CLAIMS

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

~~1. Use of a MASP-2 inhibitory agent in the manufacture of a medicament for treating, inhibiting, alleviating or preventing acute respiratory distress syndrome, pneumonia or some other pulmonary or other acute manifestation of COVID-19, such as thrombosis, in a mammalian subject infected with SARS-CoV-2, the use comprising~~

~~(i) determining the level of MASP-2/C1-INH complex in a biological sample obtained from the subject, wherein an increased level of MASP-2/C1-INH complex as compared to a healthy control sample is indicative of an increased risk of developing one or more acute manifestations of COVID-19; and~~

~~(ii) wherein an amount of the MASP-2 inhibitory agent effective to inhibit MASP-2-dependent complement activation is to be administered to the subject having an increased level of MASP-2/C1-INH complex, optionally, wherein the amount of said MASP-2 inhibitory agent is sufficient to reduce the level of MASP-2/C1-INH to a control level or reference standard.~~

~~2. The use of claim 1, wherein the MASP-2 inhibitory agent is a MASP-2 monoclonal antibody, or fragment thereof that specifically binds to a portion of SEQ ID NO:6.~~

~~3. The use of claim 1, wherein the MASP-2 inhibitory agent is a small molecule MASP-2 inhibitory compound.~~

~~4. The use of claim 3, wherein the MASP-2 inhibitory compound is a synthetic or semi-synthetic small molecule.~~

~~5. The use of claim 1, wherein the MASP-2 inhibitory agent is an expression inhibitor of MASP-2.~~

~~6. The use of claim 2, wherein the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising CDR-H1, CDR-H2 and CDR-H3 of the amino acid sequence set forth as SEQ ID NO:67 and a light chain variable region comprising CDR-L1, CDR-L2 and CDR-L3 of the amino acid sequence set forth as SEQ ID NO:69.~~

~~7. Use of a MASP-2 inhibitory agent in the manufacture of a medicament for treating, ameliorating, preventing or reducing the risk of developing one or more COVID-19-related long-term sequelae in a mammalian subject that has been infected with SARS-CoV-2, the use comprising~~

~~(i) determining the level of MASP-2/C1-INH complex in a biological sample obtained from the subject, wherein an increased level of MASP-2/C1-INH complex as compared to a healthy control sample is indicative of an increased risk of developing one or more COVID-19-related long-term sequelae; and~~

~~(ii) wherein an amount of a MASP-2 inhibitory agent effective to inhibit MASP-2-dependent complement activation is to be administered to the subject having an increased level of MASP-2/C1-INH complex.~~

~~8. The use of claim 7, wherein the MASP-2 inhibitory agent is a MASP-2 monoclonal antibody, or fragment thereof that specifically binds to a portion of SEQ ID NO:6.~~

~~9. The use of claim 7, wherein the MASP-2 inhibitory agent is a small molecule MASP-2 inhibitory compound.~~

~~10. The use of claim 7, wherein the MASP-2 inhibitory compound is a synthetic or semi-synthetic small molecule.~~

~~11. The use of claim 7, wherein the MASP-2 inhibitory agent is an expression inhibitor of MASP-2.~~

~~12. The use of claim 8, wherein the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising CDR-H1, CDR-H2 and CDR-H3 of the amino acid sequence set forth as SEQ ID NO:67 and a light chain~~

~~variable region comprising CDR-L1, CDR-L2 and CDR-L3 of the amino acid sequence set forth as SEQ ID NO:69.~~

~~13. The use of claim 7, wherein the one or more COVID-19 related long term sequelae is selected from the group consisting of a cardiovascular complication (including myocardial injury, cardiomyopathy, myocarditis, intravascular coagulation, stroke, venous and arterial complications and pulmonary thrombosis); a neurological complication (including cognitive difficulties, confusion, memory loss, also referred to as "brain fog," headache, stroke, dizziness, syncope, seizure, anorexia, insomnia, anosmia, ageusia, myoclonus, neuropathic pain, myalgias, development of neurological disease such as Alzheimer's disease, Guillian Barre Syndrome, Miller Fisher Syndrome, Parkinson's disease) kidney injury (such as acute kidney injury (AKI); a pulmonary complication (including lung fibrosis, dyspnea, pulmonary embolism),an inflammatory condition such as Kawasaki disease, Kawasaki-like disease, multisystem inflammatory syndrome in children, multi-system organ failure, extreme fatigue, muscle weakness, low grade fever, inability to concentrate, memory lapses, changes in mood, sleep difficulties, needle pains in arms and legs, diarrhea and vomiting, loss of taste and smell, sore throat and difficulties in swallowing, new onset of diabetes and hypertension, skin rash, shortness of breath, chest pains and palpitations.~~

~~14. A monoclonal antibody, or antigen binding fragment thereof, that specifically binds to human MASP-2 in complex with C1-INH, wherein the antibody comprises a binding domain comprising (a) HC-CDR1, HC-CDR2 and HC-CDR3 in a heavy chain variable region set forth as SEQ ID NO:87 and comprising LC-CDR1, LC-CDR2 and LC-CDR3 in a light chain variable region set forth as SEQ ID NO:88, or (b) HC-CDR1, HC-CDR2 and HC-CDR3 in a heavy chain variable region set forth as SEQ ID NO:97 and comprising LC-CDR1, LC-CDR2 and LC-CDR3 in a light chain variable region set forth as SEQ ID NO:98,~~

~~wherein the CDRs are numbered according to the Kabat numbering system.~~

15. A method of measuring the amount of MASP-2/C1-INH in a biological sample comprising:

(a) providing a test biological sample from a human subject;

(b) performing an immunoassay comprising capturing and detecting MASP-2/C1-INH complex in the test sample, wherein MASP-2/C1-INH is captured with a monoclonal antibody that specifically binds to human MASP-2; and the MASP-2/C1-INH complex is detected directly or indirectly with an antibody that specifically binds to C1-INH; and

(c) comparing the level of MASP-2/C1-INH complex detected in accordance with (b) with a predetermined level or control sample wherein the level of MASP-2/C1-INH complex detected in the test sample is indicative of the extent of Lectin Pathway Complement activation.

162. The method of claim 15, wherein the biological sample is a fluid sample selected from the group consisting of whole blood, serum, plasma, urine and cerebrospinal fluid.

173. The method of claim 15, wherein the antibody that specifically binds to MASP-2 comprises a binding domain comprising (a) HC-CDR1, HC-CDR2 and HC-CDR3 in a heavy chain variable region set forth as SEQ ID NO:87 and comprising LC-CDR1, LC-CDR2 and LC-CDR3 in a light chain variable region set forth as SEQ ID NO:88, or (b) HC-CDR1, HC-CDR2 and HC-CDR3 in a heavy chain variable region set forth as SEQ ID NO:97 and comprising LC-CDR1, LC-CDR2 and LC-CDR3 in a light chain variable region set forth as SEQ ID NO:98, wherein the CDRs are numbered according to the Kabat numbering system.

184. The method of claim 15, wherein the human subject is currently infected with SARS-CoV-2, or has previously been infected with SARS-CoV-2, or wherein the subject is suffering or at risk for developing another lectin-pathway disease or condition (e.g., HSCT-TMA, IgAN, GvHD or other lectin pathway disease or disorder).

19. A method of determining the risk of a subject that is or has been infected with SARS-CoV-2 for developing COVID-19 related ARDS or other poor outcome, or long term sequelae associated with COVID-19 comprising:

(a) measuring a level of MASP-2/C1-INH complex in a biological sample obtained from the subject;

(b) comparing the measured level with a predetermined level of MASP-2/C1-INH complex or a reference standard to assess the risk of developing COVID-19 related ARDS and/or long-term sequelae associated with COVID-19; and

(c) determining the risk of the subject for developing COVID-19 related ARDS or other poor outcome and/or long term sequelae associated with COVID-19 and reporting the results to the patient, physician or database;

wherein a treatment is to be optionally administered to the subject determined to be likely to develop acute disease and/or long-term sequelae associated with COVID-19 infection.

20. The method of claim 19, wherein the level of MASP-2/C1-INH complex is measured in an immunoassay.

21. A method for monitoring the efficacy of treatment with a MASP-2 inhibitory antibody, or antigen binding fragment thereof, in a mammalian subject in need thereof, the method comprising:

(a) assessing a first level of MASP-2/C1-INH complex in a biological sample obtained from the subject after a dose of a MASP-2 inhibitory antibody, or antigen-binding fragment thereof, has been administered to the subject at a first point in time;

(b) assessing a second level of MASP-2/C1-INH complex in a biological sample obtained from the subject after the subject has been treated with the MASP-2 inhibitory antibody, or antigen-binding fragment thereof, at a second point in time; and

(c) comparing the level of MASP-2/C1-INH complex assessed in step (a) with the level of MASP-2/C1-INH complex assessed in step (b) to determine the efficacy of the MASP-2 inhibitory antibody or antigen-binding fragment thereof in the mammalian subject.

~~22. The method of claim 21, wherein the method further comprises adjusting the dose of the MASP-2 inhibitory antibody or antigen-binding fragment thereof.~~