

models of arthritis, including a reduction in the destruction of bone and cartilage and a reduction in macrophage numbers. *See, e.g., Kitaura et al., J. Clin. Invest.* 115: 3418-3427 (2005).

[006] Mature differentiated myeloid lineage cells such as macrophages, microglial cells, and osteoclasts contribute to pathology of various diseases such as rheumatoid arthritis, multiple sclerosis and diseases of bone loss. Differentiated myeloid lineage cells are derived from peripheral blood monocyte intermediates. CSF1R stimulation contributes to development of monocytes from bone marrow precursors, to monocyte proliferation and survival, and to differentiation of peripheral blood monocytes into differentiated myeloid lineage cells such as macrophages, microglial cells, and osteoclasts. CSF1R stimulation thus contributes to proliferation, survival, activation, and maturation of differentiated myeloid lineage cells, and in the pathologic setting, CSF1R stimulation contributes to the ability of differentiated myeloid lineage cells to mediate disease pathology.

SUMMARY

[006a] In one aspect, provided herein is a use of an antibody that binds human colony stimulating factor 1 receptor (CSF1R) in the manufacture of a medicament for treating a CD16+ disorder in a human subject, wherein the antibody blocks binding of human colony stimulating factor 1 (CSF1) to human CSF1R and blocks binding of human IL-34 to human CSF1R, and wherein the antibody comprises a heavy chain (HC) comprising a HC CDR1 comprising the sequence of SEQ ID NO: 15, an HC CDR2 comprising the sequence of SEQ ID NO: 16, and an HC CDR3 comprising the sequence of SEQ ID NO: 17, and comprises a light chain (LC) comprising a LC CDR1 comprising the sequence of SEQ ID NO: 18, a LC CDR2 comprising the sequence of SEQ ID NO: 19, and a LC CDR3 comprising the sequence of SEQ ID NO: 20; wherein the antibody is to be administered to the subject at a dose of 3 to 10 mg/kg at least twice and at a dosing frequency of once per two weeks or longer; and wherein administration of the antibody is sufficient to reduce the number of nonclassical CD16+ monocytes in the subject by at least 70% for at least two weeks after administration of at least one dose of the antibody.

[007] In some ~~embodiments~~ examples, methods of treating rheumatoid arthritis are provided, comprising administering an effective amount of an antibody that binds colony stimulating factor 1 receptor (CSF1R) to a human subject with rheumatoid arthritis, wherein the antibody blocks binding of colony stimulating factor 1 (CSF1) to CSF1R and blocks binding of IL-34 to CSF1R, wherein the effective amount is sufficient

to reduce the number of CD16+ monocytes in the subject by at least 50% for at least 4 weeks after two doses. In some embodimentexamples, the effective dose is between 0.2 mg/kg and 10 mg/kg, or between 1 and 10 mg/kg, or between 1 and 5 mg/kg. In some embodimentexamples, the antibody is administered at a dosing frequency of once per two weeks or longer.

[008] In some embodimentexamples, methods of treating rheumatoid arthritis are provided. In some embodimentexamples, the method comprises administering an antibody that binds colony stimulating factor 1 receptor (CSF1R) to a subject with rheumatoid arthritis, wherein the antibody blocks binding of colony stimulating factor 1 (CSF1) to CSF1R and blocks binding of IL-34 to CSF1R, and wherein the antibody is administered at a dose between 0.2 mg/kg and 10 mg/kg and at a dosing frequency of once per two weeks or longer. In some embodimentexamples, the dosing frequency is less than once per two weeks, once per two weeks, once per three weeks, once per four weeks, once per month, once per five weeks, once per six weeks, once per seven weeks, once per two months, once per three months, or four times per year. In some embodimentexamples, the dose is between 1 mg/kg and 10 mg/kg. In some embodimentexamples, the dose is between 3 mg/kg and 10 mg/kg. In some embodimentexamples, the

method comprises administering one dose of the antibody. In some ~~embodiment~~examples, the method comprises administering two doses of the antibody. In some ~~embodiment~~examples, the doses are administered at least one week apart, or at least two weeks apart.

[009] In some ~~embodiment~~examples, following administration of at least one dose of the antibody, the number of CD16+ monocytes is reduced in the subject by at least 50%. In some ~~embodiment~~examples, the number of CD16- monocytes is not reduced or is reduced by less than 20%. In some ~~embodiment~~examples, the number of CD16+ monocytes is reduced in the subject by at least 75%. In some ~~embodiment~~examples, the number of CD16+ monocytes is reduced by at least 50% for at least one week, at least two weeks, at least three weeks, at least four weeks, at least five weeks, at least six weeks, at least seven weeks, or at least eight weeks. In some ~~embodiment~~examples, the CD16+ monocytes are CD16+ peripheral blood monocytes.

[010] In some ~~embodiment~~examples, the level of at least one marker of bone resorption is reduced following administration of at least one dose of the antibody. In some ~~embodiment~~examples, the level of at least one marker of bone resorption is reduced by at least 20%. In some ~~embodiment~~examples, the level of at least one marker of bone resorption is reduced by at least 50%. In some ~~embodiment~~examples, the at least one marker of bone resorption is selected from CTx and TRAP5b. In some ~~embodiment~~examples, the at least one marker of bone resorption is CTx.

[011] In some ~~embodiment~~examples, the antibody is detectable in serum from the subject at least two weeks, at least three weeks, at least four weeks, at least one month, at least six weeks, or at least two months after administration of a dose. In some ~~embodiment~~examples, the antibody is detectable in serum from the subject at least four weeks, at least one month, at least six weeks, or at least two months after administration of a dose. In some ~~embodiment~~examples, the dose is between 3 mg/kg and 10 mg/kg. In some ~~embodiment~~examples, the half-life of the antibody in the subject is greater than 2 days. In some ~~embodiment~~examples, the half-life of the antibody is greater than 4 days. In some ~~embodiment~~examples, the half-life of the antibody is greater than 15 days. In some such ~~embodiment~~examples, the dose is between 3 mg/kg and 10 mg/kg.

[012] In any of the ~~embodiment~~examples of the methods described herein, the antibody heavy chain and/or the antibody light chain may have the following structure.

[013] In some ~~embodiment~~examples, the heavy chain comprises a sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from SEQ ID NOs: 9, 11, 13, and 39 to 45. In some ~~embodiment~~examples, the light chain comprises a sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a

sequence selected from SEQ ID NOs: 10, 12, 14, and 46 to 52. In some ~~embodiment~~examples, the heavy chain comprises a sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from SEQ ID NOs: 9, 11, 13, and 39 to 45, and the light chain comprises a sequence that is at least 90%, at least 95%, at least 97%, at least 99%, or 100% identical to a sequence selected from SEQ ID NOs: 10, 12, 14, and 46 to 52.

[014] In some ~~embodiment~~examples, the HC CDR1, HC CDR2, and HC CDR3 comprise a set of sequences selected from: (a) SEQ ID NOs: 15, 16, and 17; (b) SEQ ID NOs: 21, 22, and 23; and (c) SEQ ID NOs: 27, 28, and 29. In some ~~embodiment~~examples, the LC CDR1, LC CDR2, and LC CDR3 comprise a set of sequences selected from: (a) SEQ ID NOs: 18, 19, and 20; (b) SEQ ID NOs: 24, 25, and 26; and (c) SEQ ID NOs: 30, 31, and 32.

[015] In some ~~embodiment~~examples, the heavy chain comprises an HC CDR1, HC CDR2, and HC CDR3, wherein the HC CDR1, HC CDR2, and HC CDR3 comprise a set of sequences selected from: (a) SEQ ID NOs: 15, 16, and 17; (b) SEQ ID NOs: 21, 22, and 23; and (c) SEQ ID NOs: 27, 28, and 29; and the light chain comprises an LC CDR1, LC CDR2, and LC CDR3, wherein the LC CDR1, LC CDR2, and LC CDR3 comprise a set of sequences selected from: (a) SEQ ID NOs: 18, 19, and 20; (b) SEQ ID NOs: 24, 25, and 26; and (c) SEQ ID NOs: 30, 31, and 32.

[016] In some ~~embodiment~~examples, the antibody comprises a heavy chain and a light chain, wherein the antibody comprises: (a) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 9 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 10; (b) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 11 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 12; (c) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 13 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 14; (d) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 39 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 46; (e) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 40 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 46; (f) a heavy chain comprising a sequence that is at least 95%, at least 97%,

sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 51; or (s) a heavy chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 45 and a light chain comprising a sequence that is at least 95%, at least 97%, at least 99%, or 100% identical to SEQ ID NO: 52.

[017] In some ~~embodiment~~examples, the antibody comprises a heavy chain and a light chain, wherein the antibody comprises: (a) a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 15, an HC CDR2 having the sequence of SEQ ID NO: 16, and an HC CDR3 having the sequence of SEQ ID NO: 17, and a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 18, a LC CDR2 having the sequence of SEQ ID NO: 19, and a LC CDR3 having the sequence of SEQ ID NO: 20; (b) a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 21, an HC CDR2 having the sequence of SEQ ID NO: 22, and an HC CDR3 having the sequence of SEQ ID NO: 23, and a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 24, a LC CDR2 having the sequence of SEQ ID NO: 25, and a LC CDR3 having the sequence of SEQ ID NO: 26; or (c) a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 27, an HC CDR2 having the sequence of SEQ ID NO: 28, and an HC CDR3 having the sequence of SEQ ID NO: 29, and a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 30, a LC CDR2 having the sequence of SEQ ID NO: 31, and a LC CDR3 having the sequence of SEQ ID NO: 32.

[018] In some ~~embodiment~~examples, the antibody comprises a heavy chain and a light chain, wherein the antibody comprises: (a) a heavy chain comprising a sequence of SEQ ID NO: 53 and a light chain comprising a sequence of SEQ ID NO: 60; (b) a heavy chain comprising a sequence of SEQ ID NO: 53 and a light chain comprising a sequence of SEQ ID NO: 61; or (c) a heavy chain comprising a sequence of SEQ ID NO: 58 and a light chain comprising a sequence of SEQ ID NO: 65. In some ~~embodiment~~examples, the antibody comprises a heavy chain and a light chain, wherein the antibody comprises: (a) a heavy chain consisting of the sequence of SEQ ID NO: 53 and a light chain consisting of the sequence of SEQ ID NO: 60; (b) a heavy chain consisting of the sequence of SEQ ID NO: 53 and a light chain consisting of the sequence of SEQ ID NO: 61; or (c) a heavy chain consisting of the sequence of SEQ ID NO: 58 and a light chain consisting of the sequence of SEQ ID NO: 65.

[019] In some ~~embodiment~~examples, the antibody is a humanized antibody. In some ~~embodiment~~examples, the antibody is selected from a Fab, an Fv, an scFv, a Fab', and a (Fab')₂. In some ~~embodiment~~examples, the antibody is a chimeric antibody. In some ~~embodiment~~examples, the

antibody is selected from an IgA, an IgG, and an IgD. In some ~~embodiment~~examples, the antibody is an IgG. In some ~~embodiment~~examples, the antibody is an IgG4. In some ~~embodiment~~examples, the antibody is an IgG4 comprising an S241P mutation in at least one IgG4 heavy chain constant region.

[020] In some ~~embodiment~~examples, the antibody binds to human CSF1R and/or binds to cynomolgus CSF1R. In some ~~embodiment~~examples, the antibody blocks ligand binding to CSF1R. In some ~~embodiment~~examples, an antibody blocks binding of CSF1 and/or IL-34 to CSF1R. In some ~~embodiment~~examples, the antibody blocks binding of both CSF1 and IL-34 to CSF1R. In some ~~embodiment~~examples, the antibody inhibits ligand-induced CSF1R phosphorylation. In some ~~embodiment~~examples, the antibody inhibits CSF1- and/or IL-34-induced CSF1R phosphorylation. In some ~~embodiment~~examples, an antibody binds to human CSF1R with an affinity (K_D) of less than 1 nM. In some ~~embodiment~~examples, the antibody inhibits monocyte proliferation and/or survival responses in the presence of CSF1 or IL-34.

[021] In some ~~embodiment~~examples, a pharmaceutical composition comprising an antibody that binds CSF1R is provided.

[022] In some ~~embodiment~~examples, compositions comprising antibodies that bind CSF1R are provided for use in methods of treatment of human or animals. In some ~~embodiment~~examples, antibodies that bind CSF1R and compositions comprising antibodies that bind CSF1R are provided for use in a method of treating rheumatoid arthritis in a human or animal.

BRIEF DESCRIPTION OF THE FIGURES

[023] **FIG. 1A-C** shows an alignment of the humanized heavy chain variable regions for each of humanized antibodies huAb1 to huAb16, as discussed in Example 1. Boxed residues are amino acids in the human acceptor sequence that were changed back to the corresponding mouse residue.

[024] **FIG. 2A-C** shows an alignment of the humanized light chain variable regions for each of humanized antibodies huAb1 to huAb16, as discussed in Example 1. Boxed amino acids are residues in the human acceptor sequence that were changed back to the corresponding mouse residue.

[025] **FIG. 3A-B** show clearance of serum huAb1 (“FPA008”) in humans following a single administration at the indicated dose, as described in Example 2.

CLAIMS

1. ~~A method of treating rheumatoid arthritis comprising administering an effective amount of~~ Use of an antibody that binds human colony stimulating factor 1 receptor (CSF1R) in the manufacture of a medicament for treating a CD16+ disorder in ~~to a human subject with rheumatoid arthritis,~~ wherein the antibody blocks binding of human colony stimulating factor 1 (CSF1) to human CSF1R and blocks binding of human IL-34 to human CSF1R, and wherein the antibody comprises a heavy chain (HC) comprising a HC CDR1 comprising the sequence of SEQ ID NO: 15, an HC CDR2 comprising the sequence of SEQ ID NO: 16, and an HC CDR3 comprising the sequence of SEQ ID NO: 17, and comprises a light chain (LC) comprising a LC CDR1 comprising the sequence of SEQ ID NO: 18, a LC CDR2 comprising the sequence of SEQ ID NO: 19, and a LC CDR3 comprising the sequence of SEQ ID NO: 20; wherein the antibody is to be administered to the subject at a dose of 3 to 10 mg/kg at least twice and at a dosing frequency of once per two weeks or longer; and wherein administration of the antibody ~~the effective amount~~ is sufficient to reduce the number of nonclassical CD16+ monocytes in the subject by at least ~~50~~70% for at least ~~4~~two weeks after administration of at least one dose of the antibody~~two doses~~.

2. Use of an antibody that binds human colony stimulating factor 1 receptor (CSF1R) in the manufacture of a medicament for reducing the number of nonclassical CD16+ monocytes in a human subject with a CD16+ disorder, wherein the antibody blocks binding of human colony stimulating factor 1 (CSF1) to human CSF1R and blocks binding of human IL-34 to human CSF1R, and wherein the antibody comprises a heavy chain (HC) comprising a HC CDR1 comprising the sequence of SEQ ID NO: 15, an HC CDR2 comprising the sequence of SEQ ID NO: 16, and an HC CDR3 comprising the sequence of SEQ ID NO: 17, and comprises a light chain (LC) comprising a LC CDR1 comprising the sequence of SEQ ID NO: 18, a LC CDR2 comprising the sequence of SEQ ID NO: 19, and a LC CDR3 comprising the sequence of SEQ ID NO: 20; wherein the antibody is to be administered to the subject at a dose of 3 to 10 mg/kg at least twice and at a dosing frequency of once per two weeks or longer; and wherein administration of the antibody is sufficient to reduce the number of nonclassical CD16+ monocytes in the subject by at least 70 % for at least two weeks after administration of at least one dose of the antibody.

3. Use of an antibody that binds human colony stimulating factor 1 receptor (CSF1R) in the manufacture of a medicament for reducing the number of nonclassical CD16+ monocytes in a human subject with a CD16+ disorder, wherein the antibody blocks binding of human colony stimulating factor 1 (CSF1) to human CSF1R and blocks binding of human IL-34 to human CSF1R, and wherein the antibody comprises a heavy chain (HC) comprising a HC CDR1 comprising the sequence of SEQ ID NO: 15, an HC CDR2 comprising the sequence of SEQ ID NO: 16, and an HC CDR3 comprising the sequence of SEQ ID NO: 17, and comprises a light chain (LC) comprising a LC CDR1 comprising the sequence of SEQ ID NO: 18, a LC CDR2 comprising the sequence of SEQ ID NO: 19, and a LC CDR3 comprising the sequence of SEQ ID NO: 20;

wherein the antibody is to be administered to the subject at a dose of 3 to 10 mg/kg at least twice and at a dosing frequency of once per two weeks or longer; and

wherein the number of nonclassical CD16+ monocytes detected in a peripheral blood sample from the subject two to six weeks following administration of at least one dose of the antibody is reduced by at least 70 % compared to the number in a peripheral blood sample from the subject prior to administration of the antibody.

2.4. The method use of any one of claims 1-3, wherein the effective dose is between 0.2 mg/kg and 10 mg/kg, or between 1 and 10 mg/kg, or between 1 and 5 mg/kg dose is 3 mg/kg.

3.5. The method of claim 1 or claim 2 use of any one of claims 1-4, wherein the antibody is administered at a dosing frequency of is once per two weeks or longer.

6. The use of any one of claims 1-4, wherein the dosing frequency is once per three weeks.

7. The use of any one of claims 1-4, wherein the dosing frequency is once per month or once per four weeks.

4. A method of treating rheumatoid arthritis comprising administering an antibody that binds colony stimulating factor 1 receptor (CSF1R) to a human subject with rheumatoid arthritis, wherein the antibody blocks binding of colony stimulating factor 1 (CSF1) to CSF1R and blocks binding of IL-34 to CSF1R, wherein the antibody is administered at a dose between 0.2 mg/kg and 10 mg/kg and at a dosing frequency of once per two weeks or longer.

5. The method of any one of the preceding claims, wherein the dosing frequency is less than once per two weeks, once per two weeks, once per three weeks, once per four weeks,

~~once per month, once per five weeks, once per six weeks, once per seven weeks, once per two months, once per three months, or four times per year.~~

~~6. — The method of any one of the preceding claims, wherein the method comprises administering one dose of the antibody.~~

~~7. — The method of any one of claims 1 to 5, wherein the method comprises administering two doses of the antibody.~~

~~8. — The method of claim 7, wherein the doses are administered at least one week apart.~~

~~9. — The method of claim 7, wherein the doses are administered at least two weeks apart.~~

~~10. — The method of any one of the preceding claims, wherein the dose is between 1 mg/kg and 10 mg/kg.~~

~~11. — The method of any one of the preceding claims, wherein the dose is between 3 mg/kg and 10 mg/kg.~~

~~12. — The method of any one of the preceding claims, wherein following administration of at least one dose of the antibody, the number of CD16+ monocytes is reduced in the subject by at least 50%.~~

~~13-8. The method use of any one of the preceding claimsclaims 1-7, wherein the number of CD16- monocytes is not reduced or is reduced by less than 20%.~~

9. The use of any one of claims 1-8, wherein the administration of the antibody is sufficient to reduce the number of nonclassical CD16+ monocytes in the subject by at least 70 % for at least four weeks after administration of at least one dose of the antibody.

14.10. The use of any one of claims 1-9method of any one of the preceding claims, wherein following administration of one dose of the antibody, the number of nonclassical CD16+ monocytes is reduced in the subject by at least 75% for at least two weeks.

11. The use of any one of claims 1-10, wherein the administration of the antibody is sufficient to reduce the number of nonclassical CD16+ monocytes in the subject by at least 90 % for at least two weeks after administration of at least one dose of the antibody.

12. The use of any one of claims 1-11, wherein following administration of one dose of the antibody, the number of nonclassical CD16+ monocytes is reduced in the subject by at least 90 % for at least two weeks.

~~13. The use of any one of claims 1-12, wherein the CD16+ disorder is neoplasia.~~

~~15. The method of any one of the preceding claims, wherein the number of CD16+ monocytes is reduced by at least 50% for at least one week, at least two weeks, at least three weeks, at least four weeks, at least five weeks, at least six weeks, at least seven weeks, or at least eight weeks.~~

~~16.~~14. The use of any one of claims 1-13~~method of any one of claims 2 to 15~~, wherein the nonclassical CD16+ monocytes are CD16+ peripheral blood monocytes.

~~17. The method of any one of the preceding claims, wherein the level of at least one marker of bone resorption is reduced following administration of at least one dose of the antibody.~~

~~18. The method of claim 17, wherein the level of at least one marker of bone resorption is reduced by at least 20%.~~

~~19. The method of claim 17, wherein the level of at least one marker of bone resorption is reduced by at least 50%.~~

~~20. The method of any one of claims 17 to 19, wherein the at least one marker of bone resorption is selected from CTx and TRAP5b.~~

~~21. The method of claim 20, wherein the at least one marker of bone resorption is CTx.~~

~~22.~~15. The use of any one of claims 1-14~~method of any one of the preceding claims~~, wherein the antibody is selected from:

a) ~~an antibody comprising~~ comprises a heavy chain~~HC~~ comprising the sequence of SEQ ID NO: 39 and a light chain~~LC~~ comprising the sequence of SEQ ID NO: 46;

b) ~~an antibody comprising a heavy chain comprising a heavy chain (HC) CDR1 having the sequence of SEQ ID NO: 15, an HC CDR2 having the sequence of SEQ ID NO: 16, and an HC CDR3 having the sequence of SEQ ID NO: 17, and a light chain comprising a light chain (LC) CDR1 having the sequence of SEQ ID NO: 18, a LC CDR2 having the sequence of SEQ ID NO: 19, and a LC CDR3 having the sequence of SEQ ID NO: 20; and~~

c) ~~an antibody comprising a heavy chain comprising the sequence of SEQ ID NO: 53 and a light chain comprising the sequence of SEQ ID NO: 60.~~

~~23.~~16. The ~~method of use of any one of claims 1-15~~claim 22, wherein the antibody is a humanized antibody.

~~24.17.~~ The use of any one of claims 1-16~~method of claim 22 or claim 23~~, wherein the antibody is selected from a Fab, an Fv, an scFv, a Fab', and a (Fab')₂.

18. The use of any one of claims 1-16, wherein the antibody comprises a HC comprising the sequence of SEQ ID NO: 53 and a LC comprising the sequence of SEQ ID NO: 60.

~~25.19.~~ The use of any one of claims 1-18~~method of any one of the preceding claims~~, wherein the antibody is detectable in serum from the subject at least two weeks~~, at least three weeks, at least four weeks, at least one month, at least six weeks, or at least two months after~~ administration of a dose.

20. The use of claim 19, wherein the antibody is detectable in serum from the subject at least four weeks after administration of a dose.

~~26.~~ ~~The method of claim 25, wherein the antibody is detectable in serum from the subject at least four weeks, at least one month, at least six weeks, or at least two months after administration of a dose.~~

~~27.~~ ~~The method of claim 26, wherein the dose is between 3 mg/kg and 10 mg/kg.~~

~~28.~~ ~~The method of any one of the preceding claims, wherein the half-life of the antibody in the subject is greater than 2 days.~~

~~29.~~ ~~The method of claim 28, wherein the half-life of the antibody is greater than 4 days.~~

~~30.21.~~ The use of any one of claims 1-20~~method of claim 28~~, wherein the half-life of the antibody in human blood is greater than 15 days.

~~31.22.~~ The use of claim 21~~method of claim 28~~, wherein the half-life of the antibody in human blood is greater than 28 days.

~~32.23.~~ The use of claim 21~~method of claim 28~~, wherein the half-life of the antibody in human blood is greater than 42 days.

~~33.~~ ~~The method of any one of claims 28 of claim 32, wherein the dose is between 3 mg/kg and 10 mg/kg.~~