

All three pathways (i.e., the classical, lectin and alternative) have been thought to converge at C5, which is cleaved to form products with multiple proinflammatory effects. The converged pathway has been referred to as the terminal complement pathway. C5a is the most potent anaphylatoxin, inducing alterations in smooth muscle and vascular tone, as well as vascular permeability. It is also a powerful chemotaxin and activator of both neutrophils and monocytes. C5a-mediated cellular activation can significantly amplify inflammatory responses by inducing the release of multiple additional inflammatory mediators, including cytokines, hydrolytic enzymes, arachidonic acid metabolites, and reactive oxygen species. C5 cleavage leads to the formation of C5b-9, also known as the membrane attack complex (MAC). There is now strong evidence that sublytic MAC deposition may play an important role in inflammation in addition to its role as a lytic pore-forming complex.

In addition to its essential role in immune defense, the complement system contributes to tissue damage in many clinical conditions. Thus, there is a pressing need to develop therapeutically effective complement inhibitors to prevent these adverse effects.

SUMMARY

This summary is provided to introduce a selection of concepts in a simplified form that are further described below in the Detailed Description. This summary is not intended to identify key features of the claimed subject matter, nor is it intended to be used as an aid in determining the scope of the claimed subject matter.

In one aspectexample, the present inventiondisclosure provides a method of treating a human subject suffering from idiopathic pneumonia syndrome (IPS) following hematopoietic stem cell transplant (HSCT-IPS) comprising administering to the subject a composition comprising an amount of a MASP-2 inhibitory antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation and thereby improve at least one symptom of HSCT-IPS. In one embodimentexample, the method comprises administering the composition to a subject who has previously undergone an allogeneic hematopoietic stem cell transplant. In one embodimentexample, the method comprises administering the composition to a subject who has previously undergone an autologous hematopoietic stem cell transplant. In one embodimentexample, the method further comprises identifying a human subject suffering from idiopathic pneumonia syndrome (IPS) prior to the step of administering to the subject a composition comprising an amount of a MASP-

2 inhibitory antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation. In one [embodimentexample](#), the subject suffering from idiopathic pneumonia syndrome (IPS) is determined to not have DAH. In one [embodimentexample](#), the MASP-2 inhibitory antibody is a monoclonal antibody, or fragment thereof that specifically binds to human MASP-2. In one [embodimentexample](#), the MASP-2 inhibitory antibody or fragment thereof is selected from the group consisting of a recombinant antibody, an antibody having reduced effector function, a chimeric antibody, a humanized antibody, and a human antibody. In one [embodimentexample](#), the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway. In one [embodimentexample](#), the MASP-2 inhibitory antibody inhibits C3b deposition in 90% human serum with an IC₅₀ of 30 nM or less. In one [embodimentexample](#), the MASP-2 inhibitory antibody is delivered to the subject systemically. In one [embodimentexample](#), 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:70. In one [embodimentexample](#), the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence set forth as SEQ ID NO:67 and a light chain variable region comprising the amino acid sequence set forth as SEQ ID NO:70. In some [embodimentexamples](#), the method comprises administering to a subject suffering from HSCT-IPS a composition comprising a MASP-2 inhibitory antibody, or antigen binding fragment thereof comprising a heavy-chain variable region comprising the amino acid sequence set forth as SEQ ID NO:67 and a light-chain variable region comprising the amino acid sequence set forth as SEQ ID NO:70 in a dosage from 1 mg/kg to 10 mg/kg (i.e., 1 mg/kg, 2 mg/kg, 3 mg/kg, 4 mg/kg, 5 mg/kg, 6 mg/kg, 7 mg/kg, 8 mg/kg, 9 mg/kg or 10 mg/kg) at least once weekly (such as at least twice weekly or at least three times weekly) for a period of at least 2 weeks, or at least 3 weeks, or for at least 4 weeks, or for at least 5 weeks, or for at least 6 weeks, or for at least 7 weeks, or for at least 8 weeks, or at least 9 weeks, or at least 10 weeks, or at least 11 weeks, or at least 12 weeks. In one [embodimentexample](#), the dosage of MASP-2 inhibitory antibody is about 4 mg/kg (i.e., from 3.6 mg/kg to 4.4 mg/kg). In one [embodimentexample](#), dosage of the MASP-2 inhibitory antibody is a fixed dose from about 300 mg to about 450 mg (i.e., from about 300 mg to about 400 mg, or from about 350 mg to about 400

mg), such as about 300 mg, about 305 mg, about 310 mg, about 315 mg, about 320 mg, about 325 mg, about 330 mg, about 335 mg, about 340 mg, about 345 mg, about 350 mg, about 355 mg, about 360 mg, about 365 mg, about 370 mg, about 375 mg, about 380 mg, about 385 mg, about 390 mg, about 395 mg, about 400 mg, about 405 mg, about 410 mg, about 415 mg, about 420 mg, about 425 mg, about 430 mg, about 435 mg, about 440 mg, about 445 mg or about 450 mg. In one embodimentexample, the dosage of the MASP-2 inhibitory antibody is a fixed dose of about 370 mg ($\pm 10\%$). In one embodimentexample, method comprises administering a fixed dosage of MASP-2 inhibitory antibody at about 370 mg ($\pm 10\%$) suffering from HSCT-IPS twice weekly intravenously for a treatment period of at least 8 weeks.

In one aspect, the present disclosure refers to use of a composition comprising an amount of a MASP-2 inhibitory monoclonal antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation, in the manufacture of a medicament for treating a human subject suffering from idiopathic pneumonia syndrome following hematopoietic stem cell transplant (HSCT-IPS), wherein the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway.

In another aspectexample, the present inventiondisclosure provides a method of treating a human subject suffering from capillary leak syndrome (CLS) following hematopoietic stem cell transplant (HSCT-CLS) comprising administering to the subject a composition comprising an amount of a MASP-2 inhibitory antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation and thereby improve at least one symptom of HSCT-CLS. In one embodimentexample, the method comprises administering the composition to a subject who has previously undergone an allogeneic hematopoietic stem cell transplant. In one embodimentexample, the method comprises administering the composition to a subject who has previously undergone an autologous hematopoietic stem cell transplant. In one embodimentexample, the method further comprises identifying a human subject suffering from capillary leak syndrome (CLS) prior to the step of administering to the subject a composition comprising an amount of a MASP-2 inhibitory antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation. In one embodimentexample, the subject suffering from CLS is determined to not have VOD. In one embodimentexample, the MASP-2 inhibitory antibody is a monoclonal antibody, or fragment thereof that specifically binds to human MASP-2. In one embodimentexample, the MASP-2 inhibitory antibody or fragment thereof is selected from the group consisting of a recombinant antibody, an antibody having reduced effector function, a chimeric antibody, a humanized antibody, and a human antibody. In one embodimentexample, the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway. In one embodimentexample, the MASP-2 inhibitory antibody inhibits C3b deposition in 90% human serum with an IC_{50} of 30 nM or less. In one embodimentexample, the MASP-2 inhibitory antibody is delivered to the subject systemically. In one embodimentexample, the

5 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:70. In one
10 embodimentexample, the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence set forth as SEQ ID NO:67 and a light chain variable region comprising the amino acid sequence set forth as SEQ ID NO:70. In some embodimentexamples, the method comprises administering to a subject suffering from HSCT-CLS a composition
15 comprising a MASP-2 inhibitory antibody, or antigen binding fragment thereof comprising a heavy-chain variable region comprising the amino acid sequence set forth as SEQ ID NO:67 and a light-chain variable region comprising the amino acid sequence set forth as SEQ ID NO:70 in a dosage from 1 mg/kg to 10 mg/kg (i.e., 1 mg/kg, 2 mg/kg, 3 mg/kg, 4 mg/kg, 5 mg/kg, 6 mg/kg, 7 mg/kg, 8 mg/kg, 9 mg/kg or 10 mg/kg) at least
20 once weekly (such as at least twice weekly or at least three times weekly) for a period of at least 2 weeks, or at least 3 weeks, or for at least 4 weeks, or for at least 5 weeks, or for at least 6 weeks, or for at least 7 weeks, or for at least 8 weeks, or at least 9 weeks, or at least 10 weeks, or at least 11 weeks, or at least 12 weeks. In one embodimentexample, the dosage of MASP-2 inhibitory antibody is about 4 mg/kg (i.e., from 3.6 mg/kg to 4.4 mg/kg). In one embodimentexample, dosage of the MASP-2 inhibitory antibody is a fixed dose from about 300 mg to about 450 mg (i.e., from about 300 mg to about 400 mg, or from about 350 mg to about 400 mg), such as about 300 mg, about 305 mg, about 310 mg, about 315 mg, about 320 mg, about 325 mg, about 330 mg, about 335 mg, about 340 mg, about 345 mg, about 350 mg, about 355 mg, about 360 mg, about 365 mg, about 370 mg, about 375 mg, about 380 mg, about 385 mg, about 390 mg, about 395 mg, about 400 mg, about 405 mg, about 410 mg, about 415 mg, about 420 mg, about 425 mg, about 430 mg, about 435 mg, about 440 mg, about 445 mg or about 450 mg. In one
25 embodimentexample, the dosage of the MASP-2 inhibitory antibody is a fixed dose of about 370 mg ($\pm 10\%$). In one embodimentexample, method comprises administering a fixed dosage of MASP-2 inhibitory antibody at about 370 mg ($\pm 10\%$) to a subject suffering from HSCT-CLS twice weekly intravenously for a treatment period of at least 8 weeks.

35 In one aspect, the present disclosure refers to use of a composition comprising an amount of a MASP-2 inhibitory monoclonal antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation, in the manufacture of a medicament for treating a human subject suffering from capillary leak syndrome following hematopoietic stem cell transplant (HSCT-CLS), wherein the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway.

40 In another aspectexample, the present inventiondisclosure provides a method of treating a human subject suffering from fluid overload (FO) following hematopoietic stem cell transplant

(HSCT-FO) comprising administering to the subject a composition comprising an amount of a MASP-2 inhibitory antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation and thereby improve at least one symptom of HSCT-FO. In one [embodimentexample](#), the method comprises administering the composition to a subject who has previously undergone an allogeneic hematopoietic stem cell transplant. In one [embodimentexample](#), the method comprises administering the composition to a subject who has previously undergone an autologous hematopoietic stem cell transplant. In one [embodimentexample](#), the method further comprises identifying a human subject suffering from fluid overload (FO) prior to the step of administering to the subject a composition comprising an amount of a MASP-2 inhibitory antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation. In one [embodimentexample](#), the MASP-2 inhibitory antibody is a monoclonal antibody, or fragment thereof that specifically binds to human MASP-2. In one [embodimentexample](#), the MASP-2 inhibitory antibody or fragment thereof is selected from the group consisting of a recombinant antibody, an antibody having reduced effector function, a chimeric antibody, a humanized antibody, and a human antibody. In one [embodimentexample](#), the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway. In one [embodimentexample](#), the MASP-2 inhibitory antibody inhibits C3b deposition in 90% human serum with an IC₅₀ of 30 nM or less. In one [embodimentexample](#), the MASP-2 inhibitory antibody is delivered to the subject systemically. In one [embodimentexample](#), 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:70. In one [embodimentexample](#), the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence set forth as SEQ ID NO:67 and a light chain variable region comprising the amino acid sequence set forth as SEQ ID NO:70. In some [embodimentexamples](#), the method comprises administering to a subject suffering from HSCT-FO a composition comprising a MASP-2 inhibitory antibody, or antigen binding fragment thereof comprising a heavy-chain variable region comprising the amino acid sequence set forth as SEQ ID NO:67 and a light-chain variable region comprising the amino acid sequence set forth as SEQ ID NO:70 in a dosage from 1 mg/kg to 10 mg/kg (i.e., 1 mg/kg, 2 mg/kg, 3 mg/kg, 4 mg/kg, 5 mg/kg, 6 mg/kg, 7

mg/kg, 8 mg/kg, 9 mg/kg or 10 mg/kg) at least once weekly (such as at least twice weekly or at least three times weekly) for a period of at least 2 weeks, or for at least 3 weeks, or for at least 4 weeks, or for at least 5 weeks, or for at least 6 weeks, or for at least 7 weeks, or for at least 8 weeks, or at least 9 weeks, or at least 10 weeks, or at least 11 weeks, or at least 12 weeks. In one embodimentexample, the dosage of MASP-2 inhibitory antibody is about 4 mg/kg (i.e., from 3.6 mg/kg to 4.4 mg/kg). In one embodimentexample, dosage of the MASP-2 inhibitory antibody is a fixed dose from about 300 mg to about 450 mg (i.e., from about 300 mg to about 400 mg, or from about 350 mg to about 400 mg), such as about 300 mg, about 305 mg, about 310 mg, about 315 mg, about 320 mg, about 325 mg, about 330 mg, about 335 mg, about 340 mg, about 345 mg, about 350 mg, about 355 mg, about 360 mg, about 365 mg, about 370 mg, about 375 mg, about 380 mg, about 385 mg, about 390 mg, about 395 mg, about 400 mg, about 405 mg, about 410 mg, about 415 mg, about 420 mg, about 425 mg, about 430 mg, about 435 mg, about 440 mg, about 445 mg or about 450 mg. In one embodimentexample, the dosage of the MASP-2 inhibitory antibody is a fixed dose of about 370 mg ($\pm 10\%$). In one embodimentexample, method comprises administering a fixed dosage of MASP-2 inhibitory antibody at about 370 mg ($\pm 10\%$) to a subject suffering from HSCT-FO twice weekly intravenously for a treatment period of at least 8 weeks.

In one aspect, the present disclosure refers to use of a composition comprising an amount of a MASP-2 inhibitory monoclonal antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation, in the manufacture of a medicament for treating a human subject suffering from fluid overload following hematopoietic stem cell transplant (HSCT-FO), wherein the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway.

In another aspectexample, the present inventiondisclosure provides a method of treating a human subject suffering from engraftment syndrome (ES) following hematopoietic stem cell transplant (HSCT-ES) comprising administering to the subject a composition comprising an amount of a MASP-2 inhibitory antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation and thereby improve at least one symptom of HSCT-ES. In one embodimentexample, the method comprises administering the composition to a subject who has previously undergone an allogeneic hematopoietic stem cell transplant. In one embodimentexample, the method comprises administering the composition to a subject who has previously undergone an autologous hematopoietic stem cell transplant. In one embodimentexample, the method further comprises identifying a human subject suffering from post-transplant engraftment syndrome (HSCT-ES) prior to the step of administering to the subject a composition comprising an amount of a MASP-2 inhibitory antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation. In one embodimentexample, the MASP-2 inhibitory antibody is a monoclonal antibody, or fragment thereof that specifically binds

to human MASP-2. In one [embodimentexample](#), the MASP-2 inhibitory antibody or fragment thereof is selected from the group consisting of a recombinant antibody, an antibody having reduced effector function, a chimeric antibody, a humanized antibody, and a human antibody. In one [embodimentexample](#), the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway. In one [embodimentexample](#), the MASP-2 inhibitory antibody inhibits C3b deposition in 90% human serum with an IC₅₀ of 30 nM or less. In one [embodimentexample](#), the MASP-2 inhibitory antibody is delivered to the subject systemically. In one [embodimentexample](#), 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:70. In one [embodimentexample](#), the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence set forth as SEQ ID NO:67 and a light chain variable region comprising the amino acid sequence set forth as SEQ ID NO:70. In some [embodimentexamples](#), the method comprises administering to a subject suffering from HSCT-ES a composition comprising a MASP-2 inhibitory antibody, or antigen binding fragment thereof comprising a heavy-chain variable region comprising the amino acid sequence set forth as SEQ ID NO:67 and a light-chain variable region comprising the amino acid sequence set forth as SEQ ID NO:70 in a dosage from 1 mg/kg to 10 mg/kg (i.e., 1 mg/kg, 2 mg/kg, 3 mg/kg, 4 mg/kg, 5 mg/kg, 6 mg/kg, 7 mg/kg, 8 mg/kg, 9 mg/kg or 10 mg/kg) at least once weekly (such as at least twice weekly or at least three times weekly) for a period of at least 2 weeks, or for at least 3 weeks, or for at least 4 weeks, or for at least 5 weeks, or for at least 6 weeks, or for at least 7 weeks, or for at least 8 weeks, or at least 9 weeks, or at least 10 weeks, or at least 11 weeks, or at least 12 weeks. In one [embodimentexample](#), the dosage of MASP-2 inhibitory antibody is about 4 mg/kg (i.e., from 3.6 mg/kg to 4.4 mg/kg). In one [embodimentexample](#), dosage of the MASP-2 inhibitory antibody is a fixed dose from about 300 mg to about 450 mg (i.e., from about 300 mg to about 400 mg, or from about 350 mg to about 400 mg), such as about 300 mg, about 305 mg, about 310 mg, about 315 mg, about 320 mg, about 325 mg, about 330 mg, about 335 mg, about 340 mg, about 345 mg, about 350 mg, about 355 mg, about 360 mg, about 365 mg, about 370 mg, about 375 mg, about 380 mg, about 385 mg, about 390 mg, about 395 mg, about 400 mg, about 405 mg, about 410 mg, about 415 mg, about 420 mg, about 425 mg, about 430 mg,

about 435 mg, about 440 mg, about 445 mg or about 450 mg. in one embodimentexample, the dosage of the masp-2 inhibitory antibody is a fixed dose of about 370 mg ($\pm 10\%$). in one embodimentexample, method comprises administering a fixed dosage of masp-2 inhibitory antibody at about 370 mg ($\pm 10\%$) to a subject suffering from hsct-es twice weekly intravenously for a treatment period of at least 8 weeks.

In one aspect, the present disclosure refers to use of a composition comprising an amount of a MASP-2 inhibitory monoclonal antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation, in the manufacture of a medicament for treating a human subject suffering from engraftment syndrome following hematopoietic stem cell transplant (HSCT-ES), wherein the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway.

The methods, compositions and medicaments of the inventiondisclosure are useful for inhibiting the adverse effects of MASP-2-dependent complement activation *in vivo* in mammalian subjects, including humans suffering from or at risk for developing HSCT-IPS (i.e., post-stem cell transplant IPS) and/or a subject suffering from, or at risk for developing HSCT-CLS (i.e., post-stem cell transplant CLS), and/or a subject suffering from, or at risk for developing HSCT-FO (i.e., post-stem cell transplant FO) and or a subject suffering from, or at risk for developing HSCT-ES (i.e., post-stem cell transplant ES) as further described herein. In another aspectexample, the present inventiondisclosure provides compositions for inhibiting the adverse effects of MASP-2-dependent complement activation, comprising a therapeutically effective amount of a MASP-2 inhibitory agent, such as a MASP-2 inhibitory antibody and a pharmaceutically acceptable carrier. Methods are also provided for manufacturing a medicament for use in inhibiting the adverse effects of MASP-2-dependent complement activation in living subjects in need thereof, comprising a therapeutically effective amount of a MASP-2 inhibitory agent in a pharmaceutical carrier. Methods are also provided for manufacturing medicaments for use in inhibiting MASP-2-dependent complement activation for treatment of each of the conditions, diseases and disorders described herein below.

DESCRIPTION OF THE DRAWINGS

The foregoing aspects and many of the attendant advantages of this invention will become more readily appreciated as the same become better understood by reference to the following detailed description, when taken in conjunction with the accompanying drawings, wherein:

FIGURE 1 is a diagram illustrating the genomic structure of human MASP-2;

FIGURE 2A is a schematic diagram illustrating the domain structure of human MASP-2 protein;

CLAIMS

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

1. ~~Use of A method of treating a human subject suffering from idiopathic pneumonia syndrome following hematopoietic stem cell transplant (HSCT-IPS) comprising administering to the subject~~ a composition comprising an amount of a MASP-2 inhibitory monoclonal antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation, in the manufacture of a medicament for treating a human subject suffering from idiopathic pneumonia syndrome following hematopoietic stem cell transplant (HSCT-IPS), wherein the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway.

~~2. The method of claim 1, wherein the MASP-2 inhibitory antibody is a monoclonal antibody, or fragment thereof that specifically binds to human MASP-2.~~

~~3. The method of claim 1, wherein the antibody or fragment thereof is selected from the group consisting of a recombinant antibody, an antibody having reduced effector function, a chimeric antibody, a humanized antibody, and a human antibody.~~

~~4. The method of claim 1, wherein the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway.~~

~~5. The method of claim 1, wherein the MASP-2 inhibitory antibody inhibits C3b deposition in 90% human serum with an IC₅₀ of 30 nM or less.~~

~~6. The method of claim 1, wherein the MASP-2 inhibitory antibody is delivered to the subject systemically.~~

7.2. The ~~method-use~~ of claim 1, wherein the ~~method-use~~ further comprises identifying a human subject suffering from idiopathic pneumonia syndrome following hematopoietic stem cell transplant (HSCT-IPS) prior to the step of administering to the subject a composition comprising an amount of a MASP-2 inhibitory antibody, or

antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation.

~~8.3. The method-use of claim 1, wherein the subject has previously undergone an allogeneic hematopoietic stem cell transplant.~~

5 ~~9.4. The method-use of claim 1, wherein the subject has previously undergone an autologous hematopoietic stem cell transplant.~~

~~10. The method of claim 1, wherein the subject does not have diffuse alveolar hemorrhage (DAH).~~

10 ~~11.5. The method-use of claim 1, 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:70.~~

15 ~~12. The method of claim 1, wherein the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising SEQ ID NO:67 and a light chain variable region comprising SEQ ID NO:70.~~

~~13. The method of any of claims 1-12, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 4 mg/kg at least once weekly for a treatment period of at least 4 weeks.~~

20 ~~14. The method of claim 13, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 4 mg/kg at least twice weekly for a treatment period of at least 4 weeks.~~

25 ~~15. The method of any of claims 1-12, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 370 mg at least once weekly for a treatment period of at least 4 weeks.~~

~~16. The method of claim 15, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 370 mg at least twice weekly for a treatment period of at least 4 weeks.~~

17.6. ~~Use of A method of treating a human subject suffering from capillary leak syndrome following hematopoietic stem cell transplant (HSCT-CLS) comprising administering to the subject a composition comprising an amount of a MASP-2 inhibitory monoclonal antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation, in the manufacture of a medicament for treating a human subject suffering from capillary leak syndrome following hematopoietic stem cell transplant (HSCT-CLS), wherein the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway.~~

18. ~~The method of claim 17, wherein the MASP-2 inhibitory antibody is a monoclonal antibody, or fragment thereof that specifically binds to human MASP-2.~~

19. ~~The method of claim 17, wherein the antibody or fragment thereof is selected from the group consisting of a recombinant antibody, an antibody having reduced effector function, a chimeric antibody, a humanized antibody, and a human antibody.~~

20. ~~The method of claim 17, wherein the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway.~~

21. ~~The method of claim 17, wherein the MASP-2 inhibitory antibody inhibits C3b deposition in 90% human serum with an IC₅₀ of 30 nM or less.~~

22. ~~The method of claim 17, wherein the MASP-2 inhibitory antibody is delivered to the subject systemically.~~

23.7. ~~The method-use~~ of claim ~~617~~, wherein the ~~method-use~~ further comprises identifying a human subject suffering from capillary leak syndrome following hematopoietic stem cell transplant (HSCT-CLS) prior to the step of administering to the subject a composition comprising an amount of a MASP-2 inhibitory antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation.

24.8. ~~The method-use~~ of claim ~~617~~, wherein the subject has previously undergone an allogeneic hematopoietic stem cell transplant.

~~25.9.~~ The ~~method-use~~ of claim ~~617~~, wherein the subject has previously undergone an autologous hematopoietic stem cell transplant.

~~26. The method of claim 17, wherein the subject does not have veno-occlusive disease (VOD).~~

5 ~~27.10.~~ The ~~method-use~~ of claim ~~617~~, 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:70.

10 ~~28. The method of claim 17, wherein the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising SEQ ID NO:67 and a light chain variable region comprising SEQ ID NO:70.~~

15 ~~29. The method of any of claims 17-28, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 4 mg/kg at least once weekly for a treatment period of at least 4 weeks.~~

~~30. The method of claim 29, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 4 mg/kg at least twice weekly for a treatment period of at least 4 weeks.~~

20 ~~31. The method of any of claims 17-28, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 370 mg at least once weekly for a treatment period of at least 4 weeks.~~

~~32. The method of claim 31, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 370 mg at least twice weekly for a treatment period of at least 4 weeks.~~

25 ~~33.11.~~ Use of A method of treating a human subject suffering from fluid overload following hematopoietic stem cell transplant (HSCT-FO) comprising administering to the subject a composition comprising an amount of a MASP-2 inhibitory monoclonal antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent

complement activation, in the manufacture of a medicament for treating a human subject suffering from fluid overload following hematopoietic stem cell transplant (HSCT-FO), wherein the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway.

5 ~~34. The method of claim 33, wherein the MASP-2 inhibitory antibody is a monoclonal antibody, or fragment thereof that specifically binds to human MASP-2.~~

~~35. The method of claim 33, wherein the antibody or fragment thereof is selected from the group consisting of a recombinant antibody, an antibody having reduced effector function, a chimeric antibody, a humanized antibody, and a human antibody.~~

10 ~~36. The method of claim 33, wherein the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway.~~

~~37. The method of claim 33, wherein the MASP-2 inhibitory antibody inhibits C3b deposition in 90% human serum with an IC₅₀ of 30 nM or less.~~

15 ~~38. The method of claim 33, wherein the MASP-2 inhibitory antibody is delivered to the subject systemically.~~

39.12. The method-use of claim 1133, wherein the method-use further comprises identifying a human subject suffering from fluid overload following hematopoietic stem cell transplant (HSCT-FO) prior to the step of administering to the subject a composition comprising an amount of a MASP-2 inhibitory antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation.

40.13. The method-use of claim 1133, wherein the subject has previously undergone an allogeneic hematopoietic stem cell transplant.

41.14. The method-use of claim 1133, wherein the subject has previously undergone an autologous hematopoietic stem cell transplant.

25 42.15. The method-use of claim 1133, 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:70.

~~43. The method of claim 33, wherein the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising SEQ ID NO:67 and a light chain variable region comprising SEQ ID NO:70.~~

~~44. The method of any of claims 33-43, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 4 mg/kg at least once weekly for a treatment period of at least 4 weeks.~~

~~45. The method of claim 44, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 4 mg/kg at least twice weekly for a treatment period of at least 4 weeks.~~

~~46. The method of any of claims 33-43, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 370 mg at least once weekly for a treatment period of at least 4 weeks.~~

~~47. The method of claim 46, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 370 mg at least twice weekly for a treatment period of at least 4 weeks.~~

~~48.16. Use of A method of treating a human subject suffering from engraftment syndrome following hematopoietic stem cell transplant (HSCT-ES) comprising administering to the subject a composition comprising an amount of a MASP-2 inhibitory monoclonal antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation, in the manufacture of a medicament for treating a human subject suffering from engraftment syndrome following hematopoietic stem cell transplant (HSCT-ES), wherein the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway.~~

~~49. The method of claim 48, wherein the MASP-2 inhibitory antibody is a monoclonal antibody, or fragment thereof that specifically binds to human MASP-2.~~

~~50. The method of claim 48, wherein the antibody or fragment thereof is selected from the group consisting of a recombinant antibody, an antibody having reduced effector function, a chimeric antibody, a humanized antibody, and a human antibody.~~

~~51. The method of claim 48, wherein the MASP-2 inhibitory antibody does not substantially inhibit the classical pathway.~~

~~52. The method of claim 48, wherein the MASP-2 inhibitory antibody inhibits C3b deposition in 90% human serum with an IC₅₀ of 30 nM or less.~~

~~53. The method of claim 48, wherein the MASP-2 inhibitory antibody is delivered to the subject systemically.~~

~~54.17. The method-use of claim 1648, wherein the method-use further comprises identifying a human subject suffering from engraftment syndrome following hematopoietic stem cell transplant (HSCT-ES) prior to the step of administering to the subject a composition comprising an amount of a MASP-2 inhibitory antibody, or antigen-binding fragment thereof, effective to inhibit MASP-2-dependent complement activation.~~

~~55.18. The method-use of claim 1648, wherein the subject has previously undergone an allogeneic hematopoietic stem cell transplant.~~

~~56.19. The method-use of claim 1648, wherein the subject has previously undergone an autologous hematopoietic stem cell transplant.~~

~~57.20. The method-use of claim 1648, 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:70.~~

~~58. The method of claim 48, wherein the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising SEQ ID NO:67 and a light chain variable region comprising SEQ ID NO:70.~~

~~59. The method of any of claims 48-58, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 4 mg/kg at least once weekly for a treatment period of at least 4 weeks.~~

5 ~~60. The method of claim 59, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 4 mg/kg at least twice weekly for a treatment period of at least 4 weeks.~~

~~61. The method of any of claims 48-58, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 370 mg at least once weekly for a treatment period of at least 4 weeks.~~

10 ~~62. The method of claim 61, wherein the method comprises administering to the subject a composition comprising said MASP-2 inhibitory antibody having a dosage of about 370 mg at least twice weekly for a treatment period of at least 4 weeks.~~