

What is claimed is:

CLAIMS

1. ~~A method comprising administering to a subject an anti-C1s antibody; measuring a level of IL-6, and/or IL-10 in a sample from the subject; and optionally assessing fatigue in the subject.~~
21. A method of assessing fatigue in a subject being treated with an anti-C1s antibody, comprising measuring a level of IL-6, and/or IL-10 in a sample from a the subject ~~being treated with an anti-C1s antibody; and optionally assessing fatigue in the subject.~~
32. The method of ~~any one of the preceding claims~~claim 1, wherein the subject has a complement-mediated disease, optionally a classical complement-mediated disease, further optionally cold agglutinin disease (CAD).
4. ~~The method of any one of the preceding claims, wherein the subject has fatigue.~~
53. A method comprising ~~treating a subject with~~Use of an anti-C1s antibody in the manufacture of a medicament for treating a subject, wherein the subject has fatigue; ~~measuring a level of IL-6, and/or IL-10 in a sample from the subject; and optionally assessing fatigue in the subject.~~
64. The ~~method-use~~ of claim 53, wherein the subject has a complement-mediated disease, optionally a classical complement-mediated disease, further optionally cold agglutinin disease (CAD).
7. ~~A method comprising~~

~~—treating a subject with an anti-C1s antibody, wherein the subject has a complement mediated disease, optionally cold agglutinin disease (CAD);
measuring a level of IL-6, and/or IL-10 in a sample from the subject; and
optionally assessing fatigue in the subject.~~

8. ~~The method of claim 7, wherein the subject has fatigue.~~

9. ~~The method of any one of the preceding claims, wherein the subject has a baseline level of IL-6, and/or IL-10 prior to treatment with the anti-C1s antibody, and/or wherein the subject has a baseline level of fatigue prior to treatment with the anti-C1s antibody.~~

105. Use of an anti-C1s antibody in the manufacture of a medicament for treating a complement-mediated disease in a subject~~The method of claim 9, wherein the subject has a baseline level of IL-6, and/or IL-10 prior to treatment with the anti-C1s antibody, and/or wherein the subject has a baseline level of fatigue prior to treatment with the anti-C1s antibody; and~~

(aa1) if the level of IL-6, and/or IL-10 in ~~the a~~ sample from the subject is reduced after an administration of the medicament, optionally by at least 10%, relative to baseline and/or fatigue in the subject is improved relative to baseline, ~~the method further comprises continuing with the current anti-C1s antibody treatment~~the medicament is to be continued to be administered to the subject; or

(ba2) if the level of IL-6, and/or IL-10 in ~~the a~~ sample from the subject is within 10% of baseline and/or fatigue in the subject is maintained or worsens relative to baseline after administration of the medicament, ~~the method further comprises altering the current anti-C1s antibody treatment~~administration of the medicament is to be altered.

116. ~~The method-use~~ of claim 105, wherein the altering~~alteration of the administration of the medicament comprises the current anti-C1s antibody treatment comprises adjusting~~ the dosage and/or frequency of the ~~treatment with~~administration of the anti-C1s antibody being adjusted.

~~127.~~ The ~~method-use of claim 5 or 6 of claim 10 or 11~~, wherein the alteration of the administration of the medicament comprises the medicament being administered ~~altering the current anti-C1s antibody treatment comprises further treatment of the subject~~ with an anti-inflammatory agent.

~~138.~~ The ~~method-use~~ of any one of claims ~~5-7~~10-12, wherein the alteration of the administration of the medicament ~~altering the current anti-C1s antibody treatment~~ comprises the medicament being administered with a further treatment of the subject to improve fatigue.

~~149.~~ The method of claim 1 or 2 or the method-use of any one of ~~the preceding claims~~claim 3-8, further comprising monitoring wherein levels of IL-6, and/or IL-10 in the subject are monitored over a period of time.

~~1510.~~ The method or use of any one of the preceding claims, wherein the subject has undergone a blood transfusion.

~~1611.~~ The method or use of any one of the preceding claims, wherein the fatigue is assessed based on a Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) score, optionally wherein an improvement in fatigue is a change by at least 3 points on a FACIT-F score relative to baseline.

~~1712.~~ The method or use of any one of the preceding claims, wherein the anti-C1s antibody comprises a heavy chain (HC) complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO: 5, an HC complementarity determining region 2 (CDR2) comprising the amino acid sequence of SEQ ID NO: 6, an HC complementarity determining region 3 (CDR3) comprising the amino acid sequence of SEQ ID NO: 7, a light chain (LC) CDR1 that comprises the amino acid sequence of SEQ ID NO: 8, an LC CDR2 comprising the amino acid sequence of SEQ ID NO: 9, and an LC CDR3 comprising the amino acid sequence of SEQ ID NO: 10.

~~18~~13. The method or use of any one of the preceding claims, wherein the anti-C1s antibody comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 3 and comprises a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 4.

~~19~~14. The method or use of any one of the preceding claims, wherein the anti-C1s antibody comprises an HC comprising the amino acid sequence of SEQ ID NO: 1 and an LC comprising the amino acid sequence of SEQ ID NO: 2.

~~20~~15. The method or use of any one of claims 1-~~16~~11, wherein the anti-C1s antibody comprises an HC CDR1 comprising the amino acid sequence of SEQ ID NO: 15, an HC CDR2 comprising the amino acid sequence of SEQ ID NO: 16, an HC CDR3 comprising the amino acid sequence of SEQ ID NO: 17, an LC CDR1 comprising the amino acid sequence of SEQ ID NO: 18, an LC CDR2 comprising the amino acid sequence of SEQ ID NO: 19, and an LC CDR3 comprising the amino acid sequence of SEQ ID NO: 20.

~~21~~16. The method or use of any one of claims 1-~~16~~11 and ~~20~~15, wherein the anti-C1s antibody comprises a VH comprising the amino acid sequence of SEQ ID NO: 13 and comprises a VL comprising the amino acid sequence of SEQ ID NO: 14.

~~22~~17. The method or use of any one of claims 1-~~16~~11, ~~20~~15, and ~~21~~16, wherein the anti-C1s antibody comprises an HC comprising the amino acid sequence of SEQ ID NO: 11 and an LC comprising the amino acid sequence of SEQ ID NO: 12.

~~23~~18. The method or use of any one of the preceding claims, wherein the anti-C1s antibody comprises an IgG4 constant region.