/structure/6XDG) were included for comparison. Results are summarized in Table 17.

TABLE 17

Summary of Neutralization by Antibodies Against SARS CoV-2 Variants					
Variant Mutation	S309	N55Q	MLNS	REGN10933	REGN10987
N501Y (UK, South African, and Brazilian mutant)	Y		Y	Y	
S477N	Y		Y	Y	
N439K (Scottish mutant)	Y		Y	N	
L452R (Californian mutant)	Y		P	P	
E484K (South African and Brazilian mutant)	Y		N	Y	
Y453F (mink mutant)	Y		N	N (4x decrease)	
A520S	Y		Y	Y	
K417N (South African mutant)	Y		N	Y	(K417N/E/V)
(K417N/V)					
S494P	Y		N	P	
S477R	P		?	P	
V367F	Y		Y	Y	
P384L	Y		P	P	
A522S	Y		P	P	
A522V	Y		P	P	
V382L	Y		P	P	
N501T	Y		P	P	
P330S	Y		P	P	
T478I	Y		?	P	
S477I	Y		?	P	
P479S	Y		P	P	

Y = less than three-fold decrease in neutralizing of live virus or pseudovirus

N = greater than three-fold decrease in neutralizing of live virus or pseudovirus

P = neutralization by antibody is predicted due to variant amino acid being outside of epitope

? = unknown.

diminished engagement to Fc γ receptors. This was further confirmed by the reduced binding of S309-N297A variant to hamster monocytes in the spleen. The in vivo efficacy measured with the N297A mAb is similar or just slightly inferior to the wt S309, suggesting that neutralizing capacity of the mAb is prevailing upon its effector function capacity in these conditions. The serum concentration of S309 required to reduce the viral RNA in the lung by 90% was 9 μ g/ml.

Example 49

Antibody Activity Against SARS-CoV-2 Variants

[1218] A number of SARS-CoV-2 variants have emerged, with increasing numbers of infection by variants reported in late 2020. The Receptor Binding Motif (RBM) appears to be particularly variable to mutation. Notable emerging variants have been observed in Scotland, the UK, South Africa, California, Columbus, and in minks in Denmark, and some mutations have been reported to confer escape from antibodies or serum neutralization. Experiments were performed to assess the ability of S309 antibodies to neutralize variants. S309 N55Q MLNS (VH: SEQ ID NO.: 113; VL: SEQ ID NO.: 168; with M428L and N434S Fc mutations) was tested against SARS-CoV-2 bearing a panel of the 20 most-frequent SARS-CoV-2 RBD variant mutations, as deter-

[1219] Total counts of SARS-CoV-2 sequenced mutants known to escape the antibodies (as of Jan. 29, 2021) were: S309 N55Q MLNS=29; REGN10987=10,425; REGN10933=3,621.

[1220] Binding of S309 antibodies to SARS-CoV-2 variant RBDs was assessed by BLI. S309 (VH: SEQ ID NO.: 105; VL: SEQ ID NO.: 168) with wild-type Fc and S309 N55Q (VH: SEQ ID NO.: 113; VL: SEQ ID NO.: 168) bearing MLNS or MLNS+GAALIE Fc mutations were assessed. REGN10987 and REGN10933 were included as comparators. Briefly, antibodies were diluted in kinetics buffer at 3 μ g/ml and loaded on Protein-A sensors for 75 seconds. After a short equilibration step in kinetics buffer, loaded sensors were moved in wells containing the RBD variants at 5 μ g/ml in kinetics buffer and association was recorded during 3 minutes. Dissociation of the complex was performed in kinetics buffer for 3 minutes. Data are shown in FIGS. 71A-71B; “WT”=Wuhan-Hu-1 with D614G; “Triple Mutant” in lower row=Wuhan-Hu-1 with D614G and added South Africa variant B.1.351 RBD mutations K417N, E484K, and N501Y. Other mutations present in the South Africa variant B.1.351 were not present in the “SA” RBD tested.

[1221] Neutralization of S309 antibodies against SARS-CoV-2 variants was assessed using MLV pseudovirus and Vero-E6 target cells expressing TMPRSS2. S309 (VH: SEQ ID NO.: 105; VL: SEQ ID NO.: 168) with wild-type Fc and S309 N55Q (VH: SEQ ID NO.: 113; VL: SEQ ID NO.: 168) bearing MLNS or MLNS+GAALIE Fc mutations were

assessed. REGN10987, REGN10933, and the combination of REGN10987+REGN10933, were also assessed. S309 antibodies neutralized the SARS-CoV-2 variants.

[1222] The various embodiments described above can be combined to provide further embodiments. All of the U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications referred to in this specification and/or listed in the Application Data Sheet, including U.S. Patent Application No. 63/038,738, filed Jun. 12, 2020, U.S. Patent Application No. 63/066,966, filed Aug. 18, 2020, U.S. Patent Application No. 63/141,430, filed Jan. 25, 2021, U.S. Patent Application No. 63/159,404, filed Mar. 10, 2021, U.S. Patent Application No. 63/186,055, filed May 7, 2021, and

U.S. Patent Application No. 63/196,089, filed Jun. 2, 2021, are incorporated herein by reference, in their entirety. Aspects of the embodiments can be modified, if necessary to employ concepts of the various patents, applications and publications to provide yet further embodiments.

[1223] These and other changes can be made to the embodiments in light of the above-detailed description. In general, in the following claims, the terms used should not be construed to limit the claims to the specific embodiments disclosed in the specification and the claims, but should be construed to include all possible embodiments along with the full scope of equivalents to which such claims are entitled. Accordingly, the claims are not limited by the disclosure.

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
 20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
 35 40 45

Gly Trp Val Asn Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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Gly Tyr Thr Phe Thr Asp Tyr Tyr
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Gln Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Pro Ser Ser
20 25 30

Cys Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Gly Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

Pro Leu Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 6
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Gln Ser Val Pro Ser Ser Cys
1 5

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1           5           10           15
```

```
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20          25          30
```

```
Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35          40          45
```

```
Gly Trp Val Gln Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50          55          60
```

```
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80
```

```
Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85          90          95
```

```
Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Asp Asn
100         105         110
```

```
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115         120
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```
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1           5           10           15
```

```
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20          25          30
```

```
Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35          40          45
```

```
Gly Trp Val Asn Ala Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50          55          60
```

```
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80
```

```
Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85          90          95
```

```
Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Asp Asn
100         105         110
```

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Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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<400> SEQUENCE: 11

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Trp Val Asn Ser Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 12
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v1.4 mAb VH

<400> SEQUENCE: 12

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1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Trp Val Asn Pro Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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<212> TYPE: PRT

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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v1.5 mAb VH

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
 20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
 35 40 45

Gly Trp Val Asn Gln Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln	Gly	Arg	Val	Thr	Met	Thr	Arg	Asp	Thr	Ser	Ile	Ser	Thr	Ala	Tyr
65					70					75					80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
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<210> SEQ ID NO 14
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v1.6 mAb VH

<400> SEQUENCE: 14

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
 20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Trp Val Leu Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln	Gly	Arg	Val	Thr	Met	Thr	Arg	Asp	Thr	Ser	Ile	Ser	Thr	Ala	Tyr
65					70					75					80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met
100 105

<210> SEQ ID NO 1

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<212> TYPE: PRT

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Trp Val Thr Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 16

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v1.1 mAb
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<400> SEQUENCE: 16

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<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v1.2 mAb
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<220> FEATURE:

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CDRH2

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CDRH2

<400> SEQUENCE: 20

Val Asn Gln Tyr Ser Gly Ala Thr
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<210> SEQ ID NO 21
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CDRH2

<400> SEQUENCE: 21

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<400> SEQUENCE: 22

Val Thr Gly Tyr Ser Gly Ala Thr
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<210> SEQ ID NO 23
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v1.8 mAb VH

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1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Trp Val Asn Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Phe Ala Met Tyr Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

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115

120

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Trp Val Asn Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Tyr Ala Met Tyr Phe Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v1.8 mAb
CDRH3

<400> SEQUENCE: 25

Ala Arg Asp Arg Pro Ser His Glu Phe Ala Met Tyr Phe Phe Asp Asn
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v1.9 mAb
CDRH3

<400> SEQUENCE: 26

Ala Arg Asp Arg Pro Ser His Glu Tyr Ala Met Tyr Phe Phe Asp Asn
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<210> SEQ ID NO 27
<211> LENGTH: 123
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v2 mAb VH

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Phe Val Asn Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
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<210> SEQ ID NO 28
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1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Phe Val Gln Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v2.2 mAb VH

<400> SEQUENCE: 29

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Phe Val Asn Ala Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr

-continued

50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Phe Asp Asn
100 105 110Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 30

<211> LENGTH: 123

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v2.3 mAb VH

<400> SEQUENCE: 30

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45Gly Phe Val Asn Ser Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Phe Asp Asn
100 105 110Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 31

<211> LENGTH: 123

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v2.4 mAb VH

<400> SEQUENCE: 31

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45Gly Phe Val Asn Pro Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

-continued

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 32
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v2.5 mAb VH

<400> SEQUENCE: 32

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Phe Val Asn Gln Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 33
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v2.6 mAb VH

<400> SEQUENCE: 33

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Phe Val Leu Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 34

-continued

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<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v2.7 mAb VH

<400> SEQUENCE: 34

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Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1															
															15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr															
															30
Tyr	Ile	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Pro	Glu	Trp	Leu
35															45
Gly	Phe	Val	Thr	Gly	Tyr	Ser	Gly	Ala	Thr	Arg	Tyr	Ala	Gln	Lys	Tyr
50															60
Gln	Gly	Arg	Val	Thr	Met	Thr	Arg	Asp	Thr	Ser	Ile	Ser	Thr	Ala	Tyr
65															80
Met	Gln	Leu	Ser	Arg	Leu	Arg	Pro	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
85															95
Ala	Arg	Asp	Arg	Pro	Ser	His	Glu	Trp	Ala	Met	Tyr	Phe	Phe	Asp	Asn
100															110
Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser					
115															120

```

<210> SEQ ID NO 35
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v2.8 mAb VH

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<400> SEQUENCE: 35

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Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1															
															15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr															
															30
Tyr	Ile	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Pro	Glu	Trp	Leu
35															45
Gly	Phe	Val	Asn	Gly	Tyr	Ser	Gly	Ala	Thr	Arg	Tyr	Ala	Gln	Lys	Tyr
50															60
Gln	Gly	Arg	Val	Thr	Met	Thr	Arg	Asp	Thr	Ser	Ile	Ser	Thr	Ala	Tyr
65															80
Met	Gln	Leu	Ser	Arg	Leu	Arg	Pro	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
85															95
Ala	Arg	Asp	Arg	Pro	Ser	His	Glu	Phe	Ala	Met	Tyr	Phe	Phe	Asp	Asn
100															110
Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser					
115															120

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<210> SEQ ID NO 36
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v2.9 mAb VH

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<400> SEQUENCE: 36

-continued

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Phe Val Asn Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Tyr Ala Met Tyr Phe Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 37
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v3 mAb VH

<400> SEQUENCE: 37

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Tyr Val Asn Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 38
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v3.1 mAb VH

<400> SEQUENCE: 38

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

-continued

Gly Tyr Val Gln Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 39

<211> LENGTH: 123

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v3.2 mAb VH

<400> SEQUENCE: 39

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Tyr Val Asn Ala Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 40

<211> LENGTH: 123

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v3.3 mAb VH

<400> SEQUENCE: 40

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Tyr Val Asn Ser Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys

-continued

85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 41
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v3.4 mAb VH

<400> SEQUENCE: 41

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Tyr Val Asn Pro Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 42
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v3.5 mAb VH

<400> SEQUENCE: 42

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Tyr Val Asn Gln Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

-continued

<210> SEQ ID NO 43
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v3.6 mAb VH

<400> SEQUENCE: 43

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Tyr Val Leu Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 44
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v3.7 mAb VH

<400> SEQUENCE: 44

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35 40 45

Gly Tyr Val Thr Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Pro Ser His Glu Trp Ala Met Tyr Phe Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 45
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v3.8 mAb VH

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<400> SEQUENCE: 45

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5          10          15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20          25          30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35          40          45

Gly Tyr Val Asn Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50          55          60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85          90          95

Ala Arg Asp Arg Pro Ser His Glu Phe Ala Met Tyr Phe Phe Asp Asn
100         105         110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115         120

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<210> SEQ ID NO 46

<211> LENGTH: 123

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v3.9 mAb VH

<400> SEQUENCE: 46

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5          10          15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20          25          30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu
35          40          45

Gly Tyr Val Asn Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr
50          55          60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65          70          75          80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys
85          90          95

Ala Arg Asp Arg Pro Ser His Glu Tyr Ala Met Tyr Phe Phe Asp Asn
100         105         110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115         120

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<210> SEQ ID NO 47

<211> LENGTH: 109

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v10 mAb VL
(VK)

<400> SEQUENCE: 47

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Gln Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1           5          10          15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Pro Ser Ser
20          25          30

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-continued

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Gly Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

Pro Leu Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 48

<211> LENGTH: 109

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v11 mAb VL
(VK)

<400> SEQUENCE: 48

Gln Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Pro Ser Ser
20 25 30

Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Gly Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

Pro Leu Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 49

<211> LENGTH: 109

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v12 mAb VL
(VK)

<400> SEQUENCE: 49

Gln Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Pro Ser Ser
20 25 30

Thr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Gly Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

-continued

Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 50
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v13 mAb VL
(VK)

<400> SEQUENCE: 50

Gln Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Pro Ser Ser
20 25 30

Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Gly Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

Pro Leu Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 51
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v10 mAb
CDRL1

<400> SEQUENCE: 51

Gln Ser Val Pro Ser Ser Tyr
1 5

<210> SEQ ID NO 52
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v11 mAb
CDRL1

<400> SEQUENCE: 52

Gln Ser Val Pro Ser Ser Ser
1 5

<210> SEQ ID NO 53
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v12 mAb
CDRL1

<400> SEQUENCE: 53

Gln Ser Val Pro Ser Ser Thr

-continued

1 5

<210> SEQ ID NO 54
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v13 mAb CDR1

<400> SEQUENCE: 54

Gln Ser Val Pro Ser Ser Ala
1 5

<210> SEQ ID NO 55
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S302 mAb VH

<400> SEQUENCE: 55

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Asp Ile Ser Ser Gly Trp Asp Arg Val Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 56
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S302 mAb CDRH1

<400> SEQUENCE: 56

Gly Phe Thr Phe Ser Ser Tyr Gly
1 5

<210> SEQ ID NO 57
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S302 mAb CDRH2

<400> SEQUENCE: 57

Ile Ser Tyr Asp Gly Ser Asn Lys
1 5

-continued

<210> SEQ ID NO 58
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S302 mAb CDRH3

<400> SEQUENCE: 58

Ala Lys Asp Ile Ser Ser Gly Trp Asp Arg Val Phe Asp Tyr
1 5 10

<210> SEQ ID NO 59
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S302 mAb VL (VK)

<400> SEQUENCE: 59

Glu Ile Leu Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Thr Ser Gln Ser Val Gly Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Ala Ala Ser Ser Arg Ala Ile Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 60
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S302 mAb CDRL1

<400> SEQUENCE: 60

Gln Ser Val Gly Ser Ser Tyr
1 5

<210> SEQ ID NO 61
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S302 mAb CDRL2

<400> SEQUENCE: 61

Ala Ala Ser

1

<210> SEQ ID NO 62
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S302 mAb CDRL3

<400> SEQUENCE: 62

Gln Gln Tyr Gly Ser Ser Pro Trp Thr
1 5

<210> SEQ ID NO 63

<211> LENGTH: 124

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v1 mAb VH

<400> SEQUENCE: 63

Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Leu Thr Tyr
20 25 30

Ser Met Asn Trp Val Arg Gln Thr Pro Gly Lys Arg Leu Gln Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ala Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Thr Val Thr Ala Asp Asp Thr Ala Ile Tyr Phe Cys
85 90 95

Ala Arg Glu Arg Asp Asp Ile Phe Pro Met Gly Leu Asn Ala Phe Asp
100 105 110

Ile Trp Gly Gln Gly Ala Met Val Ile Val Ser Ser
115 120

<210> SEQ ID NO 64

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v1 mAb CDRH1

<400> SEQUENCE: 64

Gly Phe Thr Phe Leu Thr Tyr Ser
1 5

<210> SEQ ID NO 65

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v1 mAb CDRH2

<400> SEQUENCE: 65

Ile Ser Gly Ser Gly Gly Ala Thr
1 5

<210> SEQ ID NO 66

<211> LENGTH: 17

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v1 mAb CDRH3

<400> SEQUENCE: 66

-continued

Ala Arg Glu Arg Asp Asp Ile Phe Pro Met Gly Leu Asn Ala Phe Asp
1 5 10 15

Ile

<210> SEQ ID NO 67

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v1 mAb VL (VK)

<400> SEQUENCE: 67

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Asn Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Thr Tyr Ser Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 68

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v1 mAb CDRL1

<400> SEQUENCE: 68

Gln Ser Ile Ser Asn Trp
1 5

<210> SEQ ID NO 69

<211> LENGTH: 3

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v1 mAb CDRL2

<400> SEQUENCE: 69

Lys Ala Ser
1

<210> SEQ ID NO 70

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v1 mAb CDRL3

<400> SEQUENCE: 70

Gln Gln Tyr Asp Thr Tyr Ser Trp Thr
1 5

-continued

<210> SEQ ID NO 71
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v2 mAb VL
(VK)

<400> SEQUENCE: 71

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Asn Phe
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Asp Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Thr Tyr Ser Trp
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 72
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v3 mAb VL
(VK)

<400> SEQUENCE: 72

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Asn Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Asp Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Thr Tyr Ser Trp
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 73
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v2 mAb CDRL1

<400> SEQUENCE: 73

Gln Ser Ile Ser Asn Phe

-continued

1 5

<210> SEQ ID NO 74
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v3 mAb CDRL1
<400> SEQUENCE: 74

Gln Ser Ile Ser Asn Tyr
1 5

<210> SEQ ID NO 75
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v4 mAb VL
(VK)

<400> SEQUENCE: 75

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Asn Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Thr Tyr Ser Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 76
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v5 mAb VL
(VK)

<400> SEQUENCE: 76

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Asn Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Thr Tyr Ser Tyr
85 90 95

-continued

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 77
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v4 mAb CDRL3

<400> SEQUENCE: 77

Gln Gln Tyr Asp Thr Tyr Ser Phe Thr
1 5

<210> SEQ ID NO 78
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S303-v5 mAb CDRL3

<400> SEQUENCE: 78

Gln Gln Tyr Asp Thr Tyr Ser Tyr Thr
1 5

<210> SEQ ID NO 79
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S304 mAb VH

<400> SEQUENCE: 79

Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Asp Met His Trp Val Arg Gln Thr Thr Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Thr Ile Gly Thr Ala Gly Asp Thr Tyr Tyr Pro Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Glu Asp Ala Lys Asn Ser Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Gly Asp Ser Ser Gly Tyr Tyr Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Leu Thr Val Ser Ser
115 120

<210> SEQ ID NO 80
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S304 mAb CDRH1

<400> SEQUENCE: 80

Gly Phe Thr Phe Ser Ser Tyr Asp
1 5

-continued

<210> SEQ ID NO 81
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S304 mAb CDRH2

<400> SEQUENCE: 81

Ile Gly Thr Ala Gly Asp Thr
1 5

<210> SEQ ID NO 82
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S304 mAb CDRH3

<400> SEQUENCE: 82

Ala Arg Gly Asp Ser Ser Gly Tyr Tyr Tyr Tyr Phe Asp Tyr
1 5 10

<210> SEQ ID NO 83
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S304 mAb VL (VK)

<400> SEQUENCE: 83

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ala Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Ile Tyr Tyr Cys Gln Gln Ser Tyr Val Ser Pro Thr
85 90 95

Tyr Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> SEQ ID NO 84
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S304 mAb CDRL1

<400> SEQUENCE: 84

Gln Ser Ile Gly Ser Tyr
1 5

<210> SEQ ID NO 85
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S304 mAb CDRL2

<400> SEQUENCE: 85

Ala Ala Ser
1

<210> SEQ ID NO 86

<211> LENGTH: 10

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S304 mAb CDRL3

<400> SEQUENCE: 86

Gln Gln Ser Tyr Val Ser Pro Thr Tyr Thr
1 5 10

<210> SEQ ID NO 87

<211> LENGTH: 123

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S306 mAb VH

<400> SEQUENCE: 87

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Thr Tyr Thr Phe Thr Ser Phe
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Thr Thr Tyr Ser Gly Asp Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Ser Asp Tyr Phe Asp Ser Ser Gly Tyr Tyr His Ser Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 88

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S306 mAb CDRH1

<400> SEQUENCE: 88

Thr Tyr Thr Phe Thr Ser Phe Gly
1 5

<210> SEQ ID NO 89

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S306 mAb CDRH2

<400> SEQUENCE: 89

-continued

Ile Thr Thr Tyr Ser Gly Asp Thr
1 5

<210> SEQ ID NO 90
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S306 mAb CDRH3
<400> SEQUENCE: 90

Ala Ser Asp Tyr Phe Asp Ser Ser Gly Tyr Tyr His Ser Phe Asp Tyr
1 5 10 15

<210> SEQ ID NO 91
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S306 mAb VL (VK)
<400> SEQUENCE: 91

Glu Ile Val Leu Thr Gln Ser Pro Asp Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Lys Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro
85 90 95

Gly Cys Ser Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 92
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S306 mAb CDRL1
<400> SEQUENCE: 92

Gln Ser Val Ser Ser Tyr
1 5

<210> SEQ ID NO 93
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S306 mAb CDRL2
<400> SEQUENCE: 93

Asp Ala Ser
1

<210> SEQ ID NO 94

-continued

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<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S306 mAb CDRL3

<400> SEQUENCE: 94

Gln Gln Arg Ser Asn Trp Pro Pro Gly Cys Ser
1           5           10

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<210> SEQ ID NO 95
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S308-v1 mAb VH

<400> SEQUENCE: 95

Gln Val Gln Leu Val Glu Ser Gly Gly Val Val Gln Pro Gly Arg
1           5           10           15

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Arg Phe Thr Phe Ser Ser Tyr
20          25          30

```

```

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35          40          45

```

```

Ala Val Ile Trp His Asp Gly Asn Asn Lys His Tyr Gly Asp Ser Val
50          55          60

```

```

Lys Gly Arg Val Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65          70          75          80

```

```

Leu Gln Met Thr Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95

```

```

Ala Arg Ala Val Thr Thr Phe Lys Gly Ser Gly Arg Ala Arg Met Arg
100         105         110

```

```

Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115         120         125

```

```

<210> SEQ ID NO 96
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S308-v1 mAb CDRH1

<400> SEQUENCE: 96

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Arg Phe Thr Phe Ser Ser Tyr Gly
1           5

```

```

<210> SEQ ID NO 97
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S308-v1 mAb CDRH2

<400> SEQUENCE: 97

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```

Ile Trp His Asp Gly Asn Asn Lys
1           5

```

```

<210> SEQ ID NO 98
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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-continued

<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S308-v1 mAb CDRH3

<400> SEQUENCE: 98

Ala Arg Ala Val Thr Thr Phe Lys Gly Ser Gly Arg Ala Arg Met Arg
1 5 10 15
Gly Met Asp Val
20

<210> SEQ ID NO 99

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S308-v1 mAb VL
(VK)

<400> SEQUENCE: 99

Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Asn Thr Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Leu Asp Thr Tyr Pro Phe
85 90 95

Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> SEQ ID NO 100

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S308-v1 mAb CDRL1

<400> SEQUENCE: 100

Gln Gly Ile Asn Thr Tyr
1 5

<210> SEQ ID NO 101

<211> LENGTH: 3

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S308-v1 mAb CDRL2

<400> SEQUENCE: 101

Ala Ala Ser
1

<210> SEQ ID NO 102

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S308-v1 mAb CDRL3

-continued

<400> SEQUENCE: 102

Gln His Leu Asp Thr Tyr Pro Phe Thr
1 5

<210> SEQ ID NO 103

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S308-v2 mAb VH

<400> SEQUENCE: 103

Gln Val Gln Leu Val Glu Ser Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15Ser Leu Arg Leu Ser Cys Ala Ala Ser Arg Phe Thr Phe Ser Ser Tyr
20 25 30Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45Ala Val Ile Trp His Asp Gly Asn Asn Lys His Tyr Gly Asp Ser Val
50 55 60Lys Gly Arg Val Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80Leu Gln Met Thr Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95Ala Arg Ala Val Thr Thr Phe Lys Gly Ser Gly Arg Ala Arg Leu Arg
100 105 110Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 104

<211> LENGTH: 20

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S308-v2 mAb CDRH3

<400> SEQUENCE: 104

Ala Arg Ala Val Thr Thr Phe Lys Gly Ser Gly Arg Ala Arg Leu Arg
1 5 10 15Gly Met Asp Val
20

<210> SEQ ID NO 105

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1 mAb VH

<400> SEQUENCE: 105

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe

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50	55	60
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Gln Gly Arg Val Thr Met Thr Asp Thr Ser Thr Thr Thr Gly Tyr	70	75
		80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys	85	90
		95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly	100	105
		110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser	115	120
		125

<210> SEQ ID NO 106

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1 mAb CDRH1

<400> SEQUENCE: 106

Gly Tyr Pro Phe Thr Ser Tyr Gly	1	5
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<210> SEQ ID NO 107

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1 mAb CDRH2

<400> SEQUENCE: 107

Ile Ser Thr Tyr Asn Gly Asn Thr	1	5
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<210> SEQ ID NO 108

<211> LENGTH: 20

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1 mAb CDRH3

<400> SEQUENCE: 108

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly	1	5
		10
		15

Gly Phe Asp Asn

20

<210> SEQ ID NO 109

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1 mAb VL
(VK)

<400> SEQUENCE: 109

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Thr Ser Val Gly	1	5
		10
		15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Asn Asn Tyr	20	25
		30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile	35	40
		45

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Tyr Gly Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Arg Gly
50 55 60

Ser Gly Ser Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Val Ala Ser Tyr Tyr Cys Arg Lys Tyr Asn Ser Ala Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Arg Val Glu Ile Lys
100 105

<210> SEQ ID NO 110

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1 mAb CDRL1

<400> SEQUENCE: 110

Gln Gly Ile Asn Asn Tyr
1 5

<210> SEQ ID NO 111

<211> LENGTH: 3

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1 mAb CDRL2

<400> SEQUENCE: 111

Gly Ala Ser
1

<210> SEQ ID NO 112

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1 mAb CDRL3

<400> SEQUENCE: 112

Arg Lys Tyr Asn Ser Ala Pro Trp Thr
1 5

<210> SEQ ID NO 113

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.1 mAb VH

<400> SEQUENCE: 113

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Thr Tyr Gln Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Gly Tyr
65 70 75 80

-continued

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 114

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE: OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.2 mAb VH

<400> SEQUENCE: 114

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Thr Tyr Asn Ser Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 115

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE: OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.3 mAb VH

<400> SEQUENCE: 115

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Thr Tyr Asn Ala Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

-continued

<210> SEQ ID NO 116
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.4 mAb VH
<400> SEQUENCE: 116

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Thr Tyr Asn Gln Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 117
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.5 mAb VH
<400> SEQUENCE: 117

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Thr Tyr Leu Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 118
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.6 mAb VH

-continued

<400> SEQUENCE: 118

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Thr Tyr Thr Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Gly Tyr
65 70 75 80
Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110
Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 119

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.7 mAb VH

<400> SEQUENCE: 119

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Gly Tyr
65 70 75 80
Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Tyr Thr Arg Gly Ala Phe Phe Gly Glu Ser Leu Ile Gly
100 105 110
Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 120

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.8 mAb VH

<400> SEQUENCE: 120

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

-continued

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Tyr Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 121

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.1 mAb
CDRH2

<400> SEQUENCE: 121

Ile Ser Thr Tyr Gln Gly Asn Thr
1 5

<210> SEQ ID NO 122

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.2 mAb
CDRH2

<400> SEQUENCE: 122

Ile Ser Thr Tyr Asn Ser Asn Thr
1 5

<210> SEQ ID NO 123

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.3 mAb
CDRH2

<400> SEQUENCE: 123

Ile Ser Thr Tyr Asn Ala Asn Thr
1 5

<210> SEQ ID NO 124

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.4 mAb
CDRH2

<400> SEQUENCE: 124

Ile Ser Thr Tyr Asn Gln Asn Thr
1 5

-continued

<210> SEQ ID NO 125
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.5 mAb
CDRH2

<400> SEQUENCE: 125

Ile Ser Thr Tyr Leu Gly Asn Thr
1 5

<210> SEQ ID NO 126
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.6 mAb
CDRH2

<400> SEQUENCE: 126

Ile Ser Thr Tyr Thr Gly Asn Thr
1 5

<210> SEQ ID NO 127
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.7 mAb
CDRH3

<400> SEQUENCE: 127

Ala Arg Asp Tyr Thr Arg Gly Ala Phe Phe Gly Ser Leu Ile Gly
1 5 10 15

Gly Phe Asp Asn
20

<210> SEQ ID NO 128
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.8 mAb
CDRH3

<400> SEQUENCE: 128

Ala Arg Asp Tyr Thr Arg Gly Ala Tyr Phe Gly Glu Ser Leu Ile Gly
1 5 10 15

Gly Phe Asp Asn
20

<210> SEQ ID NO 129
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v2 mAb VH

<400> SEQUENCE: 129

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

-continued

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 130

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v2.1 mAb VH

<400> SEQUENCE: 130

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Ser Thr Tyr Gln Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 131

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v2.2 mAb VH

<400> SEQUENCE: 131

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Ser Thr Tyr Asn Ser Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Gly Tyr

-continued

65	70	75	80
Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys			
85	90	95	
Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly			
100	105	110	
Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser			
115	120	125	

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<210> SEQ ID NO 132
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v2.3 mAb VH

<400> SEQUENCE: 132

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala			
1	5	10	15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr			
20	25	30	

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met			
35	40	45	

Gly Phe Ile Ser Thr Tyr Asn Ala Asn Thr Asn Tyr Ala Gln Lys Phe			
50	55	60	

Gln Gly Arg Val Thr Met Thr Asp Thr Ser Thr Thr Thr Gly Tyr			
65	70	75	80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys			
85	90	95	

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly			
100	105	110	

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser			
115	120	125	

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<210> SEQ ID NO 133
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v2.4 mAb VH

<400> SEQUENCE: 133

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala			
1	5	10	15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr			
20	25	30	

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met			
35	40	45	

Gly Phe Ile Ser Thr Tyr Asn Gln Asn Thr Asn Tyr Ala Gln Lys Phe			
50	55	60	

Gln Gly Arg Val Thr Met Thr Asp Thr Ser Thr Thr Thr Gly Tyr			
65	70	75	80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys			
85	90	95	

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly			
100	105	110	

-continued

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 134
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v2.5 mAb VH

<400> SEQUENCE: 134

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Ser Thr Tyr Leu Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 135
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v2.6 mAb VH

<400> SEQUENCE: 135

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Ser Thr Tyr Thr Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 136
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

-continued

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 139

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v3.1 mAb VH

<400> SEQUENCE: 139

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Ser Thr Tyr Gln Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 140

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v3.2 mAb VH

<400> SEQUENCE: 140

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Ser Thr Tyr Asn Ser Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

-continued

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 141

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v3.3 mAb VH

<400> SEQUENCE: 141

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Ser Thr Tyr Asn Ala Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 142

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v3.4 mAb VH

<400> SEQUENCE: 142

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Ser Thr Tyr Asn Gln Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly

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100	105	110
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Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser	115	120
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125		
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<210> SEQ ID NO 143
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v3.5 mAb VH

<400> SEQUENCE: 143

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala	1	5
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10		15
----	--	----

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr	20	25
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30		
----	--	--

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met	35	40
---	----	----

45		
----	--	--

Gly Tyr Ile Ser Thr Tyr Leu Gly Asn Thr Asn Tyr Ala Gln Lys Phe	50	55
---	----	----

60		
----	--	--

Gln Gly Arg Val Thr Met Thr Asp Thr Ser Thr Thr Thr Gly Tyr	65	70
---	----	----

75		80
----	--	----

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys	85	90
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95		
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Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly	100	105
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110		
-----	--	--

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser	115	120
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125		
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<210> SEQ ID NO 144

<211> LENGTH: 127

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v3.6 mAb VH

<400> SEQUENCE: 144

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala	1	5
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10		15
----	--	----

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr	20	25
---	----	----

30		
----	--	--

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met	35	40
---	----	----

45		
----	--	--

Gly Tyr Ile Ser Thr Tyr Thr Gly Asn Thr Asn Tyr Ala Gln Lys Phe	50	55
---	----	----

60		
----	--	--

Gln Gly Arg Val Thr Met Thr Asp Thr Ser Thr Thr Thr Gly Tyr	65	70
---	----	----

75		80
----	--	----

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys	85	90
---	----	----

95		
----	--	--

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly	100	105
---	-----	-----

110		
-----	--	--

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser	115	120
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125		
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<210> SEQ ID NO 145

<211> LENGTH: 127

-continued

<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v3.7 mAb VH

<400> SEQUENCE: 145

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Phe Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 146
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v3.8 mAb VH

<400> SEQUENCE: 146

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
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Ala Arg Asp Tyr Thr Arg Gly Ala Tyr Phe Gly Glu Ser Leu Ile Gly
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Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
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<210> SEQ ID NO 147
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v9 mAb VL
(VK)

<400> SEQUENCE: 147

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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Asn Asn Tyr
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Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Arg Gly
50 55 60

Ser Gly Ser Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Val Ala Ser Tyr Tyr Cys Arg Lys Tyr Asn Ser Ala Pro Gly
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Thr Phe Gly Gln Gly Thr Arg Val Glu Ile Lys
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<210> SEQ ID NO 148

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v10 mAb VL
(VK)

<400> SEQUENCE: 148

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Thr Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Asn Asn Tyr
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Arg Gly
50 55 60

Ser Gly Ser Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Val Ala Ser Tyr Tyr Cys Arg Lys Tyr Asn Ser Ala Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Arg Val Glu Ile Lys
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<210> SEQ ID NO 149

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v11 mAb VL
(VK)

<400> SEQUENCE: 149

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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Asn Asn Tyr
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Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Arg Gly
50 55 60

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Ser Gly Ser Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Val Ala Ser Tyr Tyr Cys Arg Lys Tyr Asn Ser Ala Pro Phe
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Thr Phe Gly Gln Gly Thr Arg Val Glu Ile Lys
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<210> SEQ ID NO 150

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v12 mAb VL
(VK)

<400> SEQUENCE: 150

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Thr Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Asn Asn Tyr
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Arg Gly
50 55 60

Ser Gly Ser Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Val Ala Ser Tyr Tyr Cys Arg Lys Tyr Asn Ser Ala Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Arg Val Glu Ile Lys
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<210> SEQ ID NO 151

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v9 mAb CDRL3

<400> SEQUENCE: 151

Arg Lys Tyr Asn Ser Ala Pro Gly Thr

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<210> SEQ ID NO 152

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v10 mAb
CDRL3

<400> SEQUENCE: 152

Arg Lys Tyr Asn Ser Ala Pro Arg Thr

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<210> SEQ ID NO 153

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v11 mAb
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<400> SEQUENCE: 153

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<210> SEQ ID NO 154

<211> LENGTH: 9
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v12 mAb
CDRL3

<400> SEQUENCE: 154

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<210> SEQ ID NO 155

<211> LENGTH: 126
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<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S310 mAb VH

<400> SEQUENCE: 155

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<210> SEQ ID NO 156

<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S310 mAb CDRH1

<400> SEQUENCE: 156

Gly Gly Thr Phe Asn Ser Tyr Ser
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<210> SEQ ID NO 157

<211> LENGTH: 8
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S310 mAb CDRH2

<400> SEQUENCE: 157

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Ile Ile Pro Val Leu Gly Thr Ser
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<210> SEQ ID NO 158
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<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S310 mAb CDRH3

<400> SEQUENCE: 158

Ala Thr Arg Thr Tyr Asp Ser Ser Gly Tyr Arg Pro Tyr Tyr Tyr Gly
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Leu Asp Val

<210> SEQ ID NO 159
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S310 mAb VL (VK)

<400> SEQUENCE: 159

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
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Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Ser Tyr
20 25 30

Asn Leu Val Ser Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Glu Leu
35 40 45

Met Ile Tyr Glu Val Thr Lys Arg Pro Ser Gly Leu Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
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Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Cys Ser Tyr Ala Gly Ser
85 90 95

Asp Thr Val Ile Phe Gly Gly Thr Lys Val Thr Val Leu
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<210> SEQ ID NO 160
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S310 mAb CDRL1

<400> SEQUENCE: 160

Ser Ser Asp Val Gly Ser Tyr Asn Leu
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<210> SEQ ID NO 161
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S310 mAb CDRL2

<400> SEQUENCE: 161

Glu Val Thr
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<210> SEQ ID NO 162
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S310 mAb CDRL3

<400> SEQUENCE: 162

Cys Ser Tyr Ala Gly Ser Asp Thr Val Ile
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<210> SEQ ID NO 163
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<213> ORGANISM: SARS-CoV-2 betacoronavirus

<400> SEQUENCE: 163

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<212> TYPE: PRT
<213> ORGANISM: SARS-CoV-2 betacoronavirus

<400> SEQUENCE: 164

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20 25 30

Asp Ser Val Glu Glu Val Leu Ser Glu Ala Arg Gln His Leu Lys Asp
35 40 45

Gly Thr Cys Gly Leu Val Glu Val Glu Lys Gly Val Leu Pro Gln Leu
50 55 60

Glu	Gln	Pro	Tyr	Val	Phe	Ile	Lys	Arg	Ser	Asp	Ala	Arg	Thr	Ala	Pro
65					70					75					80

His Gly His Val Met Val Glu Leu Val Ala Glu Leu Glu Gly Ile Gln
85 90 95

Tyr Gly Arg Ser Gly Glu Thr Leu Gly Val Leu Val Pro His Val Gly
 100 105 110

Glu Ile Pro Val Ala Tyr Arg Lys Val Leu Leu Arg Lys Asn Gly Asn
 115 120 125

Lys Gly Ala Gly Gly His Ser Tyr Gly Ala Asp Leu Lys Ser Phe Asp
130 135 140

Leu Gly Asp Glu Leu Gly Thr Asp Pro Tyr Glu Asp Phe Gln Glu Asn
145 150 155 160

Trp Asn Thr Lys His Ser Ser Gly Val Thr Arg Glu Leu Met Arg Glu

Leu Asn Gly Gly Ala Tyr Thr Arg Tyr Val Asp Asn Asn Phe Cys Gly

Pro Asp Gly Tyr Pro Leu Glu Cys Ile Lys Asp Leu Leu Ala Arg Ala

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Lys Arg Gly Val Tyr Cys Cys Arg Glu His Glu His Glu Ile Ala Trp		
225	230	235
Tyr Thr Glu Arg Ser Glu Lys Ser Tyr Glu Leu Gln Thr Pro Phe Glu		
245	250	255
Ile Lys Leu Ala Lys Lys Phe Asp Thr Phe Asn Gly Glu Cys Pro Asn		
260	265	270
Phe Val Phe Pro Leu Asn Ser Ile Ile Lys Thr Ile Gln Pro Arg Val		
275	280	285
Glu Lys Lys Leu Asp Gly Phe Met Gly Arg Ile Arg Ser Val Tyr		
290	295	300
Pro Val Ala Ser Pro Asn Glu Cys Asn Gln Met Cys Leu Ser Thr Leu		
305	310	315
Met Lys Cys Asp His Cys Gly Glu Thr Ser Trp Gln Thr Gly Asp Phe		
325	330	335
Val Lys Ala Thr Cys Glu Phe Cys Gly Thr Glu Asn Leu Thr Lys Glu		
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Gly Ala Thr Thr Cys Gly Tyr Leu Pro Gln Asn Ala Val Val Lys Ile		
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Tyr Cys Pro Ala Cys His Asn Ser Glu Val Gly Pro Glu His Ser Leu		
370	375	380
Ala Glu Tyr His Asn Glu Ser Gly Leu Lys Thr Ile Leu Arg Lys Gly		
385	390	395
Gly Arg Thr Ile Ala Phe Gly Gly Cys Val Phe Ser Tyr Val Gly Cys		
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His Asn Lys Cys Ala Tyr Trp Val Pro Arg Ala Ser Ala Asn Ile Gly		
420	425	430
Cys Asn His Thr Gly Val Val Gly Glu Gly Ser Glu Gly Leu Asn Asp		
435	440	445
Asn Leu Leu Glu Ile Leu Gln Lys Glu Lys Val Asn Ile Asn Ile Val		
450	455	460
Gly Asp Phe Lys Leu Asn Glu Glu Ile Ala Ile Ile Leu Ala Ser Phe		
465	470	475
Ser Ala Ser Thr Ser Ala Phe Val Glu Thr Val Lys Gly Leu Asp Tyr		
485	490	495
Lys Ala Phe Lys Gln Ile Val Glu Ser Cys Gly Asn Phe Lys Val Thr		
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Lys Gly Lys Ala Lys Lys Gly Ala Trp Asn Ile Gly Glu Gln Lys Ser		
515	520	525
Ile Leu Ser Pro Leu Tyr Ala Phe Ala Ser Glu Ala Ala Arg Val Val		
530	535	540
Arg Ser Ile Phe Ser Arg Thr Leu Glu Thr Ala Gln Asn Ser Val Arg		
545	550	555
Val Leu Gln Lys Ala Ala Ile Thr Ile Leu Asp Gly Ile Ser Gln Tyr		
565	570	575
Ser Leu Arg Leu Ile Asp Ala Met Met Phe Thr Ser Asp Leu Ala Thr		
580	585	590
Asn Asn Leu Val Val Met Ala Tyr Ile Thr Gly Gly Val Val Gln Leu		
595	600	605

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 610 615 620
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 625 630 635 640
 Phe Leu Arg Asp Gly Trp Glu Ile Val Lys Phe Ile Ser Thr Cys Ala
 645 650 655
 Cys Glu Ile Val Gly Gly Gln Ile Val Thr Cys Ala Lys Glu Ile Lys
 660 665 670
 Glu Ser Val Gln Thr Phe Phe Lys Leu Val Asn Lys Phe Leu Ala Leu
 675 680 685
 Cys Ala Asp Ser Ile Ile Ile Gly Gly Ala Lys Leu Lys Ala Leu Asn
 690 695 700
 Leu Gly Glu Thr Phe Val Thr His Ser Lys Gly Leu Tyr Arg Lys Cys
 705 710 715 720
 Val Lys Ser Arg Glu Glu Thr Gly Leu Leu Met Pro Leu Lys Ala Pro
 725 730 735
 Lys Glu Ile Ile Phe Leu Glu Gly Glu Thr Leu Pro Thr Glu Val Leu
 740 745 750
 Thr Glu Glu Val Val Leu Lys Thr Gly Asp Leu Gln Pro Leu Glu Gln
 755 760 765
 Pro Thr Ser Glu Ala Val Glu Ala Pro Leu Val Gly Thr Pro Val Cys
 770 775 780
 Ile Asn Gly Leu Met Leu Leu Glu Ile Lys Asp Thr Glu Lys Tyr Cys
 785 790 795 800
 Ala Leu Ala Pro Asn Met Met Val Thr Asn Asn Thr Phe Thr Leu Lys
 805 810 815
 Gly Gly Ala Pro Thr Lys Val Thr Phe Gly Asp Asp Thr Val Ile Glu
 820 825 830
 Val Gln Gly Tyr Lys Ser Val Asn Ile Thr Phe Glu Leu Asp Glu Arg
 835 840 845
 Ile Asp Lys Val Leu Asn Glu Lys Cys Ser Ala Tyr Thr Val Glu Leu
 850 855 860
 Gly Thr Glu Val Asn Glu Phe Ala Cys Val Val Ala Asp Ala Val Ile
 865 870 875 880
 Lys Thr Leu Gln Pro Val Ser Glu Leu Leu Thr Pro Leu Gly Ile Asp
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 Leu Asp Glu Trp Ser Met Ala Thr Tyr Tyr Leu Phe Asp Glu Ser Gly
 900 905 910
 Glu Phe Lys Leu Ala Ser His Met Tyr Cys Ser Phe Tyr Pro Pro Asp
 915 920 925
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 930 935 940
 Thr Gln Tyr Glu Tyr Gly Thr Glu Asp Asp Tyr Gln Gly Lys Pro Leu
 945 950 955 960
 Glu Phe Gly Ala Thr Ser Ala Ala Leu Gln Pro Glu Glu Gln Glu
 965 970 975
 Glu Asp Trp Leu Asp Asp Asp Ser Gln Gln Thr Val Gly Gln Gln Asp
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 Gly Ser Glu Asp Asn Gln Thr Thr Thr Ile Gln Thr Ile Val Glu Val
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1025						1030						1035		
Tyr	Ile	Lys	Asn	Ala	Asp	Ile	Val	Glu	Glu	Ala	Lys	Lys	Val	Lys
1040						1045					1050			
Pro	Thr	Val	Val	Val	Asn	Ala	Ala	Asn	Val	Tyr	Leu	Lys	His	Gly
1055						1060					1065			
Gly	Gly	Val	Ala	Gly	Ala	Leu	Asn	Lys	Ala	Thr	Asn	Asn	Ala	Met
1070						1075					1080			
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1085						1090					1095			
Val	Gly	Gly	Ser	Cys	Val	Leu	Ser	Gly	His	Asn	Leu	Ala	Lys	His
1100						1105					1110			
Cys	Leu	His	Val	Val	Gly	Pro	Asn	Val	Asn	Lys	Gly	Glu	Asp	Ile
1115						1120					1125			
Gln	Leu	Leu	Lys	Ser	Ala	Tyr	Glu	Asn	Phe	Asn	Gln	His	Glu	Val
1130						1135					1140			
Leu	Leu	Ala	Pro	Leu	Leu	Ser	Ala	Gly	Ile	Phe	Gly	Ala	Asp	Pro
1145						1150					1155			
Ile	His	Ser	Leu	Arg	Val	Cys	Val	Asp	Thr	Val	Arg	Thr	Asn	Val
1160						1165					1170			
Tyr	Leu	Ala	Val	Phe	Asp	Lys	Asn	Leu	Tyr	Asp	Lys	Leu	Val	Ser
1175						1180					1185			
Ser	Phe	Leu	Glu	Met	Lys	Ser	Glu	Lys	Gln	Val	Glu	Gln	Lys	Ile
1190						1195					1200			
Ala	Glu	Ile	Pro	Lys	Glu	Glu	Val	Lys	Pro	Phe	Ile	Thr	Glu	Ser
1205						1210					1215			
Lys	Pro	Ser	Val	Glu	Gln	Arg	Lys	Gln	Asp	Asp	Lys	Lys	Ile	Lys
1220						1225					1230			
Ala	Cys	Val	Glu	Glu	Val	Thr	Thr	Leu	Glu	Glu	Thr	Lys	Phe	
1235						1240					1245			
Leu	Thr	Glu	Asn	Leu	Leu	Leu	Tyr	Ile	Asp	Ile	Asn	Gly	Asn	Leu
1250						1255					1260			
His	Pro	Asp	Ser	Ala	Thr	Leu	Val	Ser	Asp	Ile	Asp	Ile	Thr	Phe
1265						1270					1275			
Leu	Lys	Lys	Asp	Ala	Pro	Tyr	Ile	Val	Gly	Asp	Val	Val	Gln	Glu
1280						1285					1290			
Gly	Val	Leu	Thr	Ala	Val	Val	Ile	Pro	Thr	Lys	Lys	Ala	Gly	Gly
1295						1300					1305			
Thr	Thr	Glu	Met	Leu	Ala	Lys	Ala	Leu	Arg	Lys	Val	Pro	Thr	Asp
1310						1315					1320			
Asn	Tyr	Ile	Thr	Thr	Tyr	Pro	Gly	Gln	Gly	Leu	Asn	Gly	Tyr	Thr
1325						1330					1335			
Val	Glu	Glu	Ala	Lys	Thr	Val	Leu	Lys	Lys	Cys	Lys	Ser	Ala	Phe
1340						1345					1350			
Tyr	Ile	Leu	Pro	Ser	Ile	Ile	Ser	Asn	Glu	Lys	Gln	Glu	Ile	Leu
1355						1360					1365			
Gly	Thr	Val	Ser	Trp	Asn	Leu	Arg	Glu	Met	Leu	Ala	His	Ala	Glu
1370						1375					1380			
Glu	Thr	Arg	Lys	Leu	Met	Pro	Val	Cys	Val	Glu	Thr	Lys	Ala	Ile

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1385	1390	1395
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Gly Val Val Asp Tyr Gly Ala Arg Phe Tyr Phe Tyr	Thr Ser Lys	
1415	1420	1425
Thr Thr Val Ala Ser Leu Ile Asn Thr Leu Asn Asp	Leu Asn Glu	
1430	1435	1440
Thr Leu Val Thr Met Pro Leu Gly Tyr Val Thr His	Gly Leu Asn	
1445	1450	1455
Leu Glu Glu Ala Ala Arg Tyr Met Arg Ser Leu Lys	Val Pro Ala	
1460	1465	1470
Thr Val Ser Val Ser Ser Pro Asp Ala Val Thr Ala	Tyr Asn Gly	
1475	1480	1485
Tyr Leu Thr Ser Ser Ser Lys Thr Pro Glu Glu His	Phe Ile Glu	
1490	1495	1500
Thr Ile Ser Leu Ala Gly Ser Tyr Lys Asp Trp Ser	Tyr Ser Gly	
1505	1510	1515
Gln Ser Thr Gln Leu Gly Ile Glu Phe Leu Lys Arg	Gly Asp Lys	
1520	1525	1530
Ser Val Tyr Tyr Thr Ser Asn Pro Thr Thr Phe His	Leu Asp Gly	
1535	1540	1545
Glu Val Ile Thr Phe Asp Asn Leu Lys Thr Leu Leu	Ser Leu Arg	
1550	1555	1560
Glu Val Arg Thr Ile Lys Val Phe Thr Thr Val Asp	Asn Ile Asn	
1565	1570	1575
Leu His Thr Gln Val Val Asp Met Ser Met Thr Tyr	Gly Gln Gln	
1580	1585	1590
Phe Gly Pro Thr Tyr Leu Asp Gly Ala Asp Val Thr	Lys Ile Lys	
1595	1600	1605
Pro His Asn Ser His Glu Gly Lys Thr Phe Tyr Val	Leu Pro Asn	
1610	1615	1620
Asp Asp Thr Leu Arg Val Glu Ala Phe Glu Tyr Tyr	His Thr Thr	
1625	1630	1635
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1640	1645	1650
Lys Lys Trp Lys Tyr Pro Gln Val Asn Gly Leu Thr	Ser Ile Lys	
1655	1660	1665
Trp Ala Asp Asn Asn Cys Tyr Leu Ala Thr Ala Leu	Leu Thr Leu	
1670	1675	1680
Gln Gln Ile Glu Leu Lys Phe Asn Pro Pro Ala Leu	Gln Asp Ala	
1685	1690	1695
Tyr Tyr Arg Ala Arg Ala Gly Glu Ala Ala Asn Phe	Cys Ala Leu	
1700	1705	1710
Ile Leu Ala Tyr Cys Asn Lys Thr Val Gly Glu Leu	Gly Asp Val	
1715	1720	1725
Arg Glu Thr Met Ser Tyr Leu Phe Gln His Ala Asn	Leu Asp Ser	
1730	1735	1740
Cys Lys Arg Val Leu Asn Val Val Cys Lys Thr Cys	Gly Gln Gln	
1745	1750	1755
Gln Thr Thr Leu Lys Gly Val Glu Ala Val Met Tyr	Met Gly Thr	
1760	1765	1770

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Cys	Gly		Lys	Gln	Ala	Thr	Lys	Tyr	Leu	Val	Gln	Gln	Glu	Ser	Pro
1790						1795					1800				
Phe	Val	Met	Met	Ser	Ala	Pro	Pro	Ala	Gln	Tyr	Glu	Leu	Lys	His	
1805						1810					1815				
Gly	Thr	Phe	Thr	Cys	Ala	Ser	Glu	Tyr	Thr	Gly	Asn	Tyr	Gln	Cys	
1820						1825					1830				
Gly	His	Tyr	Lys	His	Ile	Thr	Ser	Lys	Glu	Thr	Leu	Tyr	Cys	Ile	
1835						1840					1845				
Asp	Gly	Ala	Leu	Leu	Thr	Lys	Ser	Ser	Glu	Tyr	Lys	Gly	Pro	Ile	
1850						1855					1860				
Thr	Asp	Val	Phe	Tyr	Lys	Glu	Asn	Ser	Tyr	Thr	Thr	Thr	Ile	Lys	
1865						1870					1875				
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1880						1885					1890				
Pro	Lys	Leu	Asp	Asn	Tyr	Tyr	Lys	Lys	Asp	Asn	Ser	Tyr	Phe	Thr	
1895						1900					1905				
Glu	Gln	Pro	Ile	Asp	Leu	Val	Pro	Asn	Gln	Pro	Tyr	Pro	Asn	Ala	
1910						1915					1920				
Ser	Phe	Asp	Asn	Phe	Lys	Phe	Val	Cys	Asp	Asn	Ile	Lys	Phe	Ala	
1925						1930					1935				
Asp	Asp	Leu	Asn	Gln	Leu	Thr	Gly	Tyr	Lys	Pro	Ala	Ser	Arg		
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Glu	Leu	Lys	Val	Thr	Phe	Phe	Pro	Asp	Leu	Asn	Gly	Asp	Val	Val	
1955						1960					1965				
Ala	Ile	Asp	Tyr	Lys	His	Tyr	Thr	Pro	Ser	Phe	Lys	Lys	Gly	Ala	
1970						1975					1980				
Lys	Leu	Leu	His	Lys	Pro	Ile	Val	Trp	His	Val	Asn	Asn	Ala	Thr	
1985						1990					1995				
Asn	Lys	Ala	Thr	Tyr	Lys	Pro	Asn	Thr	Trp	Cys	Ile	Arg	Cys	Leu	
2000						2005					2010				
Trp	Ser	Thr	Lys	Pro	Val	Glu	Thr	Ser	Asn	Ser	Phe	Asp	Val	Leu	
2015						2020					2025				
Lys	Ser	Glu	Asp	Ala	Gln	Gly	Met	Asp	Asn	Leu	Ala	Cys	Glu	Asp	
2030						2035					2040				
Leu	Lys	Pro	Val	Ser	Glu	Glu	Val	Val	Glu	Asn	Pro	Thr	Ile	Gln	
2045						2050					2055				
Lys	Asp	Val	Leu	Glu	Cys	Asn	Val	Lys	Thr	Thr	Glu	Val	Val	Gly	
2060						2065					2070				
Asp	Ile	Ile	Leu	Lys	Pro	Ala	Asn	Asn	Ser	Leu	Lys	Ile	Thr	Glu	
2075						2080					2085				
Glu	Val	Gly	His	Thr	Asp	Leu	Met	Ala	Ala	Tyr	Val	Asp	Asn	Ser	
2090						2095					2100				
Ser	Leu	Thr	Ile	Lys	Lys	Pro	Asn	Glu	Leu	Ser	Arg	Val	Leu	Gly	
2105						2110					2115				
Leu	Lys	Thr	Leu	Ala	Thr	His	Gly	Leu	Ala	Ala	Val	Asn	Ser	Val	
2120						2125					2130				
Pro	Trp	Asp	Thr	Ile	Ala	Asn	Tyr	Ala	Lys	Pro	Phe	Leu	Asn	Lys	
2135						2140					2145				

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Val	Val	Ser	Thr	Thr	Thr	Asn	Ile	Val	Thr	Arg	Cys	Leu	Asn	Arg
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Val	Cys	Thr	Asn	Tyr	Met	Pro	Tyr	Phe	Phe	Thr	Leu	Leu	Leu	Gln
2165						2170				2175				
Leu	Cys	Thr	Phe	Thr	Arg	Ser	Thr	Asn	Ser	Arg	Ile	Lys	Ala	Ser
2180						2185				2190				
Met	Pro	Thr	Thr	Ile	Ala	Lys	Asn	Thr	Val	Lys	Ser	Val	Gly	Lys
2195						2200				2205				
Phe	Cys	Leu	Glu	Ala	Ser	Phe	Asn	Tyr	Leu	Lys	Ser	Pro	Asn	Phe
2210						2215				2220				
Ser	Lys	Leu	Ile	Asn	Ile	Ile	Ile	Trp	Phe	Leu	Leu	Leu	Ser	Val
2225						2230				2235				
Cys	Leu	Gly	Ser	Leu	Ile	Tyr	Ser	Thr	Ala	Ala	Leu	Gly	Val	Leu
2240						2245				2250				
Met	Ser	Asn	Leu	Gly	Met	Pro	Ser	Tyr	Cys	Thr	Gly	Tyr	Arg	Glu
2255						2260				2265				
Gly	Tyr	Leu	Asn	Ser	Thr	Asn	Val	Thr	Ile	Ala	Thr	Tyr	Cys	Thr
2270						2275				2280				
Gly	Ser	Ile	Pro	Cys	Ser	Val	Cys	Leu	Ser	Gly	Leu	Asp	Ser	Leu
2285						2290				2295				
Asp	Thr	Tyr	Pro	Ser	Leu	Glu	Thr	Ile	Gln	Ile	Thr	Ile	Ser	Ser
2300						2305				2310				
Phe	Lys	Trp	Asp	Leu	Thr	Ala	Phe	Gly	Leu	Val	Ala	Glu	Trp	Phe
2315						2320				2325				
Leu	Ala	Tyr	Ile	Leu	Phe	Thr	Arg	Phe	Phe	Tyr	Val	Leu	Gly	Leu
2330						2335				2340				
Ala	Ala	Ile	Met	Gln	Leu	Phe	Phe	Ser	Tyr	Phe	Ala	Val	His	Phe
2345						2350				2355				
Ile	Ser	Asn	Ser	Trp	Leu	Met	Trp	Leu	Ile	Ile	Asn	Leu	Val	Gln
2360						2365				2370				
Met	Ala	Pro	Ile	Ser	Ala	Met	Val	Arg	Met	Tyr	Ile	Phe	Phe	Ala
2375						2380				2385				
Ser	Phe	Tyr	Tyr	Val	Trp	Lys	Ser	Tyr	Val	His	Val	Val	Asp	Gly
2390						2395				2400				
Cys	Asn	Ser	Ser	Thr	Cys	Met	Met	Cys	Tyr	Lys	Arg	Asn	Arg	Ala
2405						2410				2415				
Thr	Arg	Val	Glu	Cys	Thr	Thr	Ile	Val	Asn	Gly	Val	Arg	Arg	Ser
2420						2425				2430				
Phe	Tyr	Val	Tyr	Ala	Asn	Gly	Gly	Lys	Gly	Phe	Cys	Lys	Leu	His
2435						2440				2445				
Asn	Trp	Asn	Cys	Val	Asn	Cys	Asp	Thr	Phe	Cys	Ala	Gly	Ser	Thr
2450						2455				2460				
Phe	Ile	Ser	Asp	Glu	Val	Ala	Arg	Asp	Leu	Ser	Leu	Gln	Phe	Lys
2465						2470				2475				
Arg	Pro	Ile	Asn	Pro	Thr	Asp	Gln	Ser	Ser	Tyr	Ile	Val	Asp	Ser
2480						2485				2490				
Val	Thr	Val	Lys	Asn	Gly	Ser	Ile	His	Leu	Tyr	Phe	Asp	Lys	Ala
2495						2500				2505				
Gly	Gln	Lys	Thr	Tyr	Glu	Arg	His	Ser	Leu	Ser	His	Phe	Val	Asn
2510						2515				2520				
Leu	Asp	Asn	Leu	Arg	Ala	Asn	Asn	Thr	Lys	Gly	Ser	Leu	Pro	Ile

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2525	2530	2535
Asn Val Ile Val Phe Asp Gly Lys Ser Lys Cys Glu Glu Ser Ser		
2540	2545	2550
Ala Lys Ser Ala Ser Val Tyr Tyr Ser Gln Leu Met Cys Gln Pro		
2555	2560	2565
Ile Leu Leu Leu Asp Gln Ala Leu Val Ser Asp Val Gly Asp Ser		
2570	2575	2580
Ala Glu Val Ala Val Lys Met Phe Asp Ala Tyr Val Asn Thr Phe		
2585	2590	2595
Ser Ser Thr Phe Asn Val Pro Met Glu Lys Leu Lys Thr Leu Val		
2600	2605	2610
Ala Thr Ala Glu Ala Glu Leu Ala Lys Asn Val Ser Leu Asp Asn		
2615	2620	2625
Val Leu Ser Thr Phe Ile Ser Ala Ala Arg Gln Gly Phe Val Asp		
2630	2635	2640
Ser Asp Val Glu Thr Lys Asp Val Val Glu Cys Leu Lys Leu Ser		
2645	2650	2655
His Gln Ser Asp Ile Glu Val Thr Gly Asp Ser Cys Asn Asn Tyr		
2660	2665	2670
Met Leu Thr Tyr Asn Lys Val Glu Asn Met Thr Pro Arg Asp Leu		
2675	2680	2685
Gly Ala Cys Ile Asp Cys Ser Ala Arg His Ile Asn Ala Gln Val		
2690	2695	2700
Ala Lys Ser His Asn Ile Ala Leu Ile Trp Asn Val Lys Asp Phe		
2705	2710	2715
Met Ser Leu Ser Glu Gln Leu Arg Lys Gln Ile Arg Ser Ala Ala		
2720	2725	2730
Lys Lys Asn Asn Leu Pro Phe Lys Leu Thr Cys Ala Thr Thr Arg		
2735	2740	2745
Gln Val Val Asn Val Val Thr Thr Lys Ile Ala Leu Lys Gly Gly		
2750	2755	2760
Lys Ile Val Asn Asn Trp Leu Lys Gln Leu Ile Lys Val Thr Leu		
2765	2770	2775
Val Phe Leu Phe Val Ala Ala Ile Phe Tyr Leu Ile Thr Pro Val		
2780	2785	2790
His Val Met Ser Lys His Thr Asp Phe Ser Ser Glu Ile Ile Gly		
2795	2800	2805
Tyr Lys Ala Ile Asp Gly Gly Val Thr Arg Asp Ile Ala Ser Thr		
2810	2815	2820
Asp Thr Cys Phe Ala Asn Lys His Ala Asp Phe Asp Thr Trp Phe		
2825	2830	2835
Ser Gln Arg Gly Gly Ser Tyr Thr Asn Asp Lys Ala Cys Pro Leu		
2840	2845	2850
Ile Ala Ala Val Ile Thr Arg Glu Val Gly Phe Val Val Pro Gly		
2855	2860	2865
Leu Pro Gly Thr Ile Leu Arg Thr Thr Asn Gly Asp Phe Leu His		
2870	2875	2880
Phe Leu Pro Arg Val Phe Ser Ala Val Gly Asn Ile Cys Tyr Thr		
2885	2890	2895
Pro Ser Lys Leu Ile Glu Tyr Thr Asp Phe Ala Thr Ser Ala Cys		
2900	2905	2910

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Val	Leu	Ala	Ala	Glu	Cys	Thr	Ile	Phe	Lys	Asp	Ala	Ser	Gly	Lys
2915							2920							2925
Pro	Val	Pro	Tyr	Cys	Tyr	Asp	Thr	Asn	Val	Leu	Glu	Gly	Ser	Val
2930							2935							2940
Ala	Tyr	Glu	Ser	Leu	Arg	Pro	Asp	Thr	Arg	Tyr	Val	Leu	Met	Asp
2945							2950							2955
Gly	Ser	Ile	Ile	Gln	Phe	Pro	Asn	Thr	Tyr	Leu	Glu	Gly	Ser	Val
2960							2965							2970
Arg	Val	Val	Thr	Thr	Phe	Asp	Ser	Glu	Tyr	Cys	Arg	His	Gly	Thr
2975							2980							2985
Cys	Glu	Arg	Ser	Glu	Ala	Gly	Val	Cys	Val	Ser	Thr	Ser	Gly	Arg
2990							2995							3000
Trp	Val	Leu	Asn	Asn	Asp	Tyr	Tyr	Arg	Ser	Leu	Pro	Gly	Val	Phe
3005							3010							3015
Cys	Gly	Val	Asp	Ala	Val	Asn	Leu	Leu	Thr	Asn	Met	Phe	Thr	Pro
3020							3025							3030
Leu	Ile	Gln	Pro	Ile	Gly	Ala	Leu	Asp	Ile	Ser	Ala	Ser	Ile	Val
3035							3040							3045
Ala	Gly	Gly	Ile	Val	Ala	Ile	Val	Val	Thr	Cys	Leu	Ala	Tyr	Tyr
3050							3055							3060
Phe	Met	Arg	Phe	Arg	Arg	Ala	Phe	Gly	Glu	Tyr	Ser	His	Val	Val
3065							3070							3075
Ala	Phe	Asn	Thr	Leu	Leu	Phe	Leu	Met	Ser	Phe	Thr	Val	Leu	Cys
3080							3085							3090
Leu	Thr	Pro	Val	Tyr	Ser	Phe	Leu	Pro	Gly	Val	Tyr	Ser	Val	Ile
3095							3100							3105
Tyr	Leu	Tyr	Leu	Thr	Phe	Tyr	Leu	Thr	Asn	Asp	Val	Ser	Phe	Leu
3110							3115							3120
Ala	His	Ile	Gln	Trp	Met	Val	Met	Phe	Thr	Pro	Leu	Val	Pro	Phe
3125							3130							3135
Trp	Ile	Thr	Ile	Ala	Tyr	Ile	Ile	Cys	Ile	Ser	Thr	Lys	His	Phe
3140							3145							3150
Tyr	Trp	Phe	Phe	Ser	Asn	Tyr	Leu	Lys	Arg	Arg	Val	Val	Phe	Asn
3155							3160							3165
Gly	Val	Ser	Phe	Ser	Thr	Phe	Glu	Glu	Ala	Ala	Leu	Cys	Thr	Phe
3170							3175							3180
Leu	Leu	Asn	Lys	Glu	Met	Tyr	Leu	Lys	Leu	Arg	Ser	Asp	Val	Leu
3185							3190							3195
Leu	Pro	Leu	Thr	Gln	Tyr	Asn	Arg	Tyr	Leu	Ala	Leu	Tyr	Asn	Lys
3200							3205							3210
Tyr	Lys	Tyr	Phe	Ser	Gly	Ala	Met	Asp	Thr	Thr	Ser	Tyr	Arg	Glu
3215							3220							3225
Ala	Ala	Cys	Cys	His	Leu	Ala	Lys	Ala	Leu	Asn	Asp	Phe	Ser	Asn
3230							3235							3240
Ser	Gly	Ser	Asp	Val	Leu	Tyr	Gln	Pro	Pro	Gln	Thr	Ser	Ile	Thr
3245							3250							3255
Ser	Ala	Val	Leu	Gln	Ser	Gly	Phe	Arg	Lys	Met	Ala	Phe	Pro	Ser
3260							3265							3270
Gly	Lys	Val	Glu	Gly	Cys	Met	Val	Gln	Val	Thr	Cys	Gly	Thr	Thr
3275							3280							3285

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Thr	Leu	Asn	Gly	Leu	Trp	Leu	Asp	Asp	Val	Val	Tyr	Cys	Pro	Arg
3290					3295						3300			
His	Val	Ile	Cys	Thr	Ser	Glu	Asp	Met	Leu	Asn	Pro	Asn	Tyr	Glu
3305					3310						3315			
Asp	Leu	Leu	Ile	Arg	Lys	Ser	Asn	His	Asn	Phe	Leu	Val	Gln	Ala
3320					3325						3330			
Gly	Asn	Val	Gln	Leu	Arg	Val	Ile	Gly	His	Ser	Met	Gln	Asn	Cys
3335					3340						3345			
Val	Leu	Lys	Leu	Lys	Val	Asp	Thr	Ala	Asn	Pro	Lys	Thr	Pro	Lys
3350					3355						3360			
Tyr	Lys	Phe	Val	Arg	Ile	Gln	Pro	Gly	Gln	Thr	Phe	Ser	Val	Leu
3365					3370						3375			
Ala	Cys	Tyr	Asn	Gly	Ser	Pro	Ser	Gly	Val	Tyr	Gln	Cys	Ala	Met
3380					3385						3390			
Arg	Pro	Asn	Phe	Thr	Ile	Lys	Gly	Ser	Phe	Leu	Asn	Gly	Ser	Cys
3395					3400						3405			
Gly	Ser	Val	Gly	Phe	Asn	Ile	Asp	Tyr	Asp	Cys	Val	Ser	Phe	Cys
3410					3415						3420			
Tyr	Met	His	His	Met	Glu	Leu	Pro	Thr	Gly	Val	His	Ala	Gly	Thr
3425					3430						3435			
Asp	Leu	Glu	Gly	Asn	Phe	Tyr	Gly	Pro	Phe	Val	Asp	Arg	Gln	Thr
3440					3445						3450			
Ala	Gln	Ala	Ala	Gly	Thr	Asp	Thr	Thr	Ile	Thr	Val	Asn	Val	Leu
3455					3460						3465			
Ala	Trp	Leu	Tyr	Ala	Ala	Val	Ile	Asn	Gly	Asp	Arg	Trp	Phe	Leu
3470					3475						3480			
Asn	Arg	Phe	Thr	Thr	Thr	Leu	Asn	Asp	Phe	Asn	Leu	Val	Ala	Met
3485					3490						3495			
Lys	Tyr	Asn	Tyr	Glu	Pro	Leu	Thr	Gln	Asp	His	Val	Asp	Ile	Leu
3500					3505						3510			
Gly	Pro	Leu	Ser	Ala	Gln	Thr	Gly	Ile	Ala	Val	Leu	Asp	Met	Cys
3515					3520						3525			
Ala	Ser	Leu	Lys	Glu	Leu	Leu	Gln	Asn	Gly	Met	Asn	Gly	Arg	Thr
3530					3535						3540			
Ile	Leu	Gly	Ser	Ala	Leu	Leu	Glu	Asp	Glu	Phe	Thr	Pro	Phe	Asp
3545					3550						3555			
Val	Val	Arg	Gln	Cys	Ser	Gly	Val	Thr	Phe	Gln	Ser	Ala	Val	Lys
3560					3565						3570			
Arg	Thr	Ile	Lys	Gly	Thr	His	His	Trp	Leu	Leu	Leu	Thr	Ile	Leu
3575					3580						3585			
Thr	Ser	Leu	Leu	Val	Leu	Val	Gln	Ser	Thr	Gln	Trp	Ser	Leu	Phe
3590					3595						3600			
Phe	Phe	Leu	Tyr	Glu	Asn	Ala	Phe	Leu	Pro	Phe	Ala	Met	Gly	Ile
3605					3610						3615			
Ile	Ala	Met	Ser	Ala	Phe	Ala	Met	Met	Phe	Val	Lys	His	Lys	His
3620					3625						3630			
Ala	Phe	Leu	Cys	Leu	Phe	Leu	Leu	Pro	Ser	Leu	Ala	Thr	Val	Ala
3635					3640						3645			
Tyr	Phe	Asn	Met	Val	Tyr	Met	Pro	Ala	Ser	Trp	Val	Met	Arg	Ile
3650					3655						3660			
Met	Thr	Trp	Leu	Asp	Met	Val	Asp	Thr	Ser	Leu	Ser	Gly	Phe	Lys

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3665	3670	3675
Leu Lys Asp Cys Val Met Tyr	Ala Ser Ala Val Val	Leu Leu Ile
3680	3685	3690
Leu Met Thr Ala Arg Thr Val	Tyr Asp Asp Gly Ala	Arg Arg Val
3695	3700	3705
Trp Thr Leu Met Asn Val	Leu Thr Leu Val Tyr Lys	Val Tyr Tyr
3710	3715	3720
Gly Asn Ala Leu Asp Gln Ala	Ile Ser Met Trp Ala	Leu Ile Ile
3725	3730	3735
Ser Val Thr Ser Asn Tyr Ser	Gly Val Val Thr Thr	Val Met Phe
3740	3745	3750
Leu Ala Arg Gly Ile Val Phe	Met Cys Val Glu Tyr	Cys Pro Ile
3755	3760	3765
Phe Phe Ile Thr Gly Asn Thr	Leu Gln Cys Ile Met	Leu Val Tyr
3770	3775	3780
Cys Phe Leu Gly Tyr Phe Cys	Thr Cys Tyr Phe Gly	Leu Phe Cys
3785	3790	3795
Leu Leu Asn Arg Tyr Phe Arg	Leu Thr Leu Gly Val	Tyr Asp Tyr
3800	3805	3810
Leu Val Ser Thr Gln Glu Phe	Arg Tyr Met Asn Ser	Gln Gly Leu
3815	3820	3825
Leu Pro Pro Lys Asn Ser Ile	Asp Ala Phe Lys Leu	Asn Ile Lys
3830	3835	3840
Leu Leu Gly Val Gly Gly Lys	Pro Cys Ile Lys Val	Ala Thr Val
3845	3850	3855
Gln Ser Lys Met Ser Asp Val	Lys Cys Thr Ser Val	Val Leu Leu
3860	3865	3870
Ser Val Leu Gln Gln Leu Arg	Val Glu Ser Ser Ser	Lys Leu Trp
3875	3880	3885
Ala Gln Cys Val Gln Leu His	Asn Asp Ile Leu Leu	Ala Lys Asp
3890	3895	3900
Thr Thr Glu Ala Phe Glu Lys	Met Val Ser Leu Leu	Ser Val Leu
3905	3910	3915
Leu Ser Met Gln Gly Ala Val	Asp Ile Asn Lys Leu	Cys Glu Glu
3920	3925	3930
Met Leu Asp Asn Arg Ala Thr	Leu Gln Ala Ile Ala	Ser Glu Phe
3935	3940	3945
Ser Ser Leu Pro Ser Tyr Ala	Ala Phe Ala Thr Ala	Gln Glu Ala
3950	3955	3960
Tyr Glu Gln Ala Val Ala Asn	Gly Asp Ser Glu Val	Val Leu Lys
3965	3970	3975
Lys Leu Lys Lys Ser Leu Asn	Val Ala Lys Ser Glu	Phe Asp Arg
3980	3985	3990
Asp Ala Ala Met Gln Arg Lys	Leu Glu Lys Met Ala	Asp Gln Ala
3995	4000	4005
Met Thr Gln Met Tyr Lys Gln	Ala Arg Ser Glu Asp	Lys Arg Ala
4010	4015	4020
Lys Val Thr Ser Ala Met Gln	Thr Met Leu Phe Thr	Met Leu Arg
4025	4030	4035
Lys Leu Asp Asn Asp Ala Leu	Asn Asn Ile Ile Asn	Asn Ala Arg
4040	4045	4050

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Asp	Gly	Cys	Val	Pro	Leu	Asn	Ile	Ile	Pro	Leu	Thr	Thr	Ala	Ala
4055					4060					4065				
Lys	Leu	Met	Val	Val	Ile	Pro	Asp	Tyr	Asn	Thr	Tyr	Lys	Asn	Thr
4070						4075				4080				
Cys	Asp	Gly	Thr	Thr	Phe	Thr	Tyr	Ala	Ser	Ala	Leu	Trp	Glu	Ile
4085						4090				4095				
Gln	Gln	Val	Val	Asp	Ala	Asp	Ser	Lys	Ile	Val	Gln	Leu	Ser	Glu
4100						4105				4110				
Ile	Ser	Met	Asp	Asn	Ser	Pro	Asn	Leu	Ala	Trp	Pro	Leu	Ile	Val
4115						4120				4125				
Thr	Ala	Leu	Arg	Ala	Asn	Ser	Ala	Val	Lys	Leu	Gln	Asn	Asn	Glu
4130						4135				4140				
Leu	Ser	Pro	Val	Ala	Leu	Arg	Gln	Met	Ser	Cys	Ala	Ala	Gly	Thr
4145						4150				4155				
Thr	Gln	Thr	Ala	Cys	Thr	Asp	Asp	Asn	Ala	Leu	Ala	Tyr	Tyr	Asn
4160						4165				4170				
Thr	Thr	Lys	Gly	Gly	Arg	Phe	Val	Leu	Ala	Leu	Leu	Ser	Asp	Leu
4175						4180				4185				
Gln	Asp	Leu	Lys	Trp	Ala	Arg	Phe	Pro	Lys	Ser	Asp	Gly	Thr	Gly
4190						4195				4200				
Thr	Ile	Tyr	Thr	Glu	Leu	Glu	Pro	Pro	Cys	Arg	Phe	Val	Thr	Asp
4205						4210				4215				
Thr	Pro	Lys	Gly	Pro	Lys	Val	Lys	Tyr	Leu	Tyr	Phe	Ile	Lys	Gly
4220						4225				4230				
Leu	Asn	Asn	Leu	Asn	Arg	Gly	Met	Val	Leu	Gly	Ser	Leu	Ala	Ala
4235						4240				4245				
Thr	Val	Arg	Leu	Gln	Ala	Gly	Asn	Ala	Thr	Glu	Val	Pro	Ala	Asn
4250						4255				4260				
Ser	Thr	Val	Leu	Ser	Phe	Cys	Ala	Phe	Ala	Val	Asp	Ala	Ala	Lys
4265						4270				4275				
Ala	Tyr	Lys	Asp	Tyr	Leu	Ala	Ser	Gly	Gly	Gln	Pro	Ile	Thr	Asn
4280						4285				4290				
Cys	Val	Lys	Met	Leu	Cys	Thr	His	Thr	Gly	Thr	Gly	Gln	Ala	Ile
4295						4300				4305				
Thr	Val	Thr	Pro	Glu	Ala	Asn	Met	Asp	Gln	Glu	Ser	Phe	Gly	Gly
4310						4315				4320				
Ala	Ser	Cys	Cys	Leu	Tyr	Cys	Arg	Cys	His	Ile	Asp	His	Pro	Asn
4325						4330				4335				
Pro	Lys	Gly	Phe	Cys	Asp	Leu	Lys	Gly	Lys	Tyr	Val	Gln	Ile	Pro
4340						4345				4350				
Thr	Thr	Cys	Ala	Asn	Asp	Pro	Val	Gly	Phe	Thr	Leu	Lys	Asn	Thr
4355						4360				4365				
Val	Cys	Thr	Val	Cys	Gly	Met	Trp	Lys	Gly	Tyr	Gly	Cys	Ser	Cys
4370						4375				4380				
Asp	Gln	Leu	Arg	Glu	Pro	Met	Leu	Gln	Ser	Ala	Asp	Ala	Gln	Ser
4385						4390				4395				
Phe	Leu	Asn	Arg	Val	Cys	Gly	Val	Ser	Ala	Ala	Arg	Leu	Thr	Pro
4400						4405				4410				
Cys	Gly	Thr	Gly	Thr	Ser	Thr	Asp	Val	Val	Tyr	Arg	Ala	Phe	Asp
4415						4420				4425				

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Ile	Tyr	Asn	Asp	Lys	Val	Ala	Gly	Phe	Ala	Lys	Phe	Leu	Lys	Thr
4430					4435					4440				
Asn	Cys	Cys	Arg	Phe	Gln	Glu	Lys	Asp	Glu	Asp	Asp	Asn	Leu	Ile
4445					4450					4455				
Asp	Ser	Tyr	Phe	Val	Val	Lys	Arg	His	Thr	Phe	Ser	Asn	Tyr	Gln
4460					4465					4470				
His	Glu	Glu	Thr	Ile	Tyr	Asn	Leu	Leu	Lys	Asp	Cys	Pro	Ala	Val
4475					4480					4485				
Ala	Lys	His	Asp	Phe	Phe	Lys	Phe	Arg	Ile	Asp	Gly	Asp	Met	Val
4490					4495					4500				
Pro	His	Ile	Ser	Arg	Gln	Arg	Leu	Thr	Lys	Tyr	Thr	Met	Ala	Asp
4505					4510					4515				
Leu	Val	Tyr	Ala	Leu	Arg	His	Phe	Asp	Glu	Gly	Asn	Cys	Asp	Thr
4520					4525					4530				
Leu	Lys	Glu	Ile	Leu	Val	Thr	Tyr	Asn	Cys	Cys	Asp	Asp	Asp	Tyr
4535					4540					4545				
Phe	Asn	Lys	Lys	Asp	Trp	Tyr	Asp	Phe	Val	Glu	Asn	Pro	Asp	Ile
4550					4555					4560				
Leu	Arg	Val	Tyr	Ala	Asn	Leu	Gly	Glu	Arg	Val	Arg	Gln	Ala	Leu
4565					4570					4575				
Leu	Lys	Thr	Val	Gln	Phe	Cys	Asp	Ala	Met	Arg	Asn	Ala	Gly	Ile
4580					4585					4590				
Val	Gly	Val	Leu	Thr	Leu	Asp	Asn	Gln	Asp	Leu	Asn	Gly	Asn	Trp
4595					4600					4605				
Tyr	Asp	Phe	Gly	Asp	Phe	Ile	Gln	Thr	Thr	Pro	Gly	Ser	Gly	Val
4610					4615					4620				
Pro	Val	Val	Asp	Ser	Tyr	Tyr	Ser	Leu	Leu	Met	Pro	Ile	Leu	Thr
4625					4630					4635				
Leu	Thr	Arg	Ala	Leu	Thr	Ala	Glu	Ser	His	Val	Asp	Thr	Asp	Leu
4640					4645					4650				
Thr	Lys	Pro	Tyr	Ile	Lys	Trp	Asp	Leu	Leu	Lys	Tyr	Asp	Phe	Thr
4655					4660					4665				
Glu	Glu	Arg	Leu	Lys	Leu	Phe	Asp	Arg	Tyr	Phe	Lys	Tyr	Trp	Asp
4670					4675					4680				
Gln	Thr	Tyr	His	Pro	Asn	Cys	Val	Asn	Cys	Leu	Asp	Asp	Arg	Cys
4685					4690					4695				
Ile	Leu	His	Cys	Ala	Asn	Phe	Asn	Val	Leu	Phe	Ser	Thr	Val	Phe
4700					4705					4710				
Pro	Pro	Thr	Ser	Phe	Gly	Pro	Leu	Val	Arg	Lys	Ile	Phe	Val	Asp
4715					4720					4725				
Gly	Val	Pro	Phe	Val	Val	Ser	Thr	Gly	Tyr	His	Phe	Arg	Glu	Leu
4730					4735					4740				
Gly	Val	Val	His	Asn	Gln	Asp	Val	Asn	Leu	His	Ser	Ser	Arg	Leu
4745					4750					4755				
Ser	Phe	Lys	Glu	Leu	Leu	Val	Tyr	Ala	Ala	Asp	Pro	Ala	Met	His
4760					4765					4770				
Ala	Ala	Ser	Gly	Asn	Leu	Leu	Leu	Asp	Lys	Arg	Thr	Thr	Cys	Phe
4775					4780					4785				
Ser	Val	Ala	Ala	Leu	Thr	Asn	Asn	Val	Ala	Phe	Gln	Thr	Val	Lys
4790					4795					4800				
Pro	Gly	Asn	Phe	Asn	Lys	Asp	Phe	Tyr	Asp	Phe	Ala	Val	Ser	Lys

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4805	4810	4815
Gly Phe Phe Lys Glu Gly Ser	Ser Val Glu Leu Lys His Phe Phe	
4820	4825	4830
Phe Ala Gln Asp Gly Asn Ala	Ala Ile Ser Asp Tyr Asp Tyr Tyr	
4835	4840	4845
Arg Tyr Asn Leu Pro Thr Met Cys	Asp Ile Arg Gln Leu Leu Phe	
4850	4855	4860
Val Val Glu Val Val Asp Lys	Tyr Phe Asp Cys Tyr Asp Gly Gly	
4865	4870	4875
Cys Ile Asn Ala Asn Gln Val	Ile Val Asn Asn Leu Asp Lys Ser	
4880	4885	4890
Ala Gly Phe Pro Phe Asn Lys	Trp Gly Lys Ala Arg Leu Tyr Tyr	
4895	4900	4905
Asp Ser Met Ser Tyr Glu Asp	Gln Asp Ala Leu Phe Ala Tyr Thr	
4910	4915	4920
Lys Arg Asn Val Ile Pro Thr	Ile Thr Gln Met Asn Leu Lys Tyr	
4925	4930	4935
Ala Ile Ser Ala Lys Asn Arg	Ala Arg Thr Val Ala Gly Val Ser	
4940	4945	4950
Ile Cys Ser Thr Met Thr Asn	Arg Gln Phe His Gln Lys Leu Leu	
4955	4960	4965
Lys Ser Ile Ala Ala Thr Arg	Gly Ala Thr Val Val Ile Gly Thr	
4970	4975	4980
Ser Lys Phe Tyr Gly Gly Trp	His Asn Met Leu Lys Thr Val Tyr	
4985	4990	4995
Ser Asp Val Glu Asn Pro His	Leu Met Gly Trp Asp Tyr Pro Lys	
5000	5005	5010
Cys Asp Arg Ala Met Pro Asn	Met Leu Arg Ile Met Ala Ser Leu	
5015	5020	5025
Val Leu Ala Arg Lys His	Thr Thr Cys Cys Ser Leu Ser His Arg	
5030	5035	5040
Phe Tyr Arg Leu Ala Asn Glu	Cys Ala Gln Val Leu Ser Glu Met	
5045	5050	5055
Val Met Cys Gly Gly Ser	Leu Tyr Val Lys Pro Gly Gly Thr Ser	
5060	5065	5070
Ser Gly Asp Ala Thr Thr Ala	Tyr Ala Asn Ser Val Phe Asn Ile	
5075	5080	5085
Cys Gln Ala Val Thr Ala Asn	Val Asn Ala Leu Leu Ser Thr Asp	
5090	5095	5100
Gly Asn Lys Ile Ala Asp Lys	Tyr Val Arg Asn Leu Gln His Arg	
5105	5110	5115
Leu Tyr Glu Cys Leu Tyr Arg	Asn Arg Asp Val Asp Thr Asp Phe	
5120	5125	5130
Val Asn Glu Phe Tyr Ala Tyr	Leu Arg Lys His Phe Ser Met Met	
5135	5140	5145
Ile Leu Ser Asp Asp Ala Val	Val Cys Phe Asn Ser Thr Tyr Ala	
5150	5155	5160
Ser Gln Gly Leu Val Ala Ser	Ile Lys Asn Phe Lys Ser Val Leu	
5165	5170	5175
Tyr Tyr Gln Asn Asn Val Phe	Met Ser Glu Ala Lys Cys Trp Thr	
5180	5185	5190

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Glu	Thr	Asp	Leu	Thr	Lys	Gly	Pro	His	Glu	Phe	Cys	Ser	Gln	His
5195						5200					5205			
Thr	Met	Leu	Val	Lys	Gln	Gly	Asp	Asp	Tyr	Val	Tyr	Leu	Pro	Tyr
5210						5215					5220			
Pro	Asp	Pro	Ser	Arg	Ile	Leu	Gly	Ala	Gly	Cys	Phe	Val	Asp	Asp
5225						5230					5235			
Ile	Val	Lys	Thr	Asp	Gly	Thr	Leu	Met	Ile	Glu	Arg	Phe	Val	Ser
5240						5245					5250			
Leu	Ala	Ile	Asp	Ala	Tyr	Pro	Leu	Thr	Lys	His	Pro	Asn	Gln	Glu
5255						5260					5265			
Tyr	Ala	Asp	Val	Phe	His	Leu	Tyr	Leu	Gln	Tyr	Ile	Arg	Lys	Leu
5270						5275					5280			
His	Asp	Glu	Leu	Thr	Gly	His	Met	Leu	Asp	Met	Tyr	Ser	Val	Met
5285						5290					5295			
Leu	Thr	Asn	Asp	Asn	Thr	Ser	Arg	Tyr	Trp	Glu	Pro	Glu	Phe	Tyr
5300						5305					5310			
Glu	Ala	Met	Tyr	Thr	Pro	His	Thr	Val	Leu	Gln	Ala	Val	Gly	Ala
5315						5320					5325			
Cys	Val	Leu	Cys	Asn	Ser	Gln	Thr	Ser	Leu	Arg	Cys	Gly	Ala	Cys
5330						5335					5340			
Ile	Arg	Arg	Pro	Phe	Leu	Cys	Cys	Lys	Cys	Cys	Tyr	Asp	His	Val
5345						5350					5355			
Ile	Ser	Thr	Ser	His	Lys	Leu	Val	Leu	Ser	Val	Asn	Pro	Tyr	Val
5360						5365					5370			
Cys	Asn	Ala	Pro	Gly	Cys	Asp	Val	Thr	Asp	Val	Thr	Gln	Leu	Tyr
5375						5380					5385			
Leu	Gly	Gly	Met	Ser	Tyr	Tyr	Cys	Lys	Ser	His	Lys	Pro	Pro	Ile
5390						5395					5400			
Ser	Phe	Pro	Leu	Cys	Ala	Asn	Gly	Gln	Val	Phe	Gly	Leu	Tyr	Lys
5405						5410					5415			
Asn	Thr	Cys	Val	Gly	Ser	Asp	Asn	Val	Thr	Asp	Phe	Asn	Ala	Ile
5420						5425					5430			
Ala	Thr	Cys	Asp	Trp	Thr	Asn	Ala	Gly	Asp	Tyr	Ile	Leu	Ala	Asn
5435						5440					5445			
Thr	Cys	Thr	Glu	Arg	Leu	Lys	Leu	Phe	Ala	Ala	Glu	Thr	Leu	Lys
5450						5455					5460			
Ala	Thr	Glu	Glu	Thr	Phe	Lys	Leu	Ser	Tyr	Gly	Ile	Ala	Thr	Val
5465						5470					5475			
Arg	Glu	Val	Leu	Ser	Asp	Arg	Glu	Leu	His	Leu	Ser	Trp	Glu	Val
5480						5485					5490			
Gly	Lys	Pro	Arg	Pro	Pro	Leu	Asn	Arg	Asn	Tyr	Val	Phe	Thr	Gly
5495						5500					5505			
Tyr	Arg	Val	Thr	Lys	Asn	Ser	Lys	Val	Gln	Ile	Gly	Glu	Tyr	Thr
5510						5515					5520			
Phe	Glu	Lys	Gly	Asp	Tyr	Gly	Asp	Ala	Val	Val	Tyr	Arg	Gly	Thr
5525						5530					5535			
Thr	Thr	Tyr	Lys	Leu	Asn	Val	Gly	Asp	Tyr	Phe	Val	Leu	Thr	Ser
5540						5545					5550			
His	Thr	Val	Met	Pro	Leu	Ser	Ala	Pro	Thr	Leu	Val	Pro	Gln	Glu
5555						5560					5565			

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His	Tyr	Val	Arg	Ile	Thr	Gly	Leu	Tyr	Pro	Thr	Leu	Asn	Ile	Ser
5570						5575					5580			
Asp	Glu	Phe	Ser	Ser	Asn	Val	Ala	Asn	Tyr	Gln	Lys	Val	Gly	Met
5585						5590					5595			
Gln	Lys	Tyr	Ser	Thr	Leu	Gln	Gly	Pro	Pro	Gly	Thr	Gly	Lys	Ser
5600						5605					5610			
His	Phe	Ala	Ile	Gly	Leu	Ala	Leu	Tyr	Tyr	Pro	Ser	Ala	Arg	Ile
5615						5620					5625			
Val	Tyr	Thr	Ala	Cys	Ser	His	Ala	Ala	Val	Asp	Ala	Leu	Cys	Glu
5630						5635					5640			
Lys	Ala	Leu	Lys	Tyr	Leu	Pro	Ile	Asp	Lys	Cys	Ser	Arg	Ile	Ile
5645						5650					5655			
Pro	Ala	Arg	Ala	Arg	Val	Glu	Cys	Phe	Asp	Lys	Phe	Lys	Val	Asn
5660						5665					5670			
Ser	Thr	Leu	Glu	Gln	Tyr	Val	Phe	Cys	Thr	Val	Asn	Ala	Leu	Pro
5675						5680					5685			
Glu	Thr	Thr	Ala	Asp	Ile	Val	Val	Phe	Asp	Glu	Ile	Ser	Met	Ala
5690						5695					5700			
Thr	Asn	Tyr	Asp	Leu	Ser	Val	Val	Asn	Ala	Arg	Leu	Arg	Ala	Lys
5705						5710					5715			
His	Tyr	Val	Tyr	Ile	Gly	Asp	Pro	Ala	Gln	Leu	Pro	Ala	Pro	Arg
5720						5725					5730			
Thr	Leu	Leu	Thr	Lys	Gly	Thr	Leu	Glu	Pro	Glu	Tyr	Phe	Asn	Ser
5735						5740					5745			
Val	Cys	Arg	Leu	Met	Lys	Thr	Ile	Gly	Pro	Asp	Met	Phe	Leu	Gly
5750						5755					5760			
Thr	Cys	Arg	Arg	Cys	Pro	Ala	Glu	Ile	Val	Asp	Thr	Val	Ser	Ala
5765						5770					5775			
Leu	Val	Tyr	Asp	Asn	Lys	Leu	Lys	Ala	His	Lys	Asp	Lys	Ser	Ala
5780						5785					5790			
Gln	Cys	Phe	Lys	Met	Phe	Tyr	Lys	Gly	Val	Ile	Thr	His	Asp	Val
5795						5800					5805			
Ser	Ser	Ala	Ile	Asn	Arg	Pro	Gln	Ile	Gly	Val	Val	Arg	Glu	Phe
5810						5815					5820			
Leu	Thr	Arg	Asn	Pro	Ala	Trp	Arg	Lys	Ala	Val	Phe	Ile	Ser	Pro
5825						5830					5835			
Tyr	Asn	Ser	Gln	Asn	Ala	Val	Ala	Ser	Lys	Ile	Leu	Gly	Leu	Pro
5840						5845					5850			
Thr	Gln	Thr	Val	Asp	Ser	Ser	Gln	Gly	Ser	Glu	Tyr	Asp	Tyr	Val
5855						5860					5865			
Ile	Phe	Thr	Gln	Thr	Thr	Glu	Thr	Ala	His	Ser	Cys	Asn	Val	Asn
5870						5875					5880			
Arg	Phe	Asn	Val	Ala	Ile	Thr	Arg	Ala	Lys	Val	Gly	Ile	Leu	Cys
5885						5890					5895			
Ile	Met	Ser	Asp	Arg	Asp	Leu	Tyr	Asp	Lys	Leu	Gln	Phe	Thr	Ser
5900						5905					5910			
Leu	Glu	Ile	Pro	Arg	Arg	Asn	Val	Ala	Thr	Leu	Gln	Ala	Glu	Asn
5915						5920					5925			
Val	Thr	Gly	Leu	Phe	Lys	Asp	Cys	Ser	Lys	Val	Ile	Thr	Gly	Leu
5930						5935					5940			
His	Pro	Thr	Gln	Ala	Pro	Thr	His	Leu	Ser	Val	Asp	Thr	Lys	Phe

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5945	5950	5955
Lys Thr Glu Gly Leu Cys Val Asp Ile Pro Gly Ile Pro Lys Asp		
5960	5965	5970
Met Thr Tyr Arg Arg Leu Ile Ser Met Met Gly Phe Lys Met Asn		
5975	5980	5985
Tyr Gln Val Asn Gly Tyr Pro Asn Met Phe Ile Thr Arg Glu Glu		
5990	5995	6000
Ala Ile Arg His Val Arg Ala Trp Ile Gly Phe Asp Val Glu Gly		
6005	6010	6015
Cys His Ala Thr Arg Glu Ala Val Gly Thr Asn Leu Pro Leu Gln		
6020	6025	6030
Leu Gly Phe Ser Thr Gly Val Asn Leu Val Ala Val Pro Thr Gly		
6035	6040	6045
Tyr Val Asp Thr Pro Asn Asn Thr Asp Phe Ser Arg Val Ser Ala		
6050	6055	6060
Lys Pro Pro Pro Gly Asp Gln Phe Lys His Leu Ile Pro Leu Met		
6065	6070	6075
Tyr Lys Gly Leu Pro Trp Asn Val Val Arg Ile Lys Ile Val Gln		
6080	6085	6090
Met Leu Ser Asp Thr Leu Lys Asn Leu Ser Asp Arg Val Val Phe		
6095	6100	6105
Val Leu Trp Ala His Gly Phe Glu Leu Thr Ser Met Lys Tyr Phe		
6110	6115	6120
Val Lys Ile Gly Pro Glu Arg Thr Cys Cys Leu Cys Asp Arg Arg		
6125	6130	6135
Ala Thr Cys Phe Ser Thr Ala Ser Asp Thr Tyr Ala Cys Trp His		
6140	6145	6150
His Ser Ile Gly Phe Asp Tyr Val Tyr Asn Pro Phe Met Ile Asp		
6155	6160	6165
Val Gln Gln Trp Gly Phe Thr Gly Asn Leu Gln Ser Asn His Asp		
6170	6175	6180
Leu Tyr Cys Gln Val His Gly Asn Ala His Val Ala Ser Cys Asp		
6185	6190	6195
Ala Ile Met Thr Arg Cys Leu Ala Val His Glu Cys Phe Val Lys		
6200	6205	6210
Arg Val Asp Trp Thr Ile Glu Tyr Pro Ile Ile Gly Asp Glu Leu		
6215	6220	6225
Lys Ile Asn Ala Ala Cys Arg Lys Val Gln His Met Val Val Lys		
6230	6235	6240
Ala Ala Leu Leu Ala Asp Lys Phe Pro Val Leu His Asp Ile Gly		
6245	6250	6255
Asn Pro Lys Ala Ile Lys Cys Val Pro Gln Ala Asp Val Glu Trp		
6260	6265	6270
Lys Phe Tyr Asp Ala Gln Pro Cys Ser Asp Lys Ala Tyr Lys Ile		
6275	6280	6285
Glu Glu Leu Phe Tyr Ser Tyr Ala Thr His Ser Asp Lys Phe Thr		
6290	6295	6300
Asp Gly Val Cys Leu Phe Trp Asn Cys Asn Val Asp Arg Tyr Pro		
6305	6310	6315
Ala Asn Ser Ile Val Cys Arg Phe Asp Thr Arg Val Leu Ser Asn		
6320	6325	6330

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Leu	Asn	Leu	Pro	Gly	Cys	Asp	Gly	Gly	Ser	Leu	Tyr	Val	Asn	Lys
6335						6340					6345			
His	Ala	Phe	His	Thr	Pro	Ala	Phe	Asp	Lys	Ser	Ala	Phe	Val	Asn
6350							6355				6360			
Leu	Lys	Gln	Leu	Pro	Phe	Phe	Tyr	Tyr	Ser	Asp	Ser	Pro	Cys	Glu
6365							6370				6375			
Ser	His	Gly	Lys	Gln	Val	Val	Ser	Asp	Ile	Asp	Tyr	Val	Pro	Leu
6380							6385				6390			
Lys	Ser	Ala	Thr	Cys	Ile	Thr	Arg	Cys	Asn	Leu	Gly	Gly	Ala	Val
6395							6400				6405			
Cys	Arg	His	His	Ala	Asn	Glu	Tyr	Arg	Leu	Tyr	Leu	Asp	Ala	Tyr
6410							6415				6420			
Asn	Met	Met	Ile	Ser	Ala	Gly	Phe	Ser	Leu	Trp	Val	Tyr	Lys	Gln
6425							6430				6435			
Phe	Asp	Thr	Tyr	Asn	Leu	Trp	Asn	Thr	Phe	Thr	Arg	Leu	Gln	Ser
6440							6445				6450			
Leu	Glu	Asn	Val	Ala	Phe	Asn	Val	Val	Asn	Lys	Gly	His	Phe	Asp
6455							6460				6465			
Gly	Gln	Gln	Gly	Glut	Val	Pro	Val	Ser	Ile	Ile	Asn	Asn	Thr	Val
6470							6475				6480			
Tyr	Thr	Lys	Val	Asp	Gly	Val	Asp	Val	Glu	Leu	Phe	Glu	Asn	Lys
6485							6490				6495			
Thr	Thr	Leu	Pro	Val	Asn	Val	Ala	Phe	Glu	Leu	Trp	Ala	Lys	Arg
6500							6505				6510			
Asn	Ile	Lys	Pro	Val	Pro	Glu	Val	Lys	Ile	Leu	Asn	Asn	Leu	Gly
6515							6520				6525			
Val	Asp	Ile	Ala	Ala	Asn	Thr	Val	Ile	Trp	Asp	Tyr	Lys	Arg	Asp
6530							6535				6540			
Ala	Pro	Ala	His	Ile	Ser	Thr	Ile	Gly	Val	Cys	Ser	Met	Thr	Asp
6545							6550				6555			
Ile	Ala	Lys	Lys	Pro	Thr	Glu	Thr	Ile	Cys	Ala	Pro	Leu	Thr	Val
6560							6565				6570			
Phe	Phe	Asp	Gly	Arg	Val	Asp	Gly	Gln	Val	Asp	Leu	Phe	Arg	Asn
6575							6580				6585			
Ala	Arg	Asn	Gly	Val	Leu	Ile	Thr	Glu	Gly	Ser	Val	Lys	Gly	Leu
6590							6595				6600			
Gln	Pro	Ser	Val	Gly	Pro	Lys	Gln	Ala	Ser	Leu	Asn	Gly	Val	Thr
6605							6610				6615			
Leu	Ile	Gly	Glu	Ala	Val	Lys	Thr	Gln	Phe	Asn	Tyr	Tyr	Lys	Lys
6620							6625				6630			
Val	Asp	Gly	Val	Val	Gln	Gln	Leu	Pro	Glu	Thr	Tyr	Phe	Thr	Gln
6635							6640				6645			
Ser	Arg	Asn	Leu	Gln	Glu	Phe	Lys	Pro	Arg	Ser	Gln	Met	Glu	Ile
6650							6655				6660			
Asp	Phe	Leu	Glu	Leu	Ala	Met	Asp	Glu	Phe	Ile	Glu	Arg	Tyr	Lys
6665							6670				6675			
Leu	Glu	Gly	Tyr	Ala	Phe	Glu	His	Ile	Val	Tyr	Gly	Asp	Phe	Ser
6680							6685				6690			
His	Ser	Gln	Leu	Gly	Gly	Leu	His	Leu	Leu	Ile	Gly	Leu	Ala	Lys
6695							6700				6705			

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Arg	Phe	Lys	Glu	Ser	Pro	Phe	Glu	Leu	Glu	Asp	Phe	Ile	Pro	Met
6710						6715					6720			
Asp	Ser	Thr	Val	Lys	Asn	Tyr	Phe	Ile	Thr	Asp	Ala	Gln	Thr	Gly
6725						6730					6735			
Ser	Ser	Lys	Cys	Val	Cys	Ser	Val	Ile	Asp	Leu	Leu	Leu	Asp	Asp
6740						6745					6750			
Phe	Val	Glu	Ile	Ile	Lys	Ser	Gln	Asp	Leu	Ser	Val	Val	Ser	Lys
6755						6760					6765			
Val	Val	Lys	Val	Thr	Ile	Asp	Tyr	Thr	Glu	Ile	Ser	Phe	Met	Leu
6770						6775					6780			
Trp	Cys	Lys	Asp	Gly	His	Val	Glu	Thr	Phe	Tyr	Pro	Lys	Leu	Gln
6785						6790					6795			
Ser	Ser	Gln	Ala	Trp	Gln	Pro	Gly	Val	Ala	Met	Pro	Asn	Leu	Tyr
6800						6805					6810			
Lys	Met	Gln	Arg	Met	Leu	Leu	Glu	Lys	Cys	Asp	Leu	Gln	Asn	Tyr
6815						6820					6825			
Gly	Asp	Ser	Ala	Thr	Leu	Pro	Lys	Gly	Ile	Met	Met	Asn	Val	Ala
6830						6835					6840			
Lys	Tyr	Thr	Gln	Leu	Cys	Gln	Tyr	Leu	Asn	Thr	Leu	Thr	Leu	Ala
6845						6850					6855			
Val	Pro	Tyr	Asn	Met	Arg	Val	Ile	His	Phe	Gly	Ala	Gly	Ser	Asp
6860						6865					6870			
Lys	Gly	Val	Ala	Pro	Gly	Thr	Ala	Val	Leu	Arg	Gln	Trp	Leu	Pro
6875						6880					6885			
Thr	Gly	Thr	Leu	Leu	Val	Asp	Ser	Asp	Leu	Asn	Asp	Phe	Val	Ser
6890						6895					6900			
Asp	Ala	Asp	Ser	Thr	Leu	Ile	Gly	Asp	Cys	Ala	Thr	Val	His	Thr
6905						6910					6915			
Ala	Asn	Lys	Trp	Asp	Leu	Ile	Ile	Ser	Asp	Met	Tyr	Asp	Pro	Lys
6920						6925					6930			
Thr	Lys	Asn	Val	Thr	Lys	Glu	Asn	Asp	Ser	Lys	Glu	Gly	Phe	Phe
6935						6940					6945			
Thr	Tyr	Ile	Cys	Gly	Phe	Ile	Gln	Gln	Lys	Leu	Ala	Leu	Gly	Gly
6950						6955					6960			
Ser	Val	Ala	Ile	Lys	Ile	Thr	Glu	His	Ser	Trp	Asn	Ala	Asp	Leu
6965						6970					6975			
Tyr	Lys	Leu	Met	Gly	His	Phe	Ala	Trp	Trp	Thr	Ala	Phe	Val	Thr
6980						6985					6990			
Asn	Val	Asn	Ala	Ser	Ser	Ser	Glu	Ala	Phe	Leu	Ile	Gly	Cys	Asn
6995						7000					7005			
Tyr	Leu	Gly	Lys	Pro	Arg	Glu	Gln	Ile	Asp	Gly	Tyr	Val	Met	His
7010						7015					7020			
Ala	Asn	Tyr	Ile	Phe	Trp	Arg	Asn	Thr	Asn	Pro	Ile	Gln	Leu	Ser
7025						7030					7035			
Ser	Tyr	Ser	Leu	Phe	Asp	Met	Ser	Lys	Phe	Pro	Leu	Lys	Leu	Arg
7040						7045					7050			
Gly	Thr	Ala	Val	Met	Ser	Leu	Lys	Glu	Gly	Gln	Ile	Asn	Asp	Met
7055						7060					7065			
Ile	Leu	Ser	Leu	Leu	Ser	Lys	Gly	Arg	Leu	Ile	Ile	Arg	Glu	Asn
7070						7075					7080			
Asn	Arg	Val	Val	Ile	Ser	Ser	Asp	Val	Leu	Val	Asn	Asn		

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7085

7090

7095

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<210> SEQ ID NO 165
<211> LENGTH: 1273
<212> TYPE: PRT
<213> ORGANISM: SARS-CoV-2 betacoronavirus

<400> SEQUENCE: 165

Met Phe Val Phe Leu Val Leu Pro Leu Val Ser Ser Gln Cys Val
1           5          10          15

Asn Leu Thr Thr Arg Thr Gln Leu Pro Pro Ala Tyr Thr Asn Ser Phe
20          25          30

Thr Arg Gly Val Tyr Tyr Pro Asp Lys Val Phe Arg Ser Ser Val Leu
35          40          45

His Ser Thr Gln Asp Leu Phe Leu Pro Phe Phe Ser Asn Val Thr Trp
50          55          60

Phe His Ala Ile His Val Ser Gly Thr Asn Gly Thr Lys Arg Phe Asp
65          70          75          80

Asn Pro Val Leu Pro Phe Asn Asp Gly Val Tyr Phe Ala Ser Thr Glu
85          90          95

Lys Ser Asn Ile Ile Arg Gly Trp Ile Phe Gly Thr Thr Leu Asp Ser
100         105         110

Lys Thr Gln Ser Leu Leu Ile Val Asn Asn Ala Thr Asn Val Val Ile
115         120         125

Lys Val Cys Glu Phe Gln Phe Cys Asn Asp Pro Phe Leu Gly Val Tyr
130         135         140

Tyr His Lys Asn Asn Lys Ser Trp Met Glu Ser Glu Phe Arg Val Tyr
145         150         155         160

Ser Ser Ala Asn Asn Cys Thr Phe Glu Tyr Val Ser Gln Pro Phe Leu
165         170         175

Met Asp Leu Glu Gly Lys Gln Gly Asn Phe Lys Asn Leu Arg Glu Phe
180         185         190

Val Phe Lys Asn Ile Asp Gly Tyr Phe Lys Ile Tyr Ser Lys His Thr
195         200         205

Pro Ile Asn Leu Val Arg Asp Leu Pro Gln Gly Phe Ser Ala Leu Glu
210         215         220

Pro Leu Val Asp Leu Pro Ile Gly Ile Asn Ile Thr Arg Phe Gln Thr
225         230         235         240

Leu Leu Ala Leu His Arg Ser Tyr Leu Thr Pro Gly Asp Ser Ser Ser
245         250         255

Gly Trp Thr Ala Gly Ala Ala Ala Tyr Tyr Val Gly Tyr Leu Gln Pro
260         265         270

Arg Thr Phe Leu Leu Lys Tyr Asn Glu Asn Gly Thr Ile Thr Asp Ala
275         280         285

Val Asp Cys Ala Leu Asp Pro Leu Ser Glu Thr Lys Cys Thr Leu Lys
290         295         300

Ser Phe Thr Val Glu Lys Gly Ile Tyr Gln Thr Ser Asn Phe Arg Val
305         310         315         320

Gln Pro Thr Glu Ser Ile Val Arg Phe Pro Asn Ile Thr Asn Leu Cys
325         330         335

Pro Phe Gly Glu Val Phe Asn Ala Thr Arg Phe Ala Ser Val Tyr Ala
340         345         350

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Trp	Asn	Arg	Lys	Arg	Ile	Ser	Asn	Cys	Val	Ala	Asp	Tyr	Ser	Val	Leu
355					360										365
Tyr	Asn	Ser	Ala	Ser	Phe	Ser	Thr	Phe	Lys	Cys	Tyr	Gly	Val	Ser	Pro
370					375										380
Thr	Lys	Leu	Asn	Asp	Leu	Cys	Phe	Thr	Asn	Val	Tyr	Ala	Asp	Ser	Phe
385					390										400
Val	Ile	Arg	Gly	Asp	Glu	Val	Arg	Gln	Ile	Ala	Pro	Gly	Gln	Thr	Gly
	405					410									415
Lys	Ile	Ala	Asp	Tyr	Asn	Tyr	Lys	Leu	Pro	Asp	Asp	Phe	Thr	Gly	Cys
	420					425									430
Val	Ile	Ala	Trp	Asn	Ser	Asn	Asn	Leu	Asp	Ser	Lys	Val	Gly	Gly	Asn
	435					440									445
Tyr	Asn	Tyr	Leu	Tyr	Arg	Leu	Phe	Arg	Lys	Ser	Asn	Leu	Lys	Pro	Phe
	450					455									460
Glu	Arg	Asp	Ile	Ser	Thr	Glu	Ile	Tyr	Gln	Ala	Gly	Ser	Thr	Pro	Cys
	465					470									480
Asn	Gly	Val	Glu	Gly	Phe	Asn	Cys	Tyr	Phe	Pro	Leu	Gln	Ser	Tyr	Gly
	485					490									495
Phe	Gln	Pro	Thr	Asn	Gly	Val	Gly	Tyr	Gln	Pro	Tyr	Arg	Val	Val	Val
	500					505									510
Leu	Ser	Phe	Glu	Leu	Leu	His	Ala	Pro	Ala	Thr	Val	Cys	Gly	Pro	Lys
	515					520									525
Lys	Ser	Thr	Asn	Leu	Val	Lys	Asn	Lys	Cys	Val	Asn	Phe	Asn	Phe	Asn
	530					535									540
Gly	Leu	Thr	Gly	Thr	Gly	Val	Leu	Thr	Glu	Ser	Asn	Lys	Lys	Phe	Leu
	545					550									560
Pro	Phe	Gln	Gln	Phe	Gly	Arg	Asp	Ile	Ala	Asp	Thr	Thr	Asp	Ala	Val
	565					570									575
Arg	Asp	Pro	Gln	Thr	Leu	Glu	Ile	Leu	Asp	Ile	Thr	Pro	Cys	Ser	Phe
	580					585									590
Gly	Gly	Val	Ser	Val	Ile	Thr	Pro	Gly	Thr	Asn	Thr	Ser	Asn	Gln	Val
	595					600									605
Ala	Val	Leu	Tyr	Gln	Asp	Val	Asn	Cys	Thr	Glu	Val	Pro	Val	Ala	Ile
	610					615									620
His	Ala	Asp	Gln	Leu	Thr	Pro	Thr	Trp	Arg	Val	Tyr	Ser	Thr	Gly	Ser
	625					630									640
Asn	Val	Phe	Gln	Thr	Arg	Ala	Gly	Cys	Leu	Ile	Gly	Ala	Glu	His	Val
	645					650									655
Asn	Asn	Ser	Tyr	Glu	Cys	Asp	Ile	Pro	Ile	Gly	Ala	Gly	Ile	Cys	Ala
	660					665									670
Ser	Tyr	Gln	Thr	Gln	Thr	Asn	Ser	Pro	Arg	Arg	Ala	Arg	Ser	Val	Ala
	675					680									685
Ser	Gln	Ser	Ile	Ile	Ala	Tyr	Thr	Met	Ser	Leu	Gly	Ala	Glu	Asn	Ser
	690					695									700
Val	Ala	Tyr	Ser	Asn	Asn	Ser	Ile	Ala	Ile	Pro	Thr	Asn	Phe	Thr	Ile
	705					710									720
Ser	Val	Thr	Thr	Glu	Ile	Leu	Pro	Val	Ser	Met	Thr	Lys	Thr	Ser	Val
	725					730									735
Asp	Cys	Thr	Met	Tyr	Ile	Cys	Gly	Asp	Ser	Thr	Glu	Cys	Ser	Asn	Leu
	740					745									750
Leu	Leu	Gln	Tyr	Gly	Ser	Phe	Cys	Thr	Gln	Leu	Asn	Arg	Ala	Leu	Thr

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755	760	765
Gly Ile Ala Val Glu Gln Asp Lys Asn Thr Gln Glu Val Phe Ala Gln		
770	775	780
Val Lys Gln Ile Tyr Lys Thr Pro Pro Ile Lys Asp Phe Gly Gly Phe		
785	790	795 800
Asn Phe Ser Gln Ile Leu Pro Asp Pro Ser Lys Pro Ser Lys Arg Ser		
805	810	815
Phe Ile Glu Asp Leu Leu Phe Asn Lys Val Thr Leu Ala Asp Ala Gly		
820	825	830
Phe Ile Lys Gln Tyr Gly Asp Cys Leu Gly Asp Ile Ala Ala Arg Asp		
835	840	845
Leu Ile Cys Ala Gln Lys Phe Asn Gly Leu Thr Val Leu Pro Pro Leu		
850	855	860
Leu Thr Asp Glu Met Ile Ala Gln Tyr Thr Ser Ala Leu Leu Ala Gly		
865	870	875 880
Thr Ile Thr Ser Gly Trp Thr Phe Gly Ala Gly Ala Ala Leu Gln Ile		
885	890	895
Pro Phe Ala Met Gln Met Ala Tyr Arg Phe Asn Gly Ile Gly Val Thr		
900	905	910
Gln Asn Val Leu Tyr Glu Asn Gln Lys Leu Ile Ala Asn Gln Phe Asn		
915	920	925
Ser Ala Ile Gly Lys Ile Gln Asp Ser Leu Ser Ser Thr Ala Ser Ala		
930	935	940
Leu Gly Lys Leu Gln Asp Val Val Asn Gln Asn Ala Gln Ala Leu Asn		
945	950	955 960
Thr Leu Val Lys Gln Leu Ser Ser Asn Phe Gly Ala Ile Ser Ser Val		
965	970	975
Leu Asn Asp Ile Leu Ser Arg Leu Asp Lys Val Glu Ala Glu Val Gln		
980	985	990
Ile Asp Arg Leu Ile Thr Gly Arg Leu Gln Ser Leu Gln Thr Tyr Val		
995	1000	1005
Thr Gln Gln Leu Ile Arg Ala Ala Glu Ile Arg Ala Ser Ala Asn		
1010	1015	1020
Leu Ala Ala Thr Lys Met Ser Glu Cys Val Leu Gly Gln Ser Lys		
1025	1030	1035
Arg Val Asp Phe Cys Gly Lys Gly Tyr His Leu Met Ser Phe Pro		
1040	1045	1050
Gln Ser Ala Pro His Gly Val Val Phe Leu His Val Thr Tyr Val		
1055	1060	1065
Pro Ala Gln Glu Lys Asn Phe Thr Thr Ala Pro Ala Ile Cys His		
1070	1075	1080
Asp Gly Lys Ala His Phe Pro Arg Glu Gly Val Phe Val Ser Asn		
1085	1090	1095
Gly Thr His Trp Phe Val Thr Gln Arg Asn Phe Tyr Glu Pro Gln		
1100	1105	1110
Ile Ile Thr Thr Asp Asn Thr Phe Val Ser Gly Asn Cys Asp Val		
1115	1120	1125
Val Ile Gly Ile Val Asn Asn Thr Val Tyr Asp Pro Leu Gln Pro		
1130	1135	1140
Glu Leu Asp Ser Phe Lys Glu Glu Leu Asp Lys Tyr Phe Lys Asn		
1145	1150	1155

-continued

His Thr Ser Pro Asp Val Asp Leu Gly Asp Ile Ser Gly Ile Asn
1160 1165 1170

Ala Ser Val Val Asn Ile Gln Lys Glu Ile Asp Arg Leu Asn Glu
1175 1180 1185

Val Ala Lys Asn Leu Asn Glu Ser Leu Ile Asp Leu Gln Glu Leu
1190 1195 1200

Gly Lys Tyr Glu Gln Tyr Ile Lys Trp Pro Trp Tyr Ile Trp Leu
1205 1210 1215

Gly Phe Ile Ala Gly Leu Ile Ala Ile Val Met Val Thr Ile Met
1220 1225 1230

Leu Cys Cys Met Thr Ser Cys Cys Ser Cys Leu Lys Gly Cys Cys
1235 1240 1245

Ser Cys Gly Ser Cys Cys Lys Phe Asp Glu Asp Asp Ser Glu Pro
1250 1255 1260

Val Leu Lys Gly Val Lys Leu His Tyr Thr
1265 1270

<210> SEQ ID NO 166
<211> LENGTH: 220
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence surface glycoprotein RBD
[Wuhan seafood market pneumonia virus]; GenBank: QHD43416.1;
January 23, 2020

<400> SEQUENCE: 166

Asn Ile Thr Asn Leu Cys Pro Phe Gly Glu Val Phe Asn Ala Thr Arg
1 5 10 15

Phe Ala Ser Val Tyr Ala Trp Asn Arg Lys Arg Ile Ser Asn Cys Val
20 25 30

Ala Asp Tyr Ser Val Leu Tyr Asn Ser Ala Ser Phe Ser Thr Phe Lys
35 40 45

Cys Tyr Gly Val Ser Pro Thr Lys Leu Asn Asp Leu Cys Phe Thr Asn
50 55 60

Val Tyr Ala Asp Ser Phe Val Ile Arg Gly Asp Glu Val Arg Gln Ile
65 70 75 80

Ala Pro Gly Gln Thr Gly Lys Ile Ala Asp Tyr Asn Tyr Lys Leu Pro
85 90 95

Asp Asp Phe Thr Gly Cys Val Ile Ala Trp Asn Ser Asn Asn Leu Asp
100 105 110

Ser Lys Val Gly Gly Asn Tyr Asn Tyr Leu Tyr Arg Leu Phe Arg Lys
115 120 125

Ser Asn Leu Lys Pro Phe Glu Arg Asp Ile Ser Thr Glu Ile Tyr Gln
130 135 140

Ala Gly Ser Thr Pro Cys Asn Gly Val Glu Gly Phe Asn Cys Tyr Phe
145 150 155 160

Pro Leu Gln Ser Tyr Gly Phe Gln Pro Thr Asn Gly Val Gly Tyr Gln
165 170 175

Pro Tyr Arg Val Val Leu Ser Phe Glu Leu Leu His Ala Pro Ala
180 185 190

Thr Val Cys Gly Pro Lys Lys Ser Thr Asn Leu Val Lys Asn Lys Cys
195 200 205

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Val Asn Phe Asn Phe Asn Gly Leu Thr Gly Thr Gly
210 215 220

<210> SEQ ID NO 167
<211> LENGTH: 72
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence Receptor Binding Motif
(RBM) in surface glycoprotein RBD [Wuhan seafood market pneumonia
virus]; GenBank: QHD43416.1; January 23, 2020

<400> SEQUENCE: 167

Asn Ser Asn Asn Leu Asp Ser Lys Val Gly Gly Asn Tyr Asn Tyr Leu
1 5 10 15

Tyr Arg Leu Phe Arg Lys Ser Asn Leu Lys Pro Phe Glu Arg Asp Ile
20 25 30

Ser Thr Glu Ile Tyr Gln Ala Gly Ser Thr Pro Cys Asn Gly Val Glu
35 40 45

Gly Phe Asn Cys Tyr Phe Pro Leu Gln Ser Tyr Gly Phe Gln Pro Thr
50 55 60

Asn Gly Val Gly Tyr Gln Pro Tyr
65 70

<210> SEQ ID NO 168

<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v13 mAb VL
(VK)

<400> SEQUENCE: 168

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr
20 25 30

Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu
85 90 95

Thr Phe Gly Gly Threonine Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 169

<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v13 mAb
CDRL1

<400> SEQUENCE: 169

Gln Thr Val Ser Ser Thr Ser
1 5

-continued

<210> SEQ ID NO 170
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v13 mAb
CDRL2

<400> SEQUENCE: 170

Gly Ala Ser
1

<210> SEQ ID NO 171
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v13 mAb
CDRL3

<400> SEQUENCE: 171

Gln Gln His Asp Thr Ser Leu Thr
1 5

<210> SEQ ID NO 172
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v2.9 mAb VH

<400> SEQUENCE: 172

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Ser Thr Tyr Asn Ala Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Phe Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 173
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 CH1-CH3 Gm17;
IgG1*01 LS

<400> SEQUENCE: 173

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

-continued

<210> SEQ ID NO 174
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 mAb CL (Ck)
IgKC*01 k1m3

<400> SEQUENCE: 174

-continued

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65 70 75 80

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
85 90 95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 175

<211> LENGTH: 330

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 CH1-CH3 G1m17;
IgG1*01 LS GAALIE

<400> SEQUENCE: 175

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Ala Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Leu Pro Glu Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225 230 235 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn

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260	265	270
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Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe		
275	280	285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn		
290	295	300

Val Phe Ser Cys Ser Val Leu His Glu Ala Leu His Ser His Tyr Thr			
305	310	315	320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys		
325	330	

<210> SEQ ID NO 176

<211> LENGTH: 123

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v2.10 mAb VH

<400> SEQUENCE: 176

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala			
1	5	10	15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr		
20	25	30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu		
35	40	45

Gly Phe Val Asn Ala Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr		
50	55	60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr			
65	70	75	80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys		
85	90	95

Ala Arg Asp Arg Pro Ser His Glu Phe Ala Met Tyr Phe Phe Asp Asn		
100	105	110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser		
115	120	

<210> SEQ ID NO 177

<211> LENGTH: 123

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v2.11 mAb VH

<400> SEQUENCE: 177

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala			
1	5	10	15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr		
20	25	30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Pro Glu Trp Leu		
35	40	45

Gly Phe Val Gln Gly Tyr Ser Gly Ala Thr Arg Tyr Ala Gln Lys Tyr		
50	55	60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr			
65	70	75	80

Met Gln Leu Ser Arg Leu Arg Pro Asp Asp Thr Ala Val Tyr Tyr Cys		
85	90	95

-continued

Ala Arg Asp Arg Pro Ser His Glu Phe Ala Met Tyr Phe Phe Asp Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 178
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v1 mAb VH

<400> SEQUENCE: 178

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Trp Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Leu Trp Trp Asn Asp Gln Ala His Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 179
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v1 mAb CDRH1

<400> SEQUENCE: 179

Gly Phe Thr Phe Ser Asn Tyr Trp
1 5

<210> SEQ ID NO 180
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v1 mAb CDRH2

<400> SEQUENCE: 180

Ile Lys Gln Asp Gly Ser Glu Lys
1 5

<210> SEQ ID NO 181
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v1 mAb CDRH3

<400> SEQUENCE: 181

-continued

Ala Arg Asp Leu Trp Trp Asn Asp Gln Ala His Tyr Tyr Gly Met Asp
1 5 10 15

Val

<210> SEQ ID NO 182
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v1 mAb VL

<400> SEQUENCE: 182

Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Phe Pro Asn Gln Tyr Ala
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Met Leu Ile Tyr
35 40 45

Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Phe Gly Ser
50 55 60

Ser Ser Gly Thr Thr Val Thr Leu Thr Ile Arg Gly Val Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Val
85 90 95

Phe Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> SEQ ID NO 183
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v1 mAb CDRL1

<400> SEQUENCE: 183

Ala Phe Pro Asn Gln Tyr
1 5

<210> SEQ ID NO 184
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v1 mAb CDRL2

<400> SEQUENCE: 184

Lys Asp Ser
1

<210> SEQ ID NO 185
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v1 mAb CDRL3

<400> SEQUENCE: 185

Gln Ser Ala Asp Ser Ser Gly Thr Val
1 5

-continued

```

<210> SEQ ID NO 186
<211> LENGTH: 373
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v1 mAb VH

```

<400> SEQUENCE: 186

gaggtgcagc tggggaggc ttgggtccagc ctggggggtc cctgagactc	60
tccctgtcgac cctctggatt caccttagt aattattggc tgacctgggt ccgccaggct	120
ccagggaaagg ggctggagtg ggtggccaac ataaagcaag atggaaagtga gaaatactat	180
gtggactctg tgaaggcccg attaccatc tccagagaca acgccaagaa ctcactgtat	240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatctt	300
tggtggAACG accaggctca ctactacggt atggacgtct ggggccaagg gaccacggc	360
accgtctcct cag	373

<210> SEQ ID NO 187

```

<211> LENGTH: 319
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v1 mAb VL

```

<400> SEQUENCE: 187

tccttatgagc tgacacagcc accctcggtg tcagtgtccc caggacagac ggccaggatc	60
acctgctctg gagatgcatt cccaaaccaa tatgcttatt ggtaccagca gaagccaggc	120
caggccccctg tgatgtgtat ctataaagac agtgagggc cctcaggat ccctgagcga	180
ttctttggct ccagctcagg gacaacagtc acgttgacca tcagaggagt ccaggcagaa	240
gacgaggctg actattactg tcaatcagca gacagcagtg gtaccgttt cggcggaggg	300
accaagctga ccgtcctag	319

<210> SEQ ID NO 188

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<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v1 mAb VH
  (nt - codon optimized)

```

<400> SEQUENCE: 188

gaagtgcagc ttgtcgagag cggcgaggc ctcgttcagc caggtggag tctccgttt	60
tcatgcggc cttcaggatt tacgttctcc aactactggc tgacatgggt gaggcaggca	120
cctggaaagg ggctggagtg ggtggctaac atcaaggagg acggatctga aaaatattat	180
gttagattctg tgaagggcgt gtttaccatc tcaagggata atgccaaaaa ctctttgtat	240
ttacagatga actctttcg agccgaggac accggcgttt actactgtgc ccgagatcta	300
tggtggaatg accaggctca ctattatggc atggacgtgt ggggcccagg tactaccgtt	360
accgtctcct ca	372

<210> SEQ ID NO 189

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<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

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-continued

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v1 mAb VL
(nt- codon optimized)

<400> SEQUENCE: 189

tcttacgagg tcacccagcc accctcagtgc tcaatggaccc ctggccaaac agctcgcatc	60
acctgttcag gtgacgcctt tccaaatcag tacgcctact ggtatcagca gaaacccggc	120
caggcacccg ttatgcctat ctacaagat tctgagcggc catccggtat ccccgaaacgc	180
tttttcggaa gctccagttgg gactacagtt acacttacta tccggggagt gcaagctgaa	240
gtatggggccg actattatgt ccagagcgca gactcctcag gcacagtgtt tggggggccgg	300
actaaaactaa ctgtqctq	318

<210> SEQ ID NO 190

<211> LENGTH: 106

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v2 mAb VLP

<400> SEQUENCE: 190

Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
 1 5 10 15

Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Phe Pro Asn Gln Tyr Ala
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Met Leu Ile Tyr
 35 40 45

Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Phe Gly Ser
50 55 60

Ser Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu

Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Val

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 100 105

-310- SEO ID NO. 181

<210> SEQ ID NO 19
<211> LENGTH: 318

<211> LENGTH: 313

<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

<213> ORGANISM
220 DEPARTMENT

<220> FEATURE: 223 OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-V3 mAb VLP

400 SEQUENCE 101

<210> SEQ ID NO 192

<211> LENGTH: 318

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<213> ORGANISM
<230> FEATURE:

-continued

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v2 mAb VL
(nt - codon optimized)

<400> SEQUENCE: 192

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tcctacgagc tcacccagcc cccctcagtc tctgtgtctc ctggacagac agccagaatc 60
acctgctcgagatgcttt tcccaaccaa tacgcctact ggtaccaaca gaaaccagg 120
caggcgcctgtcatgtat ttataaagac tcagagggc cttcaggaaat tcccgaaaga 180
tttcttcggaa gttcaagcgg aactaccgtg accttaacca taagccccgt gcaggccgaa 240
gatgaagcag actattatgg ccagagtgcc gatagtagtg gcacagtctt tggggggggg 300
acaaagctga cagta 318
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<210> SEQ ID NO 193

<211> LENGTH: 106

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 mAb CL IgLC*01

<400> SEQUENCE: 193

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Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser 1
15
Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp 20
25
30
Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro 35
40
45
Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn 50
55
60
Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys 65
70
75
80
Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val 85
90
95
Glu Lys Thr Val Ala Pro Thr Glu Cys Ser 100
105
```

<210> SEQ ID NO 194

<211> LENGTH: 124

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v3 mAb VH

<400> SEQUENCE: 194

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly 1
5
10
15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr 20
25
30
Phe Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35
40
45
Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val 50
55
60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr 65
70
75
80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 85
90
95
```

-continued

Ala Arg Asp Leu Trp Trp Asn Asp Gln Ala His Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 195
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v3 mAb CDRH1
<400> SEQUENCE: 195

Gly Phe Thr Phe Ser Asn Tyr Phe
1 5

<210> SEQ ID NO 196
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v4 mAb VH
<400> SEQUENCE: 196

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Trp Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Asn Ile Lys Gln Asp Ala Ser Glu Lys Tyr Tyr Val Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Leu Trp Trp Asn Asp Gln Ala His Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 197
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v4 mAb CDRH2
<400> SEQUENCE: 197

Ile Lys Gln Asp Ala Ser Glu Lys
1 5

<210> SEQ ID NO 198
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v5 mAb VH
<400> SEQUENCE: 198

-continued

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
1					5			10					15		
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Asn	Tyr
					20			25					30		
Trp	Met	Thr	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
					35			40				45			
Ala	Asn	Ile	Lys	Gln	Glu	Gly	Ser	Glu	Lys	Tyr	Tyr	Val	Asp	Ser	Val
					50			55				60			
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Leu	Tyr
					65			70			75		80		
Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
					85			90			95				
Ala	Arg	Asp	Leu	Trp	Trp	Asn	Asp	Gln	Ala	His	Tyr	Tyr	Gly	Met	Asp
					100			105			110				
Val	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser				
					115			120							

<210> SEQ ID NO 199
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v5 mAb CDRH2
<400> SEQUENCE: 199

Ile	Lys	Gln	Glu	Gly	Ser	Glu	Lys
1					5		

<210> SEQ ID NO 200
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v6 mAb VH
<400> SEQUENCE: 200

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
1					5			10				15			

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Asn	Tyr
					20			25				30			

Trp	Met	Thr	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
					35			40				45			

Ala	Asn	Ile	Lys	Gln	Asp	Gly	Ser	Glu	Lys	Tyr	Tyr	Val	Asp	Ser	Val
					50			55				60			

Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Leu	Tyr
					65			70			75		80		

Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
					85			90			95				

Ala	Arg	Asp	Leu	Phe	Trp	Asn	Asp	Gln	Ala	His	Tyr	Tyr	Gly	Met	Asp
					100			105			110				

Val	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser				
					115			120							

<210> SEQ ID NO 201
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v6 mAb CDRH3

<400> SEQUENCE: 201

Ala Arg Asp Leu Phe Trp Asn Asp Gln Ala His Tyr Tyr Gly Met Asp
1 5 10 15

Val

<210> SEQ ID NO 202

<211> LENGTH: 124

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v7 mAb VH

<400> SEQUENCE: 202

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Trp Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Leu Trp Phe Asn Asp Gln Ala His Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 203

<211> LENGTH: 17

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S315-v7 mAb CDRH3

<400> SEQUENCE: 203

Ala Arg Asp Leu Trp Phe Asn Asp Gln Ala His Tyr Tyr Gly Met Asp
1 5 10 15

Val

<210> SEQ ID NO 204

<211> LENGTH: 230

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 Heavy Chain
IgHG1*01 Fd

<400> SEQUENCE: 204

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

-continued

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly	Leu Glu Trp Met		
35	40	45	
Gly Trp Ile Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe			
50	55	60	
Gln Gly Arg Val Thr Met Thr Asp Thr Ser Thr Thr Gly Tyr			
65	70	75	80
Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys			
85	90	95	
Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly			
100	105	110	
Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala			
115	120	125	
Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser			
130	135	140	
Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe			
145	150	155	160
Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly			
165	170	175	
Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu			
180	185	190	
Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr			
195	200	205	
Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg			
210	215	220	
Val Glu Pro Lys Ser Cys			
225	230		

<210> SEQ ID NO 205
<211> LENGTH: 214
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 Light Chain
IgKC*01

<400> SEQUENCE: 205

Glu Ile Val Leu Thr Gln Ser Pro Gly	Thr Leu Ser Leu Ser Pro Gly		
1	5	10	15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr			
20	25	30	
Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu			
35	40	45	
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser			
50	55	60	
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu			
65	70	75	80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu			
85	90	95	
Thr Phe Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala			
100	105	110	
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly			
115	120	125	
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala			
130	135	140	

-continued

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> SEQ ID NO 206
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic linker sequence

<400> SEQUENCE: 206
Gly Ser Thr Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr
1 5 10 15

Lys Gly

<210> SEQ ID NO 207
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic linker sequence

<400> SEQUENCE: 207
Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly
1 5 10

<210> SEQ ID NO 208
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic linker sequence

<400> SEQUENCE: 208
Gly Lys Pro Gly Ser Gly Glu Gly
1 5

<210> SEQ ID NO 209
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic linker sequence

<400> SEQUENCE: 209
Ser Gly Lys Pro Gly Ser Gly Glu
1 5

<210> SEQ ID NO 210
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

-continued

```

<223> OTHER INFORMATION: Synthetic linker sequence
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Xaa =positively charged amino acid
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (3)..(5)
<223> OTHER INFORMATION: Xaa = glycine (G) or serine (S)
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Xaa = glycine (G) or a negatively charged
amino acid

```

<400> SEQUENCE: 210

Xaa	Pro	Xaa	Xaa	Xaa	Xaa
1					5

```

<210> SEQ ID NO 211
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic linker sequence
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (2)..(10)
<223> OTHER INFORMATION: any one or all of amino acids 2-10 can either
be present or absent
<220> FEATURE:
<221> NAME/KEY: VARIANT
<222> LOCATION: (12)..(110)
<223> OTHER INFORMATION: any one or all of amino acids 12-110 can
either be present or absent

```

<400> SEQUENCE: 211

Gly	Ser	Gly	Gly	Gly	Gly	Gly						
1							10					15

Gly	Gly	Gly	Gly	Ser	Gly							
				20		25		30				

Ser	Gly	Ser	Gly	Gly	Gly	Gly						
				35		40		45				

Gly	Gly	Gly	Gly	Gly	Ser	Gly						
				50		55		60				

Gly	Ser	Gly	Gly	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly
65				70		75		80				

Gly	Gly	Gly	Gly	Gly	Ser	Gly						
				85		90		95				

Gly	Gly	Ser	Gly	Ser	Gly						
			100		105		110				

```

<210> SEQ ID NO 212
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic linker sequence

```

<400> SEQUENCE: 212

Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Gly	Ser
1				5		10		15		

<210> SEQ ID NO 213

-continued

<211> LENGTH: 50
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic linker sequence

<400> SEQUENCE: 213

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly
1 5 10 15
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
20 25 30
Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
35 40 45
Gly Ser
50

<210> SEQ ID NO 214
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic linker sequence

<400> SEQUENCE: 214

Gly Ser Thr Ser Gly Gly Ser Gly Gly Ser Gly Gly Gly
1 5 10 15
Ser Ser

<210> SEQ ID NO 215
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic linker sequence

<400> SEQUENCE: 215

Glu Gly Lys Ser Ser Gly Ser Gly Ser Glu Ser Lys Val Asp
1 5 10

<210> SEQ ID NO 216
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic linker sequence

<400> SEQUENCE: 216

Lys Glu Ser Gly Ser Val Ser Ser Gly Gln Leu Ala Gln Phe Arg Ser
1 5 10 15

Leu Asp

<210> SEQ ID NO 217
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic linker sequence

<400> SEQUENCE: 217

Gly Gly Gly Gly Ser
1 5

-continued

<210> SEQ ID NO 218
<211> LENGTH: 494
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-scFab (H-L)

<400> SEQUENCE: 218

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
115 120 125

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
130 135 140

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
145 150 155 160

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
165 170 175

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
180 185 190

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
195 200 205

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg
210 215 220

Val Glu Pro Lys Ser Cys Gly Gly Ser Gly Gly Gly Ser
225 230 235 240

Gly Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser Gly
245 250 255

Gly Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser Gly Gly
260 265 270

Gly Gly Ser Gly Gly Ser Gly Ile Val Leu Thr Gln Ser Pro
275 280 285

Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
290 295 300

Ala Ser Gln Thr Val Ser Ser Thr Ser Leu Ala Trp Tyr Gln Gln Lys
305 310 315 320

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala
325 330 335

Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Thr Asp Phe
340 345 350

-continued

Thr	Leu	Thr	Ile	Ser	Arg	Leu	Glu	Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr
355						360					365				
Cys	Gln	Gln	His	Asp	Thr	Ser	Leu	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Val
370						375				380					
Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro
385						390				395				400	
Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly	Thr	Ala	Ser	Val	Val	Cys	Leu	Leu
											410			415	
Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala	Lys	Val	Gln	Trp	Lys	Val	Asp	Asn
											425			430	
Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln	Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser
											440			445	
Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser	Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala
											455			460	
Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr	Ala	Cys	Glu	Val	Thr	His	Gln	Gly
465						470				475				480	
Leu	Ser	Ser	Pro	Val	Thr	Lys	Ser	Phe	Asn	Arg	Gly	Glu	Cys		
											485			490	

```

<210> SEQ_ID NO 219
<211> LENGTH: 494
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-scFab (L-H)

<400> SEQUENCE: 219

```

Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Gly	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1							5			10			15		
Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Thr	Val	Ser	Ser	Thr
							20			25			30		
Ser	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu
							35			40			45		
Ile	Tyr	Gly	Ala	Ser	Ser	Arg	Ala	Thr	Gly	Ile	Pro	Asp	Arg	Phe	Ser
							50			55			60		
Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Arg	Leu	Glu
							65			70			75		80
Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	His	Asp	Thr	Ser	Leu
							85			90			95		
Thr	Phe	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	
							100			105			110		
Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly
							115			120			125		
Thr	Ala	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala
							130			135			140		
Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln
							145			150			155		160
Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser
							165			170			175		
Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr
							180			185			190		
Ala	Cys	Glu	Val	Thr	His	Gln	Gly	Leu	Ser	Ser	Pro	Val	Thr	Lys	Ser
							195			200			205		

-continued

Phe	Asn	Arg	Gly	Glu	Cys	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Ser			
210						215				220						
Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Ser	Gly		
225						230				235				240		
Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Ser	Gly		
245						250				255				255		
Gly	Gly	Ser	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Ser	Gly	Gly	Ser	Gly		
260						265				270						
Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala	Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	
275						280				285						
Ser	Gly	Tyr	Pro	Phe	Thr	Ser	Tyr	Gly	Ile	Ser	Trp	Val	Arg	Gln	Ala	
290						295				300						
Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met	Gly	Trp	Ile	Ser	Thr	Tyr	Asn	Gly	
305						310				315					320	
Asn	Thr	Asn	Tyr	Ala	Gln	Lys	Phe	Gln	Gly	Arg	Val	Thr	Met	Thr	Thr	
325						330				335						
Asp	Thr	Ser	Thr	Thr	Gly	Tyr	Met	Glu	Leu	Arg	Arg	Leu	Arg	Ser		
340						345				350						
Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Asp	Tyr	Thr	Arg	Gly	Ala	
355						360				365						
Trp	Phe	Gly	Glu	Ser	Leu	Ile	Gly	Gly	Phe	Asp	Asn	Trp	Gly	Gln	Gly	
370						375				380						
Thr	Leu	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	
385						390				395					400	
Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	Leu	
405						410				415						
Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	
420						425				430						
Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu	
435						440				445						
Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Val	Thr	Val	Pro	Ser
450						455				460						
Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro	
465						470				475						480
Ser	Asn	Thr	Lys	Val	Asp	Lys	Arg	Val	Glu	Pro	Lys	Ser	Cys			
485						490										

```

<210> SEQ_ID NO 220
<211> LENGTH: 249
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-scFv (VH-VL)

```

<400> SEQUENCE: 220

Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1						5			10			15			
Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Pro	Phe	Thr	Ser	Tyr
20						25				30					
Gly	Ile	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met
35						40				45					
Gly	Trp	Ile	Ser	Thr	Tyr	Asn	Gly	Asn	Thr	Asn	Tyr	Ala	Gln	Lys	Phe
50						55				60					

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Gln	Gly	Arg	Val	Thr	Met	Thr	Thr	Asp	Thr	Ser	Thr	Thr	Thr	Gly	Tyr
65					70					75					80
Met	Glu	Leu	Arg	Arg	Leu	Arg	Ser	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
	85						90						95		
Ala	Arg	Asp	Tyr	Thr	Arg	Gly	Ala	Trp	Phe	Gly	Glu	Ser	Leu	Ile	Gly
	100						105				110				
Gly	Phe	Asp	Asn	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly
	115					120					125				
Gly	Gly	Gly	Ser	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Ser	Glu	Ile		
	130				135			140							
Val	Leu	Thr	Gln	Ser	Pro	Gly	Thr	Leu	Ser	Leu	Ser	Pro	Gly	Glu	Arg
145					150				155				160		
Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Thr	Val	Ser	Ser	Thr	Ser	Leu
	165					170				175					
Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Ile	Tyr	
	180					185				190					
Gly	Ala	Ser	Ser	Arg	Ala	Thr	Gly	Ile	Pro	Asp	Arg	Phe	Ser	Gly	Ser
	195					200				205					
Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Arg	Leu	Glu	Pro	Glu
	210				215				220						
Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	His	Asp	Thr	Ser	Leu	Thr	Phe
225					230				235				240		
Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys							
				245											

<210> SEQ_ID NO 221															
<211> LENGTH: 249															
<212> TYPE: PRT															
<213> ORGANISM: Artificial Sequence															
<220> FEATURE:															
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-scFv (VL-VH)															
<400> SEQUENCE: 221															
Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Gly	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1					5				10				15		
Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Thr	Val	Ser	Ser	Thr
				20				25				30			
Ser	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu
					35			40				45			
Ile	Tyr	Gly	Ala	Ser	Ser	Arg	Ala	Thr	Gly	Ile	Pro	Asp	Arg	Phe	Ser
	50				55			60							
Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Arg	Leu	Glu
	65				70			75			80				
Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	His	Asp	Thr	Ser	Leu
					85			90			95				
Thr	Phe	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys	Gly	Gly	Gly	Ser		
	100				105			110							
Gly	Gly	Gly	Ser	Gly	Gly	Ser	Gln	Val	Gln	Leu	Val	Gln			
	115				120			125							
Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala	Ser	Val	Lys	Val	Ser	Cys
	130				135			140							
Lys	Ala	Ser	Gly	Tyr	Pro	Phe	Thr	Ser	Tyr	Gly	Ile	Ser	Trp	Val	Arg
	145				150			155			160				

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Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Ser Thr Tyr
165 170 175

Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met
180 185 190

Thr Thr Asp Thr Ser Thr Thr Gly Tyr Met Glu Leu Arg Arg Leu
195 200 205

Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Tyr Thr Arg
210 215 220

Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp Asn Trp Gly
225 230 235 240

Gln Gly Thr Leu Val Thr Val Ser Ser
245

<210> SEQ ID NO 222

<211> LENGTH: 518

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-scFv
(VH-VL) - (VH-VL)

<400> SEQUENCE: 222

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Ile
130 135 140

Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg
145 150 155 160

Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr Ser Leu
165 170 175

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
180 185 190

Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu
210 215 220

Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu Thr Phe
225 230 235 240

Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Ser Gly Gly
245 250 255

-continued

Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser Gln Val Gln
260 265 270

Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
275 280 285

Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr Gly Ile Ser
290 295 300

Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile
305 310 315 320

Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg
325 330 335

Val Thr Met Thr Thr Asp Thr Ser Thr Thr Gly Tyr Met Glu Leu
340 345 350

Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp
355 360 365

Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp
370 375 380

Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
385 390 395 400

Ser Gly Gly Gly Ser Gly Gly Gly Ser Glu Ile Val Leu Thr
405 410 415

Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu
420 425 430

Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr Ser Leu Ala Trp Tyr
435 440 445

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser
450 455 460

Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly
465 470 475 480

Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala
485 490 495

Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu Thr Phe Gly Gly Gly
500 505 510

Thr Lys Val Glu Ile Lys
515

<210> SEQ_ID NO 223
<211> LENGTH: 518
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2
S309-scFv- (VH-VL) - (VL-VH)

<400> SEQUENCE: 223

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Asp Thr Ser Thr Thr Gly Tyr

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65	70	75	80
Met	Glu	Leu	Arg
85	Arg	Arg	Leu
Met	Arg	Arg	Asp
85	Asp	Asp	Thr
Met	Ala	Val	Tyr
85	Tyr	Tyr	Cys
Ala	Arg	Asp	Tyr
100	Tyr	Thr	Arg
Ala	Trp	Phe	Gly
100	105	105	95
Gly	Phe	Asp	Ser
115	Asn	Trp	Gly
115	Gly	Gly	Thr
115	120	120	125
Gly	Gly	Ser	Gly
130	Gly	Gly	Ser
130	135	135	140
Val	Gly	Gly	Gly
145	150	150	155
Val	Leu	Thr	Gln
145	Thr	Gln	Ser
145	Pro	Gly	Thr
145	Leu	Ser	Leu
145	Ser	Pro	Gly
145	Glu	Glu	Arg
Ala	Thr	Leu	Ser
165	Ser	Cys	Arg
165	Ala	Ser	Gln
165	Gln	Thr	Val
165	Thr	Val	Ser
165	Ser	Ser	Thr
165	Ser	Leu	Ile
Ala	Trp	Tyr	Gln
180	Gln	Gln	Lys
180	Pro	Gly	Ala
180	Ala	Pro	Arg
180	Arg	Leu	Leu
180	Leu	Ile	Tyr
Gly	Ala	Ser	Ser
195	Arg	Ala	Thr
195	Thr	Gly	Ile
195	Gly	Ile	Pro
195	Ile	Pro	Asp
195	Asp	Arg	Phe
195	Phe	Ser	Gly
Gly	Ser	Gly	Thr
210	Thr	Asp	Phe
210	Phe	Thr	Leu
210	Leu	Thr	Ile
210	Thr	Ser	Arg
210	Arg	Leu	Glu
210	Glu	Pro	Glu
Asp	Phe	Ala	Val
225	Val	Tyr	Tyr
225	Tyr	Cys	Gln
225	Gln	Gln	His
225	His	Asp	Thr
225	Asp	Ser	Leu
225	Ser	Leu	Thr
225	Leu	Thr	Phe
Gly	Gly	Gly	Thr
245	lys	Val	Glu
245	Glu	Ile	Lys
245	Ile	Lys	Gly
245	Lys	Gly	Gly
245	Gly	Gly	Ser
245	Ser	Gly	Gly
Gly	Gly	Ser	Gly
260	Gly	Gly	Gly
260	Gly	Gly	Ser
260	Ser	Glu	Ile
260	Ile	Val	Val
Leu	Thr	Gln	Ser
275	Ser	Pro	Gly
275	Pro	Gly	Thr
275	Gly	Thr	Leu
275	Leu	Ser	Leu
275	Leu	Ser	Pro
275	Pro	Gly	Glu
275	Glu	Arg	Ala
Thr	Leu	Ser	Cys
290	Cys	Arg	Ala
290	Ala	Ser	Gln
290	Gln	Thr	Val
290	Thr	Val	Ser
290	Ser	Ser	Ser
290	Ser	Leu	Ile
Trp	Tyr	Gln	Gln
305	Gln	Lys	Pro
305	Pro	Gly	Gln
305	Gly	Gln	Ala
305	Ala	Pro	Arg
305	Arg	Leu	Leu
305	Leu	Ile	Tyr
305	Tyr	Gly	Gly
Ala	Ser	Ser	Arg
325	Arg	Ala	Thr
325	Thr	Gly	Ile
325	Gly	Ile	Pro
325	Pro	Asp	Arg
325	Asp	Ser	Phe
325	Phe	Ser	Gly
Ser	Gly	Thr	Asp
340	Asp	Phe	Thr
340	Thr	Leu	Thr
340	Leu	Ile	Ser
340	Thr	Arg	Leu
340	Arg	Glu	Pro
340	Glu	Pro	Asp
Phe	Ala	Val	Tyr
355	Tyr	Tyr	Cys
355	Cys	Gln	Gln
355	Gln	Gln	His
355	His	Asp	Thr
355	Asp	Ser	Leu
355	Ser	Leu	Thr
355	Leu	Thr	Phe
Gly	Gly	Thr	Lys
370	Lys	Val	Glu
370	Val	Ile	Lys
370	Ile	Lys	Gly
370	Lys	Gly	Gly
370	Gly	Gly	Ser
370	Ser	Gly	Gly
Gly	Ser	Gly	Gly
385	Gly	Gly	Ser
385	Ser	Gln	Val
385	Gln	Val	Gln
385	Gln	Leu	Val
385	Leu	Val	Gln
385	Gln	Ser	Gly
Glu	Val	Lys	Pro
405	Pro	Gly	Ala
405	Ala	Ser	Val
405	Ser	Val	Ser
405	Val	Ser	Cys
405	Ser	Cys	Lys
405	Cys	Lys	Ala
405	Lys	Ala	Ser
Gly	Tyr	Pro	Phe
420	Phe	Thr	Ser
420	Thr	Tyr	Gly
420	Tyr	Ile	Ser
420	Ile	Ser	Trp
420	Trp	Val	Arg
420	Arg	Gln	Ala
420	Ala	Pro	Pro
Gly	Gln	Gly	Leu
435	Gly	Gly	Glu
435	Glu	Trp	Met
435	Trp	Ile	Ser
435	Ile	Ser	Thr
435	Thr	Tyr	Asn
435	Asn	Gly	Asn
Thr	Asn	Tyr	Ala
450	Ala	Gln	Lys
450	Gln	Phe	Gly
450	Phe	Gly	Arg
450	Gly	Arg	Val
450	Arg	Val	Thr
450	Thr	Met	Thr
450	Met	Thr	Asp
Thr	Ser	Thr	Thr
465	Thr	Thr	Gly
465	Gly	Tyr	Met
465	Tyr	Glu	Leu
465	Glu	Leu	Arg
465	Arg	Arg	Leu
465	Leu	Arg	Ser
465	Ser	Asp	Asp

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Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Tyr Thr Arg Gly Ala Trp
485 490 495

Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp Asn Trp Gly Gln Gly Thr
500 505 510

Leu Val Thr Val Ser Ser
515

<210> SEQ ID NO 224

<211> LENGTH: 518

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2
S309-scFv- (VL-VH) - (VH-VL)

<400> SEQUENCE: 224

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr
20 25 30

Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu
85 90 95

Thr Phe Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Ser
100 105 110

Gly Gly Gly Ser Gly Gly Ser Gln Val Gln Leu Val Gln
115 120 125

Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
130 135 140

Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr Gly Ile Ser Trp Val Arg
145 150 155 160

Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Ser Thr Tyr
165 170 175

Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met
180 185 190

Thr Thr Asp Thr Ser Thr Thr Gly Tyr Met Glu Leu Arg Arg Leu
195 200 205

Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Tyr Thr Arg
210 215 220

Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp Asn Trp Gly
225 230 235 240

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Ser Gly Gly
245 250 255

Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser Gln Val Gln
260 265 270

Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
275 280 285

Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr Gly Ile Ser

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290	295	300																																																																																							
Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile																																																																																									
305	310	315	320			Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg			325	330	335	Val Thr Met Thr Thr Asp Thr Ser Thr Thr Gly Tyr Met Glu Leu			340	345	350	Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp			355	360	365	Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp			370	375	380	Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly			385	390	395	400			Ser Gly Gly Gly Ser Gly Gly Ser Glu Ile Val Leu Thr			405	410	415	Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu			420	425	430	Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr Ser Leu Ala Trp Tyr			435	440	445	Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser			450	455	460	Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly			465	470	475	480			Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala			485	490	495	Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu Thr Phe Gly Gly Gly			500	505	510	Thr Lys Val Glu Ile Lys			515		
320																																																																																									
Ser Thr Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg																																																																																									
325	330	335																																																																																							
Val Thr Met Thr Thr Asp Thr Ser Thr Thr Gly Tyr Met Glu Leu																																																																																									
340	345	350																																																																																							
Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp																																																																																									
355	360	365																																																																																							
Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp																																																																																									
370	375	380																																																																																							
Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly																																																																																									
385	390	395	400			Ser Gly Gly Gly Ser Gly Gly Ser Glu Ile Val Leu Thr			405	410	415	Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu			420	425	430	Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr Ser Leu Ala Trp Tyr			435	440	445	Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser			450	455	460	Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly			465	470	475	480			Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala			485	490	495	Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu Thr Phe Gly Gly Gly			500	505	510	Thr Lys Val Glu Ile Lys			515																																			
400																																																																																									
Ser Gly Gly Gly Ser Gly Gly Ser Glu Ile Val Leu Thr																																																																																									
405	410	415																																																																																							
Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu																																																																																									
420	425	430																																																																																							
Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr Ser Leu Ala Trp Tyr																																																																																									
435	440	445																																																																																							
Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser																																																																																									
450	455	460																																																																																							
Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly																																																																																									
465	470	475	480			Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala			485	490	495	Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu Thr Phe Gly Gly Gly			500	505	510	Thr Lys Val Glu Ile Lys			515																																																																				
480																																																																																									
Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala																																																																																									
485	490	495																																																																																							
Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu Thr Phe Gly Gly Gly																																																																																									
500	505	510																																																																																							
Thr Lys Val Glu Ile Lys																																																																																									
515																																																																																									

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<210> SEQ ID NO 225
<211> LENGTH: 518
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2
      S309-scFv-(VL-VH) - (VL-VH)

<400> SEQUENCE: 225

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1          5          10         15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr
20         25          30

Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35         40          45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50         55          60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65         70          75          80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu
85         90          95

Thr Phe Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Ser
100        105         110

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Gly Gly Gly Ser Gly Gly Gly Ser Gln Val Gln Leu Val Gln
 115 120 125
 Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys
 130 135 140
 Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr Gly Ile Ser Trp Val Arg
 145 150 155 160
 Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Ser Thr Tyr
 165 170 175
 Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met
 180 185 190
 Thr Thr Asp Thr Ser Thr Thr Gly Tyr Met Glu Leu Arg Arg Leu
 195 200 205
 Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Tyr Thr Arg
 210 215 220
 Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp Asn Trp Gly
 225 230 235 240
 Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Ser Gly Gly
 245 250 255
 Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser Glu Ile Val
 260 265 270
 Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
 275 280 285
 Thr Leu Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr Ser Leu Ala
 290 295 300
 Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly
 305 310 315 320
 Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly
 325 330 335
 Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp
 340 345 350
 Phe Ala Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu Thr Phe Gly
 355 360 365
 Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Ser Gly Gly Gly
 370 375 380
 Gly Ser Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala
 385 390 395 400
 Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser
 405 410 415
 Gly Tyr Pro Phe Thr Ser Tyr Gly Ile Ser Trp Val Arg Gln Ala Pro
 420 425 430
 Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Ser Thr Tyr Asn Gly Asn
 435 440 445
 Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Thr Asp
 450 455 460
 Thr Ser Thr Thr Gly Tyr Met Glu Leu Arg Arg Leu Arg Ser Asp
 465 470 475 480
 Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Tyr Thr Arg Gly Ala Trp
 485 490 495
 Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp Asn Trp Gly Gln Gly Thr
 500 505 510
 Leu Val Thr Val Ser Ser

-continued

515

<210> SEQ ID NO 226
<211> LENGTH: 494
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2
S309-scFab- (H-L) v1.1

<400> SEQUENCE: 226

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Thr Tyr Gln Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Gly Tyr
65 70 75 80

Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly
100 105 110

Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
115 120 125

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
130 135 140

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
145 150 155 160

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
165 170 175

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
180 185 190

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
195 200 205

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg
210 215 220

Val Glu Pro Lys Ser Cys Gly Gly Ser Gly Gly Gly Ser
225 230 235 240

Gly Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser Gly
245 250 255

Gly Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser Gly Gly
260 265 270

Gly Gly Ser Gly Gly Ser Gly Ile Val Leu Thr Gln Ser Pro
275 280 285

Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
290 295 300

Ala Ser Gln Thr Val Ser Ser Thr Ser Leu Ala Trp Tyr Gln Gln Lys
305 310 315 320

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala
325 330 335

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Thr	Gly	Ile	Pro	Asp	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe
340							345						350		
Thr	Leu	Thr	Ile	Ser	Arg	Leu	Glu	Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr
355						360						365			
Cys	Gln	Gln	His	Asp	Thr	Ser	Leu	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Val
370						375						380			
Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro
385					390				395			400			
Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly	Thr	Ala	Ser	Val	Val	Cys	Leu	Leu
405					410				415						
Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala	Lys	Val	Gln	Trp	Lys	Val	Asp	Asn
		420			425				430						
Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln	Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser
435					440				445						
Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser	Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala
450					455				460						
Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr	Ala	Cys	Glu	Val	Thr	His	Gln	Gly
465					470				475					480	
Leu	Ser	Ser	Pro	Val	Thr	Lys	Ser	Phe	Asn	Arg	Gly	Glu	Cys		
					485			490							

<210> SEQ_ID NO 227															
<211> LENGTH: 494															
<212> TYPE: PRT															
<213> ORGANISM: Artificial Sequence															
<220> FEATURE:															
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2															
S309-scFab-(L-H) v1.1															
<400> SEQUENCE: 227															
Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Gly	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1					5				10					15	
Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Thr	Val	Ser	Ser	Thr
					20				25					30	
Ser	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu
					35			40				45			
Ile	Tyr	Gly	Ala	Ser	Ser	Arg	Ala	Thr	Gly	Ile	Pro	Asp	Arg	Phe	Ser
					50			55			60				
Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Arg	Leu	Glu
					65			70			75			80	
Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	His	Asp	Thr	Ser	Leu
					85			90			95				
Thr	Phe	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	
					100			105			110				
Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly
					115			120			125				
Thr	Ala	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala
					130			135			140				
Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln
					145			150			155			160	
Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser
					165			170			175				
Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr
					180			185			190				

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Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
 195 200 205
 Phe Asn Arg Gly Glu Cys Gly Gly Ser Gly Gly Gly Ser
 210 215 220
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly
 225 230 235 240
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
 245 250 255
 Gly Gly Ser Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly
 260 265 270
 Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala
 275 280 285
 Ser Gly Tyr Pro Phe Thr Ser Tyr Gly Ile Ser Trp Val Arg Gln Ala
 290 295 300
 Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Ser Thr Tyr Gln Gly
 305 310 315 320
 Asn Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Thr
 325 330 335
 Asp Thr Ser Thr Thr Gly Tyr Met Glu Leu Arg Arg Leu Arg Ser
 340 345 350
 Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Tyr Thr Arg Gly Ala
 355 360 365
 Trp Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp Asn Trp Gly Gln Gly
 370 375 380
 Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
 385 390 395 400
 Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
 405 410 415
 Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
 420 425 430
 Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
 435 440 445
 Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
 450 455 460
 Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
 465 470 475 480
 Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
 485 490

 <210> SEQ ID NO 228
 <211> LENGTH: 249
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2
 S309-scFv-(VH-VL) v1.1

 <400> SEQUENCE: 228

 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
 20 25 30

 Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met

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35	40	45
Gly Trp Ile Ser Thr Tyr Gln Gly Asn Thr Asn Tyr Ala Gln Lys Phe		
50	55	60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr		
65	70	75
Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys		
85	90	95
Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly		
100	105	110
Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly		
115	120	125
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Glu Ile		
130	135	140
Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg		
145	150	155
Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr Ser Leu		
165	170	175
Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr		
180	185	190
Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser		
195	200	205
Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu		
210	215	220
Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu Thr Phe		
225	230	235
Gly Gly Gly Thr Lys Val Glu Ile Lys		
245		

<210> SEQ ID NO 229
<211> LENGTH: 249
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2
S309-scFv-(VL-VH) v1.1

<400> SEQUENCE: 229

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly		
1	5	10
15		
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr		
20	25	30
30		
Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu		
35	40	45
45		
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser		
50	55	60
60		
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu		
65	70	75
75		
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu		
85	90	95
95		
Thr Phe Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Ser		
100	105	110
110		
Gly Gly Gly Ser Gly Gly Ser Gln Val Gln Leu Val Gln		
115	120	125

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Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala	Ser	Val	Lys	Val	Ser	Cys
130				135								140			
Lys	Ala	Ser	Gly	Tyr	Pro	Phe	Thr	Ser	Tyr	Gly	Ile	Ser	Trp	Val	Arg
145				150				155						160	
Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met	Gly	Trp	Ile	Ser	Thr	Tyr
						165		170				175			
Gln	Gly	Asn	Thr	Asn	Tyr	Ala	Gln	Lys	Phe	Gln	Gly	Arg	Val	Thr	Met
						180		185				190			
Thr	Thr	Asp	Thr	Ser	Thr	Thr	Thr	Gly	Tyr	Met	Glu	Leu	Arg	Arg	Leu
						195		200			205				
Arg	Ser	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Asp	Tyr	Thr	Arg
						210		215			220				
Gly	Ala	Trp	Phe	Gly	Glu	Ser	Leu	Ile	Gly	Gly	Phe	Asp	Asn	Trp	Gly
225				230				235				240			
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser							
						245									

<210>	SEQ_ID	NO	230												
<211>	LENGTH:	518													
<212>	TYPE:	PRT													
<213>	ORGANISM:	Artificial Sequence													
<220>	FEATURE:														
<223>	OTHER INFORMATION:	Synthetic sequence SARS-CoV-2 S309-scFv-(VH-VL)-(VH-VL) v1.1													
<400> SEQUENCE: 230															
Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1					5			10			15				
Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Pro	Phe	Thr	Ser	Tyr
					20			25			30				
Gly	Ile	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met
					35			40			45				
Gly	Trp	Ile	Ser	Thr	Tyr	Gln	Gly	Asn	Thr	Asn	Tyr	Ala	Gln	Lys	Phe
					50			55			60				
Gln	Gly	Arg	Val	Thr	Met	Thr	Thr	Asp	Thr	Ser	Thr	Thr	Thr	Gly	Tyr
					65			70			75			80	
Met	Glu	Leu	Arg	Arg	Leu	Arg	Ser	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
					85			90			95				
Ala	Arg	Asp	Tyr	Thr	Arg	Gly	Ala	Trp	Phe	Gly	Glu	Ser	Leu	Ile	Gly
					100			105			110				
Gly	Phe	Asp	Asn	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly
					115			120			125				
Gly	Gly	Ser	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Ile		
					130			135			140				
Val	Leu	Thr	Gln	Ser	Pro	Gly	Thr	Leu	Ser	Leu	Ser	Pro	Gly	Glu	Arg
145					150			155			160				
Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Thr	Val	Ser	Ser	Thr	Ser	Leu
					165			170			175				
Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile	Tyr
					180			185			190				
Gly	Ala	Ser	Ser	Arg	Ala	Thr	Gly	Ile	Pro	Asp	Arg	Phe	Ser	Gly	Ser
					195			200			205				
Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Arg	Leu	Glu	Pro	Glu
					210			215			220				

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Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu Thr Phe
 225 230 235 240
 Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Ser Gly Gly
 245 250 255
 Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser Gln Val Gln
 260 265 270
 Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys
 275 280 285
 Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr Gly Ile Ser
 290 295 300
 Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile
 305 310 315 320
 Ser Thr Tyr Gln Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg
 325 330 335
 Val Thr Met Thr Thr Asp Thr Ser Thr Thr Gly Tyr Met Glu Leu
 340 345 350
 Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp
 355 360 365
 Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp
 370 375 380
 Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
 385 390 395 400
 Ser Gly Gly Ser Gly Gly Ser Glu Ile Val Leu Thr
 405 410 415
 Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu
 420 425 430
 Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr Ser Leu Ala Trp Tyr
 435 440 445
 Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser
 450 455 460
 Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly
 465 470 475 480
 Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala
 485 490 495
 Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu Thr Phe Gly Gly
 500 505 510
 Thr Lys Val Glu Ile Lys
 515

<210> SEQ ID NO 231
 <211> LENGTH: 518
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2
 S309-scFv-(VH-VL)-(VL-VH) v1.1
 <400> SEQUENCE: 231

 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15

 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr
 20 25 30

 Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met

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35	40	45
Gly Trp Ile Ser Thr Tyr Gln Gly Asn Thr Asn Tyr Ala Gln Lys Phe		
50	55	60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Thr Gly Tyr		
65	70	75
Met Glu Leu Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys		
85	90	95
Ala Arg Asp Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly		
100	105	110
Gly Phe Asp Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly		
115	120	125
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Glu Ile		
130	135	140
Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg		
145	150	155
Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr Ser Leu		
165	170	175
Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr		
180	185	190
Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser		
195	200	205
Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu		
210	215	220
Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu Thr Phe		
225	230	235
Gly Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Ser Gly Gly		
245	250	255
Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Glu Ile Val		
260	265	270
Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala		
275	280	285
Thr Leu Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr Ser Leu Ala		
290	295	300
Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly		
305	310	315
Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly		
325	330	335
Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp		
340	345	350
Phe Ala Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu Thr Phe Gly		
355	360	365
Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Ser Gly Gly Gly		
370	375	380
Gly Ser Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala		
385	390	395
Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser		
405	410	415
Gly Tyr Pro Phe Thr Ser Tyr Gly Ile Ser Trp Val Arg Gln Ala Pro		
420	425	430
Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Ser Thr Tyr Gln Gly Asn		
435	440	445

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Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Thr Asp			
450	455	460	
Thr Ser Thr Thr Gly Tyr Met Glu Leu Arg Arg Leu Arg Ser Asp			
465	470	475	480
Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Tyr Thr Arg Gly Ala Trp			
485	490	495	
Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp Asn Trp Gly Gln Gly Thr			
500	505	510	
Leu Val Thr Val Ser Ser			
515			

<210> SEQ_ID NO 232			
<211> LENGTH: 518			
<212> TYPE: PRT			
<213> ORGANISM: Artificial Sequence			
<220> FEATURE:			
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2			
S309-scFv- (VL-VH) - (VH-VL) v1.1			
<400> SEQUENCE: 232			
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly			
1	5	10	15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr			
20	25	30	
Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu			
35	40	45	
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser			
50	55	60	
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu			
65	70	75	80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu			
85	90	95	
Thr Phe Gly Gly Thr Lys Val Glu Ile Lys Gly Gly Gly Ser			
100	105	110	
Gly Gly Gly Ser Gly Gly Ser Gln Val Gln Leu Val Gln			
115	120	125	
Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys			
130	135	140	
Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr Gly Ile Ser Trp Val Arg			
145	150	155	160
Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Ser Thr Tyr			
165	170	175	
Gln Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met			
180	185	190	
Thr Thr Asp Thr Ser Thr Thr Gly Tyr Met Glu Leu Arg Arg Leu			
195	200	205	
Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp Tyr Thr Arg			
210	215	220	
Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp Asn Trp Gly			
225	230	235	240
Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Ser Gly Gly			
245	250	255	
Gly Gly Ser Gly Gly Ser Gly Gly Ser Gln Val Gln			

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260	265	270
Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys		
275	280	285
Val Ser Cys Lys Ala Ser Gly Tyr Pro Phe Thr Ser Tyr Gly Ile Ser		
290	295	300
Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile		
305	310	315
Ser Thr Tyr Gln Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg		
325	330	335
Val Thr Met Thr Thr Asp Thr Ser Thr Thr Gly Tyr Met Glu Leu		
340	345	350
Arg Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Asp		
355	360	365
Tyr Thr Arg Gly Ala Trp Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp		
370	375	380
Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly		
385	390	395
Ser Gly Gly Gly Ser Gly Gly Ser Gly Ser Glu Ile Val Leu Thr		
405	410	415
Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu		
420	425	430
Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr Ser Leu Ala Trp Tyr		
435	440	445
Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser		
450	455	460
Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly		
465	470	475
Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala		
485	490	495
Val Tyr Tyr Cys Gln Gln His Asp Thr Ser Leu Thr Phe Gly Gly		
500	505	510
Thr Lys Val Glu Ile Lys		
515		

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<210> SEQ ID NO 233
<211> LENGTH: 518
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2
S309-scFv-(VL-VH) - (VL-VH) v1.1

<400> SEQUENCE: 233

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1          5          10         15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Thr
20         25          30

Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35          40          45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50          55          60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65          70          75          80

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Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	His	Asp	Thr	Ser	Leu
85								90							95
Thr	Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys	Gly	Gly	Gly	Gly	Ser
	100					105					110				
Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Ser	Gln	Val	Gln	Leu	Val	Gln	
115					120					125					
Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala	Ser	Val	Lys	Val	Ser	Cys
130					135					140					
Lys	Ala	Ser	Gly	Tyr	Pro	Phe	Thr	Ser	Tyr	Gly	Ile	Ser	Trp	Val	Arg
145					150				155					160	
Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met	Gly	Trp	Ile	Ser	Thr	Tyr
	165					170				175					
Gln	Gly	Asn	Thr	Asn	Tyr	Ala	Gln	Lys	Phe	Gln	Gly	Arg	Val	Thr	Met
	180					185				190					
Thr	Thr	Asp	Thr	Ser	Thr	Thr	Thr	Gly	Tyr	Met	Glu	Leu	Arg	Arg	Leu
	195					200				205					
Arg	Ser	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Asp	Tyr	Thr	Arg
	210				215				220						
Gly	Ala	Trp	Phe	Gly	Glu	Ser	Leu	Ile	Gly	Gly	Phe	Asp	Asn	Trp	Gly
225					230				235					240	
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Ser	Gly	Gly	
	245					250			255						
Gly	Gly	Ser	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Glu	Ile	Val	
	260				265				270						
Leu	Thr	Gln	Ser	Pro	Gly	Thr	Leu	Ser	Leu	Ser	Pro	Gly	Glu	Arg	Ala
	275				280				285						
Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Thr	Val	Ser	Ser	Thr	Ser	Leu	Ala
	290				295				300						
Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile	Tyr	Gly
	305				310				315					320	
Ala	Ser	Ser	Arg	Ala	Thr	Gly	Ile	Pro	Asp	Arg	Phe	Ser	Gly	Ser	Gly
	325					330				335					
Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Arg	Leu	Glu	Pro	Glu	Asp
	340				345				350						
Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	His	Asp	Thr	Ser	Leu	Thr	Phe	Gly
	355				360				365						
Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys	Gly	Gly	Gly	Ser	Gly	Gly	Gly	
	370				375			380							
Gly	Ser	Gly	Gly	Gly	Ser	Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	
	385				390			395			400				
Glu	Val	Lys	Pro	Gly	Ala	Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	
	405				410			415						415	
Gly	Tyr	Pro	Phe	Thr	Ser	Tyr	Gly	Ile	Ser	Trp	Val	Arg	Gln	Ala	Pro
	420				425			430							
Gly	Gln	Gly	Leu	Glu	Trp	Met	Gly	Trp	Ile	Ser	Thr	Tyr	Gln	Gly	Asn
	435				440			445							
Thr	Asn	Tyr	Ala	Gln	Lys	Phe	Gln	Gly	Arg	Val	Thr	Met	Thr	Thr	Asp
	450				455			460							
Thr	Ser	Thr	Thr	Thr	Gly	Tyr	Met	Glu	Leu	Arg	Arg	Leu	Arg	Ser	Asp
	465				470			475			480				
Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Asp	Tyr	Thr	Arg	Gly	Ala	Trp

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485	490	495
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Phe Gly Glu Ser Leu Ile Gly Gly Phe Asp Asn Trp Gly Gln Gly Thr	500	505
	505	510
Leu Val Thr Val Ser Ser		
	515	

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<210> SEQ ID NO 234
<211> LENGTH: 114
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v14 mAb VL
(VK)

```

<400> SEQUENCE: 234

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly	1	15
	5	10

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser	20	30
	25	30

Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln	35	45
	40	45

Pro Pro Lys Leu Leu Ile Ser Trp Ala Ser Thr Arg Glu Ser Gly Val	50	60
	55	60

Pro Asp Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr	65	80
	70	75

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln	85	95
	90	95

Tyr Tyr Ser Ala Pro Gly Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu	100	110
	105	110

Ile Lys

```

<210> SEQ ID NO 235
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v14 mAb
CDRL1

```

<400> SEQUENCE: 235

Gln Ser Val Leu Tyr Ser Ser Asn Asn Lys Asn Tyr	1	10
	5	10

```

<210> SEQ ID NO 236
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v14 mAb
CDRL2

```

<400> SEQUENCE: 236

Trp Ala Ser	1	
	1	

```

<210> SEQ ID NO 237
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

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-continued

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S300-v14 mAb
CDRL3

<400> SEQUENCE: 237

Gln	Gln	Tyr	Tyr	Ser	Ala	Pro	Gly	Ile	Thr
1				5				10	

<210> SEQ ID NO 238

<211> LENGTH: 343

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV2 S300-v14 mAb VL
(VK)

<400> SEQUENCE: 238

gacatcggtga	tgaccaggc	tccagactca	ctggctgtgt	ctctggcgaa	gaggggccacc	60
atcaactgtta	agtcccgcca	gagtgtttta	tacagctcca	acaataagaa	ctacttagct	120
tggtaccaggc	agaaaaccagg	acagcctcct	aagctgctca	tttcctgggc	ttctaccgg	180
gaatccgggg	tccctgaccg	attcagtggc	agcgggtctg	ggacagat	ttacttcacc	240
atcagcagcc	tgcaggctga	agatgtggca	gtttattact	gtcaacaata	ttatagtgtct	300
ccccggatca	ccttcggcca	ggggacacga	ctggagatta	aac		343

<210> SEQ ID NO 239

<211> LENGTH: 129

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV2 S307 mAb VH

<400> SEQUENCE: 239

Gln	Val	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Glu
1				5				10			15				

Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser	Gly	Gly	Ser	Val	Thr	Ser	Gly
20				25				30							

Ser	Tyr	Tyr	Trp	Ser	Trp	Ile	Arg	Gln	Pro	Pro	Gly	Lys	Gly	Leu	Glu
35				40			45								

Trp	Ile	Gly	Tyr	Met	Tyr	Tyr	Ser	Gly	Ser	Thr	Asn	Tyr	Asn	Pro	Ser
50				55			60								

Leu	Lys	Ser	Arg	Val	Thr	Ile	Ser	Val	Asp	Thr	Ser	Lys	Asn	Gln	Phe
65				70			75		80						

Ser	Leu	Lys	Leu	Ser	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	Val	Tyr	Tyr
85				90			95								

Cys	Ala	Arg	Ala	Gly	Cys	Thr	Gly	Ile	Thr	Cys	Leu	Arg	Tyr	Asp	Tyr
100				105			110								

Tyr	Tyr	Gly	Leu	Asp	Val	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser
115			120			125									

Ser

<210> SEQ ID NO 240

<211> LENGTH: 10

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Synthetic sequence SARS-CoV2 S307 mAb CDRH1

<400> SEQUENCE: 240

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Gly Gly Ser Val Thr Ser Gly Ser Tyr Tyr
1 5 10

<210> SEQ ID NO 241
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV2 S307 mAb CDRH2

<400> SEQUENCE: 241

Met Tyr Tyr Ser Gly Ser Thr
1 5

<210> SEQ ID NO 242
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV2 S307 mAb CDRH3

<400> SEQUENCE: 242

Ala Arg Ala Gly Cys Thr Gly Ile Thr Cys Leu Arg Tyr Asp Tyr Tyr
1 5 10 15

Tyr Gly Leu Asp Val
20

<210> SEQ ID NO 243
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV2 S307 mAb VL(VK)

<400> SEQUENCE: 243

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Lys Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Ala Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Ser
85 90 95

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 244
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV2 S307 mAb CDRL1

<400> SEQUENCE: 244

Gln Ser Val Ser Ser Ser Tyr
1 5

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<210> SEQ ID NO 245
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV2 S307 mAb CDRL2

<400> SEQUENCE: 245

Gly Ala Ser
1

<210> SEQ ID NO 246
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV2 S307 mAb CDRL3

<400> SEQUENCE: 246

Gln Gln Tyr Gly Ser Ser Ser Trp Thr
1 5

<210> SEQ ID NO 247
<211> LENGTH: 387
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV2 S307 mAb VH

<400> SEQUENCE: 247

cagggtgcagc tgcaggagtc gggcccagga ctgggtgaagc cttcgagac cctgtccctc	60
acctgcactg tctctggtgg ctccgtcacc agtggttagt actactggag ctggatccgg	120
cagccccccag ggaaggggact ggagtggatt gggtatatgt attacagtgg gagcaccaat	180
tacaaccctt ccctcaagag tcgagtcacc atatcagtag acacgtccaa gaaccagttc	240
tccctgaagc tgagctctgt gaccgctgctg gacacggccgc tgtattactg tgcgagggca	300
ggttgtactg gtatcacctg cttacgttac gactactact acgggtctgga cgtctggggc	360
caagggacca cggtcaccgt ctcctca	387

<210> SEQ ID NO 248
<211> LENGTH: 325
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV2 S307 mAb VL(VK)

<400> SEQUENCE: 248

gaaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccaggaa aagagccacc	60
ctctccctgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaga	120
cctggccagg ctccccaggct cctcatctat ggtgcattca gcagggccgc tggcatccca	180
gacaggttca gtggcagtgg gtctggaca gacttcactc tcaccatcag cagactggag	240
cctgaagatt ttgcagtgtt ttactgttag cagtaggtt gctcatcgtg gacgttccgc	300
caagggacca aggtggaaat caaac	325

<210> SEQ ID NO 249
<211> LENGTH: 381

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1 mAb VH

<400> SEQUENCE: 249
caggttcagc tggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggc 60
tcctgcagg cttctggta ccccttacc agttatggta tcagctgggt gcgcacaggcc 120
cctggacaag ggcttgagtg gatggatgg atcagcactt acaatggtaa cacaatttat 180
gcacagaagt tccagggcag agtcaccatg accacagaca catccacgac cacaggctac 240
atggagctga ggaggctgag atctgacgac acggccgtg attactgtgc gagagattat 300
actcggtgtg ctgggttcgg ggagtcattt atagggggct ttgacaactg gggccaggaa 360
accctggtca ccgtctccctc a 381

<210> SEQ ID NO 250
<211> LENGTH: 322
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SAES-CoV-2 S309-v13 mAb VL (VK)

<400> SEQUENCE: 250
gaaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccaggggaa aagagccacc 60
ctctcctgca gggccagtca gactgttagc ageacctctt tagcctggta ccagcagaaa 120
cctggccagg ctcccaggct cctcatctat ggtgcattcca gcagggccac tggcatccaa 180
gacaggttca gcccgcgtgg gtctggaca gacttcactc tcaccatcag cagactggag 240
cctgaagatt ttgcagtgtt ttactgtcag cagcatgata cctcaactcac tttcggcgaa 300
gggaccaagg tggagatcaa ac 322

<210> SEQ ID NO 251
<211> LENGTH: 767
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence CMV promoter

<400> SEQUENCE: 251
gacattgatt attgactagt tattaatagt aatcaattac ggggtcatta gttcatagcc 60
catatatggta gttccgcgtt acataactta cggttaatgg cccgcctggc tgaccgcca 120
acgaccccccgc cccatgacgt caataatgac gtatgttccc atagtaacgc caataggac 180
tttccatttga cgtcaatggg tggagttttt acggtaaact gcccacttgg cagtacatca 240
agtgtatcat atgccaagta cggccccat tgcgtcaat gacggtaaat ggccgcctg 300
gcattatgcc cagtacatga ctttatggta ctttcctact tggcagtaca tctacgtatt 360
agtcatcgctt attaccatgg tgcgtcggtt ttggcagtac atcaatgggc gtggatagcg 420
gtttgactca cggggatttc caagtctcca ccccattgac gtcaatggta gtttgtttg 480
gcaccaaaaat caacggggact ttccaaaatg tcgtacaacaat tccgcggcat tgacgcaat 540
ggccggtagg cgtgtacggg tggaggtcta tataaggcaga gtcgttttag tgaaccgtca 600
gatcgccctgg agacgcacatc cacgtgttt tgacctccat agaagacacc gggaccgatc 660

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cagecctccgc ggccgggaac ggtgcattgg aacgcggatt ccccggtCCA agagtgacgt	720
aagtaccgcc tataagagtct ataggcccac ccccttggct tcgttag	767
<210> SEQ ID NO 252	
<211> LENGTH: 50	
<212> TYPE: DNA	
<213> ORGANISM: Artificial Sequence	
<220> FEATURE:	
<223> OTHER INFORMATION: Synthetic sequence Signal peptide	
<400> SEQUENCE: 252	
atgggatggt catgtatcat ccttttcta gtagcaactg caaccggtgt	50
<210> SEQ ID NO 253	
<211> LENGTH: 135	
<212> TYPE: DNA	
<213> ORGANISM: Artificial Sequence	
<220> FEATURE:	
<223> OTHER INFORMATION: Synthetic sequence Poly-adenylation signal sequence	
<400> SEQUENCE: 253	
aacttgTTTA ttgcagCTTA taatggTTAC aaataaAGCA atagcatCAC aaatttCACA	60
aataaaAGCAT ttttttCACT gcattCTAGT tgtggTTTGt ccaaactCAT caatgttatCT	120
tatcatgtCT ggATC	135
<210> SEQ ID NO 254	
<211> LENGTH: 323	
<212> TYPE: DNA	
<213> ORGANISM: Artificial Sequence	
<220> FEATURE:	
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 Light Chain IgKC*01	
<400> SEQUENCE: 254	
gtacggTggc tgCaccatCT gtcttcatCT tcccGCCatC tgatgagcAG ttgaaatCTG	60
gaactgeCTC tggTgtgtgc ctgCTgaATA acttctatCC cagagaggCC aaagtacAGT	120
ggaaggTggA taacgcCCTC caatCgggTA actcccAGGA gagTgtcaca gagcaggaca	180
gcaaggacAG cac tacacAGC ctcagcAGCA ccTGacgCT gagCAAAGCA gactacgaga	240
aacacaaAGT ctacgeCTGC gaagtcaACC atcagggeCT gagCTcgCC gTCacaAAAGA	300
gCTTcaacAG gggagagtGT tag	323
<210> SEQ ID NO 255	
<211> LENGTH: 993	
<212> TYPE: DNA	
<213> ORGANISM: Artificial Sequence	
<220> FEATURE:	
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 CH1-CH3 G1m17; IgG1*01	
<400> SEQUENCE: 255	
gcgtcgaCCA agggccccATC ggtttcccc ctggcacCCt CCTCCAAGAG cacCTCTGGG	60
ggcacagCGG ccCTgggCTG cCTggTCAG gactacttCC ccGAACCTGT gacggTCTG	120
tggAAACTCAg ggcCcCTgAC cAgcggCgTg cacACCTtCC cggCTgttCt acAGtCCTCA	180
ggactCTact CCCTCAGCAG cgtggTgACC gtGCCCTCCA gCAGCTTGGG cacCCAGACC	240
tacatCTgCA acgtGAATCA caAGCCCAGC AACACCAAGG TggACAAGAG agttgagccc	300

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aaatcttgtg acaaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga	360
ccgtcagtct tccttctccc cccaaaaccc aaggacacc tcatgatctc ccggaccct	420
gaggtcacat gcgtgggtgt ggacgtgago cacgaagacc ctgaggtcaa gttcaactgg	480
tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgccggagga gcagtacaac	540
agcacgtacc gtgtggtcag cgtectcacc gtctgcacc aggactggct gaatggcaag	600
gagtacaagt gcaaggcttc caacaagcc ctcccaagcc ccatcgagaa aaccatctcc	660
aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgccccatc ccgggaggag	720
atgaccaaga accaggctcg cctgacctgc ctggtaaaact gcttctatcc cagcgcacatc	780
gccgtggagt gggagagcaa tggcagccg gagaacaact acaagaccac gcctccctg	840
ctggactccg acggctcctt cttectctat agcaagctca ccgtggacaa gagcagggtgg	900
cagcaggggaa acgttctctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg	960
cagaagagcc tctccctgtc cccgggtaaa tga	993

<210> SEQ ID NO 256
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence Signal peptide
<400> SEQUENCE: 256

Met	Gly	Trp	Ser	Cys	Ile	Ile	Leu	Phe	Leu	Val	Ala	Thr	Ala	Thr	Gly
1					5				10			15			

<210> SEQ ID NO 257
<211> LENGTH: 1431
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.1 mAb CH1-CH3 G1m17; IgGH1*01 LS; GAALIE; signal peptide
<400> SEQUENCE: 257

atggggcttgtt cctgttatcat cctgttcctg gtcgccacag ccaccggagt gcacagccaa	60
gtgcagctgg tccagagccg cgcccgagggtg aagaagcccg gcgctagcgt gaaggtgtcc	120
tgtaaagcca gcggatatcc ttaccago tacggcatct cctgggtgcg gcaggccct	180
ggccaggggcc tggaaatggat gggctggatc agcacctacc agggaaatac caactacgcc	240
cagaagttcc agggaaaggt gacaatgacc acagatacat ctacaaccac cggctacatg	300
gaactgaggc ggctgagaag cgacgacacc gccgtgtact actgcgccag agattacacc	360
agaggcgctt ggttcggcga gagectgatc ggccgttcc acaactgggg ccaggaaacc	420
ctggtgacag tgcgttagcgc ttctacccaa ggcccttctg tctttctct ggcccttct	480
agcaagtcta caagcggagg caccggccgc ctgggctgcg tggtaagga ctactcccc	540
gagccctgtga ccgtgagctg gaatagcggc gccctgacaa gcggcgtgca cacctccca	600
gctgtgtgc agacgacccg cctgtatagc ctgagcagcg tggtcaccgt gcccagcagc	660
agoctggaa cacagaccta catctgcaac gtgaaccaca agccttctaa taccaggtg	720
gataagaagg tggaaacctaa gagctgcgac aaaacacaca catgcctcc atgtctgct	780
ccagagctgc tggccggccc cagcgaaaa ctgttcccc ccaaaccctaa agacaccctg	840

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atgatcagca gaaccctga ggtgacctgt gtgggtgtgg acgtgtccca cgaagatct	900
gagggtgaagt tcaactggta cgtggatgga gtggaaatgc acaacgccaa gaccaaacct	960
agagaagagc agtacaacag cacatataga gtctgtccg tgcttacagt gctgcacca	1020
gactggctga atggaaagga atacaagtgc aagggtgtcca acaaggccct gcctctgcct	1080
gaggagaaga caatctctaa agccaaggcc caacctcggtt aacctcagggt gtacacactg	1140
cccccccagcc gggacgagct gaccaagaac cagggtgtcc tgacctgcct ggtcaaggcc	1200
ttcttacccct ctgatatacg cgtggatgg gagagcaacg gccaacactga gaacaactac	1260
aagaccaccc ctccaggctgt ggacacgcac ggcagcttct tcctgtacag caagctgacc	1320
gttgacaagt ccagatggca gcagggcaac gtgttcagct gtacgcgtcgc acacgaggcc	1380
ctgcattctc actacacccca gaagagcctg tccctcagcc ctggcaagtg a	1431

<210> SEQ ID NO 258
<211> LENGTH: 1374
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.1 mAb CH1-CH3 G1m17; IgGHG1*01 LS; GAALIE;

<400> SEQUENCE: 258	
caagtgcagc tggtccagag cggcgccgag gtgaagaacg cggcgctag cgtgaagggt	60
tcctgtaaag ccagcggata tcctttacc agtacggca tctcctgggt gggcaggcc	120
cctggccagg gcctggatg gatgggctgg atcagcacctt accaggaaa taccaactac	180
gcccagaagt tccagggaaag agtacaatg accacagata catctacaac caccggctac	240
atggaaatgtt ggcggctgag aagcgcacgc accggcgtt actactgcgc cagagattac	300
accagaggcg ctgggttcgg cgagagccctg atcggcggtc tcgacaactg gggccaggaa	360
accctgggtga cagtgtctag cgcttctacc aaaggccctt ctgtctttcc tctggccctt	420
tctagcaagt ctacaagcgg aggacccgc gcccctggctt gcctgggtgaa ggactacttc	480
cccgagcccg tgaccgtgag ctggaaatgc ggegcctgta caagcggcgt gcacacccctt	540
ccagctgtgc tgcagagcag cgccctgtat agcctgagca gctgggtcac cgtgccac	600
agcagcctgg qaacaacacat ctatctgc aacgtgaacc acaaccccttc taataccaa	660
gtggataaga aggtggaaacc taagagctgc gacaaaacac acacatgccc tccatgtcct	720
gtcccgagcc tgctggccgg ccccaagcggtt ttctgttcc ccccaaaacc taaagacacc	780
ctgtatgtca cggaaatccc tgagggtgacc tgggtgggtt tggacgtgtc ccacgaagat	840
cctgagggtga agttcaactg gtacgtggat ggagtgaaatg tgcacaacgc caagacaaa	900
ccttagagaag agcagttacaa cagcacatata agagtcgtgt ccgtgttac agtgcac	960
caggactggc tgaatggaaa ggaatacaag tgcaagggtt ccaacaaggc cctgcctctg	1020
cctgaggaga agacaatctc taaagccaaatggccaaac cttcaacotca ggtgtacaca	1080
ctggcccccac gcccggacga gctgaccaag aaccagggtt ccctgacccgt cctgggtcaag	1140
ggcttctacc cctctgtat cggcggtggaa tggagagcagc acggccaaacc tgagaacaac	1200
tacaagacca cccctccagggt gctggacago gacggcagct tcttcgttca cagcaagctg	1260
accgttgcaca agtccagatg gcagcaggcc aacgtgttca gctgtacgtt cctgcac	1320

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gccctgcatt ctcactacac ccagaagago ctgtccctca gcccggcaa gtga	1374
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<210> SEQ ID NO 259
<211> LENGTH: 1431
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.1 mAb
    CH1-CH3 G1m17; IgGHG1*01 LS; signal peptide

<400> SEQUENCE: 259

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atgggctggt cctgttatcat cctgttcctg gtcgccacag ccaccggagt gcacaggcaa	60
gtcagctgg tccagagccg cgccgagggt aagaagcccc gcgctagcgt gaagggtgtcc	120
tgtaaagcca gcgatatcc ttttaccago tacggcatct cctgggtgcg gcaggccct	180
ggccaggggcc tggaatggat gggctggatc agcacctacc agggaaatac caactacgcc	240
cagaagtcc agggaaagagt gacaatgacc acagatacat ctacaaccac cggctacatg	300
gaactgaggc ggctgagaag cgacgacacc gccgtgtact actgcgcacag agattacacc	360
agaggcgcctt ggttcggcga gagcctgatc ggcggcttcg acaactgggg ccagggaaacc	420
ctggtgacag tgtcttagcgc ttctacaaa ggccttctg tctttctct ggccttct	480
agcaagtcta caagcggagg cacccgcgc ctgggctgcc tggtaagga ctacttcccc	540
gagcccggtga ccgtgagctg gaatagcggc gcccgtacaa gcccgtgca cacctccca	600
gctgtgtgc agagcagcgg cctgtatago ctgagcagcg tggtcaccgt gcccagcagc	660
agcctggaa cacagaccta catctgcaac gtgaaccaca agccttctaa taccaaggtg	720
gataagaagg tggaacctaa gagctgcac aaaacacaca catgccttcc atgtcctgct	780
ccagagctgc tggggggccc cagcgaaaa ctgttccccc ccaaacctaa agacaccctg	840
atgatcagca gaacccctga ggtgacctgt gtgggtggg acgtgtccca cgaagatcct	900
gaggtgaagt tcaactggta cgtggatgga gtggaaagtgc acaacgccaa gaccaaacct	960
agagaagagc agtacaacag cacatataga gtcgtgtccg tgcttacagt gctgcaccag	1020
gactggctga atggaaagga atacaagtgc aagggtgtcca acaaggccct gcctggccct	1080
atcgagaaga caatctctaa agccaaggcc caacctcggg aacctcaggt gtacacactg	1140
ccccccagcc gggacgagct gaccaagaac caggtgtccc tgacctgcct ggtcaaggc	1200
ttctaccctt ctgatatcgc cgtggatgg gagagcaacg gccaacctga gaacaactac	1260
aagaccaccc ctccagtgct ggacagcgc ggcagcttct tctgtacag caagctgacc	1320
gttgacaagt ccagatggca gcaggccaa ctgttccatgt gtacgcgtc gcacgaggcc	1380
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<211> LENGTH: 1374
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 S309-v1.1 mAb
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<400> SEQUENCE: 260

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cctggccagg	gcctggaatg	gatgggctgg	atcagcacct	accaggaaa	taccaactac	180
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atggaactga	ggcggctgag	aagcgacgc	accggcgtgt	actactgcgc	cagagattac	300
accagaggcg	cttggttcgg	cgagagcctg	atcggcggct	tcgacaactg	gggccaggaa	360
accctggta	cagtgtctag	cgcttctacc	aaaggccctt	ctgtcttcc	tctggccct	420
tctagcaagt	ctacaagcgg	aggcacccgc	gcctgggt	gcctggtaa	ggactactc	480
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cctgagggtg	agttcaactg	gtacgtggat	ggagtggaa	tgcacaacgc	caagacaaa	900
ccttagagaag	agcagttacaa	cagcacata	agagtcgtgt	ccgtgtttac	agtgtgcac	960
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cctatcgaga	agacaatctc	taaagccaag	ggccaaccc	ggaaacctca	ggtgtacaca	1080
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accgttgaca	agtccagatg	gcagcagggo	aacgtgttca	gctgtagcgt	cctgeacag	1320
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IgKC*01; signal peptide

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cttgttagagc	ttctcagacc	gtgtccagca	ccagcctggc	ctggtatcag	cagaaacctg	180
gccaggcccc	tagactgctg	atctacggcg	ccagcagcag	agccacccgc	atccctgata	240
gattcagcgg	cagcgatct	ggaacccact	tcaccctgac	catcagccgg	ctggaacccg	300
aggactttgc	cgtgtactac	tgccagcaac	acgacaccag	cctgaccc	ggcgccggaa	360
caaagggtgga	aatcaagaga	accgtggccg	cccctagcgt	gttcatctc	ccccccagcg	420
acgagcagct	gaagagcgg	acagttctg	tggtgtgcct	gctgaacaac	ttctaccgc	480
gggaagccaa	ggtgcagtgg	aaggtggaca	acgccc	gagcggcaac	agccaggaga	540
gcgtgacaga	gcaggcagc	aaggcagca	cctacagect	gagcgcacc	ctgaccctga	600
gcaaggccga	ctacgagaag	cacaagggt	acgcctgt	agtgacccac	cagggcctgt	660
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<210> SEQ ID NO 262
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cctggccagg ccccttagact gctgtatctac ggccgcagca gcagagccac cggcatccct    180
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cccgaggact ttgccgtgtca ctactgccag caacacgaca ccagcctgac cttccggccgc  300
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gagagcgtga cagagcagga cagcaaggac agcacctaca gcctgagcag caccctgacc 540
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<210> SEQ ID NO 265
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<212> TYPE: PRT
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<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 CH1-CH3 G1m17;
IgG1*01 LS no C-term Lys

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Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser		
35	40	45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser		
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Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr		
65	70	75
Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys		
85	90	95
Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys		
100	105	110
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro		
115	120	125
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys		
130	135	140
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp		
145	150	155
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu		
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His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn		
195	200	205
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly		
210	215	220
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu		
225	230	235
Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr		
245	250	255
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260	265	270
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe		
275	280	285
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Asn		
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<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic sequence SARS-CoV-2 CH1-CH3 G1m17;
IgG1*01 LS GAALIE no C-term Lys

<400> SEQUENCE: 266

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50						55					60				
Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr
65						70				75		80			
Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys
	85						90					95			
Lys	Val	Glu	Pro	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys
	100						105					110			
Pro	Ala	Pro	Glu	Leu	Leu	Ala	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro
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Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys
	130					135					140				
Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp
	145					150				155		160			
Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu
	165					170				175					
Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu
	180					185					190				
His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn
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Lys	Ala	Leu	Pro	Leu	Pro	Glu	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly
	210					215					220				
Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Asp	Glu
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Leu	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr
	245					250					255				
Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn
	260					265					270				
Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe
	275					280					285				
Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn
	290					295					300				
Val	Phe	Ser	Cys	Ser	Val	Leu	His	Glu	Ala	Leu	His	Ser	His	Tyr	Thr
	305					310				315		320			
Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly							
						325									

What is claimed is:

1. A method of treating a SARS-CoV-2 infection in a subject, the method comprising administering to the subject a single dose of a composition comprising an antibody or antigen-binding fragment that is capable of binding to a surface glycoprotein of a SARS-CoV-2 expressed on a cell surface of a host cell and/or on a virion,

wherein the antibody comprises 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 CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 comprise the amino acid sequences set forth in:

(1) SEQ ID NOS.: 106, 121, 108, 169, 170, and 171, respectively; or

(2) SEQ ID NOS.: 106, 107, 108, 169, 170, and 171, respectively.

2. A method of treating a SARS-CoV-2 infection in a subject, the method comprising administering to the subject an effective amount of (i) an antibody or antigen-binding fragment that is capable of binding to a surface glycoprotein of a SARS-CoV-2 expressed on a cell surface of a host cell and/or on a virion, or (ii) a composition comprising (ii) (a) the antibody or antigen-binding fragment and (ii) (b) a pharmaceutically acceptable excipient, carrier, or diluent,

wherein the antibody comprises 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 CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 comprise the amino acid sequences set forth in:

- (1) SEQ ID NOS.: 106, 121, 108, 169, 170, and 171, respectively; or
- (2) SEQ ID NOS.: 106, 107, 108, 169, 170, and 171, respectively.

3. The method of claim **2**, wherein the method comprises administering to the subject a single dose of the antibody or antigen-binding fragment of (i) or the composition of (ii).

4. The method of any one of claims **1-3**, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO.: 113 and the VL comprises the amino acid sequence set forth in SEQ ID NO.: 168.

5. The method of any one of claims **1-3**, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO.: 105 and the VL comprises the amino acid sequence set forth in SEQ ID NO.: 168.

6. The method of any one of claims **1-5**, wherein the antibody or antigen-binding fragment further comprises an Fc polypeptide or a fragment thereof.

7. The method of any one of claims **1-6**, which is an IgG, IgA, IgM, IgE, or IgD isotype.

8. The method of any one of claims **1-7**, which is an IgG isotype selected from IgG1, IgG2, IgG3, and IgG4.

9. The method of any one of claims **1-8**, which is an IgG1 isotype.

10. The method of any one of claims **6-9**, 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.

11. The method of claim **10**, 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.

12. The method of claim **10** or **11**, 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).

13. The method of any one of claims **10-12**, wherein the mutation that enhances binding to FcRn comprises M428L/N434S.

14. The method of any one of claims **10-13**, wherein the mutation that enhances binding to a FcγR comprises S239D; I332E; A330L; G236A; or any combination thereof, and optionally does not comprise S239D.

15. The method of any one of claims **10-14**, 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.

16. The method of any one of claims **1-15**, wherein the antibody or antigen-binding fragment comprises the CH1-CH3 amino acid sequence of SEQ ID NO.: 173 or 265 and the CL amino acid sequence of SEQ ID NO.: 174.

17. The method of any one of claims **1-15**, wherein the antibody or antigen-binding fragment comprises the CH1-CH3 amino acid sequence of SEQ ID NO.: 175 or 266 and the CL amino acid sequence of SEQ ID NO.: 174.

18. The method of any one of claims **1-17**, wherein the antibody or antigen-binding fragment comprises a heavy chain polypeptide and a light chain polypeptide, wherein:

- (i) the heavy chain polypeptide comprises the VH amino acid sequence set forth in SEQ ID NO.: 113 and the CH1-CH3 amino acid sequence set forth in SEQ ID NO.: 173 or 265; and
- (ii) the light chain comprises the VL amino acid sequence set forth in SEQ ID NO.: 168 and the CL amino acid sequence set forth in SEQ ID NO.: 174, and wherein, optionally, the method comprises administering a single dose of the antibody or antigen-binding fragment to the subject.

19. The method of any one of claims **1-17**, wherein the antibody or antigen-binding fragment comprises a heavy chain polypeptide and a light chain polypeptide, wherein:

- (i) the heavy chain polypeptide comprises the VH amino acid sequence set forth in SEQ ID NO.: 113 and the CH1-CH3 amino acid sequence set forth in SEQ ID NO.: 175 or 266; and
- (ii) the light chain comprises the VL amino acid sequence set forth in SEQ ID NO.: 168 and the CL amino acid sequence set forth in SEQ ID NO.: 174, and wherein, optionally, the method comprises administering a single dose of the antibody or antigen-binding fragment to the subject.

20. The method of any one of claims **1-19**, wherein the subject:

- (i) is aged 18 to 49 years;
- (ii) is 18 years old or older;
- (iii) has mild to moderate COVID-19;
- (iv) has severe COVID-19;
- (v) has severe to critical COVID-19;
- (vi) has had fewer than seven days or 5 or fewer days since onset of symptoms;
- (vii) has had seven days or more since onset of symptoms;
- (viii) has had a positive reverse-transcriptase-polymerase-chain-reaction or antigen SARS-CoV-2 test result;
- (ix) is 55 years of age or older;
- (x) has one or more of: diabetes requiring medication, obesity (body-mass index >30 kg/m²), chronic kidney disease (estimated glomerular filtration rate <60 mL/min/1.73 m²), congestive heart failure (New York Heart Association class II or higher), chronic obstructive pulmonary disease (history of chronic bronchitis, chronic obstructive lung disease, or emphysema with dyspnea on physical exertion), and moderate to severe asthma (subject requires an inhaled steroid to control symptoms or has been prescribed a course of oral steroids in the past year); or
- (xi) any combination of (i)-(x).

21. The method of any one of claims **1-20**, comprising administering the antibody, antigen-binding fragment, or composition to the subject intravenously.

22. The method of claim **21**, comprising administering the antibody, antigen-binding fragment, or composition to the subject intravenously over the course of 30 minutes, 60 minutes, or 90 minutes.

23. The method of any one of claims **1-22**, comprising administering the antibody, antigen-binding fragment, or composition to the subject intramuscularly.

24. The method of any one of claims **1-23**, wherein the method comprises administering the antibody or antigen-binding fragment to the subject at a dose of up to 100 mg, up to 150 mg, up to 200 mg, up to 250 mg, up to 300 mg, up to 350 mg, up to 400 mg, up to 450 mg, or up to 500 mg.

25. The method of any one of claims **1-24**, wherein the method comprises administering the antibody or antigen-binding fragment to the subject at a dose in a range from about 50 mg to about 500 mg, or in a range from about 50 mg to about 250 mg, or in a range from about 100 mg to about 500 mg, or in a range from about 250 mg to about 500 mg.

26. The method of any one of claims **1-25**, wherein the method comprises administering 50, 75, 100, 125, 150, 175, 200, 225, 250, 275, 300, 325, 350, 375, 400, 425, 450, 475, or 500 mg of the antibody or antigen-binding fragment to the subject.

27. The method of any one of claims **1-26**, wherein the method comprises administering 50, 150, 250, or 500 mg of the antibody or antigen-binding fragment to the subject.

28. The method of any one of claims **1-27**, wherein the method comprises administering 500 mg of the antibody or antigen-binding fragment to the subject.

29. The method of any one of claims **1-28**, comprising administering the antibody, antigen-binding fragment, or composition to the subject 2, 3, 4, 5, 6, 7, 8, 9, or 10 times, or more.

30. The method of any one of claims **1-29**, comprising administering the antibody, antigen-binding fragment, or composition to the subject a plurality of times, wherein a second or successive administration is performed at about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 24, about 48, about 74, about 96 hours, or more, following the first or preceding administration.

31. The method of any one of claims **1-30**, wherein the subject is 18 or more years of age with laboratory-confirmed (e.g., by PCR test) SARS-CoV-2 infection.

32. The method of any one of claims **1-31**, wherein the subject has a clinical status of Grade 4 (hospitalized, oxygen by mask or nasal prongs), 5 (hospitalized, on non-invasive ventilation, or high flow oxygen), 6 (hospitalized, intubation and mechanical ventilation) or 7 (ventilation and additional organ support-pressors, renal replacement therapy (RRT), extracorporeal membrane oxygenation (ECMO)), as defined by the WHO clinical severity score, 9-point ordinal scale.

33. The method of any one of claims **1-31**, wherein the subject has mild-to-moderate COVID-19.

34. The method of claim **33**, wherein the subject is at-risk of progression to severe COVID-19.

35. The method of claim **34**, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the subject is at a reduced risk of hospitalization for COVID-19.

36. The method of claim **35**, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 10% or more.

37. The method of claim **35**, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 20% or more.

38. The method of claim **35**, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 30% or more.

39. The method of claim **35**, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 40% or more.

40. The method of claim **35**, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 50% or more.

41. The method of claim **35**, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 60% or more.

42. The method of claim **35**, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 70% or more.

43. The method of claim **35**, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 80% or more.

44. The method of claim **35**, wherein following administration of the antibody, antigen-binding fragment, or composition to the subject, the risk of hospitalization for COVID-19 is reduced by 85% or more.

45. The method of any one of claims **1-44**, wherein the subject has or is at risk for progressing to severe COVID-19, wherein, optionally, severe COVID-19 comprises (i) hypoxemia (O₂ saturation ≤93% on room air or PaO₂/FiO₂<300) requiring oxygen supplementation for more than 1 day or (ii) the subject requiring ≥4 L/min oxygen supplementation or equivalent.

46. The method of any one of claims **1-45**, wherein the subject has or is at risk for progressing to critical COVID-19, wherein, optionally, critical COVID-19 comprises respiratory failure requiring at least one of the following: invasive mechanical ventilation and ECMO; shock; and multi-organ dysfunction/failure.

47. The method of any one of claims **1-46**, wherein the subject is less than seven days since onset of symptoms.

48. The method of any one of claims **1-46**, wherein the subject is seven days or more since onset of symptoms.

49. The method of any one of claims **1-48**, wherein the subject is any one or more of (i)-(iii):

(i) 18 or older and has a positive SARS-CoV-2 test result (by any validated test e.g. RT-PCR on any specimen type);

(ii) (1) hospitalized with severe COVID-19 disease defined as requirement for supplemental oxygen or non-invasive ventilation consistent with Grade 4 or Grade 5 disease or (2) hospitalized with critical COVID-19 disease defined as those on mechanical ventilation (Grade 6 or Grade 7 disease);

(iii) is male or female, wherein, optionally, (1) the woman is non-childbearing potential (WONCBP) or (2) is a woman of child-bearing potential (WOCBP) and uses a contraceptive method.

50. The method of any one of claims **1-49**, wherein the method comprises administering 500 mg of the antibody or antigen-binding fragment to the subject.

51. The method of any one of claims **1-50**, wherein the subject had or has close contacts to a person with a confirmed SARS-CoV-2 infection.

52. The method of any one of claims **1-51**, wherein treating comprises preventing infection by SARS-CoV-2 and/or preventing COVID-19.

53. The method of any one of claims **1-52**, wherein treating comprises preventing progression of COVID-19 in the subject.

54. The method of any one of claims **1-53**, wherein treating comprises preventing contraction and/or transmission of symptomatic COVID-19.

55. The method of any one of claims **1-53**, wherein treating comprises preventing contraction and/or transmission of asymptomatic COVID-19.

56. The method of any one of claims **1-55**, wherein the subject is at-risk for contracting or progressing on COVID-19.

57. The method of any one of claims **1-56**, wherein treating comprises preventing or reducing:

- (1) one or more acute respiratory symptom selected from: cough; sputum production; sore throat; and shortness of breath; or
- (2) fever of greater than 38° C.;
- (3) two or more of the following symptoms: fatigue; myalgias/arthalgias; chills; nausea/vomiting; diarrhea; and anosmia/dysgeusia.

58. The method of any one of claims **1-57**, wherein treating comprises preventing or reducing one or more of the following symptoms: fever of greater than 38° C.; chills; cough; sore throat; malaise; headache; myalgia; a change in smell or taste; nasal congestion/rhinorrhea; vomiting; diarrhea; shortness of breath on exertion.

59. The method of any one of claims **1-58**, wherein the subject is an adult.

60. The method of any one of claims **1-59**, wherein the subject is 18 or more years of age, or is 19 or more years of age.

61. The method of any one of claims **1-60**, wherein the subject is 55 years of age or is, or is 65 years of age or is older

62. The method of any one of claims **1-61**, wherein the administering the antibody, antigen-binding fragment, or composition comprises intravenous infusion.

63. The method of any one of claims **1-62**, wherein administering the antibody, antigen-binding fragment, or composition comprises intramuscular injection.

64. The method of any one of claims **1-63**, wherein the method comprises administering 250 mg of the antibody or antigen-binding fragment to the subject.

65. The method of any one of claims **1-63**, wherein the method comprises administering 500 mg of the antibody or antigen-binding fragment to the subject.

66. The method of any one of claims **1-65**, wherein the subject has a mild-to-moderate SARS-2-CoV infection (e.g., has mild-to-moderate COVID-19) and, optionally, is at risk for progression to severe disease.

67. The method of any one of claims **1-66**, wherein the subject:

- (i) is 12 years old or older; and
- (ii) last had contact with a person with a confirmed SARS-CoV-2 infection less than three days prior to administration of the composition.

68. The method of any one of claims **1-67**, wherein the subject has mild-to-moderate COVID-19 and the method comprises administering a single dose of the antibody, antigen-binding fragment, or composition to the subject intramuscularly.

69. The method of claim **68**, wherein the single dose comprises 250 mg of the antibody or antigen-binding fragment.

70. The method of claim **68** or **69**, wherein the single dose of comprises 500 mg of the antibody or antigen-binding fragment.

71. The method of any one of claims **68-70**, wherein:

- (i) (i)(a) the subject is 12 years of age or older and is at high risk of progression of COVID-19 or (i)(b) the subject is 65 years of age or older; and/or
- (ii) the subject has a positive SARS-CoV-2 test result (e.g., by PCR test), has oxygen saturation ≥94% on room air, has COVID-19 symptoms, and is less than or equal to 7 days from onset of symptoms.

72. The method of any one of claims **1-71**, wherein:

- (i) (i)(a) the subject is 12 years of age or older and is at high risk of progression of COVID-19 or (i)(b) the subject is 65 years of age or older; and
- (ii) the subject has a positive SARS-CoV-2 test result (e.g., by PCR test), has oxygen saturation ≥94% on room air, has COVID-19 symptoms, and is less than or equal to 7 days from onset of symptoms.

73. The method of any one of claims **1-72**, wherein the subject is not hospitalized and is at high-risk for (i) hospitalization and/or (ii) progression of COVID-19.

74. The method of any one of claims **1-73**, wherein the subject is:

- (1) 12 or more years of age and, optionally, is at high risk of progression of COVID-19; and/or
- (2) is 65 or more years of age.

75. The method of any one of claims **1-74**, wherein the subject has had a positive SARS-CoV-2 test result, has oxygen saturation ≥94% on room air, has COVID-19 symptoms, and is less than or equal to 7 days from onset of symptoms.

76. The method of any one of claims **1-75**, wherein the antibody or antigen-binding fragment was obtained from a non-clonal pool of cells stably transfected with a polynucleotide encoding the antibody or antigen-binding fragment.

77. The method of any one of claims **1-75**, wherein the antibody or antigen-binding fragment was obtained from a clonal master cell bank.

78. The method of any one of claims **1-77**, wherein the subject: is a resident of a nursing home or a long-term care facility; is a hospice care worker; is a healthcare provider or healthcare worker; is a first responder; is a family member or other close contact of a subject diagnosed with or suspected of having a SARS-CoV-2 infection, is overweight or clinically obese; is or has been a smoker; has or had chronic obstructive pulmonary disease (COPD); is asthmatic (e.g., having moderate to severe asthma); has an autoimmune disease or condition (e.g., diabetes); has a compromised or depleted immune system (e.g., due to AIDS/HIV infection, a cancer such as a blood cancer, a lymphodepleting therapy such as a chemotherapy, a bone marrow or organ transplantation, or a genetic immune condition); has chronic liver

disease; has cardiovascular disease; and/or has a pulmonary or heart defect; and/or works or otherwise spends time in close proximity with others, such as in a factory, shipping center, hospital setting, or the like.

79. The method of any one of claims **1-78**, wherein the subject has received a vaccine for SARS-CoV-2 and the vaccine is determined to be ineffective, e.g., by post-vaccine infection or symptoms in the subject, by clinical diagnosis or scientific or regulatory criteria.

80. The method of any one of claims **1-78**, wherein the subject has not received a vaccine for SARS-CoV-2.

81. The method of any one of claims **1-80**, wherein the subject has received convalescent plasma therapy, remdesivir, or both, for SARS-CoV-2.

82. The method of any one of claims **1-81**, wherein treatment comprises pre-exposure or peri-exposure prophylaxis.

83. The method of any one of claims **1-82**, wherein treatment is administered to the subject having mild-to-moderate disease, optionally in an outpatient setting.

84. The method of any one of claims **1-83**, wherein treatment is administered to a subject with moderate-to-severe disease, such as requiring hospitalization.

85. The method of any one of claims **1-84**, wherein the subject is hospitalized with COVID-19.

86. The method of any one of claims **1-85**, wherein the subject having a SARS-CoV-2 infection: has mild-to-moderate COVID-19; is experiencing any one or more of: fever; cough; fatigue; shortness of breath or difficulty breathing; muscle aches; chills; sore throat; runny nose; headache; chest pain; loss of taste and/or smell; and pink eye (conjunctivitis); malaise; and abnormal imaging; has evidence of lower respiratory disease by clinical assessment or imaging and a saturation of oxygen (SaO_2) greater than ($>$) 93 percent (%) on room air at sea level, has a positive SARS-CoV-2 viral testing result, and/or is at high risk for progressing to severe COVID-19 and/or hospitalization, e.g.,

the human subject (1) is 65 years of age or older (≥ 65); has a body mass index (BMI) of 35 or greater (≥ 35); has chronic kidney disease; has diabetes; (5) has immunosuppressive disease, is receiving immunosuppressive treatment; is 55 years of age or older (≥ 55) and has cardiovascular disease, hypertension, chronic obstructive pulmonary disease, or other chronic respiratory disease; and/or is 12-17 years of age and has a BMI $\geq 85\%$ for their age and gender, or sickle cell disease, congenital or acquired heart disease, neurodevelopmental disorders (e.g., cerebral palsy), a medical-related technological dependence (e.g., tracheostomy, gastrostomy, or positive pressure ventilation not related to COVID-19), or asthma, reactive airway or other chronic respiratory disease that requires daily medication for control; has recently been diagnosed with COVID-19 (e.g., within 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days) and/or is within 10 days of symptom onset; or has or is experiencing any combination of the foregoing.

87. The method of any one of claims **1-85**, wherein the subject is (a) 18 years old or older, or (b) 55 years old or younger, provided that the subject is 18 years or older.

88. The method of any one of claims **1-87**, wherein the subject has a laboratory confirmed COVID-19 infection by positive polymerase chain reaction (PCR; e.g., RT-PCR) test; e.g., on any type of respiratory tract sample.

89. The method of any one of claims **1-88**, the subject has peripheral capillary oxygen saturation (SpO_2) $>94\%$ room air (RA), and has experienced one or more symptoms of COVID-19 for ≤ 120 h (5 days).

90. The method of any one of claims **1-89**, wherein the subject is further receiving or has received remdesivir, supplemental oxygen, ventilation therapy, respiration therapy, dexamethasone, tocilizumab, or any combination thereof.

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