

CLAIMS

1. An isolated antibody that binds human CCR8, wherein the antibody comprises:
 - i) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 12, an HCDR2 comprising the amino acid sequence of SEQ ID NO: 13, an HCDR3 comprising the amino acid sequence of SEQ ID NO: 14, an LCDR1 comprising the amino acid sequence of SEQ ID NO: 15, an LCDR2 comprising the amino acid sequence of SEQ ID NO: 16, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 17;
 - ii) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 24, an HCDR2 comprising the amino acid sequence of SEQ ID NO: 25, an HCDR3 comprising the amino acid sequence of SEQ ID NO: 26, an LCDR1 comprising the amino acid sequence of SEQ ID NO: 27, an LCDR2 comprising the amino acid sequence of SEQ ID NO: 28, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 29;
 - iii) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 36, an HCDR2 comprising the amino acid sequence of SEQ ID NO: 37, an HCDR3 comprising the amino acid sequence of SEQ ID NO: 38, an LCDR1 comprising the amino acid sequence of SEQ ID NO: 39, an LCDR2 comprising the amino acid sequence of SEQ ID NO: 40, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 41;
 - iv) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 48, an HCDR2 comprising the amino acid sequence of SEQ ID NO: 49, an HCDR3 comprising the amino acid sequence of SEQ ID NO: 50, an LCDR1 comprising the amino acid sequence of SEQ ID NO: 51, an LCDR2 comprising the amino acid sequence of SEQ ID NO: 52, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 53; or
 - v) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 60, an HCDR2 comprising the amino acid sequence of SEQ ID NO: 61, 72, or 78, an HCDR3 comprising the amino acid sequence of SEQ ID NO: 62, 73, or 79, an LCDR1 comprising the amino acid sequence of SEQ ID NO: 63, an LCDR2 comprising the amino acid sequence of SEQ ID NO: 64, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 65; or
 - vi) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 84 or 100, an HCDR2 comprising the amino acid sequence of SEQ ID NO: 85, an HCDR3 comprising the amino acid sequence of SEQ ID NO: 86, an LCDR1 comprising

the amino acid sequence of SEQ ID NO: 87, an LCDR2 comprising the amino acid sequence of SEQ ID NO: 88, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 89.

2. The isolated antibody of claim 1, wherein the antibody comprises:
 - i) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 60, an HCDR2 comprising the amino acid sequence of SEQ ID NO: 61, 72, or 78, an HCDR3 comprising the amino acid sequence of SEQ ID NO: 62, 73, or 79, an LCDR1 comprising the amino acid sequence of SEQ ID NO: 63, an LCDR2 comprising the amino acid sequence of SEQ ID NO: 64, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 65; or
 - ii) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 84 or 100, an HCDR2 comprising the amino acid sequence of SEQ ID NO: 85, an HCDR3 comprising the amino acid sequence of SEQ ID NO: 86, an LCDR1 comprising the amino acid sequence of SEQ ID NO: 87, an LCDR2 comprising the amino acid sequence of SEQ ID NO: 88, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 89.
3. The isolated antibody of claim 2, wherein the antibody comprises:
 - i) a heavy chain variable region (VH) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 68 or 74, and a light chain variable region (VL) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 69 or 75; or
 - ii) a heavy chain variable region (VH) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 92 or 96, and a light chain variable region (VL) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 93 or 97.
4. The isolated antibody of claim 2 or claim 3, wherein the antibody comprises:
 - i) a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 68 or 74, and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 69 or 75; or

- ii) a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 92 or 96, and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 93 or 97.
- 5. The isolated antibody of any one of claims 1-4, wherein the antibody is a monoclonal antibody.
- 6. The isolated antibody of any one of claims 1-5, wherein the antibody is a humanized antibody.
- 7. The isolated antibody of any one of claims 1-6, wherein the antibody is a full-length antibody.
- 8. The isolated antibody of any one of claims 1-7, wherein the antibody is an IgG1 or IgG3 antibody.
- 9. The isolated antibody of any one of claims 1-8, wherein the antibody comprises:
 - i) a heavy chain (HC) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 70 or 76, and a light chain (LC) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 71 or 77; or
 - ii) a heavy chain (HC) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 94 or 98, and a light chain (LC) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 95 or 99.
- 10. The isolated antibody of any one of claims 1-9, wherein the antibody comprises:
 - i) a heavy chain (HC) comprising the amino acid sequence of SEQ ID NO: 70 or 76, and a light chain (LC) comprising the amino acid sequence of SEQ ID NO: 71 or 77; or
 - ii) a heavy chain (HC) comprising the amino acid sequence of SEQ ID NO: 94 or 98, and a light chain (LC) comprising the amino acid sequence of SEQ ID NO: 95 or 99.
- 11. The isolated antibody of any one of claims 1-10, wherein the antibody comprises at least one modification that enhances cell killing.
- 12. The isolated antibody of claim 11, wherein the enhanced cell killing is enhanced antibody-dependent cellular cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC).

13. The isolated antibody of claim 11 or claim 12, wherein the at least one modification is afucosylation.
14. The isolated antibody of claim 11 or claim 12, wherein the at least one modification is one or more heavy chain constant regions mutations at one or more positions selected from L234, L235, G236, S239, F243, H268, D270, R292, S298, Y300, V305, K326, A330, I332, E333, K334, and P396.
15. The isolated antibody of claim 14, wherein the one or more heavy chain constant region mutations are one or more mutation selected from S239D, S239M, F243L, H268D, D270E, R292P, S298A, Y300L, V305I, K326D, A330L, A330M, I332E, E333A, K334A, K334E, and P396L.
16. The isolated antibody of claim 14, wherein the one or more heavy chain constant region mutations are selected from: F243L/R292P/Y300L/V305I/P396L, S239D/I332E, S239D/I332E/A330L, S298A/E333A/K334A, L234Y/L235Q/G236W/S239M/H268D/D270E/S298A, and D270E/K326D/A330M/K334E.
17. The isolated antibody of claim 11 or claim 12, wherein the at least one modification is galactosylation.
18. The isolated antibody of any one of claims 1-17, wherein the antibody binds human CCR8 with an affinity (K_D) of less than 10 nM, or less than 5 nM, or less than 1 nM, or less than 500 pM, or less than 250 pM, or less than 100 pM, or less than 75 pM, or less than 50 pM, or less than 25 pM.
19. The isolated antibody of any one of claims 1-18, wherein the antibody binds human CCR8 with an on-cell affinity (K_D) of less than 10 nM, or less than 5 nM, or less than 1 nM, or less than 500 pM, or less than 250 pM, or less than 100 pM, or less than 75, or less than 50 pM, or less than 25 pM.
20. The isolated antibody of claim 18 or 19, wherein the affinity (K_D) is determined by Kinetic Exclusion Assay (i.e., KinExA).
21. An isolated nucleic acid that encodes the antibody of any one of claims 1-20.
22. A vector comprising the isolated nucleic acid of claim 21.
23. A host cell comprising the nucleic acid of claim 21 or the vector of claim 22.
24. A host cell that expresses the antibody of any one of claims 1-20.
25. The host cell of claim 23 or claim 24, which is engineered to produce afucosylated antibodies.
26. A method of producing an antibody that binds CCR8 comprising culturing the host cell of any one of claims 23-25 under conditions suitable for expressing the antibody.
27. The method of claim 26, further comprising isolating the antibody.

28. A fusion protein comprising (a) CCL1 or an active fragment thereof or MC148 or an active fragment thereof, and (b) an Fc region.
29. The fusion protein of claim 28, wherein the Fc region is an IgG1 or IgG3 Fc region.
30. The fusion protein of claim 28 or claim 29, wherein the Fc region comprises the amino acid sequence of SEQ ID NO: 4.
31. The fusion protein of any one of claims 28-30, wherein the Fc region comprises at least one modification that enhances cell killing.
32. The fusion protein of claim 31, wherein the enhanced cell killing is enhanced antibody-dependent cellular cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC).
33. The fusion protein of claim 31 or claim 32, wherein the at least one modification is afucosylation.
34. The fusion protein of claim 31 or claim 32, wherein the at least one modification is one or more Fc region mutations at one or more positions selected from L234, L235, G236, S239, F243, H268, D270, R292, S298, Y300, V305, K326, A330, I332, E333, K334, and P396.
35. The fusion protein of claim 34, wherein the one or more Fc region mutations are one or more mutation selected from S239D, S239M, F243L, H268D, D270E, R292P, S298A, Y300L, V305I, K326D, A330L, A330M, I332E, E333A, K334A, K334E, and P396L.
36. The fusion protein of claim 34, wherein the one or more Fc region mutations are selected from: F243L/R292P/Y300L/V305I/P396L, S239D/I332E, S239D/I332E/A330L, S298A/E333A/K334A, L234Y/L235Q/G236W/S239M/H268D/D270E/S298A, and D270E/K326D/A330M/K334E.
37. The fusion protein of claim 31 or claim 32, wherein the at least one modification is galactosylation.
38. The fusion protein of any one of claims 28-37, wherein the fusion protein comprises CCL1 or an active fragment thereof.
39. The fusion protein of claim 38, wherein the CCL1 or active fragment thereof comprises the amino acid sequence of SEQ ID NO: 2 or amino acids 24-96 of SEQ ID NO: 2.
40. The fusion protein of claim 38 or claim 39, wherein the fusion protein comprises the amino acid sequence of SEQ ID NO: 1 or amino acids 24-316 of SEQ ID NO: 1.
41. The fusion protein of any one of claims 28-37, wherein the fusion protein comprises MC148 or an active fragment thereof.
42. The fusion protein of claim 41, wherein the MC148 or active fragment thereof comprises the amino acid sequence of SEQ ID NO: 6.

43. The fusion protein of claim 41 or claim 42, wherein the fusion protein comprises the amino acid sequence of SEQ ID NO: 5.
44. An isolated nucleic acid that encodes the fusion protein of any one of claims 28-43.
45. A vector comprising the isolated nucleic acid of claim 44.
46. A host cell comprising the nucleic acid of claim 44 or the vector of claim 45.
47. A host cell that expresses the fusion protein of any one of claims 28-43.
48. The host cell of claim 46 or claim 47, which is engineered to produce afucosylated antibodies.
49. A method of producing a fusion protein comprising culturing the host cell of any one of claims 46-48 under conditions suitable for expressing the fusion protein.
50. The method of claim 49, further comprising isolating the fusion protein.
51. A method of treating cancer, comprising administering to a subject with cancer an effective amount of the antibody of any one of claims 1-20.
52. A method of treating cancer, comprising administering to a subject with cancer an effective amount of the fusion protein of any one of claims 28-43.
53. The method of claim 51 or 52, wherein the subject has previously received treatment with a checkpoint inhibitor (CPI), and, optionally, wherein the cancer was resistant to the CPI.
54. The method of any one of claims 51-53, wherein the cancer comprises tumor-infiltrating Treg cells.
55. The method of any one of claims 51-53, wherein the cancer comprises cells that express CCR8.
56. The method of claim 55, wherein the cells that express CCR8 are Treg cells.
57. The method of claim 56, wherein CCR8 is expressed on the surface of the Treg cells at fewer than 10,000 copies per cell (as determined fluorescence-activated cell sorting (FACS) and/or flow cytometry).
58. The method of any one of claims 51-57, wherein the cancer comprises tumor cells that express CCR8.
59. The method of any one of claims 51-58, wherein the cancer is selected from breast cancer, colorectal cancer, head and neck cancer, lung cancer, ovarian cancer, gastric cancer, stomach adenocarcinoma, and thymoma.
60. The method of any one of claims 51-59, wherein the cancer is a refractory cancer or resistant to checkpoint inhibitor (CPI) therapy.

61. The method of claim 60, wherein the CPI therapy comprises an anti-PDL1 antibody, an anti-CTLA4 antibody, or an anti-TIGIT antibody.
62. The method of claim 61, wherein the anti-PDL1 antibody is selected from pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, cemiplimab-rwlc, and zimberelimab; wherein the anti-CLTA4 antibody is ipilimumab or tremelimumab; or wherein the anti-TIGIT antibody is selected from tiragolumab, vibostolimab, domvanalimab, AB308, BMS-986207, and durvalumab.
63. A method of treating blood cancer, comprising administering to a subject with blood cancer an effective amount of an antibody that binds human CCR8.
64. The method of claim 63, wherein the subject has previously received treatment with a checkpoint inhibitor (CPI), and, optionally, wherein the cancer was resistant to the CPI.
65. The method of claim 63 or 64, wherein the antibody inhibits binding of CCL1 to CCR8.
66. The method of any one of claims 63-65, wherein the blood cancer expresses CCR8.
67. The method of any one of claims 63-66, wherein the blood cancer is a refractory cancer or resistant to checkpoint inhibitor (CPI) therapy.
68. The method of claim 67, wherein the CPI therapy comprises an anti-PDL1 antibody, an anti-CTLA4 antibody, or an anti-TIGIT antibody.
69. The method of claim 68, wherein the anti-PDL1 antibody is selected from pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, cemiplimab-rwlc, and zimberelimab; wherein the anti-CLTA4 antibody is ipilimumab or tremelimumab; or wherein the anti-TIGIT antibody is selected from tiragolumab, vibostolimab, domvanalimab, AB308, BMS-986207, and durvalumab.
70. A method of selecting a subject with blood cancer for treatment with an antibody that binds human CCR8, comprising detecting CCR8 expression in a sample from the subject.
71. The method of claim 70, further comprising administering an effective amount of an antibody that binds human CCR8.
72. The method of any one of claims 63-71, wherein the antibody that binds human CCR8 is the antibody of any one of claims 1-20.
73. A method of treating blood cancer, comprising administering to a subject with blood cancer an effective amount of the fusion protein of any one of claims 28-43.
74. A method of selecting a subject with blood cancer for treatment with a fusion protein comprising (a) CCL1 or an active fragment thereof or MC148 or an active fragment

thereof, and (b) an Fc region, comprising detecting CCR8 expression in a sample from the subject.

75. The method of claim 74, further comprising administering an effective amount of a fusion protein comprising (a) CCL1 or an active fragment thereof or MC148 or an active fragment thereof, and (b) an Fc region.

76. The method of claim 75, wherein the fusion protein is the fusion protein of any one of claims 28-43.

77. The method of any one of claims 73-76, wherein the blood cancer is T-cell adult acute lymphocytic leukemia, T-cell childhood acute lymphocytic leukemia, lymphoblastic lymphoma, acute lymphocytic leukemia, cutaneous T cell lymphoma, T-cell acute lymphocytic leukemia, adult T cell leukemia/lymphoma, T cell lymphoblastic leukemia/lymphoma, or anaplastic large cell lymphoma.

78. An isolated antibody that binds human CCR8, wherein the antibody comprises a HCDR3 comprising SEQ ID NO: 86 or a variant of SEQ ID NO: 86 comprising 1, 2, or 3 mutations, and wherein the antibody binds to human CCR8 and possesses ADCC activity.

79. The isolated antibody of claim 78, wherein the mutations are selected from a substitution, an insertion, or a deletion.

80. The isolated antibody of claim 78 or 79, wherein the antibody comprises at least 2 substitutions in HCDR3.

81. The isolated antibody of any one of claims 78-80, wherein the 1, 2, or 3 mutations are located in at least one of amino acid positions 1-4, 6, 7, or 12 of SEQ ID NO: 86.

82. The isolated antibody of any one of claims 79-81, wherein the substitution is a conservative substitution.

83. The isolated antibody of claim 82, wherein the conservative substitution is at amino acid position 1, 4, or 12 of SEQ ID NO: 86.

84. The isolated antibody of any one of claims 79-81, wherein the substitution is a non-conservative substitution.

85. The isolated antibody of claim 84, wherein the non-conservative substitution is at amino acid position 7 of SEQ ID NO: 86.

86. The isolated antibody of any one of claims 79-81, wherein the mutations comprise a conservative substitution and a non-conservative substitution when more than one substitution mutation is present.

87. An isolated antibody that binds human CCR8, wherein the antibody comprises a HCDR3 that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%

identical to SEQ ID NO: 86, and wherein the antibody binds to human CCR8 and possesses ADCC activity.

88. The isolated antibody of claim 78 or 87, wherein the HCDR3 comprises an amino acid sequence selected from any one of SEQ ID NOs: 104-119.

89. The isolated antibody of any one of claims 78-87, wherein the HCDR3 comprises an amino acid sequence selected from SEQ ID NO: 86 and any one of SEQ ID NOs: 104-119.

90. The isolated antibody of any one of claims 78-89, wherein the antibody comprises a HCDR1 comprising SEQ ID NO: 84 or SEQ ID NO: 123.

91. The isolated antibody of any one of claims 78-90, wherein the antibody comprises a HCDR2 comprising SEQ ID NO: 85 or SEQ ID NO: 124.

92. The isolated antibody of any one of claims 78-91, wherein the antibody comprises a LCDR1 comprising SEQ ID NO: 87 or SEQ ID NO: 120.

93. The isolated antibody of any one of claims 78-92, wherein the antibody comprises a LCDR2 comprising SEQ ID NO: 88 or SEQ ID NO: 121.

94. The isolated antibody of any one of claims 78-93, wherein the antibody comprises a LCDR3 comprising SEQ ID NO: 89 or SEQ ID NO: 122.

95. The isolated antibody of any one of claims 78-94, wherein the antibody comprises a heavy chain variable region (VH) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NOs: 80, 92, and 96, and a light chain variable region (VL) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NOs: 81, 93, and 97.

96. The isolated antibody of any one of claims 78-95, wherein the antibody comprises a heavy chain comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NOs: 82, 90, 94, and 98, and a light chain comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NOs: 83, 91, 95, and 99.

97. The isolated antibody of any one of claims 78-96, wherein ADCC activity comprises an EC50 value of less than 200, 175, 150, 125, 100, 75, 50, 25, 20, 15, 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 ng/ml as measured by an ADCC reporter mechanism of action (MOA)-based bioassay.

98. The isolated antibody of any one of claims 78-97, wherein the ADCC activity is more potent than a 7-B16 antibody.

99. The isolated antibody of any one of claims 78-98, wherein the antibody possesses a K_D for human CCR8 that is equal to or lower than a 7-B16 antibody.
100. The isolated antibody of any one of claims 78-99, wherein the antibody possesses an on-cell K_D for human CCR8 that is equal to or lower than a 7-B16 antibody.
101. The isolated antibody of claim 99 or 100, wherein the K_D is determined by Kinetic Exclusion Assay (i.e., KinExA).
102. The isolated antibody of any one of claims 78-101, wherein the antibody comprises at least one modification that enhances cell killing.
103. The isolated antibody of claim 102, wherein the enhanced cell killing is enhanced antibody-dependent cellular cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC).
104. The isolated antibody of claim 102 or claim 103, wherein the at least one modification is afucosylation.
105. The isolated antibody of claim 102 or claim 103, wherein the at least one modification is one or more heavy chain constant regions mutations at one or more positions selected from L234, L235, G236, S239, F243, H268, D270, R292, S298, Y300, V305, K326, A330, I332, E333, K334, and P396.
106. The isolated antibody of claim 105, wherein the one or more heavy chain constant region mutations are one or more mutation selected from S239D, S239M, F243L, H268D, D270E, R292P, S298A, Y300L, V305I, K326D, A330L, A330M, I332E, E333A, K334A, K334E, and P396L.
107. The isolated antibody of claim 105, wherein the one or more heavy chain constant region mutations are selected from: F243L/R292P/Y300L/V305I/P396L, S239D/I332E, S239D/I332E/A330L, S298A/E333A/K334A, L234Y/L235Q/G236W/S239M/H268D/D270E/S298A, and D270E/K326D/A330M/K334E.
108. The isolated antibody of claim 96 or claim 97, wherein the at least one modification is galactosylation.
109. The isolated antibody of any one of claims 78-108, wherein the antibody binds human CCR8 with an affinity (K_D) of less than 10 nM, or less than 5 nM, or less than 1 nM, or less than 500 pM, or less than 250 pM, or less than 100 pM, or less than 75 pM, or less than 50 pM, or less than 25 pM.
110. The isolated antibody of any one of claims 78-109, wherein the antibody binds human CCR8 with an on-cell affinity (K_D) of less than 10 nM, or less than 5 nM, or less than 1 nM, or less than 500 pM, or less than 250 pM, or less than 100 pM, or less than 75, or less than 50 pM, or less than 25 pM.

111. The isolated antibody of claim 109 or 110, wherein the affinity (K_D) is determined by Kinetic Exclusion Assay (i.e., KinExA).
112. The isolated antibody of any one of claims 78-111, wherein the antibody is a monoclonal antibody.
113. The isolated antibody of any one of claims 78-112, wherein the antibody is a human or humanized antibody.
114. The isolated antibody of any one of claims 78-113, wherein the antibody is a full-length antibody.
115. The isolated antibody of any one of claims 78-114, wherein the antibody is an IgG1 or IgG3 antibody.
116. A nucleic acid encoding an antibody of any one of claims 78-115.
117. A method of treating cancer, comprising administering to a subject with cancer an antibody according to any one of claims 78-115.
118. The method of claim 117, wherein the cancer is a blood cancer or a solid cancer.
119. The method of claim 117 or 118, wherein the cancer expresses CCR8.
120. The method of any one of claims 117-119, wherein the cancer is T-cell adult acute lymphocytic leukemia, T-cell childhood acute lymphocytic leukemia, lymphoblastic lymphoma, acute lymphocytic leukemia, cutaneous T cell lymphoma, T-cell acute lymphocytic leukemia, adult T cell leukemia/lymphoma, T cell lymphoblastic leukemia/lymphoma, or anaplastic large cell lymphoma.
121. The method of any one of claims 117-119, wherein the cancer is selected from breast cancer, colorectal cancer, head and neck cancer, lung cancer, ovarian cancer, gastric cancer, stomach adenocarcinoma, and thymoma.
122. The method of any one of claims 117-121 further comprising administering to the subject one or more additional therapeutic agents.
123. The method of claim 122, wherein the one or more additional therapeutic agents are selected from an anti-Trop-2 antibody (*e.g.*, sacituzumab govitecan, SKB-264, JS-108 (DAC-002), datopotamab deruxtecan, BAT-8003), an anti-CD47 antibody or a CD47-blocking agent (*e.g.*, magrolimab, DSP-107, AO-176, ALX-148, IBI-188, lemozoparlimab, TTI-621, TTI-622), an anti-SIRP α antibody (*e.g.*, GS-0189), a FLT3L-Fc fusion protein (*e.g.*, GS-3583), an anti-PD-1 antibody (pembrolizumab, nivolumab, zimberelimab), a small molecule PD-L1 inhibitor (*e.g.*, GS-4224), an anti-PD-L1 antibody (*e.g.*, atezolizumab), a small molecule MCL1 inhibitor (*e.g.*, GS-9716), a small molecule HPK1 inhibitor (*e.g.*, GS-6451), an HPK1 degrader (PROTAC; *e.g.*, ARV-766), a small molecule DGK α inhibitor, a small molecule CD73 inhibitor (*e.g.*, AB680), an anti-CD73 antibody (*e.g.*, oleclumab), a dual A_{2a}/A_{2b} adenosine receptor

antagonist (*e.g.*, etrumadenant (AB928)), an anti-TIGIT antibody (*e.g.*, tiragolumab, vibostolimab, domvanalimab, AB308), an anti-TREM1 antibody (*e.g.*, PY159), an anti-TREM2 antibody (*e.g.*, PY314), a TGF β -trap (*e.g.*, bintrafusp alpha, AGEN-1423), an anti-TGF β 1 antibody (*e.g.*, SRK-181), and a CAR-T cell therapy (*e.g.*, axicabtagene ciloleucel, brexucabtagene autoleucel, tisagenlecleucel).

124. The method of claim 122, wherein the one or more additional therapeutic agents are selected from sacituzumab govitecan-hziy, magrolimab, GS-0189, GS-3583, zimberelimab, GS-4224, GS-9716, GS-6451, AB680, etrumadenant (AB928), domvanalimab, AB308, PY159, PY314, SRK-181, axicabtagene ciloleucel, and brexucabtagene autoleucel.

125. The method of any one of claims 122-124, wherein administration of the one or more additional therapeutic agents is concurrent with the administration of the antibody.

126. The method of any one of claims 122-124, wherein administration of the one or more additional therapeutic agents is before or after the administration of the antibody.

127. The method of any one of claims 117-126, wherein the cancer is a refractory cancer or resistant to checkpoint inhibitor (CPI) therapy.

128. The method of claim 127, wherein the CPI therapy comprises an anti-PDL1 antibody, an anti-CTLA4 antibody, or an anti-TIGIT antibody.

129. The method of claim 128, wherein the anti-PDL1 antibody is selected from pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, cemiplimab-rwlc, and zimberelimab; wherein the anti-CTLA4 antibody is ipilimumab or tremelimumab; or wherein the anti-TIGIT antibody is selected from tiragolumab, vibostolimab, domvanalimab, AB308, BMS-986207, and durvalumab.

130. Use of the isolated antibody of any one of claims 1-20 or 78-115 or the fusion protein of any one of claims 28-43 for treating cancer.

131. The use of claim 130, wherein the cancer is a blood cancer or a solid tumor.

132. The use of claim 130 or 131, wherein the cancer expresses CCR8.

133. The use of any one of claims 130-132, wherein the cancer is T-cell adult acute lymphocytic leukemia, T-cell childhood acute lymphocytic leukemia, lymphoblastic lymphoma, acute lymphocytic leukemia, cutaneous T cell lymphoma, T-cell acute lymphocytic leukemia, adult T cell leukemia/lymphoma, T cell lymphoblastic leukemia/lymphoma, or anaplastic large cell lymphoma.

134. The use of any one of claims 130-132, wherein the cancer is selected from breast cancer, colorectal cancer, head and neck cancer, lung cancer, ovarian cancer, gastric cancer, stomach adenocarcinoma, and thymoma.

135. The use of any one of claims 130-134 further comprising administering to the subject one or more additional therapeutic agents.

136. The use of claim 135, wherein administration of the one or more additional therapeutic agents is concurrent with the administration of the antibody.

137. The use of claim 135, wherein administration of the one or more additional therapeutic agents is before or after the administration of the antibody.

138. The use of any one of claims 130-137, wherein the cancer is a refractory cancer or resistant to checkpoint inhibitor (CPI) therapy.

139. The use of claim 138, wherein the CPI therapy comprises an anti-PDL1 antibody, an anti-CTLA4 antibody, or an anti-TIGIT antibody.

140. The use of claim 139, wherein the anti-PDL1 antibody is selected from pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, cemiplimab-rwlc, and zimberelimab; wherein the anti-CTLA4 antibody is ipilimumab or tremelimumab; or wherein the anti-TIGIT antibody is selected from tiragolumab, vibostolimab, domvanalimab, AB308, BMS-986207, and durvalumab.

141. The isolated antibody of any one of claims 1-20 or 78-115 or the fusion protein of any one of claims 28-43 for use is treating cancer.

142. The isolated antibody or fusion protein of claim 141, wherein the cancer is a blood cancer or a solid tumor.

143. The isolated antibody or fusion protein of claim 141 or 142, wherein the cancer expresses CCR8.

144. The isolated antibody or fusion protein of any one of claims 141-143, wherein the cancer is T-cell adult acute lymphocytic leukemia, T-cell childhood acute lymphocytic leukemia, lymphoblastic lymphoma, acute lymphocytic leukemia, cutaneous T cell lymphoma, T-cell acute lymphocytic leukemia, adult T cell leukemia/lymphoma, T cell lymphoblastic leukemia/lymphoma, or anaplastic large cell lymphoma.

145. The isolated antibody or fusion protein of any one of claims 141-143, wherein the cancer is selected from breast cancer, colorectal cancer, head and neck cancer, lung cancer, ovarian cancer, gastric cancer, stomach adenocarcinoma, and thymoma.

146. The isolated antibody or fusion protein of any one of claims 141-145 further comprising administering to the subject one or more additional therapeutic agents.

147. The isolated antibody or fusion protein of claim 146, wherein administration of the one or more additional therapeutic agents is concurrent with the administration of the antibody.

148. The isolated antibody or fusion protein of claim 146, wherein administration of the one or more additional therapeutic agents is before or after the administration of the antibody.

149. The isolated antibody or fusion protein of any one of claims 141-148, wherein the cancer is a refractory cancer or resistant to checkpoint inhibitor (CPI) therapy.

150. A method of treating a refractory or checkpoint inhibitor (CPI)-resistant cancer, comprising administering to a subject with cancer the isolated antibody of any one of claims 1-20 or 78-115 or the fusion protein of any one of claims 28-43, wherein the subject has previously been treated with chemotherapy or CPI therapy without responding to the chemotherapy or CPI therapy.

151. The method of claim 150, wherein the CPI therapy comprises an anti-PDL1 antibody, an anti-CTLA4 antibody, or an anti-TIGIT antibody.

152. The method of claim 151, wherein the anti-PDL1 antibody is selected from pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, cemiplimab-rwlc, and zimberelimab; wherein the anti-CTLA4 antibody is ipilimumab or tremelimumab; or wherein the anti-TIGIT antibody is selected from tiragolumab, vibostolimab, domvanalimab, AB308, BMS-986207, and durvalumab.

153. The method of any one of claims 150-152, wherein the cancer is a blood cancer or a solid cancer.

154. The method of any one of claims 150-153, wherein the cancer expresses CCR8.

155. The method of any one of claims 150-154, wherein the cancer is T-cell adult acute lymphocytic leukemia, T-cell childhood acute lymphocytic leukemia, lymphoblastic lymphoma, acute lymphocytic leukemia, cutaneous T cell lymphoma, T-cell acute lymphocytic leukemia, adult T cell leukemia/lymphoma, T cell lymphoblastic leukemia/lymphoma, or anaplastic large cell lymphoma.

156. The method of any one of claims 150-154, wherein the cancer is selected from breast cancer, colorectal cancer, head and neck cancer, lung cancer, ovarian cancer, gastric cancer, stomach adenocarcinoma, and thymoma.

157. The method of any one of claims 150-156 further comprising administering to the subject one or more additional therapeutic agents.

158. The method of claim 157, wherein the one or more additional therapeutic agents are selected from an anti-Trop-2 antibody (*e.g.*, sacituzumab govitecan, SKB-264, JS-108 (DAC-002), datopotamab deruxtecan, BAT-8003), an anti-CD47 antibody or a CD47-blocking agent (*e.g.*, magrolimab, DSP-107, AO-176, ALX-148, IBI-188, lemozoparlimab, TTI-621, TTI-622), an anti-SIRP α antibody (*e.g.*, GS-0189), a FLT3L-Fc fusion protein (*e.g.*, GS-3583), an

anti-PD-1 antibody (pembrolizumab, nivolumab, zimberelimab), a small molecule PD-L1 inhibitor (*e.g.*, GS-4224), an anti-PD-L1 antibody (*e.g.*, atezolizumab), a small molecule MCL1 inhibitor (*e.g.*, GS-9716), a small molecule HPK1 inhibitor (*e.g.*, GS-6451), an HPK1 degrader (PROTAC; *e.g.*, ARV-766), a small molecule DGK α inhibitor, a small molecule CD73 inhibitor (*e.g.*, AB680), an anti-CD73 antibody (*e.g.*, oleclumab), a dual A_{2a}/A_{2b} adenosine receptor antagonist (*e.g.*, etrumadenant (AB928)), an anti-TIGIT antibody (*e.g.*, tiragolumab, vibostolimab, domvanalimab, AB308), an anti-TREM1 antibody (*e.g.*, PY159), an anti-TREM2 antibody (*e.g.*, PY314), a TGF β -trap (*e.g.*, bintrafusp alpha, AGEN-1423), an anti-TGF β 1 antibody (*e.g.*, SRK-181), and a CAR-T cell therapy (*e.g.*, axicabtagene ciloleucel, brexucabtagene autoleucel, tisagenlecleucel).

159. The method of claim 157, wherein the one or more additional therapeutic agents are selected from sacituzumab govitecan-hziy, magrolimab, GS-0189, GS-3583, zimberelimab, GS-4224, GS-9716, GS-6451, AB680, etrumadenant (AB928), domvanalimab, AB308, PY159, PY314, SRK-181, axicabtagene ciloleucel, and brexucabtagene autoleucel.

160. The method of claim any one of claims 157-159, wherein administration of the one or more additional therapeutic agents is concurrent with the administration of the antibody.

161. The method of any one of claims 157-159, wherein administration of the one or more additional therapeutic agents is before or after the administration of the antibody.