

AMENDED CLAIMS**received by the International Bureau on 3 October 2021 (03.10.2021)**

- [Claim 1] A method of treating a fibrotic inflammatory disease in a human subject, comprising administering an effective amount of a humanized anti-CCL24 monoclonal antibody or a pharmaceutical composition thereof, wherein the anti-CCL24 monoclonal antibody comprises a heavy chain having at least 95% sequence identity to SEQ ID NO: 11 and a light chain having at least 95% sequence identity to SEQ ID NO: 12; wherein said anti-CCL24 monoclonal antibody is administered at a dose of about 2.5 mg/kg, about 5 mg/kg, about 10 mg/kg, or about 20mg/kg, and wherein the fibrotic inflammatory disease is non-alcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), primary sclerosing cholangitis (PSC), or systemic sclerosis (SSC).
- [Claim 2] A humanized anti-CCL24 monoclonal antibody or a pharmaceutical composition thereof for use in a method of treating a fibrotic inflammatory disease in a human subject, wherein said method comprises administering an effective amount of said anti-CCL24 monoclonal antibody or a pharmaceutical composition thereof to the human subject, wherein the anti-CCL24 monoclonal antibody comprises a heavy chain having at least 95% sequence identity to SEQ ID NO: 11 and a light chain having at least 95% sequence identity to SEQ ID NO: 12; wherein said anti-CCL24 monoclonal antibody is administered at a dose of about 2.5 mg/kg, about 5 mg/kg, about 10 mg/kg, or about 20mg/kg, and wherein the fibrotic inflammatory disease is non-alcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), primary sclerosing cholangitis (PSC), or systemic sclerosis (SSC).
- [Claim 3] The method or the antibody for use of any one of claims 1-2, wherein the anti-CCL24 monoclonal antibody comprises a heavy chain having 100% sequence identity to SEQ ID NO: 11.
- [Claim 4] The method or the antibody for use of any one of claims 1-3, wherein the anti-CCL24 monoclonal antibody comprises a light chain having 100% sequence identity to SEQ ID NO:
- [Claim 12]
- [Claim 5] The method of claim 1 or the antibody for use of claim 2, wherein the

anti-CCL24

monoclonal antibody comprises a heavy chain according to SEQ ID NO: 11 and a light chain according to SEQ ID NO: 12.

- [Claim 6] 6. The method or the antibody for use of claim 1 or claim 2, wherein the anti-CCL24 monoclonal antibody is administered at a dose of about 10 mg/kg.
- [Claim 7] 7. The method or the antibody for use of claim 1 or claim 2, wherein the anti-CCL24 monoclonal antibody is administered at a dose of about 5 mg/kg.
- [Claim 8] 8. The method or the antibody for use of claim 1 or 2, wherein the anti-CCL24 monoclonal antibody is administered at a dose of about 20 mg/kg.
- [Claim 9] 9. The method or the antibody for use of any one of claims 1-8, wherein the anti-CCL24 monoclonal antibody is administered subcutaneously.
- [Claim 10] 10. The method or the antibody for use of any one of claims 1-8, wherein the anti-CCL24 monoclonal antibody is administered intravenously.
- [Claim 11] The method or the antibody for use of any one of claims 1-10, wherein the anti-CCL24 monoclonal antibody is administered once every one to four weeks.
- [Claim 12] 12. The method or the antibody for use of claim 11, wherein the anti-CCL24 monoclonal antibody is administered once every two weeks.
- [Claim 13] 13. The method or the antibody for use of claim 11, wherein the anti-CCL24 monoclonal antibody is administered once every three weeks.
- [Claim 14] 14. The method or the antibody for use of claim 11, wherein the anti-CCL24 monoclonal antibody is administered once every four weeks.
- [Claim 15] 15. The method or the antibody for use of any one of claims 1-14, wherein the anti-CCL24 monoclonal antibody is administered for at least four weeks.
- [Claim 16] 16. The method or the antibody for use of claim 15, wherein the anti-CCL24 monoclonal antibody is administered for at least 15 weeks.
- [Claim 17] 17. The method or the antibody for use of claim 15, wherein the anti-CCL24 monoclonal antibody is administered for at least 24 weeks.
- [Claim 18] 18. The method or the antibody for use of any one of claims 1-17, wherein administration of the anti-CCL24 monoclonal antibody increases total sera level of CCL24 at day 4 post administration to at

least 150% of baseline total sera level of CCL24 before administering the anti-CCL24 monoclonal antibody.

[Claim 19]

19. The method or the antibody for use of any one of claims 1-18, wherein said method further comprises a step of evaluating the level of one or more circulating fibrosis markers to determine improvement in the hepatic condition of the subject.

[Claim 20]

20. The method or the antibody for use of claim 19, wherein the one or more circulating fibrosis markers are selected from the group consisting of plasma alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), PRO-C3, PRO-C4, PRO-C5, C3M, cytokeratin 18 (CK18), amino-terminal propeptide of type III procollagen (PIIINP), hyaluronic acid (HA), Tissue Inhibitor of Metalloproteinases 1 (TIMP-1), platelet derived growth factor (PDGF), Tissue Inhibitor of Metalloproteinases 2 (TIMP-2), γ -glutamyltransferase (GGT), bilirubin, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and procalcitonin (PCT).

[Claim 21]

21. The method or the antibody for use of claim 19 or 20, wherein the one or more circulating fibrosis markers are measured by Enhanced Liver Fibrosis (ELF) blood test.

[Claim 22]

A pharmaceutical composition, comprising about 1 to about 500 mg/mL of an anti-CCL24 monoclonal antibody comprising a heavy chain according to SEQ ID NO: 11 and a light chain according to SEQ ID NO: 12.

[Claim 23]

The pharmaceutical composition of claim 22, comprising about 100 to about 250 mg/mL the anti-CCL24 monoclonal antibody.

[Claim 24]

The pharmaceutical composition of claim 23, comprising about 175 mg/mL the anti-CCL24 monoclonal antibody.

[Claim 25]

The pharmaceutical composition of any one of claims 22-24, comprising a histidine buffer, optionally at about 10 mM.

[Claim 26]

The pharmaceutical composition of any one of claims 22-25, comprising a sodium or potassium phosphate buffer, optionally at about 10 mM.

[Claim 27]

The pharmaceutical composition of any one of claims 22-26, further comprising arginine, optionally at between about 30 and about 200 mM, or optionally at about 150 mM.

[Claim 28]

The pharmaceutical composition of any one of claims 22-27, further comprising glutamic acid, optionally at between about 30 and about 200 mM, or optionally at about 150 mM.

- [Claim 29] The pharmaceutical composition of any one of claims 22-28, further comprising sorbitol, optionally at about 4%.
- [Claim 30] The pharmaceutical composition of any one of claims 22-29, further comprising glycine, optionally at about 10 mM to about 100 mM, or optionally about 40 mM.
- [Claim 31] The pharmaceutical composition of any one of claims 22-30, further comprising polysorbate, optionally polysorbate-80, optionally at about 0.02% or about 0.01%.
- [Claim 32] The pharmaceutical composition of any one of claims 22-31, wherein the pharmaceutical composition has a pH of 5 to 8.
- [Claim 33] The pharmaceutical composition of any one of claims 22-31, wherein the pharmaceutical composition has a pH of 6 to 7, optionally 6.1 or 6.3.
- [Claim 34] The pharmaceutical composition of any one of claims 22-33, wherein the pharmaceutical composition is supplied in a unit dose having a fill volume of about 0.2 to about 2 mL, or about 5 to about 20 mL.
- [Claim 35] The pharmaceutical composition of any one of claims 22-34, comprising about 5 to about 20 mg/mL the anti-CCL24 monoclonal antibody.
- [Claim 36] The pharmaceutical composition of any one of claims 22-34, comprising about 10 mg/mL the anti-CCL24 monoclonal antibody.
- [Claim 37] A method of treating nonalcoholic steatohepatitis (NASH) in a human subject, comprising administering an effective amount of the pharmaceutical composition of any one of claims 22-36.
- [Claim 38] The pharmaceutical composition of any one of claims 22-36 for use in a method of treating nonalcoholic steatohepatitis (NASH) in a human subject.
- [Claim 39] A method of treating primary sclerosing cholangitis (PSC) in a human subject, comprising administering an effective amount of the pharmaceutical composition of any one of claims 22-36.
- [Claim 40] The pharmaceutical composition of any one of claims 22-36 for use in a method of treating primary sclerosing cholangitis (PSC) in a human subject.
- [Claim 41] A method of treating Systemic Sclerosis (SSc) in a human subject, comprising administering an effective amount of the pharmaceutical composition of any one of claims 22-36.
- [Claim 42] The pharmaceutical composition of any one of claims 22-36 for use in a method of treating Systemic Sclerosis (SSc) in a human subject.

- [Claim 43] The method or the pharmaceutical composition for use of any one of claims 22-42, wherein the administering step comprises subcutaneous administration.
- [Claim 44] The method or the pharmaceutical composition for use of any one of claims 22-42, wherein the administering step comprises intravenous administration.
- [Claim 45] A kit comprising the pharmaceutical composition of any one of claims 22-36 and instructions for use.

CLAIMS

1. A use of a pharmaceutical composition for the manufacture of a medicament for the treatment of a fibrotic inflammatory disease in a human subject, comprising administering an effective amount of a humanized anti-CCL24 monoclonal antibody or a pharmaceutical composition thereof, wherein the anti-CCL24 monoclonal antibody comprises a heavy chain having at least 95% sequence identity to SEQ ID NO: 11 and a light chain having at least 95% sequence identity to SEQ ID NO: 12; wherein said anti-CCL24 monoclonal antibody is administered at a dose of about 2.5 mg/kg, about 5 mg/kg, about 10 mg/kg, or about 20mg/kg, and wherein the fibrotic inflammatory disease is non-alcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), cholestatic liver diseases, primary sclerosing cholangitis (PSC), or systemic sclerosis (SSC).
2. The use of a pharmaceutical composition of claim 1, wherein the anti-CCL24 monoclonal antibody comprises a heavy chain according to SEQ ID NO: 11 and a light chain according to SEQ ID NO: 12.
3. The use of a pharmaceutical composition of claim 1, wherein the anti-CCL24 monoclonal antibody is administered at a dose of about 5 mg/kg, about 10 mg/kg, or about 20 mg/kg.
4. The use of a pharmaceutical composition of any one of claims 1-3, wherein the anti-CCL24 monoclonal antibody is administered subcutaneously or intravenously.
5. The use of a pharmaceutical composition of any one of claims 1-4, wherein the anti-CCL24 monoclonal antibody is administered once every one to four weeks, optionally once every two weeks, once every three weeks, or once every four weeks.
6. The use of a pharmaceutical composition of any one of claims 1-5, wherein the anti-CCL24 monoclonal antibody is administered for at least four weeks, optionally for at least 15 weeks, or for at least 24 weeks.
7. The use of a pharmaceutical composition of any one of claims 1-6, wherein administration of the anti-CCL24 monoclonal antibody increases total sera level of CCL24 at day 4 post administration to at least 150% of baseline total sera level of CCL24 before administering the anti-CCL24 monoclonal antibody.
8. The use of a pharmaceutical composition of any one of claims 1-7, wherein said method further comprises a step of evaluating the level of one or more circulating fibrosis markers to

determine improvement in the hepatic condition of the subject, optionally the one or more circulating fibrosis markers are selected from the group consisting of plasma alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST), PRO-C3, PRO-C4, PRO-C5, C3M, cytokeratin 18 (CK18), amino-terminal propeptide of type III procollagen (PIIINP), hyaluronic acid (HA), Tissue Inhibitor of Metalloproteinases 1 (TIMP-1), platelet derived growth factor (PDGF), Tissue Inhibitor of Metalloproteinases 2 (TIMP-2), γ -glutamyltransferase (GGT), bilirubin, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and procalcitonin (PCT).

9. A pharmaceutical composition, comprising about 1 to about 500 mg/mL, about 100 to about 250 mg/mL, or about 175 mg/mL of an anti-CCL24 monoclonal antibody comprising a heavy chain according to SEQ ID NO: 11 and a light chain according to SEQ ID NO: 12.

10. The pharmaceutical composition of claim 9, comprising a histidine buffer, or a sodium or potassium phosphate buffer, optionally at about 10 mM.

11. The pharmaceutical composition of any one of claims 9-10, further comprising arginine, optionally at between about 30 and about 200 mM, or optionally at about 150 mM.

12. The pharmaceutical composition of any one of claims 9-11, further comprising glutamic acid, optionally at between about 30 and about 200 mM, or optionally at about 150 mM.

13. The pharmaceutical composition of any one of claims 9-12, further comprising sorbitol, optionally at about 4%.

14. The pharmaceutical composition of any one of claims 9-13, further comprising glycine, optionally at about 10 mM to about 100 mM, or optionally about 40 mM.

15. The pharmaceutical composition of any one of claims 9-14, further comprising polysorbate, optionally polysorbate-80, optionally at about 0.02% or about 0.01%.

16. The pharmaceutical composition of any one of claims 9-15, wherein the pharmaceutical composition has a pH of 5 to 8, optionally a pH of 6 to 7, optionally 6.1 or 6.3.

17. The pharmaceutical composition of any one of claims 9-16, wherein the pharmaceutical composition is supplied in a unit dose having a fill volume of about 0.2 to about 2 mL, or about 5 to about 20 mL.

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18. A use of a pharmaceutical composition for the manufacture of a medicament for the treatment of one or more of nonalcoholic steatohepatitis (NASH), cholestatic liver diseases, primary sclerosing cholangitis (PSC), Systemic Sclerosis (SSc), in a human subject, comprising administering an effective amount of the pharmaceutical composition of any one of claims 11-19.

19. The pharmaceutical composition for use of any one of claims 9-18, wherein the administering step comprises subcutaneous administration or intravenous administration.

20. A kit comprising the pharmaceutical composition of any one of claims 9-17 and instructions for use.