

CLAIMS

WHAT IS CLAIMED IS:

1. An antibody, comprising:
 - (a) a light chain CDR1 sequence comprising the formula:
RASQSI X_8 YLN (SEQ ID NO: 13), wherein X_8 is S, R, K, or H; and
 - (b) a light chain CDR2 sequence comprising the formula:
AASSLQ X_9 (SEQ ID NO: 14), wherein X_9 is S, N, Q, or T; and
 - (c) a light chain CDR3 sequence comprising the formula:
QQSYST X_{10} X_{11} G X_{12} (SEQ ID NO: 15), wherein X_{10} is P, Q, T, S, N, A, or G; X_{11} is R, G, A, or S; and X_{12} is T, S, A, G, or N; and
 - (d) a heavy chain CDR1 sequence comprising the formula:
S X_1 X_2 MH (SEQ ID NO: 25), wherein X_1 is Y, E, Q, or D; and X_2 is A, D, T, V, S, G, or E; and
 - (e) a heavy chain CDR2 sequence comprising the formula:
VIS X_3 DGSNKY X_4 ADSVKG (SEQ ID NO: 26), wherein X_3 is Y, E, Q, or D; and X_4 is Y, N, H, E, D, K, Q, or R; and
 - (f) a heavy chain CDR3 sequence comprising the formula:
ENVRPYYDFW X_5 G X_6 SEYYYYG X_7 DV (SEQ ID NO: 27), wherein X_5 is S, R, K, or H; X_6 is Y, S, N, T, A, or Q; and X_7 is M, L, I, or V;provided that the antibody does not comprise a sequence as set forth in SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3.
2. The antibody of claim 1, comprising:
 - (a) a heavy chain variable region (VH) having a sequence at least 90% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, AND SEQ ID NO: 41; and
 - (b) a light chain variable region (VL) having a sequence at least 90% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, AND SEQ ID NO: 40;provided that the antibody does not comprise a light chain variable region (VL) having a sequence as set forth in SEQ ID NO: 40 and a heavy chain variable region (VH) having a sequence as set forth in SEQ ID NO. 41.

3. The antibody of claim 1, wherein:

(a) the light chain CDR1 has an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 1, SEQ ID NO: 7, and SEQ ID NO: 13; a light chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 2, SEQ ID NO: 9, and SEQ ID NO: 14; and a light chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 3, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, and SEQ ID NO: 15; and

(b) the heavy chain CDR1 has an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 4, SEQ ID NO: 16, SEQ ID NO: 19, SEQ ID NO: 22 and SEQ ID NO: 25; a heavy chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 5, SEQ ID NO: 17, SEQ ID NO: 20, SEQ ID NO: 23, and SEQ ID NO: 26; a heavy chain CDR3 having an amino acid sequence 100%, identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 6, SEQ ID NO: 18, SEQ ID NO: 21, SEQ ID NO: 24, and SEQ ID NO: 27;

provided that the antibody does not comprise a sequence at least as set forth in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6.

4. The antibody of claim 1, wherein the light chain variable region (VL) has a sequence at least 95% identical to the amino acid sequence selected from the group consisting of: SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, AND SEQ ID NO: 40.
5. The antibody of claim 1, wherein the light chain variable region (VL) has a sequence at least 99% identical to the amino acid sequence selected from the group consisting of: SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, AND SEQ ID NO: 40.
6. The antibody of claim 1, wherein the light chain variable region (VL) has a sequence 100% identical to the amino acid sequence selected from the group consisting of: SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, AND SEQ ID NO: 40.
7. The antibody of claim 1, wherein the heavy chain variable region (VH) has a sequence at least 95% identical to the amino acid sequence selected from the group consisting of:

- SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, AND SEQ ID NO: 41.
8. The antibody of claim 1, wherein the heavy chain variable region (VH) has a sequence at least 99% identical to the amino acid sequence selected from the group consisting of: SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, AND SEQ ID NO: 41.
9. The antibody of claim 1, wherein the heavy chain variable region (VH) has a sequence 100% identical to the amino acid sequence selected from the group consisting of: SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, AND SEQ ID NO: 41.
10. An antibody, comprising:
- (a) a light chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 1, SEQ ID NO: 7, and SEQ ID NO: 13; a light chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 2, SEQ ID NO: 9, and SEQ ID NO: 14; and a light chain CDR3 having an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 3, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, and SEQ ID NO: 15; and
- (b) a heavy chain CDR1 having an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 4, SEQ ID NO: 16, SEQ ID NO: 19, SEQ ID NO: 22 and SEQ ID NO: 25; a heavy chain CDR2 having an amino acid sequence 100% identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 5, SEQ ID NO: 17, SEQ ID NO: 20, SEQ ID NO: 23, and SEQ ID NO: 26; a heavy chain CDR3 having an amino acid sequence 100%, identical to an amino acid sequence set forth in the group consisting of: SEQ ID NO: 6, SEQ ID NO: 18, SEQ ID NO: 21, SEQ ID NO: 24, and SEQ ID NO: 27;
- provided that the antibody does not comprise a sequence at least as set forth in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6.
11. The antibody of claim 10, comprising:
- (a) a heavy chain variable region (VH) having a sequence at least 90% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 29, SEQ ID

NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, AND SEQ ID NO: 41; and

(b) a light chain variable region (VL) having a sequence at least 90% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, AND SEQ ID NO: 40.

12. The antibody of claim 10, comprising:

(a) a heavy chain variable region (VH) having a sequence at least 95% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, AND SEQ ID NO: 41; and

(b) a light chain variable region (VL) having a sequence at least 95% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, AND SEQ ID NO: 40.

13. The antibody of claim 10, comprising:

(a) a heavy chain variable region (VH) having a sequence at least 99% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, AND SEQ ID NO: 41; and

(b) a light chain variable region (VL) having a sequence at least 99% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, AND SEQ ID NO: 40.

14. The antibody of claim 10, comprising:

(a) a heavy chain variable region (VH) having a sequence 100% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, AND SEQ ID NO: 41; and

(b) a light chain variable region (VL) having a sequence 100% identical to an amino acid sequence selected from the group consisting of: SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, AND SEQ ID NO: 40.

15. The antibody of any one of claims 1-14, wherein the antibody further comprises a human heavy chain constant region or a human light chain constant region.
16. The antibody of any one of claims 1-15, wherein the antibody binds to an Fc receptor.
17. The antibody of claim 16, wherein the Fc receptor is expressed on the macrophage.
18. The antibody of any one of claims 1-17, wherein the antibody binds to an immunosuppressive myeloid cell.
19. The antibody of claim 17 or 18, wherein the immunosuppressive myeloid cell is a macrophage or a myeloid-derived suppressor cell.
20. The antibody of any one of claims 1-19, wherein the antibody binds to a CD163 protein.
21. The antibody of any one of claims 1-20, wherein the antibody specifically binds to a CD163 epitope comprising amino acid sequence SEQ ID NO: 42.
22. The antibody of any one of claims 1-20, wherein the antibody specifically binds to a CD163 epitope comprising amino acid sequence SEQ ID NO: 43.
23. The antibody of any one of claims 1-20, wherein the antibody specifically binds to a CD163 epitope comprising amino acid sequence SEQ ID NO: 44.
24. The antibody of any one of claims 1-20, wherein the antibody specifically binds to a CD163 epitope comprising each of amino acid sequence SEQ ID NO: 42, SEQ ID NO: 43, and SEQ ID NO: 44.
25. Use of an antibody according to any one of claims 1-24 in the manufacture of a medicament for the treatment of a cancer in a subject in need thereof, wherein the medicament is to be administered in a therapeutically effective amount to the subject.
26. Use of an antibody according to any one of claims 1-24 in the manufacture of a medicament for the treatment of a fibrotic disease or disorder associated with a presence of M2 macrophages in a subject in need thereof, wherein the medicament is to be administered in a therapeutically effective amount to the subject.
27. The use of claim 25, wherein the cancer is a lung cancer.
28. The use of claim 25, wherein the cancer is a lung carcinoma or a lung sarcoma.
29. The use of claim 25, wherein the cancer is a lung adenocarcinoma.
30. The use of any one of claims 25-29, wherein an anti-cancer therapeutic is to be further administered to the subject.
31. The use of claim 26, wherein the fibrotic disease or disorder is lung fibrosis.
32. The use of claim 26, wherein the fibrotic disease or disorder is cardiac fibrosis.
33. The use of claim 26, wherein the fibrotic disease or disorder is hepatic fibrosis.
34. The use of claim 26, wherein the fibrotic disease or disorder is renal fibrosis.

35. The use of claim 26, wherein the fibrotic disease or disorder is retinal fibrosis.
36. The use of claim 26, wherein the fibrosis is a primary fibrotic disease or disorder.
37. The use of claim 36, wherein the primary fibrotic disease or disorder is idiopathic pulmonary fibrosis (IPF).
38. The use of claim 36, wherein the primary fibrotic disease or disorder is hepatic cirrhosis.
39. The use of claim 36, wherein the primary fibrotic disease or disorder is systemic sclerosis.
40. The use of claim 36, wherein the primary fibrotic disease or disorder is radiation fibrosis.
41. The use of claim 36, wherein the primary fibrotic disease or disorder is scarring associated with a mechanical injury.
42. The use of claim 26, wherein the fibrosis is a secondary fibrotic disease.
43. The use of claim 42, wherein the secondary fibrotic disease is associated with a disease or disorder selected from the group consisting of an infection, an autoimmune disease or disorder, cancer, and an inflammatory disease or disorder.
44. The use of claim 42, wherein the secondary fibrotic disease is associated with a disease or disorder selected from the group consisting of: atherosclerosis, atrial fibrillation, chronic heart failure, peripheral artery disease, acute coronary syndromes, non-alcoholic fatty liver disease (NAFLD), acute-on-chronic liver failure, acute liver failure, acute kidney injury, acute tubular necrosis, and chronic kidney disease.
45. The use of claim 43, wherein the infection is selected from the group consisting of: sepsis, an HIV infection, a SARS-CoV-2 infection, acute viral hepatitis, chronic viral hepatitis, and malaria.
46. The use of claim 43, wherein the autoimmune or inflammatory disease or disorder or is selected from the group consisting of: acute lung injury (ALI), acute respiratory distress syndrome (ARDS), hypersensitivity pneumonitis, alcoholic hepatitis, non-alcoholic steatohepatitis, viral hepatitis, sickle cell disease, Type 1 diabetes mellitus, Type 2 diabetes mellitus, Crohn's disease, celiac disease, asthma, sarcoidosis, glomerulonephritis, lupus nephritis, systemic lupus erythematosus, rheumatoid arthritis, Sjögren's Syndrome, scleroderma, cystic fibrosis (CF), graft-versus-host disease, allograft rejection, kidney allograft rejection, sarcoidosis, pulmonary sarcoidosis, hemophagocytic lymphohistiocytosis (HLH), inflammatory arthritis, chronic obstructive pulmonary disease (COPD), asthma, osteoarthritis, fibroids, and multiple sclerosis.
47. The use according to any one of claims 25 and 31-46, wherein an anti-inflammatory therapy is to be further administered to the subject.

48. A pharmaceutical composition, comprising (a) an antibody according to any one of claims 1-20, and (b) a pharmaceutically acceptable excipient.
49. The pharmaceutical composition of claim 48, wherein the pharmaceutically acceptable excipient is selected from the group consisting of a stabilizer, buffer, surfactant, filler, solvent, tonicity agent, and antioxidant.
50. The pharmaceutical composition of claim 48, comprising two or more pharmaceutically acceptable excipients independently selected from the group consisting of stabilizers, buffers, surfactants, fillers, solvents, tonicity agents, and antioxidants.
51. Use of a composition of any one of claims 48-50 in the manufacture of a medicament for the treatment of a cancer or a fibrotic disease in a subject.
52. An antibody according to any one of claims 1-24 and a pharmaceutical composition of claim 48 for use in therapy.