

CLAIMS

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

1. ~~A method of treating a human subject suffering from persistent TMA associated with hematopoietic stem cell transplant (HSCT-TMA) comprising administering to the subject a composition comprising an amount Use of a MASP-2 inhibitory monoclonal antibody, or antigen-binding fragment thereof in the manufacture of a medicament for treating a human subject suffering from plasma therapy-resistant aHUS, effective to inhibit MASP-2 dependent complement activation.~~

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.~~

3.2. The ~~method-use~~ of ~~C~~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.

3. The use of claim 1 wherein the subject has previously undergone, or is currently undergoing, treatment with a terminal complement inhibitor that inhibits cleavage of complement protein C5.

4. The use of claim 3, wherein the terminal complement inhibitor is a humanized anti-C5 antibody or antigen-binding fragment thereof.

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

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

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

7. ~~The method of Claim 1, wherein the method further comprises identifying a human subject having persistent TMA associated with hematopoietic stem cell transplant 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. The method of Claim 1, wherein the subject has previously undergone, or is currently undergoing, treatment with a humanized anti-C5 antibody or antigen-binding fragment thereof.~~

~~9.8. The method-use of Claim 1, wherein administration of the MASP-2 inhibitory antibody ~~or antigen-binding fragment thereof is administered in an amount effective to improve~~ at least one or more of the following clinical parameters associated with persistent TMA associated with hematopoietic stem cell transplant aHUS: (i) an increase in platelet count, ~~(e.g., at least double, at least triple, at least quadruple the platelet count prior to treatment)~~; (ii) a decrease in LDH, (iii) an increase in haptoglobin; ~~(iii) a decrease in lactate dehydrogenase (LDH)~~; (iv) an increase in hemoglobin, and/or (iv) a decrease in creatinine.~~

~~10.9. 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.~~

~~10. The use 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.~~