

CLAIMS

1. A method of treating a fibrotic inflammatory disease in a human subject, comprising administering an effective amount of an anti-CCL24 monoclonal antibody.
2. An anti-CCL24 monoclonal antibody 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 to the human subject.
3. The method of claim 1, or the antibody for use of claim 2 wherein the anti-CCL24 monoclonal antibody comprises:
 - a heavy chain variable region comprising:
 - a) the complementary determining region VH CDR1 comprising the amino acid sequence denoted by SEQ ID NO: 1;
 - b) the complementary determining region VH CDR2 comprising the amino acid sequence denoted by SEQ ID NO: 2; and
 - c) the complementary determining region VH CDR3 comprising the amino acid sequence denoted by SEQ ID NO: 3; and
 - a light chain variable region comprising:
 - d) the complementary determining region VK CDR1 comprising the amino acid sequence denoted by SEQ ID NO: 4;
 - e) the complementary determining region VK CDR2 comprising the amino acid sequence denoted by SEQ ID NO: 5; and
 - f) the complementary determining region VK CDR3 comprising the amino acid sequence denoted by SEQ ID NO: 6.
4. The method or the antibody for use of any one of claims 1-3, wherein the anti-CCL24 monoclonal antibody is a humanized or human antibody.
5. The method or the antibody for use of any one of claims 1-4, wherein the anti-CCL24 monoclonal antibody comprises a heavy chain variable region having at least 95% sequence identity to SEQ ID NO: 7.

6. The method or the antibody for use of any one of claims 1-5, wherein the anti-CCL24 monoclonal antibody comprises a heavy chain having at least 95% sequence identity to SEQ ID NO: 11.
7. The method or the antibody for use of any one of claims 1-6, wherein the anti-CCL24 monoclonal antibody comprises a light chain variable region having at least 95% sequence identity to SEQ ID NO: 8.
8. The method or the antibody for use of any one of claims 1-7, wherein the anti-CCL24 monoclonal antibody comprises a light chain having at least 95% sequence identity to SEQ ID NO: 12.
9. The method or the antibody for use of any one of claims 1-8, wherein the anti-CCL24 monoclonal antibody comprises a heavy chain variable region having 100% sequence identity to SEQ ID NO: 7.
10. The method or the antibody for use of any one of claims 1-9, wherein the anti-CCL24 monoclonal antibody comprises a heavy chain having 100% sequence identity to SEQ ID NO: 11.
11. The method or the antibody for use of any one of claims 1-10, wherein the anti-CCL24 monoclonal antibody comprises a light chain variable region having 100% sequence identity to SEQ ID NO: 8.
12. The method or the antibody for use of any one of claims 1-11, wherein the anti-CCL24 monoclonal antibody comprises a light chain having 100% sequence identity to SEQ ID NO: 12.
13. 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.
14. The method or the antibody for use of any one of claims 1-13, wherein the anti-CCL24 monoclonal antibody is administered at a dose of between about 0.75 mg/kg and about 20 mg/kg.
15. The method or the antibody for use of claim 14, wherein the anti-CCL24 monoclonal antibody is administered at a dose of about 10 mg/kg.

16. The method or the antibody for use of claim 14, wherein the anti-CCL24 monoclonal antibody is administered at a dose of about 5 mg/kg.
17. The method or the antibody for use of claim 14, wherein the anti-CCL24 monoclonal antibody is administered at a dose of about 20 mg/kg.
18. The method or the antibody for use of any one of claims 1-17, wherein the anti-CCL24 monoclonal antibody is administered subcutaneously.
19. The method or the antibody for use of any one of claims 1-17, wherein the anti-CCL24 monoclonal antibody is administered intravenously.
20. The method or the antibody for use of any one of claims 1-19, wherein the anti-CCL24 monoclonal antibody is administered once every one to four weeks.
21. The method or the antibody for use of claim 20, wherein the anti-CCL24 monoclonal antibody is administered once every two weeks.
22. The method or the antibody for use of claim 20, wherein the anti-CCL24 monoclonal antibody is administered once every three weeks.
23. The method or the antibody for use of claim 20, wherein the anti-CCL24 monoclonal antibody is administered once every four weeks.
24. The method or the antibody for use of any one of claims 1-23, wherein the subject maintains a steady-state serum concentration of the anti-CCL24 monoclonal antibody of about 10 to about 1000 µg/mL.
25. The method or the antibody for use of claim 24, wherein the subject maintains a steady-state serum concentration of the anti-CCL24 monoclonal antibody of about 60 to about 90 µg/mL.
26. The method or the antibody for use of claim 24, wherein the subject maintains a steady-state serum concentration of the anti-CCL24 monoclonal antibody of about 70 to about 300 µg/mL.
27. The method or the antibody for use of any one of claims 24-26, wherein the anti-CCL24 monoclonal antibody reaches the steady-state serum concentration following three administrations.

28. The method or the antibody for use of any one of claims 1-27, wherein the anti-CCL24 monoclonal antibody is administered for at least four weeks.
29. The method or the antibody for use of claim 28, wherein the anti-CCL24 monoclonal antibody is administered for at least 15 weeks.
30. The method or the antibody for use of claim 28, wherein the anti-CCL24 monoclonal antibody is administered for at least 24 weeks.
31. The method or the antibody for use of any one of claims 1-30, wherein the half-life of the anti-CCL24 monoclonal antibody is about 10-30 days.
32. The method or the antibody for use of claim 31, wherein the half-life of the anti-CCL24 monoclonal antibody is about 17 days.
33. The method or the antibody for use of claim 31, wherein the half-life of the anti-CCL24 monoclonal antibody is about 19 days.
34. The method or the antibody for use of any one of claims 1-33, wherein the fibrotic inflammatory disease is nonalcoholic steatohepatitis (NASH).
35. The method or the antibody for use of any one of claims 1-33, wherein the fibrotic inflammatory disease is primary sclerosing cholangitis (PSC).
36. The method or the antibody for use of any one of claims 1-33, wherein the fibrotic inflammatory disease is systemic sclerosis (SSC).
37. The method or the antibody for use of any one of claims 1-36, 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.
38. The method or the antibody for use of any one of claims 1-37, wherein administration of the anti-CCL24 monoclonal antibody improves hepatic condition of the subject as evaluated by one or more circulating fibrosis markers.

39. The method or the antibody for use of claim 38, 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).
40. The method or the antibody for use of claim 38 or 39, wherein the one or more circulating fibrosis markers are measured by Enhanced Liver Fibrosis (ELF) blood test.
41. The method or the antibody for use of claim 39 or 40, wherein administration of the anti-CCL24 monoclonal antibody decreases serum level of Tissue Inhibitor of Metalloproteinases 1 (TIMP-1) by at least 10% compared to baseline before administering the anti-CCL24 monoclonal antibody.
42. The method or the antibody for use of any one of claims 39-41, wherein administration of the anti-CCL24 monoclonal antibody decreases serum level of Tissue Inhibitor of Metalloproteinases 2 (TIMP-2) by at least 5% compared to baseline before administering the anti-CCL24 monoclonal antibody.
43. The method or the antibody for use of any one of claims 39-42, wherein administration of the anti-CCL24 monoclonal antibody decreases serum level of PDGF AA by at least 5% or at least 10% compared to baseline before administering the anti-CCL24 monoclonal antibody.
44. The method or the antibody for use of any one of claims 1-43, wherein administration of the anti-CCL24 monoclonal antibody improves hepatic condition as evaluated by one or more imaging tests.
45. The method or the antibody for use of claim 44, wherein the one or more imaging tests comprise Magnetic Resonance Imaging Proton Density Fat Fraction (MRI-PDFF), liver elastography and/or FibroScan.

46. The method or the antibody for use of claim 44 or 45, wherein administration of the anti-CCL24 monoclonal antibody decreases liver fat content of the subject by at least 15% compared to baseline before administering the anti-CCL24 monoclonal antibody.
47. The method of any one of claims 44-46, wherein administration of the anti-CCL24 monoclonal antibody decreases liver stiffness by at least 0.5 kPa compared to baseline before administering the anti-CCL24 monoclonal antibody as measured by FibroScan.
48. The method or the antibody for use of any one of claims 1-47, wherein administration of the anti-CCL24 monoclonal antibody improves hepatic condition as evaluated by one or more tests for liver enzyme function.
49. The method or the antibody for use of claim 48, wherein administration of the anti-CCL24 monoclonal antibody decreases γ -glutamyltransferase (GGT) level by at least 20% compared to baseline before administering the anti-CCL24 monoclonal antibody.
50. The method or the antibody for use of claim 48 or 49, wherein administration of the anti-CCL24 monoclonal antibody decreases alanine aminotransferase (ALT) level by at least 10% compared to baseline before administering the anti-CCL24 monoclonal antibody.
51. The method or the antibody for use of any one of claims 1-50, wherein administration of the anti-CCL24 monoclonal antibody causes no dose limiting toxicity.
52. The method or the antibody for use of any one of claims 1-51, wherein administration of the anti-CCL24 monoclonal antibody causes no injection site reaction.
53. The method or the antibody for use of any one of claims 1-52, wherein administration of the anti-CCL24 monoclonal antibody causes no severe or serious adverse event (AE).
54. The method or the antibody for use of any one of claims 1-53, wherein administration of the anti-CCL24 monoclonal antibody does not elevate level of triglycerides (TG), low-density lipoprotein (LDL) and/or Cholesterol in the subject's blood.
55. A method of treating nonalcoholic steatohepatitis (NASH) in a human subject, comprising administering an effective amount of an anti-CCL24 monoclonal antibody or a pharmaceutical composition thereof.

56. An anti-CCL24 monoclonal antibody or a pharmaceutical composition thereof for use in a method of treating nonalcoholic steatohepatitis (NASH) in a human subject, said method comprising administering an effective amount of said anti-CCL24 monoclonal antibody or a pharmaceutical composition thereof to the human subject.
57. The method of claim 55 or the antibody for use of claim 56, 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.
58. The method or the antibody for use of any one of claims 55-57, wherein the anti-CCL24 monoclonal antibody is administered at a dose of about 2.5 mg/kg, about 5 mg/kg, or about 10 mg/kg.
59. The method or the antibody for use of any one of claims 55-57, wherein the anti-CCL24 monoclonal antibody is administered at a dose of about 5 mg/kg.
60. The method or the antibody for use of any one of claims 55-59, wherein the anti-CCL24 monoclonal antibody is administered subcutaneously.
61. The method or the antibody for use of any one of claims 55-60, wherein the anti-CCL24 monoclonal antibody is administered once every two weeks.
62. The method or the antibody for use of any one of claims 55-61, wherein the subject maintains a steady state serum concentration of the anti-CCL24 monoclonal antibody of about 60 to about 90 $\mu\text{g/mL}$.
63. The method or the antibody for use of any one of claims 55-62, wherein the anti-CCL24 monoclonal antibody reaches the steady state serum concentration following 3 administrations.
64. The method or the antibody for use of any one of claims 55-63, wherein the anti-CCL24 monoclonal antibody is administered for at least 14 weeks.
65. The method or the antibody for use of any one of claims 55-64, wherein the half-life of the anti-CCL24 monoclonal antibody is about 16 days.
66. The method or the antibody for use of any one of claims 55-65, 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.

67. The method or the antibody for use of any one of claims 55-66, wherein administration of the anti-CCL24 monoclonal antibody improves hepatic condition of the subject as evaluated by one or more circulating fibrosis markers.

68. The method or the antibody for use of any one of claims 55-67, wherein administration of the anti-CCL24 monoclonal antibody decreases liver fat content of the subject compared to baseline before administering the anti-CCL24 monoclonal antibody as measured by MRI-PDFF.

69. The method or the antibody for use of any one of claims 55-68, wherein administration of the anti-CCL24 monoclonal antibody decreases liver stiffness compared to baseline before administering the anti-CCL24 monoclonal antibody as measured by FibroScan.

70. A method of treating primary sclerosing cholangitis (PSC) in a human subject, comprising administering an effective amount of an anti-CCL24 monoclonal antibody or a pharmaceutical composition thereof.

71. An anti-CCL24 monoclonal antibody or a pharmaceutical composition thereof for use in a method of treating primary sclerosing cholangitis (PSC) in a human subject, said method comprising administering an effective amount of said anti-CCL24 monoclonal antibody or a pharmaceutical composition thereof to the human subject.

72. The method of claim 70 or the antibody for use of claim 71, 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.

73. The method or the antibody for use of any one of claims 70-72, wherein the anti-CCL24 monoclonal antibody is administered at a dose of about 5mg/kg, about 10 mg/kg, or about 20mg/kg.

74. The method or the antibody for use of any one of claims 70-72, wherein the anti-CCL24 monoclonal antibody is administered at a dose of about 10 mg/kg.

75. The method or the antibody for use of any one of claims 70-74, wherein the anti-CCL24 monoclonal antibody is administered intravenously.

76. The method or the antibody for use of any one of claims 70-75, wherein the anti-CCL24 monoclonal antibody is administered once every three weeks.
77. The method or the antibody for use of any one of claims 70-76, wherein the subject maintains a steady state serum concentration of the anti-CCL24 monoclonal antibody of about 70 to about 300 µg/mL.
78. The method or the antibody for use of any one of claims 70-77, wherein the anti-CCL24 monoclonal antibody reaches the steady state serum concentration following 3 administrations.
79. The method or the antibody for use of any one of claims 70-78, wherein the anti-CCL24 monoclonal antibody is administered for at least 12 weeks.
80. The method or the antibody for use of any one of claims 70-79, wherein the half-life of the anti-CCL24 monoclonal antibody is about 19 days.
81. The method or the antibody for use of any one of claims 70-80, wherein administration of the anti-CCL24 monoclonal antibody lowers the level of steady state serum concentration of CCL24 compared to baseline before administering the anti-CCL24 monoclonal antibody.
82. The method or the antibody for use of any one of claims 70-81, wherein administration of the anti-CCL24 monoclonal antibody improves hepatic condition of the subject as evaluated by one or more circulating fibrosis markers.
83. The method or the antibody for use of claim 82, wherein administration of the anti-CCL24 monoclonal antibody lowers the level of circulating alkaline phosphatase (ALP) compared to baseline before administering the anti-CCL24 monoclonal antibody.
84. The method or the antibody for use of claim 82 or 83, wherein administration of the anti-CCL24 monoclonal antibody lowers Enhanced Liver Fibrosis (ELF) score compared to baseline before administering the anti-CCL24 monoclonal antibody.
85. The method or the antibody for use of any one of claims 82-84, wherein administration of the anti-CCL24 monoclonal antibody lowers the level of circulating PRO-C3, PRO-C4, C3M, and/or PRO-C5 compared to baseline before administering the anti-CCL24 monoclonal antibody.

86. The method or the antibody for use of any one of claims 70-85, wherein administration of the anti-CCL24 monoclonal antibody decreases liver stiffness compared to baseline before administering the anti-CCL24 monoclonal antibody as measured by FibroScan.
87. A method of treating systemic sclerosis (SSc) in a human subject, comprising administering an effective amount of an anti-CCL24 monoclonal antibody or a pharmaceutical composition thereof.
88. An anti-CCL24 monoclonal antibody or a pharmaceutical composition thereof for use in a method of treating systemic sclerosis (SSc) in a human subject, said method comprising administering an effective amount of said anti-CCL24 monoclonal antibody or a pharmaceutical composition thereof to the human subject.
89. The method of claim 87 or the antibody for use of claim 88, 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.
90. The method or the antibody for use of any one of claims 87-89, wherein the anti-CCL24 monoclonal antibody is administered at a dose of about 2.5-10 mg/kg.
91. The method or the antibody for use of any one of claims 87-90, wherein the anti-CCL24 monoclonal antibody is administered intravenously.
92. The method or the antibody for use of any one of claims 87-91, wherein the anti-CCL24 monoclonal antibody is administered once every two, three, or four weeks.
93. The method or the antibody for use of any one of claims 87-92, wherein the subject maintains a steady state serum concentration of the anti-CCL24 monoclonal antibody of about 70 to about 300 $\mu\text{g/mL}$.
94. The method or the antibody for use of any one of claims 87-93, wherein the anti-CCL24 monoclonal antibody reaches the steady state serum concentration following 3 administrations.
95. The method or the antibody for use of any one of claims 87-94, wherein the anti-CCL24 monoclonal antibody is administered for at least 24 weeks.
96. The method or the antibody for use of any one of claims 87-95, 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.

97. The method or the antibody for use of any one of claims 87-96, wherein administration of the anti-CCL24 monoclonal antibody improves Combined Response Index for Systemic Sclerosis (CRISS) score of the subject compared to baseline before administering the anti-CCL24 monoclonal antibody.

98. The method or the antibody for use of any one of claims 87-97, wherein administration of the anti-CCL24 monoclonal antibody lowers the level of one or more circulating fibrosis markers compared to baseline before administering the anti-CCL24 monoclonal antibody.

99. The method or the antibody for use of any one of claims 87-98, wherein administration of the anti-CCL24 monoclonal antibody improves lung function of the subject compared to baseline before administering the anti-CCL24 monoclonal antibody.

100. 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.

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

102. The pharmaceutical composition of claim 101, comprising about 175 mg/mL the anti-CCL24 monoclonal antibody.

103. The pharmaceutical composition of any one of claims 100-102, comprising a histidine buffer, optionally at about 10 mM.

104. The pharmaceutical composition of any one of claims 100-103, comprising a sodium or potassium phosphate buffer, optionally at about 10 mM.

105. The pharmaceutical composition of any one of claims 100-104, further comprising arginine, optionally at between about 30 and about 200 mM, or optionally at about 150 mM.

106. The pharmaceutical composition of any one of claims 100-105, further comprising glutamic acid, optionally at between about 30 and about 200 mM, or optionally at about 150 mM.

107. The pharmaceutical composition of any one of claims 100-106, further comprising sorbitol, optionally at about 4%.
108. The pharmaceutical composition of any one of claims 100-107, further comprising glycine, optionally at about 10 mM to about 100 mM, or optionally about 40 mM.
109. The pharmaceutical composition of any one of claims 100-108, further comprising polysorbate, optionally polysorbate-80, optionally at about 0.02% or about 0.01%.
110. The pharmaceutical composition of any one of claims 100-109, wherein the pharmaceutical composition has a pH of 5 to 8.
111. The pharmaceutical composition of any one of claims 100-109, wherein the pharmaceutical composition has a pH of 6 to 7, optionally 6.1 or 6.3.
112. The pharmaceutical composition of any one of claims 100-111, 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.
113. The pharmaceutical composition of any one of claims 100-112, comprising about 5 to about 20 mg/mL the anti-CCL24 monoclonal antibody.
114. The pharmaceutical composition of any one of claims 100-112, comprising about 10 mg/mL the anti-CCL24 monoclonal antibody.
115. 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 100-114.
116. The pharmaceutical composition of any one of claims 100-114 for use in a method of treating nonalcoholic steatohepatitis (NASH) in a human subject.
117. 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 100-114.
118. The pharmaceutical composition of any one of claims 100-114 for use in a method of treating primary sclerosing cholangitis (PSC) in a human subject.

119. 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 100-114.
120. The pharmaceutical composition of any one of claims 100-114 for use in a method of treating Systemic Sclerosis (SSc) in a human subject.
121. The method or the pharmaceutical composition for use of any one of claims 115-120, wherein the administering step comprises subcutaneous administration.
122. The method or the pharmaceutical composition for use of any one of claims 115-120, wherein the administering step comprises intravenous administration.
123. A kit comprising the pharmaceutical composition of any one of claims 100-114 and instructions for use.