

What is claimed is:-

1. ~~A method for detecting a presence or determining an amount of at least one type of anti-SARS-CoV-2 antibody in a subject, the method comprising the steps of:~~

~~a) contacting at least one biological sample from the subject, either simultaneously or sequentially, in any order, with~~

~~at least one type of first specific binding partner comprising at least one type of β -coronavirus isolated polypeptide or variant thereof, selected from a C-terminal domain of a nucleocapsid protein, a receptor binding domain (RBD) of a spike protein, or a C-terminal domain of a nucleocapsid protein and a receptor binding domain (RBD) of a spike protein, wherein the polypeptide specifically binds to at least one type of anti-SARS-CoV-2 antibody in the sample, and~~

~~at least one type of second specific binding partner comprising a detectable label,~~

~~thereby producing one or more types of first complexes comprising the first specific binding partner-anti-SARS-CoV-2 antibody-second specific binding partner; and~~

~~b) assessing a signal from the one or more types of first complexes, wherein the amount of detectable signal from the detectable label indicates the presence or amount of at least one type of anti- β -coronavirus antibody in the sample.—~~

2. ~~The method of claim 1, wherein the at least one type of anti-SARS-CoV-2 antibody specifically binds to a variant:~~

~~a) of the nucleocapsid protein having one or more substitutions, deletions or a substitution and deletion at positions 210-419 of SEQ ID NO:2 comprising: (1) replacing serine with phenylalanine at amino acid position 235 (S235F); (2) replacing methionine with isoleucine at amino acid position 234 (M234I); (3) replacing lysine with asparagine at amino acid position 373 (K373N); (4) replacing aspartic acid with tyrosine at amino acid position 377 (D377Y); (5) replacing alanine with threonine at amino acid position 376 (A376T); or (6) any combinations of (1)-(5), either alone or combined with any other substitutions and/or deletions in amino acids 210-419 of SEQ ID NO:2 other than those recited in (1)-(5);~~

~~b) of the RBD of a spike protein having one or more substitutions, deletions or a substitution and deletion at positions 319-542 of SEQ ID NO:15 comprising (1) replacing lysine~~

with asparagine at amino acid position 417 (K417N); (2) replacing lysine with threonine at amino acid position 417 (K417T); (3) replacing leucine with arginine at amino acid position 452 (L452R); (4) replacing serine with asparagine at amino acid position 477 (S477N); (5) replacing glutamic acid with lysine at amino acid position 484 (E484K); (6) replacing asparagine with tyrosine at amino acid position 501 (N501Y); or (7) any combinations of (1)–(6), either alone or combined with any other substitutions and/or deletions in amino acids 319–542 of SEQ ID-NO:15 other than those recited in (1)–(6); or

~~c) from a SARS-CoV-2 virus comprising any combination of a) and b).~~

~~3. The method of claims 1 or 2, wherein the biological sample is whole blood, serum, plasma, saliva, a nasal mucus specimen, an anal swab specimen, an oropharyngeal specimen, or a nasopharyngeal specimen.~~

~~4. The method of any of claims 1–3, wherein the at least one type of anti-SARS-CoV-2 antibody is an IgG antibody, an IgM antibody, or IgG antibody and an IgM antibody.~~

~~5. The method of any of claims 1–4, wherein the at least one type of first specific binding partner comprises at least one isolated polypeptide from a C-terminal domain of a nucleocapsid protein from a β -coronavirus, wherein the method is carried out so that said specific binding partner specifically binds to (a) an anti- β -coronavirus IgG antibody; (b) an anti- β -coronavirus IgM antibody; or (b) both an anti- β -coronavirus IgG and an anti- β -coronavirus IgM antibody.~~

~~6. The method of any of claims 1–4, wherein the at least one type of first specific binding partner comprises at least one isolated polypeptide from a receptor binding domain (RBD) of a spike protein from a β -coronavirus, wherein the method is carried out so that said specific binding partner specifically binds to (a) an anti- β -coronavirus IgG antibody; (b) an anti- β -coronavirus IgM antibody; or (b) both an anti- β -coronavirus IgG antibody and anti- β -coronavirus IgM antibody.~~

~~7. The method of any of claims 1–6, wherein the at least one type of second specific binding partner is an anti-species IgG (e.g., anti-human IgG-IgG) antibody, an anti-species IgM (e.g., anti-human IgM-IgG) antibody, or an anti-species IgG (e.g., anti-human IgG-IgG) and an anti-species IgM (e.g., anti-human IgM-IgG) antibody.~~

~~8. The method of any of claims 1–7, wherein the at least one type of first specific binding partner is a C-terminal domain nucleocapsid protein or variant thereof that~~

(1) has an amino acid sequence of SEQ ID NO:1; (2) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQNNQ (SEQ ID NO:21), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2; (3) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQSNQ (SEQ ID NO:22), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2; or (4) has an amino acid sequence of amino acids 210 to 419 of SEQ ID NO:2.

9. The method of any of claims 1-4 or 6, wherein the at least one type of first specific binding partner is a receptor binding domain (RBD) of a spike protein or variant thereof that has an amino acid sequence of amino acids 319 to 542 of SEQ ID NO:15 or SEQ ID NO:17.

10. The method of claim 8 or claim 9, wherein the method is carried out so that the at least one type of first specific binding partner binds to (a) an anti SARS-CoV-2 IgG antibody; (b) an anti SARS-CoV-2 IgM antibody; or (c) both an anti SARS-CoV-2 IgG antibody and anti SARS-CoV-2 IgM antibody.

11. The method of any of claims 1-10, wherein the method comprises detecting:

(a) at least one anti SARS-CoV-2 IgG antibody in at least one biological sample obtained from a subject wherein the at least one type of first specific binding partner is a C-terminal domain nucleocapsid protein or variant thereof that (1) has an amino acid sequence of SEQ ID NO:1; (2) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQNNQ (SEQ ID NO:21), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2; (3) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQSNQ (SEQ ID NO:22), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2 and specifically binds to at least one anti SARS-CoV-2 IgG antibody; or (4) has an amino acid sequence of amino acids 210 to 419 of SEQ ID NO:2, and/or

(b) at least one anti SARS-CoV-2 IgM antibody in at least one biological sample obtained in a subject wherein the at least one first specific binding partner wherein the at least one first specific binding partner is a receptor binding domain (RBD) of a spike protein or variant thereof that has an amino acid sequence of amino acids 319 to 542 of SEQ ID NO:15 or SEQ ID NO:17 and specifically binds to at least one anti SARS-CoV-2 IgM antibody; and

~~wherein the at least one anti-SARS-CoV-2 IgG antibody and/or at least one anti-SARS-CoV-2 IgM antibody are detected in a single biological sample obtained from the subject or in multiple biological samples obtained from the subject; and~~

~~further wherein, when the at least one anti-SARS-CoV-2 IgG antibody and at least one anti-SARS-CoV-2 IgM antibody are detected simultaneously or sequentially, in any order, in a single biological sample obtained from the subject or in multiple biological samples obtained from the subject.~~

~~12. The method of any of claims 4-11, wherein the method quantifies up to (a) about 91% or (b) about 99% of anti-SARS-CoV-2 IgG antibodies.~~

~~13. The method of any of claims 1-12, wherein the method further comprises detecting SARS-CoV-2 from at least one biological sample obtained from the subject, said at least one biological sample being a single biological sample or multiple biological samples.~~

~~14. The method of claim 13, wherein the SARS-CoV-2 detected comprises a variant:~~
~~a) of the nucleocapsid protein having one or more substitutions, deletions or a substitution and deletion at positions 210-419 of SEQ ID NO:2 comprising: (1) replacing serine with phenylalanine at amino acid position 235 (S235F); (2) replacing methionine with isoleucine at amino acid position 234 (M234I); (3) replacing lysine with asparagine at amino acid position 373 (K373N); (4) replacing aspartic acid with tyrosine at amino acid position 377 (D377Y); (5) replacing alanine with threonine at amino acid position 376 (A376T); or (6) any combinations of (1)-(5), either alone or combined with any other substitutions and/or deletions in amino acids 210-419 of SEQ ID NO:2 other than those recited in (1)-(5);~~

~~b) of the RBD of a spike protein having one or more substitutions, deletions or a substitution and deletion at positions 319-542 of SEQ ID NO:15 comprising (1) replacing lysine with asparagine at amino acid position 417 (K417N); (2) replacing lysine with threonine at amino acid position 417 (K417T); (3) replacing leucine with arginine at amino acid position 452 (L452R); (4) replacing serine with asparagine at amino acid position 477 (S477N); (5) replacing glutamic acid with lysine at amino acid position 484 (E484K); (6) replacing asparagine with tyrosine at amino acid position 501 (N501Y); or (7) any combinations of (1)-(6), either alone or combined with any other substitutions and/or deletions in amino acids 319-542 of SEQ ID NO:15 other than those recited in (1)-(6); or~~

~~c) from a SARS-CoV-2 virus comprising any combination of a) and b).~~

~~15. The method of any of claims 12-14, wherein the SARS-CoV-2 is detected by its viral RNA using polymerase chain reaction, or by its viral antigen.~~

~~16. The method of any of claims 12-14, wherein said multiple biological samples are obtained at the same or different times.~~

~~17. The method of any of claims 12-16, wherein the method further comprises detecting whether the subject is in:~~

~~(a) an initial period of infection without any antibodies being produced, when the at least one biological sample obtained from the subject is positive for viral RNA or viral antigen, negative for anti-SARS-CoV-2 IgM antibodies, and negative for anti-SARS-CoV-2 IgG antibodies; and/or~~

~~(b) an early acute phase of infection, and is developing an immune response to the virus and producing antibodies, when the at least one biological sample obtained from the subject is positive for viral RNA or viral antigen, positive for anti-SARS-CoV-2 IgM antibodies, and negative for anti-SARS-CoV-2 IgG antibodies; and/or~~

~~(c) an early acute phase of infection or had a false negative viral RNA result or viral antigen result, or a false positive anti-SARS-CoV-2 IgM antibody result, when the at least one biological sample obtained from the subject is negative for viral RNA, positive for anti-SARS-CoV-2 IgM antibodies, and negative for anti-SARS-CoV-2 IgG antibodies; and/or~~

~~(d) an acute phase of infection, and is progressing in an immune response, when the at least one biological sample obtained from the subject is positive for viral RNA or viral antigen, positive for anti- β coronavirus IgM antibodies, and positive for anti-SARS-CoV-2 IgG antibodies; and/or~~

~~(e) a late acute phase of infection, or has developed a recurrent infection with SARS-CoV-2, when the at least one biological sample obtained from the subject is positive for viral RNA or viral antigen, negative for anti-SARS-CoV-2 IgM antibodies, and positive for anti-SARS-CoV-2 IgG antibodies;~~

~~(f) a late acute phase of infection or recovery phase, or had a false negative viral RNA result, when the at least one biological sample obtained from the subject is negative for viral RNA or viral antigen, positive for anti- β coronavirus IgM antibodies, and positive for anti-SARS-CoV-2 IgG antibodies;~~

~~—— (g) recovery phase when the at least one biological sample obtained from the subject is negative for viral RNA or viral antigen, negative for anti-SARS-CoV-2 IgM antibodies and positive for anti-SARS-CoV-2 IgG antibodies; and/or~~

~~—— (h) recovery phase when the at least one biological sample obtained from the subject is negative for viral RNA or viral antigen and negative for anti-SARS-CoV-2 IgM antibodies and anti-SARS-CoV-2 IgG antibodies.——~~

~~—— 18.—— The method any of claims 1-17, wherein the method further comprises a pre-treatment step done at the same time as, or prior to, contacting the at least one type of first-specific binding partner, the at least one type of second-specific binding partner, or the at least one type of first specific binding partner and the at least one type of second-specific binding-partner, with the biological sample, and wherein the pretreatment step optionally comprises treatment with anti-human IgG, anti-human IgM, or anti-human IgG and anti-human IgM.~~

~~—— 19.—— The method of any of claims 1-18, wherein the at least one type of first specific binding partner is immobilized on a solid support.~~

~~20.—— The method of any of claims 1-19, wherein the method is performed in from about 5 to about 20 minutes, less than about 20 minutes, and optionally is performed in less than about 5 minutes, less than about 10 minutes or less than about 15 minutes.~~

~~21.—— The method of any of claims 1-20, wherein the method further comprises use with at least one calibrator reagent, at least one control reagent, or at least one calibrator reagent and at least one control reagent.~~

~~—— 22.—— The method of any of claims 1-21, wherein the method further employs use of at least one calibrator reagent or a control reagent comprising a sequence of monoclonal antibody-CR3018 or CR3022.~~

~~—— 23.—— The method of any of claims 1-22, wherein the method is selected from the group consisting of an immunoassay, or a clinical chemistry assay.~~

~~—— 24.—— The method of any of claims 1-23, wherein the method is performed using single-molecule detection, lateral flow assay, or a point-of-care assay.——~~

~~25.—— The method of any of claims 1-24, wherein the method further comprises identifying a subject having one or more anti-SARS-CoV-2 IgG and/or anti-SARS-CoV-2 IgM antibodies as a candidate subject to provide a biological sample for use in convalescent therapy against SARS-CoV-2.~~

26. — The method of claim 25, wherein the subject is identified as a candidate to provide a biological sample for use in convalescent therapy if the level of one or more SARS-CoV-2 IgG and/or SARS-CoV-2 IgM antibodies is from at least about 100 BAU/mL to about 490 BAU/mL; at least about 110 BAU/mL to about 490 BAU/mL; at least about 200 BAU/mL to about 490 BAU/mL; at least from about 300 BAU/mL to about 490 BAU/mL; at least about 400 BAU/mL to about 490 BAU/mL; at least about 100 BAU/mL; at least about 110 BAU/mL; at least about 120 BAU/mL; at least about 130 BAU/mL; at least about 140 BAU/mL; at least about 150 BAU/mL; at least about 160 BAU/mL; at least about 170 BAU/mL; at least about 180 BAU/mL; at least about 190 BAU/mL; at least about 200 BAU/mL; at least about 210 BAU/mL; at least about 220 BAU/mL; at least about 230 BAU/mL; at least about 240 BAU/mL; at least about 250 BAU/mL; at least about 260 BAU/mL; at least about 270 BAU/mL; at least about 280 BAU/mL; at least about 290 BAU/mL; at least about 300 BAU/mL; at least about 300 BAU/mL; at least about 310 BAU/mL; at least about 320 BAU/mL; at least about 330 BAU/mL; at least about 340 BAU/mL; at least about 350 BAU/mL; at least about 360 BAU/mL; at least about 370 BAU/mL; at least about 380 BAU/mL; at least about 390 BAU/mL; at least about 400 BAU/mL; at least about 400 BAU/mL; at least about 410 BAU/mL; at least about 420 BAU/mL; at least about 430 BAU/mL; at least about 440 BAU/mL; at least about 450 BAU/mL; at least about 460 BAU/mL; at least about 470 BAU/mL; at least about 480 BAU/mL; or at least about 490 BAU/mL.

——— 27. The method of claim 26, wherein the subject is identified as a candidate to provide a biological sample for use in convalescent therapy if the level of one or more SARS-CoV-2 IgG and/or anti- β coronavirus IgM antibodies is from at least about 500 BAU/mL to about 650 BAU/mL; at least about 550 BAU/mL to about 650 BAU/mL; at least about 500 BAU/mL; from at least about 510 BAU/mL; at least about 520 BAU/mL; at least about 530 BAU/mL; at least about 540 BAU/mL; at least about 550 BAU/mL to about 650 BAU/mL; at least about 550 BAU/mL; at least about 560 BAU/mL; at least about 570 BAU/mL; at least about 580 BAU/mL; at least about 590 BAU/mL; at least about 600 BAU/mL; at least about 610 BAU/mL; at least about 620 BAU/mL; at least about 630 BAU/mL; at least about 639 BAU/mL; at least about 640 BAU/mL; or at least about 650 BAU/mL.

——— 28. — The method of any of claims 1-27, wherein the method:

~~(a) further comprises detecting at least one type of anti SARS-CoV-2 IgG neutralizing antibody;~~

~~(b) demonstrates high qualitative agreement with a plaque reduction neutralization assay;~~

~~(c) detects increasing amounts of anti SARS-CoV-2 IgG antibodies as detected by the method that are associated with increasing amounts of anti SARS-CoV-2 IgG neutralizing antibodies;~~

~~(d) has a probability profile that corresponds to high titer levels in the plaque reduction neutralization assay such that there is a high probability of the levels of anti SARS-CoV-2 IgG antibodies determined by the method being at or above the levels of anti SARS-CoV-2 IgG neutralizing antibodies determined in the plaque reduction neutralization assay; or~~

~~(e) demonstrates high qualitative agreement with an ACE2 binding inhibition assay.~~

~~29. — The method of claim 28, wherein a level of anti SARS-CoV-2 IgG antibodies of at least about 4160 AU/mL (about 590 BAU/mL) when used as a cut-off or threshold correspond to about a 0.95 probability of obtaining a plaque reduction neutralization assay ID50 at 1:250 dilution.~~

~~30. — The method of claim 28, wherein the anti SARS-CoV-2 neutralizing antibody is an anti SARS-CoV-2 IgG antibody that is an anti-nucleocapsid (N) antibody, an anti-spike antibody, or any combination thereof.~~

~~31. — The method of any of claims 1-30, wherein the method comprises obtaining the at least one biological sample from the subject at a critical time of from about fourteen (14) days to about thirty-five (35) days after onset of symptoms of SARS-CoV-2.~~

~~32. — The method of claim 31, wherein the method further comprises determining that the subject: (i) more likely than not will develop or experience at least one of a cytokine storm, acute respiratory distress syndrome (ARDS), or a combination of a cytokine storm and ARDS if anti SARS-CoV-2 IgM antibody, anti SARS-CoV-2 IgG antibody, or anti SARS-CoV-2 IgM antibody and anti SARS-CoV-2 IgG antibody are not detected in the biological sample within the critical time; or (ii) more likely than not will not develop or experience at least one of a cytokine storm, ARDS, or a combination of a cytokine storm and ARDS if anti SARS-CoV-2 IgM antibody, anti SARS-CoV-2 IgG antibody, or anti SARS-CoV-2 IgM antibody and anti SARS-CoV-2 IgG antibody are not detected in the biological sample within the critical time.~~

~~33. — The method of any of claims 1-32, wherein the subject: (1) is naïve and was not previously vaccinated against SARS-CoV-2; (2) is naïve and was previously vaccinated against~~

~~SARS-CoV-2; (3) is currently infected with SARS-CoV-2 and was not previously vaccinated against SARS-CoV-2; (4) is currently infected with SARS-CoV-2 and was previously vaccinated against SARS-CoV-2; (5) was previously infected with SARS-CoV-2, recovered, and was not previously vaccinated against SARS-CoV-2; or (6) was previously infected with SARS-CoV-2, recovered, and then was vaccinated against SARS-CoV-2.~~

~~34. The method of claim 33, wherein the method is performed to: (a) determine whether the subject can be administered a current vaccine for SARS-CoV-2; or (b) monitor the subject following the current vaccine or previous vaccination, based on detecting the presence of at least one type of anti-SARS-CoV-2 antibody in the sample.~~

~~35. The method of claim 34, performed regardless of variation in timing and/or severity of prior infection with SARS-CoV-2.~~

~~36. The method of any of claim 34 or 35, wherein the method comprises determining that the current vaccine for SARS-CoV-2:~~

~~(a) can be administered to the subject when no anti-SARS-CoV-2 antibodies, no anti-SARS-CoV-2 IgG neutralizing antibodies, or an amount of anti-SARS-CoV-2 IgG antibody or anti-SARS-CoV-2 IgG neutralizing antibody that is insufficient to impart immunity, are detected in the biological sample; and/or~~

~~(b) should not be administered to the subject if an amount of anti-SARS-CoV-2 antibody or anti-SARS-CoV-2 IgG neutralizing antibody that is sufficient to impart immunity is detected in the biological sample.~~

~~37. The method of claim 36, wherein the amount of anti-SARS-CoV-2 antibody or anti-SARS-CoV-2 IgG neutralizing antibody sufficient to impart immunity is from at least about 100 BAU/mL to about 490 BAU/mL; at least about 110 BAU/mL to about 490 BAU/mL; at least about 200 BAU/mL to about 490 BAU/mL; at least from about 300 BAU/mL to about 490 BAU/mL; at least about 400 BAU/mL to about 490 BAU/mL; at least about 100 BAU/mL; at least about 110 BAU/mL; at least about 120 BAU/mL; at least about 130 BAU/mL; at least about 140 BAU/mL; at least about 150 BAU/mL; at least about 160 BAU/mL; at least about 170 BAU/mL; at least about 180 BAU/mL; at least about 190 BAU/mL; at least about 200 BAU/mL; at least about 210 BAU/mL; at least about 220 BAU/mL; at least about 230 BAU/mL; at least about 240 BAU/mL; at least about 250 BAU/mL; at least about 260 BAU/mL; at least about 270~~

BAU/mL; at least about 280 BAU/mL; at least about 290 BAU/mL; at least about 300 BAU/mL; at least about 300 BAU/mL; at least about 310 BAU/mL; at least about 320 BAU/mL; at least about 330 BAU/mL; at least about 340 BAU/mL; at least about 350 BAU/mL; at least about 360 BAU/mL; at least about 370 BAU/mL; at least about 380 BAU/mL; at least about 390 BAU/mL; at least about 400 BAU/mL; at least about 400 BAU/mL; at least about 410 BAU/mL; at least about 420 BAU/mL; at least about 430 BAU/mL; at least about 440 BAU/mL; at least about 450 BAU/mL; at least about 460 BAU/mL; at least about 470 BAU/mL; at least about 480 BAU/mL; or at least about 490 BAU/mL.

38. — The method of claim 36, wherein the amount of anti-SARS-CoV-2 antibody or anti-SARS-CoV-2 IgG neutralizing antibody sufficient to impart immunity is: (a) from at least about 550 BAU/mL to about 650 BAU/mL; (b) at least about 550 BAU/mL; (c) at least about 560 BAU/mL; (d) at least about 570 BAU/mL; (e) at least about 580 BAU/mL; (f) at least about 590 BAU/mL; (g) at least about 600 BAU/mL; (h) at least about 610 BAU/mL; (i) at least about 620 BAU/mL; (j) at least about 630 BAU/mL; (k) at least about 639 BAU/mL; (l) at least about 640 BAU/mL; or (m) at least about 650 BAU/mL.

39. — The method of claim 34, wherein the method comprises obtaining the biological sample within a time frame after the subject has received either the current vaccine or previous vaccination for SARS-CoV-2 of at least one day, at least 2 days, at least 3 days, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, at least 17 days, at least 18 days, at least 19 days, at least 20 days, at least 21 days, at least 22 days, at least 23 days, at least 24 days, at least 25 days, at least 26 days, at least 27 days, at least 28 days, at least 29 days, at least 30 days, at least 31 days, at least 32 days, at least 33 days, at least 34 days, at least 35 days, at least 36 days, at least 37 days, at least 38 days, at least 39 days, at least 40 days, at least 41 days, at least 42 days, at least 43 days, at least 44 days, at least 45 days, at least 46 days, at least 47 days, at least 48 days, at least 49 days, or at least 50 days. —

40. — The method of claim 34, wherein the biological sample is obtained within about 7 to about 21 days after the subject has received either the current vaccine or previous vaccination.

41. — The method of claim 39 or claim 40, wherein the method comprises determining that at least one further vaccine for SARS-CoV-2:

~~(a) can be administered to the subject after the current vaccine if no anti SARS-CoV-2 antibodies, no anti SARS-CoV-2 IgG neutralizing antibodies, and/or an amount of anti SARS-CoV-2 IgG antibody or anti SARS-CoV-2 IgG neutralizing antibody that is insufficient to impart immunity, is detected in the biological sample obtained from the subject; or—~~

~~(b) should not be administered to the subject after the current vaccine if an amount of anti SARS-CoV-2 antibody or anti SARS-CoV-2 IgG neutralizing antibody that is sufficient to impart immunity is detected in the biological sample obtained from the subject.—~~

42.——~~The method of claim 41, wherein the amount of anti SARS-CoV-2 antibody or anti SARS-CoV-2 IgG neutralizing antibody sufficient to impart immunity is from at least about 100 BAU/mL to about 490 BAU/mL; at least about 110 BAU/mL to about 490 BAU/mL; at least about 200 BAU/mL to about 490 BAU/mL; at least from about 300 BAU/mL to about 490 BAU/mL; at least about 400 BAU/mL to about 490 BAU/mL; at least about 100 BAU/mL; at least about 110 BAU/mL; at least about 120 BAU/mL; at least about 130 BAU/mL; at least about 140 BAU/mL; at least about 150 BAU/mL; at least about 160 BAU/mL; at least about 170 BAU/mL; at least about 180 BAU/mL; at least about 190 BAU/mL; at least about 200 BAU/mL; at least about 210 BAU/mL; at least about 220 BAU/mL; at least about 230 BAU/mL; at least about 240 BAU/mL; at least about 250 BAU/mL; at least about 260 BAU/mL; at least about 270 BAU/mL; at least about 280 BAU/mL; at least about 290 BAU/mL; at least about 300 BAU/mL; at least about 300 BAU/mL; at least about 310 BAU/mL; at least about 320 BAU/mL; at least about 330 BAU/mL; at least about 340 BAU/mL; at least about 350 BAU/mL; at least about 360 BAU/mL; at least about 370 BAU/mL; at least about 380 BAU/mL; at least about 390 BAU/mL; at least about 400 BAU/mL; at least about 400 BAU/mL; at least about 410 BAU/mL; at least about 420 BAU/mL; at least about 430 BAU/mL; at least about 440 BAU/mL; at least about 450 BAU/mL; at least about 460 BAU/mL; at least about 470 BAU/mL; at least about 480 BAU/mL; or at least about 490 BAU/mL.~~

43.——~~The method of claim 41, wherein the amount of anti SARS-CoV-2 antibody or anti SARS-CoV-2 IgG neutralizing antibody sufficient to impart immunity is from at least about 500 BAU/mL to about 650 BAU/mL; at least about 550 BAU/mL to about 650 BAU/mL; at least about 500 BAU/mL; from at least about 510 BAU/mL; at least about 520 BAU/mL; at least about 530 BAU/mL; at least about 540 BAU/mL; at least about 550 BAU/mL to about 650~~

~~BAU/mL; at least about 550 BAU/mL; at least about 560 BAU/mL; at least about 570 BAU/mL; at least about 580 BAU/mL; at least about 590 BAU/mL; at least about 600 BAU/mL; at least about 610 BAU/mL; at least about 620 BAU/mL; at least about 630 BAU/mL; at least about 639 BAU/mL; at least about 640 BAU/mL; or at least about 650 BAU/mL.~~

~~44. The method of any of claims 28, 30, 36, 37, 38, 41, 42 or 43 wherein the anti-SARS-CoV-2 neutralizing antibody is an anti-SARS-CoV-2 IgG antibody that is an anti-nucleocapsid (N) antibody, an anti-spike antibody, or any combination thereof.~~

~~45. The method of any of claims 1-44, wherein the method further comprises (a) monitoring the subject for at least one type of anti-SARS-CoV-2 antibody, optionally, IgG and/or IgM antibodies; (b) treating the subject for SARS-CoV-2; (c) monitoring the subject for at least one type of anti-SARS-CoV-2, optionally, IgG and/or IgM antibodies and treating the subject for SARS-CoV-2; or (d) treating the subject for a SARS-CoV-2 and monitoring the subject for at least one type of anti-SARS-CoV-2 antibody, optionally, IgG and/or IgM antibodies.~~

~~46. The method of any of claims 1-45, wherein the volume of the biological sample used in the method is from about 0.30 μ L to about 0.40 μ L.~~

~~47. The method of any of claims 1-46, wherein the method comprises (a) diluting the biological sample prior to or during the method and further wherein the diluting comprises mixing about 10 μ L of the biological sample with about 290 μ L of at least one buffer to form a biological sampling mixture; and (b) removing about 10 μ L from the biological sampling mixture for use in the method.~~

~~48. The method of any of claims 1-47, wherein the method is adapted for use in an automated system or a semi-automated system.~~

~~49. A kit for performing the method of claim 1, wherein the kit comprises:~~

- ~~a. at least one type of specific binding partner comprising at least one β -coronavirus isolated polypeptide or variant thereof selected from a C-terminal domain nucleocapsid protein, a receptor binding domain (RBD) of a spike protein, or a C-terminal domain nucleocapsid protein and a receptor binding domain (RBD) of a spike protein from a β -coronavirus; and~~
- ~~b. at least one type of second specific binding partner comprising at least one detectable label.~~

50. — The kit of claim 49, wherein the at least one type of anti SARS CoV 2 antibody detected or determined specifically binds to a variant:

a) of the nucleocapsid protein having one or more substitutions, deletions or a substitution and deletion at positions 210-419 of SEQ ID NO:2 comprising: (1) replacing serine with phenylalanine at amino acid position 235 (S235F); (2) replacing methionine with isoleucine at amino acid position 234 (M234I); (3) replacing lysine with asparagine at amino acid position 373 (K373N); (4) replacing aspartic acid with tyrosine at amino acid position 377 (D377Y); (5) replacing alanine with threonine at amino acid position 376 (A376T); or (6) any combinations of (1)-(5), either alone or combined with any other substitutions and/or deletions in amino acids 210-419 of SEQ ID NO:2 other than those recited in (1)-(5);

b) of the RBD of a spike protein having one or more substitutions, deletions or a substitution and deletion at positions 319-542 of SEQ ID NO:15 comprising (1) replacing lysine with asparagine at amino acid position 417 (K417N); (2) replacing lysine with threonine at amino acid position 417 (K417T); (3) replacing leucine with arginine at amino acid position 452 (L452R); (4) replacing serine with asparagine at amino acid position 477 (S477N); (5) replacing glutamic acid with lysine at amino acid position 484 (E484K); (6) replacing asparagine with tyrosine at amino acid position 501 (N501Y); or (7) any combinations of (1)-(6), either alone or combined with any other substitutions and/or deletions in amino acids 319-542 of SEQ ID NO:15 other than those recited in (1)-(6); or

c) from a SARS-CoV-2 virus comprising any combination of a) and b).

— 51. — The kit of claim 49 or claim 50, wherein the kit further comprises, or is configured to be used with, at least one calibrator reagent, at least one control reagent, or at least one calibrator reagent and at least one control reagent.

— 52. — The kit of any of claims 49-51, wherein the kit further comprises at least one solid support.

— 53. — The kit of any of claims 49-52, wherein the kit further comprises, or is configured to be used with, at least one pretreatment reagent.

— 54. — The kit of any of claims 49-53, wherein the isolated polypeptide is a fusion polypeptide.

— 55. — The kit of any of claims 49-54, wherein the at least one type of second specific binding partner is an anti-species IgG (e.g., anti-human IgG-IgG) antibody, an anti-species IgM-

(e.g., anti human IgM IgG) antibody, or an anti species IgG (e.g., anti human IgG IgG) antibody and an anti species IgM (e.g., anti human IgM IgG) antibody.

56. The kit of any of claims 49-55, wherein the kit further comprises at least one calibrator reagent or control reagent comprising a sequence of monoclonal antibody CR3018 or CR3022.

57. The kit of any of claims 49-56, wherein the at least one type of first specific binding partner is a C-terminal domain nucleocapsid protein or variant thereof that (1) has an amino acid sequence of SEQ ID NO:1; (2) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQNQ (SEQ ID NO:21), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2; (3) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQSNQ (SEQ ID NO:22), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2; or (4) has an amino acid sequence of amino acids 210 to 419 of SEQ ID NO:2.

58. The kit of any of claims 49-57, wherein the at least one type of first specific binding partner is a receptor binding domain (RBD) of a spike protein that has an amino acid sequence of amino acids 319 to 542 of SEQ ID NO:15 or SEQ ID NO:17.

59. The kit of any of claims 49-58, wherein the at least one type of first specific binding partner binds to (a) an anti SARS-CoV-2 IgG antibody, (b) an anti SARS-CoV-2 IgM antibody, or (c) combinations of (a) and (b).

60. The kit of any of claims 49-59, wherein the kit is adapted for use with an automated or semi-automated system.

61. A system for detecting a presence or determining an amount of anti SARS-CoV-2 antibody in a biological sample obtained from a subject comprising:

at least one type of first specific binding partner comprising at least one β -coronavirus isolated polypeptide or variant thereof selected from a C-terminal domain nucleocapsid protein, a receptor binding domain (RBD) of a spike protein, or a C-terminal domain nucleocapsid protein and a receptor binding domain (RBD) of a spike protein from a β -coronavirus that specifically binds to at least one type of anti SARS-CoV-2 antibody and at least one type of second specific binding partner comprising at least one detectable label; and

~~at least one device for detecting the at least one label from the complex, wherein the amount of signal from the label indicates the presence or amount of anti-SARS-CoV-2 antibody in the sample.~~

~~62. The system of claim 61, wherein the at least one type of anti-SARS-CoV-2 antibody detected specifically binds to a variant:~~

~~a) of the nucleocapsid protein having one or more substitutions, deletions or a substitution and deletion at positions 210-419 of SEQ ID NO:2 comprising: (1) replacing serine with phenylalanine at amino acid position 235 (S235F); (2) replacing methionine with isoleucine at amino acid position 234 (M234I); (3) replacing lysine with asparagine at amino acid position 373 (K373N); (4) replacing aspartic acid with tyrosine at amino acid position 377 (D377Y); (5) replacing alanine with threonine at amino acid position 376 (A376T); or (6) any combinations of (1)-(5), either alone or combined with any other substitutions and/or deletions in amino acids 210-419 of SEQ ID NO:2 other than those recited in (1)-(5);~~

~~b) of the RBD of a spike protein having one or more substitutions, deletions or a substitution and deletion at positions 319-542 of SEQ ID NO:15 comprising (1) replacing lysine with asparagine at amino acid position 417 (K417N); (2) replacing lysine with threonine at amino acid position 417 (K417T); (3) replacing leucine with arginine at amino acid position 452 (L452R); (4) replacing serine with asparagine at amino acid position 477 (S477N); (5) replacing glutamic acid with lysine at amino acid position 484 (E484K); (6) replacing asparagine with tyrosine at amino acid position 501 (N501Y); or (7) any combinations of (1)-(6), either alone or combined with any other substitutions and/or deletions in amino acids 319-542 of SEQ ID NO:15 other than those recited in (1)-(6); or~~

~~c) from a SARS-CoV-2 virus comprising any combination of a) and b).~~

~~63. The system of claim 61 or claim 62, wherein the device for detecting the label from the complex is automated or semi-automated.~~

~~64. The system of any of claims 61-63, wherein the at least one type of anti-SARS-CoV-2 antibody is an IgG antibody, an IgM antibody, or any combination thereof.~~

~~65. The system of any of claims 61-64, wherein the at least one type of second-specific binding partner is an anti-species IgG (e.g., anti-human-IgG-IgG) antibody, an anti-species IgM (e.g., anti-human-IgM-IgG) antibody, or an anti-species IgG (e.g., anti-human-IgG-IgG) antibody, and anti-species IgM (e.g., anti-human-IgM-IgG) antibody.~~

~~66. The system of claims 61-65, wherein the at least one type of first specific binding partner is a C-terminal domain nucleocapsid protein or variant thereof that~~

~~(1) has an amino acid sequence of SEQ ID NO:1; (2) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQNN (SEQ ID NO:21), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2; (3) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQSNQ (SEQ ID NO:22), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2; or (4) has an amino acid sequence of amino acids 210 to 419 of SEQ ID NO:2.~~

~~67. The system of any of claims 61-66, wherein the at least one type of first specific binding partner is a receptor binding domain (RBD) of a spike protein or variant thereof that has an amino acid sequence of amino acids 319 to 542 of SEQ ID NO:15 or SEQ ID NO:17.~~

~~68. The system of any of claims 61-67, wherein the at least one type of first specific binding partner binds to (a) an anti-SARS-CoV-2 IgG antibody, (b) an anti-SARS-CoV-2 IgM antibody, or (c) combinations of (a) and (b).~~

~~69. In an improvement of a method of detecting at least one type of anti-SARS-CoV-2 antibody in a biological sample, wherein the method comprises detecting a complex comprising a first type of specific binding partner, said sample anti-SARS-CoV-2 antibody, and a second type of specific binding partner comprising at least one detectable label, wherein the improvement comprises using at least one type of first specific binding partner comprising at least one isolated polypeptide from a C-terminal domain of a β -coronavirus nucleocapsid protein or a variant thereof.~~

~~70. In the improvement of claim 69, wherein the at least one type of first specific binding partner is a C-terminal domain nucleocapsid protein or variant thereof that (1) has an amino acid sequence of SEQ ID NO:1; (2) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQNN (SEQ ID NO:21), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2; (3) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQSNQ (SEQ ID NO:22), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2; or (4) has an amino acid sequence of amino acids 210 to 419 of SEQ ID NO:2.~~

~~71. In an improvement of a method of detecting at least one type of anti-SARS-CoV-2 antibody in a biological sample, wherein the method comprises detecting a complex~~

comprising a first type of specific binding partner, said sample anti-SARS-CoV-2 antibody, and a second type of specific binding partner comprising at least one detectable label, wherein the improvement comprises using a first specific binding partner comprising at least one isolated polypeptide from a receptor binding domain (RBD) of a β -coronavirus spike protein or a variant thereof.—

———72.—— In the improvement of claim 71, wherein the at least one type of first specific binding partner is a receptor binding domain (RBD) of a spike protein or variant thereof that has an amino acid sequence of amino acids 319 to 542 of SEQ ID NO:15 or SEQ ID NO:17.

———73.—— In the improvement of claim 70 or claim 71, wherein the at least one first type of specific binding partner binds to (a) an anti-SARS-CoV-2 IgG antibody, (b) an anti-SARS-CoV-2 IgM antibody, or (c) combinations of (a) and (b).

74.—— The improvement of any of claims 69–73, wherein the at least one type of anti-SARS-CoV-2 antibody detected specifically binds to a variant:

a) of the nucleocapsid protein having one or more substitutions, deletions or a substitution and deletion at positions 210–419 of SEQ ID NO:2 comprising: (1) replacing serine with phenylalanine at amino acid position 235 (S235F); (2) replacing methionine with isoleucine at amino acid position 234 (M234I); (3) replacing lysine with asparagine at amino acid position 373 (K373N); (4) replacing aspartic acid with tyrosine at amino acid position 377 (D377Y); (5) replacing alanine with threonine at amino acid position 376 (A376T); or (6) any combinations of (1)–(5), either alone or combined with any other substitutions and/or deletions in amino acids 210–419 of SEQ ID NO:2 other than those recited in (1)–(5);

b) of the RBD of a spike protein having one or more substitutions, deletions or a substitution and deletion at positions 319–542 of SEQ ID NO:15 comprising (1) replacing lysine with asparagine at amino acid position 417 (K417N); (2) replacing lysine with threonine at amino acid position 417 (K417T); (3) replacing leucine with arginine at amino acid position 452 (L452R); (4) replacing serine with asparagine at amino acid position 477 (S477N); (5) replacing glutamic acid with lysine at amino acid position 484 (E484K); (6) replacing asparagine with tyrosine at amino acid position 501 (N501Y); or (7) any combinations of (1)–(6), either alone or combined with any other substitutions and/or deletions in amino acids 319–542 of SEQ ID NO:15 other than those recited in (1)–(6); or

c) from a SARS-CoV-2 virus comprising any combination of a) and b).

~~75. In an improvement of a method or system for determining an amount of an anti-SARS-CoV-2 IgG antibody in a subject based on the amount of detectable signal assessed, wherein the improvement comprises: (a) a linear assay range of up to 50,000 AU/mL; (b) determining an amount in arbitrary units rather than an index; and/or (c) improved detection of positive samples as compared to other assays.~~

~~76. A method of predicting outcome in a subject that is or was infected with SARS-CoV-2, the method comprising the steps of:~~

~~a) detecting an anti-SARS-CoV-2 IgG antibody in at least one biological sample obtained from the subject within a first ten days after onset of symptoms of SARS-CoV-2 infection;~~

~~b) detecting an anti-SARS-CoV-2 IgM antibody in the at least one biological sample obtained from the subject within the first ten days after onset of symptoms of SARS-CoV-2 infection;~~

~~c) determining which of the anti-SARS-CoV-2 IgG or anti-SARS-CoV-2 IgM antibody detected in a) and b) first appears in the subject;~~

~~d) predicting that the subject is more likely to have an unfavorable outcome if anti-SARS-CoV-2 IgG antibody first appears in the subject prior to the appearance of anti-SARS-CoV-2 IgM antibody; and~~

~~e) predicting that the subject is more likely to have a favorable outcome if anti-SARS-CoV-2 IgG antibody first appears in the subject at the same time or after the appearance of anti-SARS-CoV-2 IgM antibody.~~

~~77. The method of claim 76, wherein the subject is hospitalized for symptoms of SARS-CoV-2.~~

~~78. The method of claim 76 or claim 77, wherein (i) the anti-SARS-CoV-2 IgG antibody and the one anti-SARS-CoV-2 IgM antibody are detected in the same biological sample; or (ii) the anti-SARS-CoV-2 IgG antibody and the anti-SARS-CoV-2 IgM antibody are detected in different biological samples.~~

~~79. The method of any of claims 76-78, wherein the anti-SARS-CoV-2 IgG antibody and the anti-SARS-CoV-2 IgM antibody are (i) detected on the same day within the first ten days~~

after onset of symptoms; (ii) detected on different days within the first ten days after the onset of symptoms.

~~80. The method any of claims 76-79, wherein the anti-SARS-CoV-2 IgG antibody is detected in at least one biological sample obtained from the subject within the first day after the onset of symptoms, within the second day after the onset of symptoms, within the third day after the onset of symptoms, within the fourth day after the onset of symptoms, within the fifth day after the onset of symptoms, within the sixth day after the onset of symptoms, within the seventh date after the onset of symptoms, within the eighth day after the onset of symptoms or within the ninth day after the onset of symptoms.~~

~~81. The method of any of claims 76-80, wherein the anti-SARS-CoV-2 IgM antibody is detected in at least one biological sample obtained from the subject within the first day after the onset of symptoms, within the second day after the onset of symptoms, within the third day after the onset of symptoms, within the fourth day of infection, within the fifth day after the onset of symptoms, within the sixth day after the onset of symptoms, within the seventh date after the onset of symptoms, within the eighth day after the onset of symptoms or within the ninth day after the onset of symptoms.~~

~~82. The method of any of claims 76-81, wherein the unfavorable outcome is death.~~

~~83. A method of predicting outcome in a subject that is or was infected with SARS-CoV-2, the method comprising the steps of:—~~

~~—— a) obtaining a signal-to-calibrator ratio (S/CO) from an assay of at least one anti-SARS-CoV-2 IgM antibody in at least one biological sample obtained from the subject at least ten days after onset of symptoms of SARS-CoV-2; and~~

~~—— b) predicting that the subject is more likely than not to have an unfavorable outcome if the S/CO ratio of anti-SARS-CoV-2 IgM antibody determined in the biological sample is equal to or greater than about 10 S/CO.~~

~~84. The method of claim 83, wherein the subject is hospitalized for symptoms of SARS-CoV-2.~~

~~85. The method of claim 83 or claim 84, further comprising that the subject is more likely than not to have an unfavorable outcome if the level of anti SARS-CoV-2 IgM antibody determined in the biological sample is between about 10 S/CO to about 15 S/CO.~~

~~86. The method of any of claims 76-85, wherein the method is selected from the group consisting of an immunoassay, or a clinical chemistry assay.~~

~~87. The method of any of claims 76-86, wherein the method is performed using single molecule detection, lateral flow assay or a point-of-care assay.~~

~~88. A method of determining SARS-CoV-2 immune status of a subject, the method comprising the steps of:~~

- ~~a) determining an amount of at least one anti-SARS-CoV-2 IgG antibody and/or anti-SARS-CoV-2 IgG neutralizing antibody in at least one biological sample obtained from a subject; and~~
- ~~b) determining the subject's SARS-CoV-2 immune status, wherein the subject is determined to have immunity to SARS-CoV-2 when the amount of anti-SARS-CoV-2 IgG antibody and/or anti-SARS-CoV-2 IgG neutralizing antibody is (a) from at least about 550 BAU/mL to about 650 BAU/mL; or (b) from at least about 100 BAU/mL to about 490 BAU/mL,~~

~~wherein the method is performed irrespective of (i) the subject's prior infection and/or vaccination history with SARS-CoV-2, and/or (ii) whether there is any knowledge of the subject's prior infection and/or vaccination history with SARS-CoV-2.~~

~~89. The method of claim 88, wherein the subject has not previously been infected with SARS-CoV-2.~~

~~90. The method of claim 88, wherein the subject has previously been infected with SARS-CoV-2.~~

~~91. The method of any of claims 88-90, wherein the subject has not previously been vaccinated for SARS-CoV-2.~~

~~92. The method of any of claims 88-90, wherein the subject has previously been vaccinated for SARS-CoV-2.~~

~~93. The method of any of claims 88-92, wherein the immune status of the subject is that the subject has immunity to SARS-CoV-2.~~

~~94. The method of any of claims 88-92, wherein the immune status of the subject is that the subject does not have immunity to SARS-CoV-2.~~

~~95. The method of any of claims 88-94, wherein the method is selected from the group consisting of an immunoassay, or a clinical chemistry assay.~~

~~96. The method of any of claims 88-95, wherein the method is performed using single molecule detection, lateral flow assay or a point-of-care assay.~~

~~97. A system for assessing whether a subject is likely to have immunity from infection from SARS-CoV-2 in a biological sample obtained from a subject, the system comprising:~~

~~at least one type of first specific binding partner comprising at least one type of β -coronavirus isolated polypeptide or variant thereof selected from a C-terminal domain-nucleocapsid protein, a receptor binding domain (RBD) of a spike protein, or a C-terminal domain-nucleocapsid protein and a receptor binding domain (RBD) of a spike protein from at least one type β -coronavirus that specifically binds to at least one type of anti-SARS-CoV-2 antibody and at least one type of second specific binding partner comprising at least one detectable label;~~

~~at least one device for detecting the at least one label from the complex, wherein the amount of signal from the label indicates the presence or amount of anti-SARS-CoV-2 antibody in the sample; and~~

~~a means for assigning a differentiative rating indicating whether the subject is likely to have immunity from infection from SARS-CoV-2 based on the presence or amount of at least one type of anti-SARS-CoV-2 antibody detected in the sample.~~

~~98. The system of claim 97, wherein the differentiative rating is a color and/or number rating.~~

~~99. The system of claim 98, wherein the color and/or number rating is displayed on a mobile device through a mobile application.~~

~~100. The system of any of claims 97-99, wherein the variant:~~

~~a) is of the C-terminal domain of a nucleocapsid protein having one or more substitutions, deletions or a substitution and deletion at positions 210-419 of SEQ ID NO:2 comprising: (1) replacing serine with phenylalanine at amino acid position 235 (S235F); (2) replacing methionine with isoleucine at amino acid position 234 (M234I); (3) replacing lysine-~~

with asparagine at amino acid position 373 (K373N); (4) replacing aspartic acid with tyrosine at amino acid position 377 (D377Y); (5) replacing alanine with threonine at amino acid position 376 (A376T); or (6) any combinations of (1)–(5), either alone or combined with any other substitutions and/or deletions in amino acids 210–419 of SEQ ID NO:2 other than those recited in (1)–(5);

b) is the RBD of a spike protein having one or more substitutions, deletions or a substitution and deletion at positions 319–542 of SEQ ID NO:15 comprising (1) replacing lysine with asparagine at amino acid position 417 (K417N); (2) replacing lysine with threonine at amino acid position 417 (K417T); (3) replacing leucine with arginine at amino acid position 452 (L452R); (4) replacing serine with asparagine at amino acid position 477 (S477N); (5) replacing glutamic acid with lysine at amino acid position 484 (E484K); (6) replacing asparagine with tyrosine at amino acid position 501 (N501Y); or (7) any combinations of (1)–(6), either alone or combined with any other substitutions and/or deletions in amino acids 319–542 of SEQ ID NO:15 other than those recited in (1)–(6); or

~~c) comprises any combination of a) and b).~~

101. —The system of any of claims 97–100, wherein the device for detecting the label from the complex is automated or semi-automated.

102. —The system of claim 101, wherein the device for detecting the label from the complex is semi-automated and comprises uploading the differentiative rating using a bar code.

103. —The system of any of claims 97–102, wherein the at least one type of anti-SARS-CoV-2 antibody is an anti-SARS-CoV-2 IgG antibody, an anti-SARS-CoV-2 IgM antibody, or any combination thereof.

104. —The system of any of claims 97–103, wherein the at least one type of second-specific binding partner is an anti-species IgG (e.g., anti-human IgG IgG) antibody, an anti-species IgM (e.g., anti-human IgM IgG) antibody, or an anti-species IgG (e.g., anti-human IgG-IgG) antibody, and anti-species IgM (e.g., anti-human IgM IgG) antibody.

—105. —The system of any of claims 97–104, wherein the at least one type of first specific binding partner is a receptor binding domain (RBD) of a spike protein or variant thereof that has an amino acid sequence of amino acids 319 to 542 of SEQ ID NO:15 or SEQ ID NO:17.

~~106. The system of any of claims 97-105, wherein the at least one type of first specific binding partner binds to (a) an anti SARS-CoV-2 IgG antibody, (b) an anti SARS-CoV-2 IgM antibody, or (c) combinations of (a) and (b).~~

What is claimed is:

1. A method for detecting a presence or determining an amount of at least one type of anti-SARS-CoV-2 antibody in a subject, the method comprising the steps of:

a) contacting at least one biological sample from the subject, either simultaneously or sequentially, in any order, with at least one type of first specific binding partner comprising at least one type of β -coronavirus isolated polypeptide or variant thereof, selected from a C-terminal domain of a nucleocapsid protein, a receptor binding domain (RBD) of a spike protein, or a C-terminal domain of a nucleocapsid protein and a receptor binding domain (RBD) of a spike protein, wherein the polypeptide specifically binds to at least one type of anti-SARS-CoV-2 antibody in the sample, and

at least one type of second specific binding partner comprising a detectable label, thereby producing one or more types of first complexes comprising the first specific binding partner-anti-SARS-CoV-2 antibody-second specific binding partner; and

b) assessing a signal from the one or more types of first complexes, wherein the amount of detectable signal from the detectable label indicates the presence or amount of at least one type of anti- β -coronavirus antibody in the sample.

2. The method of claim 1, wherein the at least one type of anti-SARS-CoV-2 antibody specifically binds to a variant:

a) of the nucleocapsid protein having one or more substitutions, deletions or a substitution and deletion at positions 210-419 of SEQ ID NO:2 comprising: (1) replacing serine with phenylalanine at amino acid position 235 (S235F); (2) replacing methionine with isoleucine at amino acid position 234 (M234I); (3) replacing lysine with asparagine at amino acid position 373 (K373N); (4) replacing aspartic acid with tyrosine at amino acid position 377 (D377Y); (5) replacing alanine with threonine at amino acid position 376 (A376T); or (6) any combinations of

(1)-(5), either alone or combined with any other substitutions and/or deletions in amino acids 210-419 of SEQ ID NO:2 other than those recited in (1)-(5);

b) of the RBD of a spike protein having one or more substitutions, deletions or a substitution and deletion at positions 319-542 of SEQ ID NO:15 comprising (1) replacing lysine with asparagine at amino acid position 417 (K417N); (2) replacing lysine with threonine at amino acid position 417 (K417T); (3) replacing leucine with arginine at amino acid position 452 (L452R); (4) replacing serine with asparagine at amino acid position 477 (S477N); (5) replacing glutamic acid with lysine at amino acid position 484 (E484K); (6) replacing asparagine with tyrosine at amino acid position 501 (N501Y); or (7) any combinations of (1)-(6), either alone or combined with any other substitutions and/or deletions in amino acids 319-542 of SEQ ID NO:15 other than those recited in (1)-(6); or

c) from a SARS-CoV-2 virus comprising any combination of a) and b).

3. The method of claims 1 or 2, wherein the biological sample is whole blood, serum, plasma, saliva, a nasal mucus specimen, an anal swab specimen, an oropharyngeal specimen, or a nasopharyngeal specimen.

4. The method of any of claims 1-3, wherein the at least one type of anti-SARS-CoV-2 antibody is an IgG antibody, an IgM antibody, or IgG antibody and an IgM antibody.

5. The method of any of claims 1-4, wherein the at least one type of first specific binding partner comprises at least one isolated polypeptide from a C-terminal domain of a nucleocapsid protein from a β -coronavirus, wherein the method is carried out so that said specific binding partner specifically binds to (a) an anti- β -coronavirus IgG antibody; (b) an anti- β -coronavirus IgM antibody; or (b) both an anti- β -coronavirus IgG and an anti- β -coronavirus IgM antibody.

6. The method of any of claims 1-4, wherein the at least one type of first specific binding partner comprises at least one isolated polypeptide from a receptor binding domain (RBD) of a spike protein from a β -coronavirus, wherein the method is carried out so that said

specific binding partner specifically binds to (a) an anti- β -coronavirus IgG antibody; (b) an anti- β -coronavirus IgM antibody; or (b) both an anti- β -coronavirus IgG antibody and anti- β -coronavirus IgM antibody.

7. The method of any of claims 1-6, wherein the at least one type of second specific binding partner is an anti-species IgG (e.g., anti-human-IgG IgG) antibody, an anti-species IgM (e.g., anti-human-IgM IgG) antibody, or an anti-species IgG (e.g., anti-human-IgG IgG) and an anti-species IgM (e.g., anti-human-IgM IgG) antibody.

8. The method of any of claims 1-7, wherein the at least one type of first specific binding partner is a C-terminal domain nucleocapsid protein or variant thereof that (1) has an amino acid sequence of SEQ ID NO:1; (2) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQNQ (SEQ ID NO:21), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2; (3) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQSNQ (SEQ ID NO:22), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2; or (4) has an amino acid sequence of amino acids 210 to 419 of SEQ ID NO:2.

9. The method of any of claims 1-4 or 6, wherein the at least one type of first specific binding partner is a receptor binding domain (RBD) of a spike protein or variant thereof that has an amino acid sequence of amino acids 319 to 542 of SEQ ID NO:15 or SEQ ID NO:17.

10. The method of claim 8 or claim 9, wherein the method is carried out so that the at least one type of first specific binding partner binds to (a) an anti-SARS-CoV-2 IgG antibody; (b) an anti-SARS CoV-2 IgM antibody; or (c) both an anti-SARS-CoV-2 IgG antibody and anti-SARS-CoV-2 IgM antibody.

11. The method of any of claims 1-10, wherein the method comprises detecting:
(a) at least one anti-SARS-CoV-2 IgG antibody in at least one biological sample obtained from a subject wherein the at least one type of first specific binding partner is a C-

terminal domain nucleocapsid protein or variant thereof that (1) has an amino acid sequence of SEQ ID NO:1; (2) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQNQ (SEQ ID NO:21), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2; (3) is a fusion protein comprising an initiator amino acid methionine and the sequences GPQSNQ (SEQ ID NO:22), RSAPRITFG (SEQ ID NO:7), GPTDST (SEQ ID NO:23), and amino acids 211 to 419 of SEQ ID NO:2 and specifically binds to at least one anti-SARS-CoV-2 IgG antibody; or (4) has an amino acid sequence of amino acids 210 to 419 of SEQ ID NO:2, and/or

(b) at least one anti-SARS-CoV-2 IgM antibody in at least one biological sample obtained in a subject wherein the at least one first specific binding partner wherein the at least one first specific binding partner is a receptor binding domain (RBD) of a spike protein or variant thereof that has an amino acid sequence of amino acids 319 to 542 of SEQ ID NO:15 or SEQ ID NO:17 and specifically binds to at least one anti-SARS-CoV-2 IgM antibody; and

wherein the at least one anti-SARS-CoV-2 IgG antibody and/or at least one anti-SARS-CoV-2 IgM antibody are detected in a single biological sample obtained from the subject or in multiple biological samples obtained from the subject; and

further wherein, when the at least one anti-SARS-CoV-2 IgG antibody and at least one anti-SARS-CoV-2 IgM antibody are detected simultaneously or sequentially, in any order, in a single biological sample obtained from the subject or in multiple biological samples obtained from the subject.

12. The method of any of claims 4-11, wherein the method quantifies up to (a) about 91% or (b) about 99% of anti-SARS-CoV-2 IgG antibodies.

13. The method of any of claims 1-12, wherein the method further comprises detecting SARS-CoV-2 from at least one biological sample obtained from the subject, said at least one biological sample being a single biological sample or multiple biological samples.

14. The method of claim 13, wherein the SARS-CoV-2 detected comprises a variant:
a) of the nucleocapsid protein having one or more substitutions, deletions or a substitution and deletion at positions 210-419 of SEQ ID NO:2 comprising: (1) replacing serine

with phenylalanine at amino acid position 235 (S235F); (2) replacing methionine with isoleucine at amino acid position 234 (M234I); (3) replacing lysine with asparagine at amino acid position 373 (K373N); (4) replacing aspartic acid with tyrosine at amino acid position 377 (D377Y); (5) replacing alanine with threonine at amino acid position 376 (A376T); or (6) any combinations of (1)-(5), either alone or combined with any other substitutions and/or deletions in amino acids 210-419 of SEQ ID NO:2 other than those recited in (1)-(5);

b) of the RBD of a spike protein having one or more substitutions, deletions or a substitution and deletion at positions 319-542 of SEQ ID NO:15 comprising (1) replacing lysine with asparagine at amino acid position 417 (K417N); (2) replacing lysine with threonine at amino acid position 417 (K417T); (3) replacing leucine with arginine at amino acid position 452 (L452R); (4) replacing serine with asparagine at amino acid position 477 (S477N); (5) replacing glutamic acid with lysine at amino acid position 484 (E484K); (6) replacing asparagine with tyrosine at amino acid position 501 (N501Y); or (7) any combinations of (1)-(6), either alone or combined with any other substitutions and/or deletions in amino acids 319-542 of SEQ ID NO:15 other than those recited in (1)-(6); or

c) from a SARS-CoV-2 virus comprising any combination of a) and b).

15. The method of any of claims 12-14, wherein the SARS-CoV-2 is detected by its viral RNA using polymerase chain reaction, or by its viral antigen.

16. The method of any of claims 12-14, wherein said multiple biological samples are obtained at the same or different times.

17. The method of any of claims 12-16, wherein the method further comprises detecting whether the subject is in:

(a) an initial period of infection without any antibodies being produced, when the at least one biological sample obtained from the subject is positive for viral RNA or viral antigen, negative for anti-SARS-CoV-2 IgM antibodies, and negative for anti-SARS-CoV-2 IgG antibodies; and/or

(b) an early acute phase of infection, and is developing an immune response to the virus and producing antibodies, when the at least one biological sample obtained from the subject is

positive for viral RNA or viral antigen, positive for an anti-SARS-CoV-2 IgM antibodies, and negative for anti-SARS-CoV-2 IgG antibodies; and/or

(c) an early acute phase of infection or had a false negative viral RNA result or viral antigen result, or a false positive anti-SARS-CoV-2 IgM antibody result, when the at least one biological sample obtained from the subject is negative for viral RNA, positive for anti-SARS-CoV-2 IgM antibodies, and negative for anti-SARS-CoV-2 IgG antibodies; and/or

(d) an acute phase of infection, and is progressing in an immune response, when the at least one biological sample obtained from the subject is positive for viral RNA or viral antigen, positive for anti- β -coronavirus IgM antibodies, and positive for anti-SARS-CoV-2 IgG antibodies; and/or

(e) a late acute phase of infection, or has developed a recurrent infection with SARS-CoV-2, when the at least one biological sample obtained from the subject is positive for viral RNA or viral antigen, negative for anti-SARS-CoV-2 IgM antibodies, and positive for anti-SARS-CoV-2 IgG antibodies;

(f) a late acute phase of infection or recovery phase, or had a false negative viral RNA result, when the at least one biological sample obtained from the subject is negative for viral RNA or viral antigen, positive for anti- β -coronavirus IgM antibodies, and positive for anti-SARS-CoV-2 IgG antibodies;

(g) recovery phase when the at least one biological sample obtained from the subject is negative for viral RNA or viral antigen, negative for anti-SARS-CoV-2 IgM antibodies and positive for anti-SARS-CoV-2 IgG antibodies; and/or

(h) recovery phase when the at least one biological sample obtained from the subject is negative for viral RNA or viral antigen and negative for anti-SARS-CoV-2 IgM antibodies and anti-SARS-CoV-2 IgG antibodies.

18. The method any of claims 1-17, wherein the method further comprises a pre-treatment step done at the same time as, or prior to, contacting the at least one type of first specific binding partner, the at least one type of second specific binding partner, or the at least one type of first specific binding partner and the at least one type of second specific binding partner, with the biological sample, and wherein the pretreatment step optionally comprises treatment with anti-human IgG, anti-human IgM, or anti-human IgG and anti-human IgM.

19. The method of any of claims 1-18, wherein the at least one type of first specific binding partner is immobilized on a solid support.

20. The method of any of claims 1-19, wherein the method is performed in from about 5 to about 20 minutes, less than about 20 minutes, and optionally is performed in less than about 5 minutes, less than about 10 minutes or less than about 15 minutes.

21. The method of any of claims 1-20, wherein the method further comprises use with at least one calibrator reagent, at least one control reagent, or at least one calibrator reagent and at least one control reagent.

22. The method of any of claims 1-21, wherein the method further employs use of at least one calibrator reagent or a control reagent comprising a sequence of monoclonal antibody CR3018 or CR3022.

23. The method of any of claims 1-22, wherein the method is selected from the group consisting of an immunoassay, or a clinical chemistry assay.

24. The method of any of claims 1-23, wherein the method is performed using single molecule detection, lateral flow assay, or a point-of-care assay.

25. The method of any of claims 1-24, wherein the method further comprises identifying a subject having one or more anti-SARS-CoV-2 IgG and/or anti-SARS-CoV-2 IgM antibodies as a candidate subject to provide a biological sample for use in convalescent therapy against SARS-CoV-2.

26. The method of claim 25, wherein the subject is identified as a candidate to provide a biological sample for use in convalescent therapy if the level of one or more SARS-CoV-2 IgG and/or SARS-CoV-2 IgM antibodies is from at least about 100 BAU/mL to about

490 BAU/mL; at least about 110 BAU/mL to about 490 BAU/mL; at least about 200 BAU/mL to about 490 BAU/mL; at least from about 300 BAU/mL to about 490 BAU/mL; at least about 400 BAU/mL to about 490 BAU/mL; at least about 100 BAU/mL; at least about 110 BAU/mL; at least about 120 BAU/mL; at least about 130 BAU/mL; at least about 140 BAU/mL; at least about 150 BAU/mL; at least about 160 BAU/mL; at least about 170 BAU/mL; at least about 180 BAU/mL; at least about 190 BAU/mL; at least about 200 BAU/mL; at least about 210 BAU/mL; at least about 220 BAU/mL; at least about 230 BAU/mL; at least about 240 BAU/mL; at least about 250 BAU/mL; at least about 260 BAU/mL; at least about 270 BAU/mL; at least about 280 BAU/mL; at least about 290 BAU/mL; at least about 300 BAU/mL; at least about 300 BAU/mL; at least about 310 BAU/mL; at least about 320 BAU/mL; at least about 330 BAU/mL; at least about 340 BAU/mL; at least about 350 BAU/mL; at least about 360 BAU/mL; at least about 370 BAU/mL; at least about 380 BAU/mL; at least about 390 BAU/mL; at least about 400 BAU/mL; at least about 400 BAU/mL; at least about 410 BAU/mL; at least about 420 BAU/mL; at least about 430 BAU/mL; at least about 440 BAU/mL; at least about 450 BAU/mL; at least about 460 BAU/mL; at least about 470 BAU/mL; at least about 480 BAU/mL; or at least about 490 BAU/mL.

27. The method of claim 26, wherein the subject is identified as a candidate to provide a biological sample for use in convalescent therapy if the level of one or more SARS-CoV-2 IgG and/or anti- β -coronavirus IgM antibodies is from at least about 500 BAU/mL to about 650 BAU/mL; at least about 550 BAU/mL to about 650 BAU/mL; at least about 500 BAU/mL; from at least about 510 BAU/mL; at least about 520 BAU/mL; at least about 530 BAU/mL; at least about 540 BAU/mL; at least about 550 BAU/mL to about 650 BAU/mL; at least about 550 BAU/mL; at least about 560 BAU/mL; at least about 570 BAU/mL; at least about 580 BAU/mL; at least about 590 BAU/mL; at least about 600 BAU/mL; at least about 610 BAU/mL; at least about 620 BAU/mL; at least about 630 BAU/mL; at least about 639 BAU/mL; at least about 640 BAU/mL; or at least about 650 BAU/mL.

28. The method of any of claims 1-27, wherein the method:
(a) further comprises detecting at least one type of anti-SARS-CoV-2 IgG neutralizing antibody;

(b) demonstrates high qualitative agreement with a plaque reduction neutralization assay;

(c) detects increasing amounts of anti-SARS-CoV-2 IgG antibodies as detected by the method that are associated with increasing amounts of anti-SARS-CoV-2 IgG neutralizing antibodies;

(d) has a probability profile that corresponds to high titer levels in the plaque reduction neutralization assay such that there is a high probability of the levels of anti-SARS-CoV-2 IgG antibodies determined by the method being at or above the levels of anti-SARS-CoV-2 IgG neutralizing antibodies determined in the plaque reduction neutralization assay; or

(e) demonstrates high qualitative agreement with an ACE2 binding inhibition assay.

29. The method of claim 28, wherein a level of anti-SARS-CoV-2 IgG antibodies of at least about 4160 AU/mL (about 590 BAU/mL) when used as a cut-off or threshold correspond to about a 0.95 probability of obtaining a plaque reduction neutralization assay ID₅₀ at 1:250 dilution.

30. The method of any of claims 1-29, wherein the method comprises obtaining the at least one biological sample from the subject at a critical time of from about fourteen (14) days to about thirty-five (35) days after onset of symptoms of SARS-CoV-2.

31. The method of claim 30, wherein the method further comprises determining that the subject: (i) more likely than not will develop or experience at least one of a cytokine storm, acute respiratory distress syndrome (ARDS), or a combination of a cytokine storm and ARDS if anti-SARS-CoV-2 IgM antibody, anti-SARS-CoV-2 IgG antibody, or anti-SARS-CoV-2 IgM antibody and anti-SARS-CoV-2 IgG antibody are not detected in the biological sample within the critical time; or (ii) more likely than not will not develop or experience at least one of a cytokine storm, ARDS, or a combination of a cytokine storm and ARDS if anti-SARS-CoV-2 IgM antibody, anti-SARS-CoV-2 IgG antibody, or anti-SARS-CoV-2 IgM antibody and anti-SARS-CoV-2 IgG antibody are not detected in the biological sample within the critical time.

32. The method of any of claims 1-29 or 30-31, wherein the subject: (1) is naive and was not previously vaccinated against SARS-CoV-2; (2) is naive and was previously vaccinated against SARS-CoV-2; (3) is currently infected with SARS-CoV-2 and was not previously vaccinated against SARS-CoV-2; (4) is currently infected with SARS-CoV-2 and was previously vaccinated against SARS-CoV-2; (5) was previously infected with SARS-CoV-2, recovered, and was not previously vaccinated against SARS-CoV-2; or (6) was previously infected with SARS-CoV-2, recovered, and then was vaccinated against SARS-CoV-2.

33. The method of claim 32, wherein the method is performed to: (a) determine whether the subject can be administered a current vaccine for SARS-CoV-2; or (b) monitor the subject following the current vaccine or previous vaccination, based on detecting the presence of at least one type of anti-SARS-CoV-2 antibody in the sample.

34. The method of claim 33, wherein the method comprises determining that the current vaccine for SARS-CoV-2:

(a) can be administered to the subject when no anti-SARS-CoV-2 antibodies, no anti-SARS-CoV-2 IgG neutralizing antibodies, or an amount of anti-SARS-CoV-2 IgG antibody or anti-SARS-CoV-2 IgG neutralizing antibody that is insufficient to impart immunity, are detected in the biological sample; and/or

(b) should not be administered to the subject if an amount of anti-SARS-CoV-2 antibody or anti-SARS-CoV-2 IgG neutralizing antibody that is sufficient to impart immunity is detected in the biological sample.

35. The method of claim 34, wherein the amount of anti-SARS-CoV-2 antibody or anti-SARS-CoV-2 IgG neutralizing antibody sufficient to impart immunity is from at least about 100 BAU/mL to about 490 BAU/mL; at least about 110 BAU/mL to about 490 BAU/mL; at least about 200 BAU/mL to about 490 BAU/mL; at least from about 300 BAU/mL to about 490 BAU/mL; at least about 400 BAU/mL to about 490 BAU/mL; at least about 100 BAU/mL; at least about 110 BAU/mL; at least about 120 BAU/mL; at least about 130 BAU/mL; at least about 140 BAU/mL; at least about 150 BAU/mL; at least about 160 BAU/mL; at least about 170

BAU/mL; at least about 180 BAU/mL; at least about 190 BAU/mL; at least about 200 BAU/mL; at least about 210 BAU/mL; at least about 220 BAU/mL; at least about 230 BAU/mL; at least about 240 BAU/mL; at least about 250 BAU/mL; at least about 260 BAU/mL; at least about 270 BAU/mL; at least about 280 BAU/mL; at least about 290 BAU/mL; at least about 300 BAU/mL; at least about 300 BAU/mL; at least about 310 BAU/mL; at least about 320 BAU/mL; at least about 330 BAU/mL; at least about 340 BAU/mL; at least about 350 BAU/mL; at least about 360 BAU/mL; at least about 370 BAU/mL; at least about 380 BAU/mL; at least about 390 BAU/mL; at least about 400 BAU/mL; at least about 400 BAU/mL; at least about 410 BAU/mL; at least about 420 BAU/mL; at least about 430 BAU/mL; at least about 440 BAU/mL; at least about 450 BAU/mL; at least about 460 BAU/mL; at least about 470 BAU/mL; at least about 480 BAU/mL; or at least about 490 BAU/mL.

36. The method of claim 33, wherein the biological sample is obtained within about 7 to about 21 days after the subject has received either the current vaccine or previous vaccination.

37. The method of claim 36, wherein the method comprises determining that at least one further vaccine for SARS-CoV-2:

(a) can be administered to the subject after the current vaccine if no anti-SARS-CoV-2 antibodies, no anti-SARS-CoV-2 IgG neutralizing antibodies, and/or an amount of anti-SARS-CoV-2 IgG antibody or anti-SARS-CoV-2 IgG neutralizing antibody that is insufficient to impart immunity, is detected in the biological sample obtained from the subject; or

(b) should not be administered to the subject after the current vaccine if an amount of anti-SARS-CoV-2 antibody or anti-SARS-CoV-2 IgG neutralizing antibody that is sufficient to impart immunity is detected in the biological sample obtained from the subject.

38. The method of claim 37, wherein the amount of anti-SARS-CoV-2 antibody or anti-SARS-CoV-2 IgG neutralizing antibody sufficient to impart immunity is from at least about 100 BAU/mL to about 490 BAU/mL; at least about 110 BAU/mL to about 490 BAU/mL; at least about 200 BAU/mL to about 490 BAU/mL; at least from about 300 BAU mL to about 490

BAU/mL; at least about 400 BAU/mL to about 490 BAU/mL; at least about 100 BAU/mL; at least about 110 BAU/mL; at least about 120 BAU/mL; at least about 130 BAU/mL; at least about 140 BAU/mL; at least about 150 BAU/mL; at least about 160 BAU/mL; at least about 170 BAU/mL; at least about 180 BAU/mL; at least about 190 BAU/mL; at least about 200 BAU/mL; at least about 210 BAU/mL; at least about 220 BAU/mL; at least about 230 BAU/mL; at least about 240 BAU/mL; at least about 250 BAU/mL; at least about 260 BAU/mL; at least about 270 BAU/mL; at least about 280 BAU/mL; at least about 290 BAU/mL; at least about 300 BAU/mL; at least about 300 BAU/mL; at least about 310 BAU/mL; at least about 320 BAU/mL; at least about 330 BAU/mL; at least about 340 BAU/mL; at least about 350 BAU/mL; at least about 360 BAU/mL; at least about 370 BAU/mL; at least about 380 BAU/mL; at least about 390 BAU/mL; at least about 400 BAU/mL; at least about 400 BAU/mL; at least about 410 BAU/mL; at least about 420 BAU/mL; at least about 430 BAU/mL; at least about 440 BAU/mL; at least about 450 BAU/mL; at least about 460 BAU/mL; at least about 470 BAU/mL; at least about 480 BAU/mL; or at least about 490 BAU/mL.

39. The method of any of claims 1-35 or 36-38, wherein the volume of the biological sample used in the method is from about 0.30 μ L to about 0.40 μ L.

40. The method of any of claims 1-38 or 39, wherein the method comprises (a) diluting the biological sample prior to or during the method and further wherein the diluting comprises mixing about 10 μ L of the biological sample with about 290 μ L of at least one buffer to form a biological sampling mixture; and (b) removing about 10 μ L from the biological sampling mixture for use in the method.

41. A kit for performing the method of claim 1, wherein the kit comprises: a. at least one type of specific binding partner comprising at least one β -coronavirus isolated polypeptide or variant thereof selected from a C-terminal domain nucleocapsid protein, a receptor binding domain (RBD) of a spike protein, or a C-terminal domain nucleocapsid protein and a receptor

binding domain (RBD) of a spike protein from a β -coronavirus; and b. at least one type of second specific binding partner comprising at least one detectable label.

42. A system for detecting a presence or determining an amount of anti-SARS-CoV-2 antibody in a biological sample obtained from a subject comprising: at least one type of first specific binding partner comprising at least one β -coronavirus isolated polypeptide or variant thereof selected from a C-terminal domain nucleocapsid protein, a receptor binding domain (RBD) of a spike protein, or a C-terminal domain nucleocapsid protein and a receptor binding domain (RBD) of a spike protein from a β -coronavirus that specifically binds to at least one type of anti-SARS-CoV-2 antibody and at least one type of second specific binding partner comprising at least one detectable label; and at least one device for detecting the at least one label from the complex, wherein the amount of signal from the label indicates the presence or amount of anti- SARS-CoV-2antibody in the sample.