CCR8: a human monocyte and thymus receptor for the CC chemokine I-309", J Exp Med; Jul 7;186(1):165-70).

[0005] Recent data in multiple tumor types have demonstrated CCR8 expression is a marker for tumor specific T regulatory (Treg) cells (*see e.g.,* Plitas et al. (2016) "Regulatory T Cells Exhibit Distinct Features in Human Breast Cancer", Immunity; 45(5):1122-1134; Villarreal et al. (Sept. 2018) "Targeting CCR8 Induces Protective Antitumor Immunity and Enhances Vaccine-Induced Responses in Colon Cancer" Tumor Biol. And Immun.). CCR8 is expressed with much higher prevalence and at higher levels on the surface of tumor-resident Tregs compared to circulating or normal tissue Tregs and conventional T effector (Teff) cells. Treg cell infiltration in solid tumors is associated with poor clinical outcome, and Tregs suppress the anti-cancer immune response through inhibition of Teff cell cytotoxicity.

[0006] Some data suggest that Treg suppression of the immune response in the tumor can be reduced by blocking CCR8 function, thereby promoting an inflammatory response and reduced tumor volume. Another therapeutic strategy is to deplete tumor Treg cells via anti-CCR8 antibody dependent cell killing (such as ADCC). For ADCC, anti-CCR8 antibodies may induce redirected T cell lysis of tumor-resident CCR8+ Tregs while sparing normal tissue Tregs that have little to no CCR8 expression by preferentially binding to CCR8 on tumor-resident Tregs and depleting these tumor-resident Tregs via ADCC (e.g., Tanaka et al. (2019) "Targeting Treg cells in cancer immunotherapy" European J. of Immun.; 49(8)1140-1146).

[0007] Treg depleting antibodies such as anti-CCR8 antibodies are known in the art. For example, PCT publication No. WO 2018/181425 describes an antibody against CCR8 having ADCC activity for use in treating cancer, and it discloses the commercially available rat anti-mouse CCR8 antibody (SA214G2).

[0008] There exists a need for alternative anti-CCR8 antibodies that 1) are able to bind human and cynomolgus monkey CCR8 on tumor-resident Treg cells; 2) lead to specific depletion of tumor-resident Treg cells; 3) demonstrate an acceptable pharmacokinetic profile (compared to anti-CCR8 antibodies that bind a different epitope), and/or 4) display sufficient potency for the treatment of cancer.

[0009] There also exists a need for anti-CCR8 antibodies that do not block binding of ligand (such as CCL1) to CCR8, and/or that bind an epitope on CCR8 wherein the epitope comprises at least one residue at positions 1-12 of SEQ ID NO. 31.

SUMMARY

[0010] In one aspect, the present disclosure refers to an antibody that binds to human C-C chemokine receptor type 8 (CCR8), or an antigen-binding fragment thereof, wherein said antibody, or antigen-binding fragment thereof, comprises: (a) a heavy chain complementarity-determining region (HCDR) 1 amino acid sequence of SEQ ID NO: 1; (b) an HCDR2 amino acid sequence of SEQ ID NO: 2; (c) an HCDR3 amino acid sequence of SEQ ID NO: 3; (d) a light chain complementarity-determining region (LCDR) 1 amino acid sequence of KSSQSVLYSSNNX$_1$NYLA (SEQ ID NO: 1235), wherein X_1 is K or R, (e) an LCDR2 amino acid sequence of SEQ ID NO: 5, and (f) an LCDR3 amino acid sequence of SEQ ID NO: 6. In some examples, the antibody or antigen-binding fragment comprises an LCDR1 amino acid sequence of SEQ ID NO: 4. In some examples, the antibody or antigen binding fragment comprises a heavy chain variable region (HCVR) amino acid sequence of SEQ ID NO: 13, and a light chain variable region (LCVR) comprising the amino acid sequence: DIVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNX$_1$NYLA WYX$_2$QKPGQX$_3$PKLLISWASTRESGVPDRFSGSGSGTDFTLTINSLQAEDVAVYYCQQ YYSIPITFGGGTKVEIKR (SEQ ID NO: 1236), wherein X_1 is K or R, X_2 is H or Q, and/or X_3 is S or P. In some examples, the antibody or antigen-binding fragment comprises a heavy chain variable region (HCVR) amino acid sequence of SEQ ID NO: 13 and a light chain variable region (LCVR) amino acid sequence of SEQ ID NO: 14 or SEQ ID NO: 363. In some examples, the antibody or antigen-binding fragment comprises a heavy chain (HC) amino acid sequence of SEQ ID NO: 15 and a light chain (LC) amino acid sequence of SEQ ID NO: 16 or SEQ ID NO: 365. In other examples, the antibody or antigen-binding fragment comprises two HCs and two LCs, wherein both HCs comprise an amino acid sequence of SEQ ID NO: 15, and both LCs comprise an amino acid sequence of SEQ ID NO: 16. In some examples, the antibody or antigen-binding fragment comprises two HCs and two LCs, and wherein both HCs comprise an amino acid sequence of SEQ ID NO: 15, and both LCs comprise an amino acid sequence of SEQ ID NO: 365. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0011] The present disclosure provides an antibody that binds to human CCR8, or an antigen-binding fragment thereof, comprising a heavy chain (HC) and a light chain (LC), wherein the HC comprises a heavy chain variable region (HCVR) and wherein the LC comprises a light chain variable region (LCVR), wherein the HCVR comprises HCDR1, HCDR2, and HCDR3 and the LCVR comprises LCDR1, LCDR2, and LCDR3, and wherein HCDR1 comprises an amino acid sequence of SEQ ID NO: 1; HCDR2 comprises an amino acid sequence of SEQ ID NO: 2; HCDR3 comprises an amino acid sequence of SEQ ID NO:

3; LCDR1 comprises an amino acid sequence of SEQ ID NO: 4; LCDR2 comprises an amino acid sequence of SEQ ID NO: 5; and LCDR3 comprises an amino acid sequence of SEQ ID NO: 6. In an example, the HCVR comprises an amino acid sequence of SEQ ID NO: 13, and the LCVR comprises an amino acid sequence of SEQ ID NO: 14 or SEQ ID NO: 365. In an example, the LCVR comprises an amino acid sequence of SEQ ID NO: 14. In an example, the LCVR comprises an amino acid sequence of SEQ ID NO: 365. In an example, the HC has an amino acid sequence of SEQ ID NO: 15 or SEQ ID NO: 573, and the LC has an amino acid sequence given by SEQ ID NO: 16. In another example, the antibody comprises two HCs and two LCs, wherein each HC has an amino acid sequence of SEQ ID NO: 15 or SEQ ID NO: 573, and each LC has an amino acid sequence of SEQ ID NO: 16. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0012] The present disclosure also provides an antibody that binds to human CCR8, or an antigen-binding fragment thereof, which comprises an HCDR1 amino acid sequence of SEQ ID NO: 839; an HCDR2 amino acid sequence of SEQ ID NO: 840; an HCDR3 amino acid sequence of SEQ ID NO: 841; an LCDR1 amino acid sequence of SEQ ID NO: 842; an LCDR2 amino acid sequence of SEQ ID NO: 843; and an LCDR3 amino acid sequence of SEQ ID NO: 844. In another aspect, the present disclosure refers to an antibody that binds to human CCR8, or an antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises (a) an HCDR1 amino acid sequence of SEQ ID NO: 839, (b) an HCDR2 amino acid sequence of SEQ ID NO: 840, (c) an HCDR3 amino acid sequence of SEQ ID NO: 841, (d) an LCDR1 amino acid sequence of SEQ ID NO: 842, (e) an LCDR2 amino acid sequence of SEQ ID NO: 843, and (f) an LCDR3 amino acid sequence of SEQ ID NO: 844. In some examples, the antibody or antigen-binding fragment comprises an HCVR amino acid sequence of SEQ ID NO: 1017 and an LCVR amino acid sequence of SEQ ID NO: 1018. In some examples, the antibody comprises an HC amino acid sequence of SEQ ID NO: 1125 or SEQ ID NO: 1237 and an LC amino acid sequence of SEQ ID NO: 1126. In some examples, the antibody comprises an HC amino acid sequence of SEQ ID NO: 1125 and an LC amino acid sequence of SEQ ID NO: 1126. In some examples, the antibody comprises an HC amino acid sequence of SEQ ID NO: 1237 and an LC amino acid sequence of SEQ ID NO: 1126. For example, the antibody may comprise two HCs and two LCs, wherein both HCs comprise an amino acid sequence of SEQ ID NO: 1125 or SEQ ID NO: 1237, and both LCs comprise an amino acid sequence of SEQ ID NO: 1126. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0013] The present disclosure also provides an antibody that binds to human CCR8, or an antigen-binding fragment thereof, which comprises an HCDR1 amino acid sequence of SEQ ID NO: 845; an HCDR2 amino acid sequence of SEQ ID NO: 846; an HCDR3 amino acid sequence of SEQ ID NO: 847; an LCDR1 amino acid sequence of SEQ ID NO: 848; an LCDR2 amino acid sequence of SEQ ID NO: 849; and an LCDR3 amino acid sequence of SEQ ID NO: 850. In some examples, the antibody or antigen-binding fragment comprises

an HCVR amino acid sequence of SEQ ID NO: 1019 and an LCVR amino acid sequence of SEQ ID NO: 1020. In some examples, the antibody comprises an HC amino acid sequence of SEQ ID NO: 1127 or SEQ ID NO: 1238 and an LC amino acid sequence of SEQ ID NO: 1128.

[0014] In another aspect, the present disclosure refers to an antibody that binds to human CCR8, or an antigen-binding fragment thereof, wherein the antibody comprises: (a) an HCDR1 amino acid sequence of $X_1X_2GX_4H$, (SEQ ID NO: 1233), wherein (i) X_1 is N, S, D, G, T, or R, (ii) X_2 is C, N, Y, S, or F, and (iii) X_4 is M or F; (b) an HCDR2 amino acid sequence of SEQ ID NOs: 648, 654, 660, 666, 672, 678, 684, 690, 696, 702, 708, 714, 720, 726, 732, 738, 744, 750, 756, 762, 768, 774, 780, 786, 792, 798, 804, 810, 816, 822, 828, 834, 840, 846, 852, 858, 867, 873, 879, 885, 891, 897, 903, 909, 915, 921, 927, 933, 939, or 945, or a variant thereof that comprises 1-4 amino acid substitutions or is at least 90% identical to any one of the foregoing HCDR2 amino acid sequences; (c) an HCDR3 amino acid sequence of SEQ ID NOs: 649, 655, 661, 667, 673, 679, 685, 691, 697, 703, 709, 715, 721, 727, 733, 739, 745, 751, 757, 763, 769, 775, 781, 787, 793, 799, 805, 811, 817, 823, 829, 835, 847, 853, 859, 868, 874, 880, 886, 892, 898, 904, 910, 916, 922, 928, 934, 940, or 946 or a variant thereof that comprises 1-4 amino acid substitutions or is at least 90% identical to any one of the foregoing HCDR3 amino acid sequences; (d) an LCDR1 amino acid sequence of SEQ ID NOs: 650, 656, 662, 668, 674, 680, 686, 692, 698, 704, 710, 716, 722, 728, 734, 740, 746, 752, 758, 764, 770, 776, 782, 788, 794, 800, 806, 812, 818, 824, 830, 836, 848, 854, 860, 863, 869, 875, 881, 887, 893, 899, 905, 911, 917, 923, 929, 935, or 941 or a variant thereof that comprises 1-4 amino acid substitutions or is at least 90% identical to any one of the foregoing LCDR1 amino acid sequences; (e) an LCDR2 amino acid sequence of $RX_2X_3X_4RPS$ (SEQ ID NO: 1234), wherein (i) X_2 is A, N, D, S, or Q, (ii) X_3 is S, T, N, I, F, or A, and (iii) X_4 is N or V; and (f) an LCDR3 amino acid sequence of SEQ ID NOs: 652, 658, 664, 670, 676, 682, 688, 694, 700, 706, 712, 718, 724, 730, 736, 742, 748, 754, 760, 766, 772, 778, 784, 790, 796, 802, 808, 814, 820, 826, 832, 838, 850, 856, 862, 865, 871, 877, 883, 889, 895, 901, 907, 913, 919, 925, 931, 937, or 943 or a variant thereof that comprises 1-4 amino acid substitutions or is at least 90% identical to any one of the foregoing LCDR3 amino acid sequences. In some examples, the HCDR1 comprises an amino acid sequence of SEQ ID NOs: 647, 653, 659, 665, 671, 677, 683, 689, 695, 701, 707, 713, 719, 725, 731, 737, 743, 749, 755, 761, 767, 773, 779, 785, 791, 797, 803, 809, 815, 821, 827, 833, 845, 851, 857, 866, 872, 878, 884, 890, 896, 902, 908, 914, 920, 926, 932, 938, or 944. In some examples, the LCDR2 comprises an amino acid sequence of SEQ ID NOs: 651,

657, 663, 669, 675, 681, 687, 693, 699, 705, 711, 717, 723, 729, 735, 741, 747, 753, 759, 765, 771, 777, 783, 789, 795, 801, 807, 813, 819, 825, 831, 837 849, 855, 861, 864, 870, 876, 882, 888, 894, 900, 906, 912, 918, 924, 930, 936, or 942. In some examples, the HCVR comprises an amino acid sequence of SEQ ID NOs: 953, 955, 957, 959, 961, 963, 965, 967, 969, 971, 973, 975, 977, 979, 981, 983, 985, 987, 989, 991, 993, 995, 997, 999, 1001, 1003, 1005, 1007, 1009, 1011, 1013, 1015, 1019, 1021, 1023, 1026, 1028, 1030, 1032, 1034, 1036, 1038, 1040, 1042, 1044, 1046, 1048, 1050, or 1052. In some examples, the LCVR comprises an amino acid sequence of SEQ ID NOs: 964, 966, 968, 970, 972, 974, 976, 978, 980, 982, 984, 986, 988, 990, 992, 994, 996, 998, 1000, 1002, 1004, 1006, 1008, 1010, 1012, 1014, 1016, 1020, 1022, 1024, 1025, 1027, 1029, 1031, 1033, 1035, 1037, 1039, 1041, 1043, 1045, 1047, 1049, or 1051. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0015] In some examples, the antibody of or antigen-binding fragment comprises: (a) a HCVR comprising an amino acid sequence of SEQ ID NO: 1019 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1020; (b) a HCVR comprising an amino acid sequence of SEQ ID NO: 1021 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1022; (c) a HCVR comprising an amino acid sequence of SEQ ID NO: 1023 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1024; (d) a HCVR comprising an amino acid sequence of SEQ ID NO: 1026 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1025; (e) a HCVR comprising an amino acid sequence of SEQ ID NO: 1028 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1027; (f) a HCVR comprising an amino acid sequence of SEQ ID NO: 1030 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1029; (g) a HCVR comprising an amino acid sequence of SEQ ID NO: 1032 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1031; (h) a HCVR comprising an amino acid sequence of SEQ ID NO: 1034 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1033; (i) a HCVR comprising an amino acid sequence of SEQ ID NO: 1036 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1035; (j) a HCVR comprising an amino acid sequence of SEQ ID NO: 1038 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1037; (k) a HCVR comprising an amino acid sequence of SEQ ID NO: 1040 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1039; (l) a HCVR comprising an amino acid sequence of SEQ ID NO: 1042 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1041; (m) a HCVR comprising an amino acid sequence of SEQ ID NO: 1044 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1043; (n) a HCVR comprising an amino acid sequence of SEQ ID NO: 1046

and a LCVR comprising an amino acid sequence of SEQ ID NO: 1045; (o) a HCVR comprising an amino acid sequence of SEQ ID NO: 1048 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1047; (p) a HCVR comprising an amino acid sequence of SEQ ID NO: 1050 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1049; or (q) a HCVR comprising an amino acid sequence of SEQ ID NO: 1052 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1051. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0016] In some examples, the antibody comprises an HC amino acid sequence of SEQ ID NOs: 1127, 1129, 1131, 1134, 1136, 1138, 1140, 1142, 1144, 1146, 1148, 1150, 1152, 1154, 1156, 1158, 1160, or 1238-1254; and an LC amino acid sequence of SEQ ID NOs: 1128, 1130, 1132, 1133, 1135, 1137, 1139, 1141, 1143, 1145, 1147, 1149, 1151, 1153, 1155, 1157, or 1159. In another aspect, the present disclosure refers to a nucleic acid sequence encoding a heavy chain amino acid sequence of SEQ ID NOs: 1127, 1129, 1131, 1134, 1136, 1138, 1140, 1142, 1144, 1146, 1148, 1150, 1152, 1154, 1156, 1158, 1160, or 1238-1254. In yet another aspect, the present disclosure refers to a nucleic acid sequence encoding a light chain amino acid sequence of SEQ ID NOs: 1128, 1130, 1132, 1133, 1135, 1137, 1139, 1141, 1143, 1145, 1147, 1149, 1151, 1153, 1155, 1157, or 1159. For example, in some examples, the antibody comprises: (a) an HC amino acid sequence of SEQ ID NO: 1127 or SEQ ID NO: 1238 and a LC amino acid sequence of SEQ ID NO: 1128; (b) an HC amino acid sequence of SEQ ID NO: 1129 or SEQ ID NO: 1239 and a LC amino acid sequence of SEQ ID NO: 1130; (c) an HC amino acid sequence of SEQ ID NO: 1131 or SEQ ID NO: 1240 and a LC amino acid sequence of SEQ ID NO: 1132; (d) an HC amino acid sequence of SEQ ID NO: 1134 or SEQ ID NO: 1241 and a LC amino acid sequence of SEQ ID NO: 1133; (e) an HC amino acid sequence of SEQ ID NO: 1136 or SEQ ID NO: 1242 and a LC amino acid sequence of SEQ ID NO: 1135; (f) an HC amino acid sequence of SEQ ID NO: 1138 or SEQ ID NO: 1243 and a LC amino acid sequence of SEQ ID NO: 1137; (g) an HC amino acid sequence of SEQ ID NO: 1140 or SEQ ID NO: 1244 and a LC amino acid sequence of SEQ ID NO: 1139; (h) an HC amino acid sequence of SEQ ID NO: 1142 or SEQ ID NO: 1245 and a LC amino acid sequence of SEQ ID NO: 1141; (i) an HC amino acid sequence of SEQ ID NO: 1144 or SEQ ID NO: 1246 and a LC amino acid sequence of SEQ ID NO: 1143; (j) an HC amino acid sequence of SEQ ID NO: 1146 or SEQ ID NO: 1247 and a LC amino acid sequence of SEQ ID NO: 1145; (k) an HC amino acid sequence of SEQ ID NO: 1148 or SEQ ID NO: 1248 and a LC amino acid sequence of SEQ ID NO: 1147; (l) an HC amino acid sequence of SEQ ID NO: 1150 or SEQ ID NO: 1249 and a LC amino acid

sequence of SEQ ID NO: 1149; (m) an HC amino acid sequence of SEQ ID NO: 1152 or SEQ ID NO: 1250 and a LC amino acid sequence of SEQ ID NO: 1151; (n) an HC amino acid sequence of SEQ ID NO: 1154 or SEQ ID NO: 1251 and a LC amino acid sequence of SEQ ID NO: 1153; (o) an HC amino acid sequence of SEQ ID NO: 1156 or SEQ ID NO: 1252 and a LC amino acid sequence of SEQ ID NO: 1155; (p) an HC amino acid sequence of SEQ ID NO: 1158 or SEQ ID NO: 1253 and a LC amino acid

sequence of SEQ ID NO: 1157; or (q) an HC amino acid sequence of SEQ ID NO: 1160 or SEQ ID NO: 1254 and a LC amino acid sequence of SEQ ID NO: 1159. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0016a] In another aspect, the present disclosure refers to a vector comprising the nucleic acid sequence as described herein.

[0017] In some examples, the antibody or antigen-binding fragment thereof is an antibody. In some examples, the antibody or antigen-binding fragment thereof is an antigen-binding fragment thereof. In some examples, the antibody or antigen-binding fragment is a single chain variable fragment (scFv). In some examples, the antibody or antigen-binding fragment is a Fab. In particular examples, the antibody or antigen-binding fragment is a single chain Fab (scFab). In some examples, the antigen-binding fragment comprises an amino acid sequence of any one of the anti-CCR8 antibodies or antigen-binding fragments thereof of the present disclosure.

[0018] The present disclosure also provides an antibody or antigen-binding fragment thereof, that binds to human CCR8, comprising a heavy chain (HC) and a light chain (LC), wherein the HC comprises a heavy chain variable region (HCVR) and wherein the LC comprises a light chain variable region (LCVR), wherein the HCVR comprises HCDR1, HCDR2, and HCDR3 and the LCVR comprises LCDR1, LCDR2, and LCDR3, and wherein HCDR1 comprises an amino acid sequence of SEQ ID NO: 7; HCDR2 comprises an amino acid sequence of SEQ ID NO: 8, SEQ ID NO: 367, or SEQ ID NO: 377; HCDR3 comprises an amino acid sequence of SEQ ID NO: 9; LCDR1 comprises an amino acid sequence of SEQ ID NO: 10, SEQ ID NO: 369, or SEQ ID NO: 379; LCDR2 comprises an amino acid sequence of SEQ ID NO: 11; and LCDR3 comprises an amino acid sequence of SEQ ID NO: 12. In an example, the HCDR2 comprises an amino acid sequence of SEQ ID NO: 8. In an example, the HCDR2 comprises an amino acid sequence of SEQ ID NO: 367. In an example, the HCDR2 comprises an amino acid sequence of SEQ ID NO: 377. In an example, the LCDR1 comprises an amino acid sequence of SEQ ID NO: 10. In an example, the LCDR1 comprises an amino acid sequence of SEQ ID NO: 369. In an example, the LCDR1 comprises an amino acid sequence of SEQ ID NO: 379. In an example, the HCVR comprises an amino acid sequence of SEQ ID NO: 17, SEQ ID NO: 372, or SEQ ID NO: 382, and the LCVR comprises an amino acid sequence of SEQ ID NO: 18, SEQ ID NO: 373, or SEQ ID NO: 383. In an example, the HCVR comprises an amino acid sequence of SEQ ID NO: 17. In an example, the HCVR comprises an amino acid sequence of SEQ ID NO: 372. In an example, the HCVR comprises an amino acid sequence of SEQ ID NO: 382. In an example, the LCVR comprises an amino acid sequence of SEQ ID NO: 18. In an example, the LCVR comprises an amino acid

sequence of SEQ ID NO: 373. In an example, the LCVR comprises an amino acid sequence of SEQ ID NO: 383. In an example, the HC comprises an amino acid sequence of SEQ ID NO: 19, SEQ ID NO: 374, or SEQ ID NO: 384, and the LC comprises an amino acid sequence of SEQ ID NO: 20, SEQ ID NO: 375, or SEQ ID NO: 385. In an example, the HC comprises an amino acid sequence of SEQ ID NO: 19. In an example, the HC comprises an amino acid sequence of SEQ ID NO: 374. In an example, the HC comprises an amino acid sequence of SEQ ID NO: 384. In an example, the LC comprises an amino acid sequence of SEQ ID NO: 20. In an example, the LC comprises an amino acid sequence of SEQ ID NO: 375. In an example, the LC comprises an amino acid sequence of SEQ ID NO: 385. In another example, the antibody comprises two HCs and two LCs, wherein each HC comprises an amino acid sequence of SEQ ID NO: 19, SEQ ID NO: 374, or SEQ ID NO: 384, and each LC comprises an amino acid sequence of SEQ ID NO: 20, SEQ ID NO: 375, or SEQ ID NO: 385. In an example, each HC comprises an amino acid sequence of SEQ ID NO: 19. In an example, each HC comprises an amino acid sequence of SEQ ID NO: 374. In an example, each HC comprises an amino acid sequence of SEQ ID NO: 384. In an example, each LC comprises an amino acid sequence of SEQ ID NO: 20. In an example, each LC comprises an amino acid sequence of SEQ ID NO: 375. In an example, each LC comprises an amino acid sequence of SEQ ID NO: 385. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0019] The present disclosure provides an antibody or antigen-binding fragment thereof, that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of 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, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 352 and SEQ ID NO: 353, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 354 and 355, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 573 and 355, respectively. In an example, the antibody is Antibody 1 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0020] The present disclosure provides an antibody or antigen-binding fragment thereof, that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of

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, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 362 and SEQ ID NO: 363, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 364 and 365, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 574 and 365, respectively. In an example, the antibody is Antibody 1.1 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0021] The present disclosure provides an antibody or antigen-binding fragment thereof that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 366; SEQ ID NO: 367; SEQ ID NO: 368; SEQ ID NO: 369; SEQ ID NO: 370; and SEQ ID NO: 371, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 372 and SEQ ID NO: 373, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 374 and 375, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 575 and 375, respectively. In an example, the antibody is Antibody 2.1 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0022] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 376; SEQ ID NO: 377; SEQ ID NO: 378; SEQ ID NO: 379; SEQ ID NO: 380; and SEQ ID NO: 381, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 382 and SEQ ID NO: 383, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 384 and 385, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 576 and 385, respectively. In an example, the antibody is Antibody 2.2 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0023] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 386;

SEQ ID NO: 387; SEQ ID NO: 388; SEQ ID NO: 389; SEQ ID NO: 390; and SEQ ID NO: 391, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and an LCVR comprising amino acid sequences of SEQ ID NO: 392 and SEQ ID NO: 393, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 394 and 395, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 577 and 395, respectively. In an example, the antibody is Antibody 3.0 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0024] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 396; SEQ ID NO: 397; SEQ ID NO: 398; SEQ ID NO: 399; SEQ ID NO: 400; and SEQ ID NO: 401; respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 402 and SEQ ID NO: 403, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 404 and 405, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 578 and 405, respectively. In an example, the antibody is Antibody 4.0 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0025] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 406; SEQ ID NO: 407; SEQ ID NO: 408; SEQ ID NO: 409; SEQ ID NO: 410; and SEQ ID NO: 411; respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 412 and SEQ ID NO: 413, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 414 and 415, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 579 and 415, respectively. In an example, the antibody is Antibody 4.1 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0026] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 416; SEQ ID NO: 417; SEQ ID NO: 418; SEQ ID NO: 419; SEQ ID NO: 420; and SEQ ID NO:

421, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 422 and SEQ ID NO: 423, respectively. In another example, the antibody comprises HC and LC comprising amino acid sequences of SEQ ID NO: 424 and 425, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 580 and 425, respectively. In an example, the antibody is Antibody 4.2 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0027] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 426, SEQ ID NO: 427, SEQ ID NO: 428, SEQ ID NO: 429, SEQ ID NO: 430, and SEQ ID NO: 431, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 432 and SEQ ID NO: 433, respectively. In another example, the antibody comprises an HC and LC comprising amino acid sequences of SEQ ID NO: 434 and 435, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 581 and 435, respectively. In an example, the antibody is Antibody 5.0 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0028] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 436, SEQ ID NO: 437, SEQ ID NO: 438, SEQ ID NO: 439, SEQ ID NO: 440, and SEQ ID NO: 441, respectively. In an example, the antibody or antigen-binding fragment comprises HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 442 and SEQ ID NO: 443, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 444 and 445, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 582 and 445, respectively. In an example, the antibody is Antibody 5.1 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0029] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 446; SEQ ID NO: 447; SEQ ID NO: 448; SEQ ID NO: 449; SEQ ID NO: 450; and SEQ ID NO: 451, respectively. In an example, the antibody or antigen-binding fragment comprises an

HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 452 and SEQ ID NO: 453, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 454 and 455, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 583 and 455, respectively. In an example, the antibody is Antibody 5.2 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0030] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 456, SEQ ID NO: 457, SEQ ID NO: 458, SEQ ID NO: 459, SEQ ID NO: 460, and SEQ ID NO: 461, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising the amino acid sequences of SEQ ID NO: 462 and SEQ ID NO: 463, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 464 and 465, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 584 and 465, respectively. In an example, the antibody is Antibody 5.3 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0031] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 466, SEQ ID NO: 467, SEQ ID NO: 468, SEQ ID NO: 469, SEQ ID NO: 470, and SEQ ID NO: 471, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising the amino acid sequences of SEQ ID NO: 472 and SEQ ID NO: 473, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 474 and 475, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 585 and 475, respectively. In an example, the antibody is Antibody 5.4 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0032] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 476, SEQ ID NO: 477, SEQ ID NO: 478, SEQ ID NO: 479, SEQ ID NO: 480, and SEQ ID NO: 481, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 482 and SEQ ID NO:

483, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 484 and 485, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 586 and 485, respectively. In an example, the antibody is Antibody 5.5 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0033] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 486; SEQ ID NO: 487; SEQ ID NO: 488; SEQ ID NO: 489; SEQ ID NO: 490; and SEQ ID NO: 491, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 492 and SEQ ID NO: 493, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 494 and 495, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 587 and 495, respectively. In an example, the antibody is Antibody 5.6 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0034] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 496; SEQ ID NO: 497; SEQ ID NO: 498; SEQ ID NO: 499; SEQ ID NO: 500; and SEQ ID NO: 501, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 502 and SEQ ID NO: 503, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 504 and 505, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 588 and 505, respectively. In an example, the antibody is Antibody 5.7 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0035] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 506; SEQ ID NO: 507; SEQ ID NO: 508; SEQ ID NO: 509; SEQ ID NO: 510; and SEQ ID NO: 511; respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 512 and SEQ ID NO: 513, respectively. In another example, the antibody comprises an HC and LC comprising

the amino acid sequences of SEQ ID NO: 514 and 515, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 589 and 515, respectively. In an example, the antibody is Antibody 5.8 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0036] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 516; SEQ ID NO: 517; SEQ ID NO: 518; SEQ ID NO: 519; SEQ ID NO: 520; and SEQ ID NO: 521, respectively. In an example, the antibody or antigen-binding fragment comprises HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 522 and SEQ ID NO: 523, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 524 and 525, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 590 and 525, respectively. In an example, the antibody is Antibody 5.9 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0037] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 526; SEQ ID NO: 527; SEQ ID NO: 528; SEQ ID NO: 529; SEQ ID NO: 530; and SEQ ID NO: 531; respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 532 and SEQ ID NO: 533, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 534 and 535, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 591 and 535, respectively. In an example, the antibody is Antibody 6.0 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0038] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 536; SEQ ID NO: 537; SEQ ID NO: 538; SEQ ID NO: 539; SEQ ID NO: 540; and SEQ ID NO: 541, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising the amino acid sequences of SEQ ID NO: 542 and SEQ ID NO: 543, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 544 and 545, respectively. In another

example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 592 and 545, respectively. In an example, the antibody is Antibody 6.1 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0039] The present disclosure provides an antibody or antigen-binding fragment that binds CCR8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3 comprising amino acid sequences of SEQ ID NO: 546; SEQ ID NO: 547; SEQ ID NO: 548; SEQ ID NO: 549; SEQ ID NO: 550; and SEQ ID NO: 551, respectively. In an example, the antibody or antigen-binding fragment comprises an HCVR and LCVR comprising amino acid sequences of SEQ ID NO: 552 and SEQ ID NO: 553, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 554 and 555, respectively. In another example, the antibody comprises an HC and LC comprising the amino acid sequences of SEQ ID NO: 593 and 555, respectively. In an example, the antibody is Antibody 6.2 IgG1. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0040] In some examples, the anti-CCR8 antibody or antigen-binding fragment thereof comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, LCDR3, HCVR, LCVR, HC, and/or LC amino acid residues as disclosed in Table 16, Table 17, Table 19, and/or Table 20.

[0041] In another example, the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and/or LCDR3 of an antibody or antigen-binding fragment of the present disclosure comprises a sequence of amino acids that is at least 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of a HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and/or LCDR3 sequence of an anti-CCR8 antibody or antigen-binding fragment of the present disclosure listed herein. In an example, the sequence of amino acids is at least 70% identical. In an example, the sequence of amino acids is at least 80% identical. In an example, the sequence of amino acids is at least 90% identical. In another example, the sequence of amino acids is at least 95% identical. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0042] In another example, the HCVR and/or LCVR comprises a sequence of amino acids that is at least 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of a HCVR and/or LCVR sequence of an anti-CCR8 antibody or antigen-binding fragment of the present disclosure listed herein. In an example, the sequence of amino acids is at least 70% identical. In an example, the sequence of amino acids is at least 80% identical. In an example, the sequence of amino

acids is at least 90% identical. In another example, the sequence of amino acids is at least 95% identical. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0043] In another example, the HC and/or LC comprises a sequence of amino acids that is at least 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identical to the sequence of a HC and/or LC sequence of an anti-CCR8 antibody or antigen-binding fragment of the present disclosure listed herein. In an example, the sequence of amino acids is at least 70% identical. In an example, the sequence of amino acids is at least 80% identical. In an example, the sequence of amino acids is at least 90% identical. In another example, the sequence of amino acids is at least 95% identical. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0044] In an example, the present disclosure provides an afucosylated antibody of the present disclosure. In an example, an anti-CCR8 antibody of the present disclosure is human or humanized.

[0045] In some examples, an anti-CCR8 antibody or antigen-binding fragment of the present disclosure can be administered concurrently with, before, or after a variety of drugs and treatments widely employed in cancer treatment such as, for example, chemotherapeutic agents, non-chemotherapeutic agents (e.g., checkpoint inhibitors including anti-PD-1 or anti-PD-L1 inhibitors, such as antagonist antibodies), anti-neoplastic agents, and/or radiation. For example, administration can occur before, during, and/or after any of the treatments described herein. Examples of chemotherapeutic agents are discussed herein and include, but are not limited to, cisplatin, taxol, etoposide, mitoxantrone (Novantrone®), actinomycin D, cycloheximide, camptothecin (or water soluble derivatives thereof), methotrexate, mitomycin (e.g., mitomycin C), dacarbazine (DTIC), anti-neoplastic antibiotics such as adriamycin (doxorubicin) and daunomycin, and all the chemotherapeutic agents mentioned herein. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0046] In some examples, an anti-CCR8 antibody or antigen-binding fragment of the present disclosure may be administered concurrently with, before, or after a checkpoint inhibitor such as a PD-1 antagonist antibody or a PD-L1 antagonist antibody. The term "PD-1 antagonist antibody" refers to an antibody that specifically binds to PD-1 and decreases, blocks, inhibits, abrogates, or interferes with signal transduction resulting from the interaction of PD-1 and one or more of its ligands, such as PD-L1 and PD-L2. In some examples, a

PD-1 antagonist antibody inhibits the binding of PD-1 to PD-L1 and/or PD-L2. The term "PD-L1 antagonist antibody" refers to an antibody that specifically binds to PD-L1 and decreases, blocks, inhibits, abrogates, or interferes with signal transduction resulting from the interaction of PD-L1 with the PD-1 receptor. In some examples, a PD-L1 antagonist antibody inhibits the binding of PD-L1 to PD-1. In some examples, the PD-1 antagonist antibody is any one of Antibody 20C1.006 (comprising LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, HCDR3 amino acid sequences of SEQ ID NOs 72-77, respectively; VL and VH amino acid sequences of SEQ ID NOs 78 and 79, respectively; and LC and HC amino acid sequences of SEQ ID NOs 80 and 81, respectively); zeluvalimab (comprising LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, HCDR3 amino acid sequences of SEQ ID NOs 32-37, respectively; VL and VH amino acid sequences of SEQ ID NOs 38 and 39 respectively; LC amino acid sequence of SEQ ID NO: 40; and HC amino acid sequences of SEQ ID NOs 41 or 636); Antibody 20A2.003 (comprising LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, HCDR3 amino acid sequences of SEQ ID NOs 42-47, respectively; VL and VH amino acid sequences of SEQ ID NOs 48 and 49, respectively; and LC and HC amino acid sequences of SEQ ID NOs 50 and 51, respectively); Antibody 22D4.006 (comprising LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, HCDR3 amino acid sequences of SEQ ID NOs 52-57, respectively; VL and VH amino acid sequences of SEQ ID NOs 58 and 59, respectively; and LC and HC amino acid sequences of SEQ ID NOs 60 and 61, respectively); or Antibody 22D4.017 (comprising LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, HCDR3 amino acid sequences of SEQ ID NOs 62-67, respectively; VL and VH amino acid sequences of SEQ ID NOs 68 and 69, respectively; and LC and HC amino acid sequences of SEQ ID NOs 70 and 71, respectively). In one example, the PD-1 antagonist antibody is pembrolizumab. In another example, the PD-1 antagonist antibody is nivolumab. In yet another example, the PD-1 antagonist antibody is cemiplimab. In a particular example, the PD-1 antagonist antibody is zeluvalimab. Zeluvalimab is also known as AMG 404 and is also known as 20C1.009. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0046a] In another aspect, the present disclosure refers to the use of the antibody as described herein, or the composition as described herein in the manufacture of a medicament for treating cancer in a patient.

[0047] The present disclosure provides a method of treating cancer in a patient comprising administering an effective amount of an anti-CCR8 antibody or antigen-binding fragment, wherein the anti-CCR8 antibody or antigen-binding fragment does not block ligand binding to CCR8. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0048] The present disclosure provides a method of treating cancer in a patient comprising administering an effective amount of an anti-CCR8 antibody, wherein the anti-CCR8 antibody has ADCC.

[0049] The present disclosure provides a method of treating cancer in a patient comprising administering an effective amount of an anti-CCR8 antibody, wherein the anti-CCR8 antibody does not block ligand binding to CCR8 and wherein the anti-CCR8 antibody has ADCC. In an example, the anti-CCR8 antibody further has an acceptable PK. In an example, the anti-CCR8 antibody binds an epitope wherein the epitope comprises at least one residue at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises at least two residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises at least three residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises at least four residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises at least five residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises six or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises seven or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises eight or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises nine or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises ten or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises eleven or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises all twelve amino acid residues at positions 1-12 of SEQ ID NO: 31. In a particular example, the epitope comprises a threonine at position 4 of SEQ ID NO: 31. In a particular example, the epitope comprises a threonine at position 4 of SEQ ID NO: 22. The amino acid sequence of amino acid residues 1-12 of SEQ ID NO: 31 is SEQ ID NO: 82. In an example, the epitope is determined by epitope binning. In an example, the epitope is determined by antibody binding to CCR8 peptide-nanobody complexes. In an example, the epitope is determined by screening antibody binding to CCR8 by phage display. In an example, the epitope is determined by determining binding to a CCR8 peptide expressed in human cells, wherein the peptide comprises an amino acid sequence given by SEQ ID NO: 82. In some examples, the epitope is determined by anti-CCR8 antibody binding to the T4R mutation in cynomolgus monkey CCR8. In an example, binding to the T4R mutation is determined in a cell based affinity assay, wherein antibody binding to cells expressing cynomolgus monkey cells CCR8 containing a T4R mutation is compared to antibody binding to cells expressing wild-type cynomolgus monkey CCR8

(comprising a threonine at position four). In some examples, an anti-CCR8 antibody binds threonine at position four if it shows reduced binding to CCR8 comprising a T4R mutation. In particular examples, an anti-CCR8 antibody binds threonine at position four if it shows no detectable binding to CCR8 comprising a T4R mutation. In some examples, wild-type cynomolgus monkey CCR8 comprises an amino acid sequence given by SEQ ID NO: 22. In some examples, cynomolgus monkey CCR8 comprising a T4R mutation comprises an amino acid sequence given by SEQ ID NO: 556.

[0050] The present disclosure provides a method of treating cancer in a patient comprising administering an effective amount of an anti-CCR8 antibody, wherein the anti-CCR8 antibody does not block ligand binding to CCR8 and wherein the anti-CCR8 antibody has ADCC. In an example, the anti-CCR8 antibody further has an acceptable PK. In an example, the anti-CCR8 antibody binds an epitope wherein the epitope consists of at least one residue at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of at least two residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of at least three residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of at least four residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comp consists of rises at least five residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of six or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of seven or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of eight or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of nine or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of ten or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of eleven or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of all twelve amino acid residues at positions 1-12 of SEQ ID NO: 31. In a particular example, the epitope consists of a threonine at position 4 of SEQ ID NO: 31. In a particular example, the epitope consists of a threonine at position 4 of SEQ ID NO: 22. In an example, the epitope is determined by epitope binning. In an example, the epitope is determined by antibody binding to CCR8 peptide-nanobody complexes. In an example, the epitope is determined by screening antibody binding to CCR8 by phage display. In an example, the epitope is determined by determining binding to a CCR8 peptide expressed in human cells, wherein the peptide comprises an amino acid sequence given by SEQ ID NO: 82. In some examples, the epitope is determined by anti-CCR8 antibody binding to the T4R mutation in cynomolgus monkey CCR8. In an

example, binding to the T4R mutation is determined in a cell based affinity assay, wherein antibody binding to cells expressing cynomolgus monkey CCR8 containing a T4R mutation is compared to antibody binding to cells expressing wild-type cynomolgus monkey CCR8 (comprising a threonine at position four). In some examples, an anti-CCR8 antibody binds threonine at position four if it shows reduced binding to CCR8 comprising a T4R mutation. In particular examples, an anti-CCR8 antibody binds threonine at position four if it shows no detectable binding to CCR8 comprising a T4R mutation. In some examples, wild-type cynomolgus monkey CCR8 comprises an amino acid sequence given by SEQ ID NO: 22. In some examples, cynomolgus monkey CCR8 comprising a T4R mutation comprises an amino acid sequence given by SEQ ID NO: 556.

[0051] The present disclosure provides a method of treating cancer in a patient comprising administering an effective amount of an anti-CCR8 antibody, wherein the anti-CCR8 antibody does not block ligand binding to CCR8 and wherein the anti-CCR8 antibody has ADCC. In an example, the anti-CCR8 antibody further has an acceptable PK. In an example, the anti-CCR8 antibody binds an epitope wherein the epitope comprises at least one residue of SEQ ID NO: 82. In an example, the epitope comprises at least two residues of SEQ ID NO: 82. In an example, the epitope comprises at least three residues of SEQ ID NO: 82. In an example, the epitope comprises at least four residues of SEQ ID NO: 82. In an example, the epitope comprises at least five residues of SEQ ID NO: 82. In an example, the epitope comprises six or more residues of SEQ ID NO: 82. In an example, the epitope comprises seven or more residues of SEQ ID NO: 82. In an example, the epitope comprises eight or more residues of SEQ ID NO: 82. In an example, the epitope comprises nine or more residues of SEQ ID NO: 82. In an example, the epitope comprises ten or more residues of SEQ ID NO: 82. In an example, the epitope comprises eleven or more residues of SEQ ID NO: 82. In an example, the epitope comprises all twelve amino acid residues of SEQ ID NO: 82. In an example, the epitope is determined by epitope binning. In an example, the epitope is determined by antibody binding to CCR8 peptide-nanobody complexes. In an example, the epitope is determined by screening antibody binding to CCR8 by phage display. In an example, the epitope is determined by determining binding to a CCR8 peptide expressed in human cells, wherein the peptide comprises an amino acid sequence given by SEQ ID NO: 82. In a particular example, the epitope comprises a threonine at position 4 of SEQ ID NO: 82. In a particular example, the epitope comprises a threonine at position 4 of SEQ ID NO: 22. In some examples, the epitope is determined by anti-CCR8 antibody binding

to the T4R mutation in cynomolgus monkey CCR8. In an example, binding to the T4R mutation is determined in a cell based affinity assay, wherein antibody binding to cells expressing cynomolgus monkey CCR8 containing a T4R mutation is compared to antibody binding to cells expressing wild-type cynomolgus monkey CCR8 (comprising a threonine at position four). In some examples, an anti-CCR8 antibody binds threonine at position four if it shows reduced binding to CCR8 comprising a T4R mutation. In particular examples, an anti-CCR8 antibody binds threonine at position four if it shows no detectable binding to CCR8 comprising a T4R mutation. In some examples, wild-type cynomolgus monkey CCR8 comprises an amino acid sequence given by SEQ ID NO: 22. In some examples, cynomolgus monkey CCR8 comprising a T4R mutation comprises an amino acid sequence given by SEQ ID NO: 556.

[0052] The present disclosure provides a method of treating cancer in a patient comprising administering an effective amount of an anti-CCR8 antibody, wherein the anti-CCR8 antibody does not block ligand binding to CCR8 and wherein the anti-CCR8 antibody has ADCC. In an example, the anti-CCR8 antibody further has an acceptable PK. In an example, the anti-CCR8 antibody binds an epitope wherein the epitope consists of at least one residue of SEQ ID NO: 82. In an example, the epitope consists of at least two residues of SEQ ID NO: 82. In an example, the epitope consists of at least three residues of SEQ ID NO: 82. In an example, the epitope consists of at least four residues of SEQ ID NO: 82. In an example, the epitope consists of rises at least five residues of SEQ ID NO: 82. In an example, the epitope consists of six or more residues of SEQ ID NO: 82. In an example, the epitope consists of seven or more residues of SEQ ID NO: 82. In an example, the epitope consists of eight or more residues of SEQ ID NO: 82. In an example, the epitope consists of nine or more residues of SEQ ID NO: 82. In an example, the epitope consists of ten or more residues of SEQ ID NO: 82. In an example, the epitope consists of eleven or more residues of SEQ ID NO: 82. In an example, the epitope consists of all twelve amino acid residues of SEQ ID NO: 82. In a particular example, the epitope consists of a threonine at position 4 of SEQ ID NO: 82. In a particular example, the epitope consists of a threonine at position 4 of SEQ ID NO: 22. In an example, the epitope is determined by epitope binning. In an example, the epitope is determined by antibody binding to CCR8 peptide-nanobody complexes. In an example, the epitope is determined by screening antibody binding to CCR8 by phage display. In an example, the epitope is determined by determining binding to a CCR8 peptide expressed in human cells, wherein the peptide comprises an amino acid sequence

given by SEQ ID NO: 82. In some examples, the epitope is determined by anti-CCR8 antibody binding to the T4R mutation in cynomolgus monkey CCR8. In an example, binding to the T4R mutation is determined in a cell based affinity assay, wherein antibody binding to cells expressing cynomolgus monkey CCR8 containing a T4R mutation is compared to antibody binding to cells expressing wild-type cynomolgus monkey CCR8 (comprising a threonine at position four). In some examples, an anti-CCR8 antibody binds threonine at position four if it shows reduced binding to CCR8 comprising a T4R mutation. In particular examples, an anti-CCR8 antibody binds threonine at position four if it shows no detectable binding to CCR8 comprising a T4R mutation. In some examples, wild-type cynomolgus monkey CCR8 comprises an amino acid sequence given by SEQ ID NO: 22. In some examples, cynomolgus monkey CCR8 comprising a T4R mutation comprises an amino acid sequence given by SEQ ID NO: 556.

[0053] The present disclosure also provides a method of treating cancer in a patient comprising administering an effective amount of an anti-CCR8 antibody or antigen-binding fragment of the present disclosure to the patient. In an example, the cancer is a solid tumor. In a more particular example, the cancer is non-small cell lung cancer, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, triple-negative breast cancer, colorectal cancer, pancreatic cancer, or metastatic castrate-resistant prostate cancer. In an example, the cancer is non-small cell lung cancer, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, or triple-negative breast cancer. In an example, the cancer is non-small cell lung cancer. In an example, the cancer is colorectal cancer. In an example, the cancer is head and neck squamous cell carcinoma. In some examples, the method further comprises administering to the patient a PD-1 antagonist antibody or a PD-L1 antagonist antibody. In some such examples, the PD-1 antagonist antibody or PD-L1 antagonist antibody is administered prior to, concurrently with, and/or after administration of the anti-CCR8 antibody or antigen-binding fragment. In particular examples, the PD-1 antagonist antibody is pembrolizumab, nivolumab, cemiplimab, or zeluvalimab. In other particular examples, the PD-L1 antagonist antibody is atezolizumab, avelumab, or durvalumab. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0054] In some examples, the method further comprises administering to the patient a chemotherapeutic agent. In some examples, the method comprises administering to the patient an anti-CCR8 antibody or antigen-binding fragment of the present disclosure and a chemotherapeutic agent. In some such examples, the

chemotherapeutic agent may be administered prior to, concurrently with, or after administration of the anti-CCR8 antibody or antigen-binding fragment of the present disclosure. In some examples, the method comprises administering to the patient an anti-CCR8 antibody of the present disclosure, a PD-1 or PD-L1 antagonist antibody, and a chemotherapeutic agent. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0055] The present disclosure provides a method of treating cancer in a patient comprising administering to the patient an effective amount of a Treg depleting antibody, a bispecific T-cell engager molecule, an agonist of a T cell co-stimulatory receptor, and/or an antagonist of the PD-1/PD-L1 pathway. In some examples, the patient is administered two of a Treg depleting antibody, a bispecific T-cell engager molecule, an agonist of a T cell co-stimulatory receptor, and an antagonist of the PD-1/PD-L1 pathway. In some examples, the patient is administered three of a Treg depleting antibody, a bispecific T-cell engager molecule, an agonist of a T cell co-stimulatory receptor, and an antagonist of the PD-1/PD-L1 pathway. In some examples, the patient is administered each of a Treg depleting antibody, a bispecific T-cell engager molecule, an agonist of a T cell co-stimulatory receptor, and an antagonist of the PD-1/PD-L1 pathway. In some examples, the patient is administered a bispecific T-cell engager molecule, an agonist of a T cell co-stimulatory receptor, and an antagonist of the PD-1/PD-L1 pathway.

[0056] The present disclosure also provides a method of treating cancer in a patient comprising administering to the patient an effective amount of a Treg depleting antibody and one or more of a bispecific T-cell engager molecule, an agonist of a T cell co-stimulatory receptor, and an antagonist of the PD-1/PD-L1 pathway. In another aspect, the present disclosure refers to the use of a Treg depleting antibody and one or more of a bispecific T-cell engager molecule, an agonist of a T cell co-stimulatory receptor, and an antagonist of the PD-1/PD-L1 pathway in the manufacture of a medicament for treating cancer in a patient. In an example, the method comprises administering to the patient an effective amount of a Treg depleting antibody and a bispecific T-cell engager molecule. In an example, the method comprises administering to the patient an effective amount of a Treg depleting antibody and an antagonist of the PD-1/PD-L1 pathway. In an example, the method comprises administering to the patient an effective amount of a Treg depleting antibody and an agonist of a T cell co-stimulatory receptor. In an example, the method comprises administering to the patient an effective amount of a Treg depleting antibody, a bispecific T-cell engager molecule, and an antagonist of the PD-1/PD-L1 pathway. In an example, the method comprises administering to the patient an effective amount of a Treg depleting antibody, a bispecific T-cell engager molecule, an antagonist of the PD-1/PD-L1 pathway, and an agonist of a T cell co-stimulatory receptor.

[0057] In some examples, the Treg depleting antibody is an anti-CCR8 antibody. In some examples, the Treg depleting antibody is an anti-CTLA4 antibody. In an example, the method comprises administering to the patient an effective amount of an anti-CCR8 antibody and a bispecific T-cell engager molecule. In an example, the method comprises administering to the patient an effective amount of an anti-CCR8 antibody of the present disclosure and a bispecific T-cell engager molecule. In an example, the method comprises administering to the patient an effective amount of an anti-CTLA-4 antibody and a bispecific T-cell engager molecule. In an example, the method comprises administering to the patient an effective amount of an anti-CCR8 antibody and an antagonist of the PD-1/PD-L1 pathway. In an example, the method comprises administering to the patient an effective amount of an anti-CCR8 antibody of the present disclosure and an antagonist of the PD-1/PD-L1 pathway. In some such examples, the antagonist of the PD-1/PD-L1 pathway is an PD-1 antagonist antibody. Antibody 20C1.006 (comprising LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, HCDR3 amino acid sequences of SEQ ID NOs 72-77, respectively; VL and VH amino acid sequences of SEQ ID NOs 78 and 79, respectively; and LC and HC amino acid sequences of SEQ ID NOs 80 and 81, respectively), zeluvalimab (comprising LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, HCDR3 amino acid sequences of SEQ ID NOs 32-37, respectively; VL and VH amino acid sequences of SEQ ID NOs 38 and 39 respectively; LC amino acid sequence of SEQ ID NO: 40; and HC amino acid sequences of SEQ ID NOs 41 or 636), Antibody 20A2.003 (comprising LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, HCDR3 amino acid sequences of SEQ ID NOs 42-47, respectively; VL and VH amino acid sequences of SEQ ID NOs 48 and 49, respectively; and LC and HC amino acid sequences of SEQ ID NOs 50 and 51, respectively), Antibody 22D4.006 (comprising LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, HCDR3 amino acid sequences of SEQ ID NOs 52-57, respectively; VL and VH amino acid sequences of SEQ ID NOs 58 and 59, respectively; and LC and HC amino acid sequences of SEQ ID NOs 60 and 61, respectively), or Antibody 22D4.017 (comprising LCDR1, LCDR2, LCDR3, HCDR1, HCDR2, HCDR3 amino acid sequences of SEQ ID NOs 62-67, respectively; VL and VH amino acid sequences of SEQ ID NOs 68 and 69, respectively; and LC and HC amino acid sequences of SEQ ID NOs 70 and 71, respectively). In one example, the PD-1 antagonist antibody is pembrolizumab. In another example, the PD-1 antagonist antibody is nivolumab. In yet another example, the PD-1 antagonist antibody is cemiplimab. In a particular example, the PD-1 antagonist antibody is zeluvalimab.

[0058] In an example, the method comprises administering to the patient an effective amount of an anti-CCR8 antibody, a bispecific T-cell engager molecule, and an PD-1 antagonist antibody. In an example, the method comprises administering to the patient an effective amount of an anti-CCR8 antibody of the present disclosure, a bispecific T-cell engager molecule, and an PD-1 antagonist antibody. In an example, the method comprises administering to the patient an effective amount of an anti-CTLA-4 antibody, a bispecific T-cell engager molecule, and an PD-1 antagonist antibody.

[0059] In an example, the method comprises administering to the patient an effective amount of an anti-CCR8 antibody, a bispecific T-cell engager molecule, an PD-1 antagonist antibody, and an agonist of a T cell co-stimulatory receptor. In an example, the method comprises administering to the patient an effective amount of an anti-CCR8 antibody of the present disclosure, a bispecific T-cell engager molecule, an PD-1 antagonist antibody, and an agonist of a T cell co-stimulatory receptor. In an example, the method comprises administering to the patient an effective amount of an anti-CTLA-4 antibody, a bispecific T-cell engager molecule, an PD-1 antagonist antibody, and an agonist of a T cell co-stimulatory receptor.

[0060] In some examples, the agonist of a T cell co-stimulatory receptor is an agonist of 4-1BB.

[0061] In some examples, the bispecific T-cell engager molecule comprises an amino acid sequence of any one of SEQ ID NOs. 87-345 in Table 15.

[0062] In some examples, the Treg depleting antibody is an antibody against CTLA-4, CCR8, CD25, TIGIT, CCR4, CD27, CD28, CD39, CD40, CD73, ICOS, OX40, 4-1BB, GITR, LAYN, IL1R2, or IL21R.

[0063] In some examples, the Treg depleting antibody is an anti-CTLA-4 antibody.

[0064] In some examples, the Treg depleting antibody is an anti-CCR8 antibody. In some such examples, the anti-CCR8 antibody is capable of depleting Treg cells. In some examples, the anti-CCR8 antibody is an anti-CCR8 antibody that has ADCC activity. In some examples, the anti-CCR8 antibody does not block ligand binding to CCR8. In some examples, the anti-CCR8 antibody binds human and cynomolgus monkey CCR8 on tumor-resident Treg cells. In some examples, the anti-CCR8 antibody binds an epitope on CCR8 wherein the epitope comprises at least one residue at positions 1-12 of SEQ ID NO.

31. In some examples, the anti-CCR8 antibody binds an epitope on CCR8 wherein the epitope consists of at least one residue at positions 1-12 of SEQ ID NO. 31. In a particular example, the epitope comprises a threonine at position 4 of SEQ ID NO: 22. The amino acid sequence of amino acid residues 1-12 of SEQ ID NO: 31 is SEQ ID NO: 82. In an example, the epitope is determined by epitope binning. In an example, the epitope is determined by antibody binding to CCR8 peptide-nanobody complexes. In an example, the epitope is determined by screening antibody binding to CCR8 by phage display. In an example, the epitope is determined by determining binding to a CCR8 peptide expressed in human cells, wherein the peptide comprises an amino acid sequence given by SEQ ID NO: 82. In some examples, the epitope is determined by anti-CCR8 antibody binding to the T4R mutation in cynomolgus monkey CCR8. In an example, binding to the T4R mutation is determined in a cell based affinity assay, wherein antibody binding to cells expressing cynomolgus monkey CCR8 containing a T4R mutation is compared to antibody binding to cells expressing wild-type cynomolgus monkey CCR8 (comprising a threonine at position four). In some examples, an anti-CCR8 antibody binds threonine at position four if it shows reduced binding to CCR8 comprising a T4R mutation. In particular examples, an anti-CCR8 antibody binds threonine at position four if it shows no detectable binding to CCR8 comprising a T4R mutation. In some examples, wild-type cynomolgus monkey CCR8 comprises an amino acid sequence given by SEQ ID NO: 22. In some examples, cynomolgus monkey CCR8 comprising a T4R mutation comprises an amino acid sequence given by SEQ ID NO: 556.In some examples, the anti-CCR8 antibody demonstrates an acceptable pharmacokinetic profile. In a particular example, the anti-CCR8 antibody is an anti-CCR8 antibody of the present disclosure.

[0065] In an example, the agonist of an immune cell co-stimulatory receptor is an agonist of CD2, TNFRSF4 (OX40), TNFRSF5 (CD40), TNFRSF7 (CD27), TNFRSF8 (CD30), TNFRSF9 (4-1BB), TNFRSF14 (HVEM), TNFRSF18 (GITR), TNFR2, or ICOS. In a particular example, the agonist of an immune cell co-stimulatory receptor is a 4-1BB agonist antibody.

[0066] In an example, the antagonist of the PD-1/PD-L1 pathway is a PD-1 antagonist antibody or a PD-L1 antagonist antibody as described herein. In some examples, the PD-1 antagonist antibody is any one of Antibody 20C1.006, zeluvalimab, Antibody 20A2.003, Antibody 22D4.006, or Antibody 22D4.017. In one example, the PD-1 antagonist antibody is pembrolizumab. In another example, the PD-1 antagonist antibody is nivolumab. In yet another example, the PD-1 antagonist antibody is cemiplimab. In a particular example, the PD-1 antagonist antibody is zeluvalimab.

[0067] In an example, the Treg depleting antibody is administered at the same time as the bispecific T-cell engager molecule, agonist of an immune cell co-stimulatory receptor, and/or an antagonist of the PD-1/PD-L1 pathway. In an example, the Treg depleting antibody, bispecific T-cell engager molecule, agonist of an immune cell co-stimulatory receptor, and/or an antagonist of the PD-1/PD-L1 pathway are administered at different times. In a particular example, the patient is administered a Treg depleting antibody, a bispecific T-cell engager molecule, an agonist of an immune cell co-stimulatory receptor, and an antagonist of the PD-1/PD-L1 pathway. In another particular example, the patient is administered an anti-CCR8 antibody, a bispecific T-cell engager molecule, a 4-1BB agonist antibody, and an antagonist of the PD-1/PD-L1 pathway. In a particular example, the anti-CCR8 antibody is an anti-CCR8 antibody of the present disclosure.

[0068] In an example, the cancer is a solid tumor. In a more particular example, the cancer is non-small cell lung cancer, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, triple-negative breast cancer, colorectal cancer, pancreatic cancer, or metastatic castrate-resistant prostate cancer. In an example, the cancer is non-small cell lung cancer, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, or triple-negative breast cancer. In an example, the cancer is non-small cell lung cancer. In an example, the cancer is colorectal cancer. In an example, the cancer is head and neck squamous cell carcinoma.

[0069] The present disclosure provides an anti-CCR8 antibody or antigen-binding fragment of the present disclosure for use in therapy. The present disclosure also provides an anti-CCR8 antibody or antigen-binding fragment of the present disclosure for use in treating cancer. In an example, the cancer is a solid tumor. In an example, the cancer is non-small cell lung cancer, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, triple-negative breast cancer, colorectal cancer, pancreatic cancer, or metastatic castrate-resistant prostate cancer. In a more particular example, the cancer is non-small cell lung cancer, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, or triple-negative breast cancer. In some examples, the use further comprises administering to the patient a PD-1 antagonist antibody or a PD-L1 antagonist antibody. In some such examples, the PD-1 antagonist antibody or PD-L1 antagonist antibody is administered prior to, concurrently with, and/or after administration of the anti-CCR8 antibody or antigen-binding fragment. In particular examples, the PD-1 antagonist antibody is pembrolizumab, nivolumab, cemiplimab, or zeluvalimab. In other particular examples, the PD-L1 antagonist antibody is atezolizumab, avelumab, or durvalumab. In

some examples, the use further comprises administering to the patient a chemotherapeutic agent. In some such examples, the chemotherapeutic agent may be administered prior to, concurrently with, or after administration of the anti-CCR8 antibody or antigen-binding fragment. In some examples, the use comprises administering to the patient an anti-CCR8 antibody or antigen-binding fragment of the present disclosure and a chemotherapeutic agent. In some examples, the use comprises administering to the patient an anti-CCR8 antibody or antigen-binding fragment of the present disclosure, a PD-1 or PD-L1 antagonist antibody, and a chemotherapeutic agent. In an example, the anti-CCR8 antibody or antigen-binding fragment thereof, is an antibody.

[0070] The present disclosure provides an anti-CCR8 antibody or antigen-binding fragment of the present disclosure for the manufacture of a medicament for the treatment of cancer. In an example, the cancer is a solid tumor. In an example, the cancer is non-small cell lung cancer, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, triple-negative breast cancer, colorectal cancer, pancreatic cancer, or metastatic castrate-resistant prostate cancer. In a more particular example, the cancer is non-small cell lung cancer, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, or triple-negative breast cancer. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[0071] The present disclosure also provides a pharmaceutical composition comprising an anti-CCR8 antibody of the present disclosure, or an antigen-binding fragment thereof, and one or more pharmaceutically acceptable carriers, diluents, or excipients. In an example, the antibody or antigen-binding fragment thereof, is an antibody. In yet another aspect, the present disclosure refers to a pharmaceutical composition comprising the antibody or antigen-binding fragment as described herein and a pharmaceutically acceptable carrier.

[0072] In an example, the anti-CCR8 antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 594 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 595. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 354, and the LC comprises an amino acid sequence of SEQ ID NO: 355. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 573, and the LC comprises an amino acid sequence of SEQ ID NO: 355.

[0073] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 596 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 597. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 364, and the LC comprises an amino acid sequence of SEQ ID NO: 365. In another particular example, the HC comprises an amino

acid sequence of SEQ ID NO: 574, and the LC comprises an amino acid sequence of SEQ ID NO: 365.

[0074] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 598 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 599. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 374, and the LC comprises an amino acid sequence of SEQ ID NO: 375. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 575, and the LC comprises an amino acid sequence of SEQ ID NO: 375.

[0075] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 600 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 601. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 384, and the LC comprises an amino acid sequence of SEQ ID NO: 385. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 576, and the LC comprises an amino acid sequence of SEQ ID NO: 385.

[0076] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 602 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 603. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 394, and the LC comprises an amino acid sequence of SEQ ID NO: 395. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 577, and the LC comprises an amino acid sequence of SEQ ID NO: 395.

[0077] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 604 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 605. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 404, and the LC comprises an amino acid sequence of SEQ ID NO: 405. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 578, and the LC comprises an amino acid sequence of SEQ ID NO: 405.

[0078] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 606 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 607. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 414, and the LC comprises an amino acid

sequence of SEQ ID NO: 415. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 579, and the LC comprises an amino acid sequence of SEQ ID NO: 415.

[0079] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 608 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 609. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 424, and the LC comprises an amino acid sequence of SEQ ID NO: 425. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 580, and the LC comprises an amino acid sequence of SEQ ID NO: 425.

[0080] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 610 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 611. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 434, and the LC comprises an amino acid sequence of SEQ ID NO: 435. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 581, and the LC comprises an amino acid sequence of SEQ ID NO: 435.

[0081] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 612 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 613. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 444, and the LC comprises an amino acid sequence of SEQ ID NO: 445. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 582, and the LC comprises an amino acid sequence of SEQ ID NO: 445.

[0082] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 614 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 615. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 454, and the LC comprises an amino acid sequence of SEQ ID NO: 455. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 583, and the LC comprises an amino acid sequence of SEQ ID NO: 455.

[0083] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 616 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 617. In a particular example, the HC

comprises an amino acid sequence of SEQ ID NO: 464, and the LC comprises an amino acid sequence of SEQ ID NO: 465. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 584, and the LC comprises an amino acid sequence of SEQ ID NO: 465.

[0084] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 618 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 619. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 474, and the LC comprises an amino acid sequence of SEQ ID NO: 475. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 585, and the LC comprises an amino acid sequence of SEQ ID NO: 475.

[0085] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 620 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 621. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 484, and the LC comprises an amino acid sequence of SEQ ID NO: 485. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 586, and the LC comprises an amino acid sequence of SEQ ID NO: 485.

[0086] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 622 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 623. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 494, and the LC comprises an amino acid sequence of SEQ ID NO: 495. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 587, and the LC comprises an amino acid sequence of SEQ ID NO: 495.

[0087] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 624 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 625. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 504, and the LC comprises an amino acid sequence of SEQ ID NO: 505. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 588, and the LC comprises an amino acid sequence of SEQ ID NO: 505.

[0088] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 626 and a LC encoded by a

polynucleotide sequence comprising SEQ ID NO: 627. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 514, and the LC comprises an amino acid sequence of SEQ ID NO: 515. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 589, and the LC comprises an amino acid sequence of SEQ ID NO: 515.

[0089] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 628 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 629. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 524, and the LC comprises an amino acid sequence of SEQ ID NO: 525. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 590, and the LC comprises an amino acid sequence of SEQ ID NO: 525.

[0090] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 630 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 631. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 534, and the LC comprises an amino acid sequence of SEQ ID NO: 535. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 591, and the LC comprises an amino acid sequence of SEQ ID NO: 535.

[0091] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 632 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 633. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 544, and the LC comprises an amino acid sequence of SEQ ID NO: 545. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 592, and the LC comprises an amino acid sequence of SEQ ID NO: 545.

[0092] In an example, the antibody of the present disclosure comprises a HC encoded by a polynucleotide sequence comprising SEQ ID NO: 634 and a LC encoded by a polynucleotide sequence comprising SEQ ID NO: 635. In a particular example, the HC comprises an amino acid sequence of SEQ ID NO: 554, and the LC comprises an amino acid sequence of SEQ ID NO: 555. In another particular example, the HC comprises an amino acid sequence of SEQ ID NO: 593, and the LC comprises an amino acid sequence of SEQ ID NO: 555.

[0093] Also provided herein are one or more nucleic acid sequences encoding the anti-CCR8 antibody or antigen-binding fragment of the present disclosure. In yet another aspect, the present disclosure refers to a nucleic acid sequence encoding the antibody or antigen-binding fragment as described herein. In some examples, the present disclosure provides a DNA molecule comprising a polynucleotide that encodes a HC of an antibody of the present disclosure. The present disclosure also provides a DNA molecule comprising a polynucleotide that encodes a LC of an antibody of the present disclosure. The present disclosure also provides a DNA molecule comprising a polynucleotide that encodes both a LC of an antibody of the present disclosure and a HC of an antibody of the present disclosure. In some examples, the disclosure provides a nucleic acid sequence encoding a heavy chain amino acid sequence of SEQ ID NOs: 1127, 1129, 1131, 1134, 1136, 1138, 1140, 1142, 1144, 1146, 1148, 1150, 1152, 1154, 1156, 1158, or 1160. In other examples, the disclosure provides a nucleic acid sequence encoding a light chain amino acid sequence of SEQ ID NOs: 1128, 1130, 1132, 1133, 1135, 1137, 1139, 1141, 1143, 1145, 1147, 1149, 1151, 1153, 1155, 1157, or 1159.

[0094] The present disclosure also provides a DNA molecule comprising a polynucleotide that encodes an antibody LC wherein the LC has an amino acid sequence of SEQ ID NO: 16. In an example, the polynucleotide comprises a polynucleotide sequence of SEQ ID NO: 28. The present disclosure also provides DNA molecules where one DNA molecule comprises a polynucleotide that encodes an antibody HC wherein the HC has an amino acid sequence of SEQ ID NO: 15, and another DNA molecule comprises a polynucleotide that encodes a LC wherein the LC has an amino acid sequence of SEQ ID NO: 16. In an example, the polynucleotide that encodes the antibody HC comprises a polynucleotide sequence of SEQ ID NO: 27, and the polynucleotide that encodes the LC comprises a polynucleotide sequence of SEQ ID NO: 28.

[0095] The present disclosure further provides a mammalian cell transformed with a DNA molecule of the present disclosure, wherein the transformed mammalian cell is capable of expressing an antibody of the present disclosure, wherein the antibody comprises two HCs and two LCs.

[0096] The present disclosure further provides a mammalian cell transformed with a DNA molecule of the present disclosure, wherein the transformed mammalian cell is capable of expressing an antibody comprising two HCs and two LCs, wherein each HC comprises an amino acid sequence of SEQ ID NO: 15, and each LC comprises an amino acid sequence of SEQ ID NO: 16.

[0096a] In another aspect, the present disclosure refers to a mammalian cell comprising the nucleic acid sequence as described herein or the vector as described herein.

[0097] The present disclosure also provides a process for producing an antibody of the present disclosure, wherein the antibody comprises two HCs and two LCs, and wherein the

process comprises cultivating a mammalian cell under conditions such that the antibody is expressed and recovering the expressed antibody. In an example, the mammalian cell is transformed with a DNA molecule of the present disclosure, wherein the transformed mammalian cell is capable of expressing an antibody of the present disclosure comprising two HCs and two LCs. The present disclosure also provides an antibody obtainable by the process.

[0098] The present disclosure also provides a process for producing an antibody, wherein the antibody comprises two HCs and two LCs, each HC comprises an amino acid sequence of SEQ ID NO: 15 and each LC comprises an amino acid sequence of SEQ ID NO: 16. In an example, the process comprises cultivating a mammalian cell under conditions such that the antibody is expressed and recovering the expressed antibody, and wherein the mammalian cell is transformed with a DNA molecule of the present disclosure, wherein the transformed mammalian cell is capable of expressing an antibody comprising two HCs and two LCs, wherein each HC comprises an amino acid sequence of SEQ ID NO: 15, and each LC comprises an amino acid sequence of SEQ ID NO: 16. The present disclosure also provides an antibody obtainable by the process.

[0099] The present disclosure provides a DNA molecule comprising a polynucleotide that encodes an antibody HC, wherein the HC has an amino acid sequence of SEQ ID NO: 19. In an example, the polynucleotide sequence comprises SEQ ID NO: 29.

[00100] The present disclosure provides a DNA molecule comprising a polynucleotide that encodes an antibody LC wherein the LC has an amino acid sequence of SEQ ID NO: 20. In an example, the polynucleotide sequence comprises SEQ ID NO: 30.

[00101] The present disclosure provides a DNA molecule comprising a polynucleotide that encodes an antibody HC wherein the HC has an amino acid sequence of SEQ ID NO: 19. In an example, the polynucleotide that encodes the antibody HC comprises a polynucleotide sequence of SEQ ID NO: 29. The present disclosure also provides a DNA molecule comprising a polynucleotide that encodes an antibody LC wherein the LC has an amino acid sequence of SEQ ID NO: 20. In an example, the polynucleotide that encodes the LC comprises a polynucleotide sequence of SEQ ID NO: 30. The present disclosure also provides a mammalian cell transformed with a DNA molecule of the present disclosure, wherein the transformed mammalian cell is capable of expressing an antibody comprising two HCs and two LCs, wherein each HC comprises an amino acid sequence of SEQ ID NO: 19, and each LC comprises an amino acid sequence of SEQ ID NO: 20.

[00102] In some examples, a nucleic acid sequence encoding an HC described herein may comprise any one of SEQ ID NOs: 1195, 1197, 1199, 1201, 1204, 1206, 1208, 1210, 1212, 1214, 1216, 1218, 1220, 1222, 1224, 1226, 1228, or 1230.

[00103] In some examples, a nucleic acid sequence encoding an LC described herein may comprise any one of SEQ ID NOs: 1196, 1198, 1200, 1202, 1203, 1205, 1207, 1209, 1211, 1213, 1215, 1217, 1219, 1221, 1223, 1225, 1227, or 1229.

[00104] In some examples, a nucleic acid sequence encoding an scFv described herein may comprise any one of SEQ ID NOs: 1163-1194.

[00105] The present disclosure also provides a process for producing an antibody, wherein the antibody comprises two HCs and two LCs, each HC comprises an amino acid sequence of SEQ ID NO: 19 and each LC comprises an amino acid sequence of SEQ ID NO: 20. In an example, the process comprises cultivating a mammalian cell under conditions such that the antibody is expressed and recovering the expressed antibody, and wherein the mammalian cell is transformed with a DNA molecule of the present disclosure. In an example, the transformed mammalian cell is capable of expressing an antibody comprising two HCs and two LCs, wherein each HC comprises an amino acid sequence of SEQ ID NO: 19, and each LC comprises an amino acid sequence of SEQ ID NO: 20. The present disclosure also provides an antibody obtainable by the process.

[00106] The present disclosure also provides a process for producing an antibody comprising two HCs and two LCs, wherein the process comprises cultivating the above-described mammalian cell under conditions such that the antibody is expressed and recovering the expressed antibody, wherein: (a) both HCs comprise an amino acid sequence of SEQ ID NOs: 15, 1125, 1127, 1129, 1131, 1134, 1136, 1138, 1140, 1142, 1144, 1146, 1148, 1150, 1152, 1154, 1156, 1158, or 1160, or an amino acid sequence that is at least 90% identical to any one of the foregoing HC amino acid sequences; and (b) both LCs comprise an amino acid sequence of SEQ ID NOs: 16, 365, 1126, 1128, 1130, 1132, 1133, 1135, 1137, 1139, 1141, 1143, 1145, 1147, 1149, 1151, 1153, 1155, 1157, or 1159, or an amino acid sequence that is at least 90% identical to any one of the foregoing LC amino acid sequences.

[00106a] In another aspect, the present disclosure refers to a process for producing an antibody comprising two HCs and two LCs, wherein the process comprises cultivating the mammalian cell of claim 28 under conditions such that the antibody is expressed and recovering the expressed antibody, and wherein: (a) both HCs comprise an amino acid sequence of SEQ ID NOs: 15, 573, 1125, 1127, 1129, 1131, 1134, 1136, 1138, 1140, 1142,

1144, 1146, 1148, 1150, 1152, 1154, 1156, 1158, 1160, 1238-1254, or an amino acid sequence that is at least 90% identical to any one of the foregoing HC amino acid sequences; and (b) both LCs comprise an amino acid sequence of SEQ ID NOs: 16, 365, 1126, 1128, 1130, 1132, 1133, 1135, 1137, 1139, 1141, 1143, 1145, 1147, 1149, 1151, 1153, 1155, 1157, or 1159, or an amino acid sequence that is at least 90% identical to any one of the foregoing LC amino acid sequences.

[00106b] In yet another aspect, the present disclosure refers to an antibody obtainable by the process as described herein.

[00106c] In another aspect, the present disclosure refers to the use of the antibody as described herein in the manufacture of a medicament for treating cancer.

[00107] In another example, the present disclosure provides an antibody or antigen-binding fragment thereof that binds human CCR8 at an epitope wherein the epitope comprises at least one residue at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises at least two residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises at least three residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises at least four residues at positions 1-12 of SEQ

ID NO: 31. In an example, the epitope comprises at least five residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises six or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises seven or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises eight or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises nine or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises ten or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises eleven or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises all twelve amino acid residues at positions 1-12 of SEQ ID NO: 31. In a particular example, the epitope comprises a threonine at position 4 of SEQ ID NO: 31. The amino acid sequence of amino acid residues 1-12 of SEQ ID NO: 31 is SEQ ID NO: 82. In a particular example, the epitope comprises a threonine at position 4 of SEQ ID NO: 22. In some such examples, the anti-CCR8 antibody does not block the binding of CCL1 to CCR8. In an example, the epitope is determined by epitope binning. In an example, the epitope is determined by antibody binding to CCR8 peptide-nanobody complexes. In an example, the epitope is determined by determining binding to a CCR8 peptide expressed in human cells, wherein the peptide comprises an amino acid sequence given by SEQ ID NO: 82. In an example, the epitope is determined by screening antibody binding to CCR8 by phage display. In another example, the present disclosure provides an antibody or antigen-binding fragment thereof that binds human CCR8 at an epitope wherein the epitope consists of at least one residue at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of at least two residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of at least three residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of at least four residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of at least five residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of six or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of seven or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of eight or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of nine or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of ten or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of eleven or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of all twelve amino acid residues at positions 1-12 of SEQ ID NO: 31. In a particular example, the

epitope consists of a threonine at position 4 of SEQ ID NO: 31. The amino acid sequence of amino acid residues 1-12 of SEQ ID NO: 31 is SEQ ID NO: 82. In a particular example, the epitope consists of a threonine at position 4 of SEQ ID NO: 22. In some such examples, the anti-CCR8 antibody does not block the binding of CCL1 to CCR8. In an example, the epitope is determined by epitope binning. In an example, the epitope is determined by antibody binding to CCR8 peptide-nanobody complexes. In an example, the epitope is determined by screening antibody binding to CCR8 by phage display. In an example, the epitope is determined by determining binding to a CCR8 peptide expressed in human cells, wherein the peptide comprises an amino acid sequence given by SEQ ID NO: 82. In some examples, the epitope is determined by anti-CCR8 antibody or antigen-binding fragment thereof binding to the T4R mutation in cynomolgus monkey CCR8. In an example, binding to the T4R mutation is determined in a cell based affinity assay, wherein antibody binding to cells expressing cynomolgus monkey CCR8 containing a T4R mutation is compared to antibody binding to cells expressing wild-type cynomolgus monkey CCR8 (comprising a threonine at position four). In some examples, an anti-CCR8 antibody or antigen-binding fragment thereof binds threonine at position four if it shows reduced binding to CCR8 comprising a T4R mutation. In particular examples, an anti-CCR8 antibody or antigen-binding fragment thereof binds threonine at position four if it shows no detectable binding to CCR8 comprising a T4R mutation. In some examples, wild-type cynomolgus monkey CCR8 comprises an amino acid sequence given by SEQ ID NO: 22. In some examples, cynomolgus monkey CCR8 comprising a T4R mutation comprises an amino acid sequence given by SEQ ID NO: 556. In an example, the anti-CCR8 antibody or fragment thereof is an antibody.

[00108] In another example, the present disclosure provides an antibody or antigen-binding fragment thereof that binds human CCR8 at an epitope wherein the epitope comprises at least one residue of SEQ ID NO: 82. In an example, the epitope comprises at least two residues of SEQ ID NO: 82. In an example, the epitope comprises at least three residues of SEQ ID NO: 82. In an example, the epitope comprises at least four residues of SEQ ID NO: 82. In an example, the epitope comprises at least five residues of SEQ ID NO: 82. In an example, the epitope comprises six or more residues of SEQ ID NO: 82. In an example, the epitope comprises seven or more residues of SEQ ID NO: 82. In an example, the epitope comprises eight or more residues of SEQ ID NO: 82. In an example, the epitope comprises nine or more residues of SEQ ID NO: 82. In an example, the epitope comprises ten or more residues of SEQ ID NO: 82. In an

example, the epitope comprises eleven or more residues of SEQ ID NO: 82. In an example, the epitope comprises all twelve amino acid residues of SEQ ID NO: 82. In a particular example, the epitope comprises a threonine at position 4 of SEQ ID NO: 82. In a particular example, the epitope comprises a threonine at position 4 of SEQ ID NO: 22. In some such examples, the anti-CCR8 antibody does not block the binding of CCL1 to CCR8. In an example, the epitope is determined by epitope binning. In an example, the epitope is determined by antibody binding to CCR8 peptide-nanobody complexes. In an example, the epitope is determined by screening antibody binding to CCR8 by phage display. In an example, the epitope is determined by determining binding to a CCR8 peptide expressed in human cells, wherein the peptide comprises an amino acid sequence given by SEQ ID NO: 82. In some examples, the epitope is determined by anti-CCR8 antibody or antigen-binding fragment thereof binding to the T4R mutation in cynomolgus monkey CCR8. In an example, binding to the T4R mutation is determined in a cell based affinity assay, wherein antibody binding to cells expressing cynomolgus monkey CCR8 containing a T4R mutation is compared to antibody binding to cells expressing wild-type cynomolgus monkey CCR8 (comprising a threonine at position four). In some examples, an anti-CCR8 antibody or antigen-binding fragment thereof binds threonine at position four if it shows reduced binding to CCR8 comprising a T4R mutation. In particular examples, an anti-CCR8 antibody or antigen-binding fragment thereof binds threonine at position four if it shows no detectable binding to CCR8 comprising a T4R mutation. In some examples, wild-type cynomolgus monkey CCR8 comprises an amino acid sequence given by SEQ ID NO: 22. In some examples, cynomolgus monkey CCR8 comprising a T4R mutation comprises an amino acid sequence given by SEQ ID NO: 556. In an example, the anti-CCR8 antibody or fragment thereof is an antibody.

[00109] In another example, the present disclosure provides an antibody or antigen-binding fragment thereof that binds human CCR8 at an epitope wherein the epitope consists of at least one residue of SEQ ID NO: 82. In an example, the epitope consists of at least two residues of SEQ ID NO: 82. In an example, the epitope consists of at least three residues of SEQ ID NO: 82. In an example, the epitope consists of at least four residues of SEQ ID NO: 82. In an example, the epitope consists of at least five residues of SEQ ID NO: 82. In an example, the epitope consists of six or more residues of SEQ ID NO: 82. In an example, the epitope consists of seven or more residues of SEQ ID NO: 82. In an example, the epitope consists of eight or more residues of SEQ ID NO: 82. In an example, the epitope consists of nine or more residues of SEQ ID NO: 82. In an

example, the epitope consists of ten or more residues of SEQ ID NO: 82. In an example, the epitope consists of eleven or more residues of SEQ ID NO: 82. In an example, the epitope consists of all twelve amino acid residues of SEQ ID NO: 82. In a particular example, the epitope consists of a threonine at position 4 of SEQ ID NO: 82. In a particular example, the epitope consists of a threonine at position 4 of SEQ ID NO: 22. In some such examples, the anti-CCR8 antibody does not block the binding of CCL1 to CCR8. In an example, the epitope is determined by epitope binning. In an example, the epitope is determined by antibody binding to CCR8 peptide-nanobody complexes. In an example, the epitope is determined by screening antibody binding to CCR8 by phage display. In an example, the epitope is determined by determining binding to a CCR8 peptide expressed in human cells, wherein the peptide comprises an amino acid sequence given by SEQ ID NO: 82. In some examples, the epitope is determined by anti-CCR8 antibody or antigen-binding fragment thereof binding to the T4R mutation in cynomolgus monkey CCR8. In an example, binding to the T4R mutation is determined in a cell based affinity assay, wherein antibody binding to cells expressing cynomolgus monkey CCR8 containing a T4R mutation is compared to antibody binding to cells expressing wild-type cynomolgus monkey CCR8 (comprising a threonine at position four). In some examples, an anti-CCR8 antibody or antigen-binding fragment thereof binds threonine at position four if it shows reduced binding to CCR8 comprising a T4R mutation. In particular examples, an anti-CCR8 antibody or antigen-binding fragment thereof binds threonine at position four if it shows no detectable binding to CCR8 comprising a T4R mutation. In some examples, wild-type cynomolgus monkey CCR8 comprises an amino acid sequence given by SEQ ID NO: 22. In some examples, cynomolgus monkey CCR8 comprising a T4R mutation comprises an amino acid sequence given by SEQ ID NO: 556. In an example, the anti-CCR8 antibody or fragment thereof is an antibody.

[00110] In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope comprising amino acids of SEQ ID NO: 83. In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope comprising amino acids of SEQ ID NO: 86. In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope comprising amino acids of SEQ ID NO: 84. In some examples, the epitope is determined by antibody binding to a peptide of amino acids of SEQ ID NO: 85, SEQ ID NO: 83, SEQ ID NO: 86, and/or SEQ ID NO: 84. In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope comprising amino acids at positions

13 through 35 of SEQ ID NO: 31. In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope comprising amino acids at positions 13, 14, or 15 of SEQ ID NO: 31.

[00111] In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope consisting of amino acids of SEQ ID NO: 83. In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope consisting of amino acids of SEQ ID NO: 86. In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope consisting of amino acids of SEQ ID NO: 84. In some examples, the epitope is determined by antibody binding to a peptide of amino acids of SEQ ID NO: 85, SEQ ID NO: 83, SEQ ID NO: 86, and/or SEQ ID NO: 84. In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope consisting of amino acids at positions 13 through 35 of SEQ ID NO: 31. In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope consisting of amino acids at positions 13, 14, or 15 of SEQ ID NO: 31

[00112] In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope comprising amino acids residues at position 13-24 of SEQ ID NO: 31. In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope comprising amino acids residues at position 19-30 of SEQ ID NO: 31. In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope comprising amino acids residues at position 25-35 of SEQ ID NO: 31. In some examples, the epitope is determined by antibody binding to a peptide of amino acids of SEQ ID NO: 85, SEQ ID NO: 83, SEQ ID NO: 86, and/or SEQ ID NO: 84.

[00113] In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope consisting of amino acids residues at position 13-24 of SEQ ID NO: 31. In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope consisting of amino acids residues at position 19-30 of SEQ ID NO: 31. In some examples, an anti-CCR8 antibody or fragment thereof of the present disclosure does not bind an epitope consisting of amino acids residues at position 25-35 of SEQ ID NO: 31. In some examples, the epitope is determined by antibody binding to a peptide of amino acids of SEQ ID NO: 85, SEQ ID NO: 83, SEQ ID NO: 86, and/or SEQ ID NO: 84.

[00114] The term "epitope" as used herein refers to sites of an antigen that are in contact with the variable region of an antibody. The epitope may be continuous or non-continuous, and may be determined by a method known to a person of ordinary skill, including flow cytometry of bound antibody to peptides, hydrogen-deuterium exchange, alanine scanning, and/or x-ray crystallography.

[00115] The epitope may be an epitope comprising or consisting of amino acid residues that are determined by antibody binding to a peptide as described herein. In some such examples, the peptide comprises an amino acid sequence of SEQ ID NO: 82. In some such examples, the peptide comprises an amino acid sequence of residues at positions 1-12 of SEQ ID NO: 31.

[00116] The epitope may be an epitope comprising or consisting of amino acid residues that are determined by epitope binning. In some such examples, the epitope binning is performed with biotinylated N-terminus CCR8 peptides.

[00117] The epitope may be an epitope comprising or consisting of amino acid residues that are determined by antibody binding to CCR8 peptide-nanobody complexes.

[00118] The epitope may be an epitope comprising or consisting of amino acid residues that are determined by screening antibody binding to CCR8 by phage display.

[00119] The epitope may be an epitope comprising or consisting of threonine at position four of the N-terminal region of CCR8 as determined by reduced binding to CCR8 comprising a T4R mutation compared to binding to wild-type CCR8. Binding to the T4R mutation may be tested, for example, by determining binding to wild-type cynomolgus monkey CCR8 (comprising an amino acid sequence given by SEQ ID NO: 22) compared to binding cynomolgus monkey CCR8 comprising a T4R mutation (comprising an amino acid sequence given by SEQ ID NO: 556).

[00120] The epitope may be an epitope comprising or consisting of amino acid residues that are determined by determining binding to a CCR8 peptide expressed in human cells, wherein the peptide comprises an amino acid sequence given by SEQ ID NO: 82. The CCR8 peptide may be fused to a nanobody, or other protein or Fc, for expression in human cells.

[00121] The present disclosure further provides an antibody or antigen-binding fragment that binds to an epitope on human CCR8, wherein said epitope comprises or consists of SEQ ID NO: 82. In some examples, the present disclosure also provides an antibody or antigen-binding fragment, wherein said antibody or antigen-binding fragment: (a) binds to an epitope on human CCR8, wherein said epitope comprises or consists of SEQ ID

NO: 82; and (b) does not block the binding of CCL1 to CCR8. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[00122] In some examples, the present disclosure provides a molecule that competes for binding to CCR8 with an anti-CCR8 antibody or antigen-binding fragment of the present disclosure. Such molecule that competes for binding may be, for example, an antibody, antibody fragment, or polypeptide. In some examples, the present disclosure provides a molecule that binds the same epitope as an anti-CCR8 antibody or antigen-binding fragment of the present disclosure. In an example, the anti-CCR8 antibody or antigen-binding fragment thereof, is an antibody.

[00123] The present disclosure provides a method of treating cancer in a patient comprising administering to the patient an effective amount of an antibody or antigen-binding fragment that binds human CCR8 at an epitope wherein the epitope comprises at least one residue at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises at least two residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises at least three residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises at least four residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises at least five residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises six or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises seven or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises eight or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises nine or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises ten or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises eleven or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope comprises all twelve amino acid residues at positions 1-12 of SEQ ID NO: 31. In a particular example, the epitope comprises a threonine at position 4 of SEQ ID NO: 31. The amino acid sequence of amino acid residues 1-12 of SEQ ID NO: 31 is SEQ ID NO: 82. In a particular example, the epitope comprises a threonine at position 4 of SEQ ID NO: 22. In some such examples, the anti-CCR8 antibody or antigen-binding fragment does not block the binding of CCL1 to CCR8. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[00124] The present disclosure provides a method of treating cancer in a patient comprising administering to the patient an effective amount of an antibody or antigen-binding fragment that binds human CCR8 at an epitope wherein the epitope consists of at least one

residue at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of at least two residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of at least three residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of at least four residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of at least five residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of six or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of seven or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of eight or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of nine or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of ten or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of eleven or more residues at positions 1-12 of SEQ ID NO: 31. In an example, the epitope consists of all twelve amino acid residues at positions 1-12 of SEQ ID NO: 31. In a particular example, the epitope consists of a threonine at position 4 of SEQ ID NO: 31. The amino acid sequence of amino acid residues 1-12 of SEQ ID NO: 31 is SEQ ID NO: 82. In a particular example, the epitope consists of a threonine at position 4 of SEQ ID NO: 22. In some such examples, the anti-CCR8 antibody or antigen-binding fragment does not block the binding of CCL1 to CCR8. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[00125] The present disclosure provides a method of treating cancer in a patient comprising administering to the patient an effective amount of an antibody or antigen-binding fragment that binds human CCR8 at an epitope wherein the epitope comprises at least one residue of SEQ ID NO: 82. In another aspect, the present disclosure refers to an anti-CCR8 antibody or antigen-binding fragment thereof, that binds human CCR8 at an epitope, wherein the epitope comprises at least one residue of SEQ ID NO: 82. In an example, the epitope comprises at least two residues of SEQ ID NO: 82. In an example, the epitope comprises at least three residues of SEQ ID NO: 82. In an example, the epitope comprises at least four residues of SEQ ID NO: 82. In an example, the epitope comprises at least five residues of SEQ ID NO: 82. In an example, the epitope comprises six or more residues of SEQ ID NO: 82. In an example, the epitope comprises seven or more residues of SEQ ID NO: 82. In an example, the epitope comprises eight or more residues of SEQ ID NO: 82. In an example, the epitope comprises nine or more residues of SEQ ID NO: 82. In an example, the epitope comprises ten or more residues of SEQ ID NO: 82. In an example, the epitope comprises eleven or more residues of SEQ ID NO: 82. In an example, the epitope comprises all twelve amino acid residues of SEQ ID NO: 82. In a particular example, the epitope comprises a threonine at position 4 of SEQ ID NO: 82. In

a particular example, the epitope comprises a threonine at position 4 of SEQ ID NO: 22. In some such examples, the anti-CCR8 antibody or antigen-binding fragment does not block the binding of CCL1 to CCR8. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[00125a] In another aspect, the present disclosure refers to the use of an antibody or antigen-binding fragment thereof that binds human CCR8 at an epitope in the manufacture of a medicament for treating cancer in a patient, wherein the epitope comprises at least one residue of SEQ ID NO: 82.

[00125b] In yet another aspect, the present disclosure refers to the use of an antibody or antigen-binding fragment thereof that binds human CCR8 at an epitope in the manufacture of a medicament for treating cancer in a patient, wherein the epitope consists of threonine at position 4 of SEQ ID NO: 82.

[00126] The present disclosure provides a method of treating cancer in a patient comprising administering to the patient an effective amount of an antibody or antigen-binding fragment that binds human CCR8 at an epitope wherein the epitope consists of at least one residue of SEQ ID NO: 82. In an example, the epitope consists of at least two residues of SEQ ID NO: 82. In an example, the epitope consists of at least three residues of SEQ ID NO: 82. In an example, the epitope consists of at least four residues of SEQ ID NO: 82. In an example, the epitope consists of at least five residues of SEQ ID NO: 82. In an example, the epitope consists of six or more residues of SEQ ID NO: 82. In an example, the epitope consists of seven or more residues of SEQ ID NO: 82. In an example, the epitope consists of eight or more residues of SEQ ID NO: 82. In an example, the epitope consists of nine or more residues of SEQ ID NO: 82. In an example, the epitope consists of ten or more residues of SEQ ID NO: 82. In an example, the epitope consists of eleven or more residues of SEQ ID NO: 82. In an example, the epitope consists of all twelve amino acid residues of SEQ ID NO: 82. In a particular example, the epitope consists of a threonine at position 4 of SEQ ID NO: 82. In a particular example, the epitope consists of a threonine at position 4 of SEQ ID NO: 22. In some such examples, the anti-CCR8 antibody or antigen-binding fragment does not block the binding of CCL1 to CCR8. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

[00127] In some examples, the present disclosure provides a method of treating cancer in a patient comprising administering to the patient an effective

amount of a molecule that competes for binding to CCR8 with an anti-CCR8 antibody or antigen-binding fragment of the present disclosure. Such molecule that competes for binding may be, for example, an antibody, antibody fragment, or polypeptide. In some examples, the present disclosure provides a molecule that binds the same epitope as an anti-CCR8 antibody of the present disclosure. In an example, the anti-CCR8 antibody or antigen-binding fragment thereof, is an antibody.

[00128] In some examples, an anti-CCR8 antibody or antigen-binding fragment of the present disclosure binds CCR8 from a non-human species. In some examples, an anti-CCR8 antibody or antigen-binding fragment of the present disclosure binds cynomolgus

monkey CCR8. In some examples, an anti-CCR8 antibody or antigen-binding fragment of the present disclosure binds murine CCR8. In some examples, the anti-CCR8 antibody or antigen-binding fragment of the present disclosure binds both cynomolgus monkey CCR8 and human CCR8. In a particular example, an anti-CCR8 antibody or antigen-binding fragment of the present disclosure bind cynomolgus monkey CCR8 and human CCR8 with affinities that are within 10-fold of one another. In an example, the antibody or antigen-binding fragment thereof, is an antibody.

BRIEF DESCRIPTION OF THE DRAWINGS

[00129] **Figure 1.** Anti-tumor activity of single agent muCLDN18.2 bispecific T-cell engager molecule (BiTE®) molecule (□), muCLDN18.2 BiTE molecule /anti-CTLA4 dual combination (△), muCLDN18.2 BiTE molecule /anti-PD-1/anti-4-1BB triple combination (◇), control BiTE molecule /anti-PD-1/anti-4-1BB/anti-CTLA4 quadruple combination (■), or muCLDN18.2 BiTE molecule /anti-PD-1/anti-4-1BB/anti-CTLA4 quadruple combination (▽) therapy in the KPC-M5 model.

[00130] **Figure 2.** Anti-tumor activity of CCR8 afucosylated mIgG2a antibody in an MC38 syngeneic mouse model. Individual tumor growth for isotype control mIgG2a antibody (dashed lines) or CCR8 afucosylated mIgG2a antibody (solid lines) are shown in Figures 2C and 2B, respectively. Figure 2A demonstrates the mean tumor volume for each group through day 24. **** indicates $p<0.0001$.

[00131] **Figure 3.** Percent survival of mice inoculated with MC38 tumor cells and treated with either isotype control mIgG2a antibody (dashed lines) or CCR8 afucosylated mIgG2a antibody (solid lines). **** indicates $p<0.0001$.

[00132] **Figure 4.** CD8+/Treg ratio in MC38 tumor-bearing mice treated with either isotype control mIgG2a antibody (▪) or CCR8 afucosylated mIgG2a antibody (•). Figures 4A, 4B, 4C, and 4D represent % Foxp3+Treg, % CD25+Foxp3+Treg, CD8/Treg (Foxp3+), and CD8/Treg (CD25+Foxp3+), respectively.

[00133] **Figure 5.** Anti-tumor activity of CCR8 afucosylated mIgG2a as monotherapy and in combination with TAA-BiTE molecule in the B16F10 syngeneic tumor model expressing tumor-associated antigen (TAA). Individual tumor growth for the treatment groups is depicted as spider plots (Figures 5A to 5D). Animals with no measurable tumors defined as Complete Responders (CRs) have been assessed until day 48.

CLAIMS

We claim:

1. An antibody that binds to human C-C chemokine receptor type 8 (CCR8), or an antigen-binding fragment thereof, wherein said antibody or antigen-binding fragment thereof comprises:

(a) a heavy chain complementarity-determining region (HCDR) 1 amino acid sequence of SEQ ID NO: 1;

(b) an HCDR2 amino acid sequence of SEQ ID NO: 2,

(c) an HCDR3 amino acid sequence of SEQ ID NO: 3,

(d) a light chain complementarity-determining region (LCDR) 1 amino acid sequence of KSSQSVLYSSNNX$_1$NYLA (SEQ ID NO: 1235), wherein X_1 is K or R,

(e) an LCDR2 amino acid sequence of SEQ ID NO: 5, and

(f) an LCDR3 amino acid sequence of SEQ ID NO: 6.

2. The antibody or antigen binding fragment of claim 1, which comprises an LCDR1 amino acid sequence of SEQ ID NO: 4.

3. The antibody or antigen binding fragment of claim 1 or claim 2, which comprises a heavy chain variable region (HCVR) amino acid sequence of SEQ ID NO: 13, and a light chain variable region (LCVR) comprising the amino acid sequence: DIVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNX$_1$NYLAWYX$_2$QKPGQX$_3$PKLLIS WASTRESGVPDRFSGSGSGTDFTLTINSLQAEDVAVYYCQQYYSIPITFGGGTKVEIK R (SEQ ID NO: 1236), wherein X_1 is K or R, X_2 is H or Q, and/or X_3 is S or P.

4. The antibody or antigen-binding fragment of any one of claims 1-3, which comprises a heavy chain variable region (HCVR) amino acid sequence of SEQ ID NO: 13 and a light chain variable region (LCVR) amino acid sequence of SEQ ID NO: 14 or SEQ ID NO: 363.

5. The antibody or antigen-binding fragment of any one of claims 1-4, which comprises a heavy chain (HC) amino acid sequence of SEQ ID NO: 15 or SEQ ID NO: 573 and a light chain (LC) amino acid sequence of SEQ ID NO: 16 or SEQ ID NO: 365.

6. The antibody or antigen-binding fragment of any one of claims 1-5, which comprises two HCs and two LCs, wherein both HCs comprise an amino acid sequence of SEQ ID NO: 15 or SEQ ID NO: 573, and both LCs comprise an amino acid sequence of SEQ ID NO: 16.

7. The antibody or antigen-binding fragment of any one of claims 1-5, which comprises two HCs and two LCs, and wherein both HCs comprise an amino acid sequence of SEQ ID NO: 15 or SEQ ID NO: 573, and both LCs comprise an amino acid sequence of SEQ ID NO: 365.

8. An antibody that binds to human CCR8, or an antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises (a) an HCDR1 amino acid sequence of SEQ ID NO: 839, (b) an HCDR2 amino acid sequence of SEQ ID NO: 840, (c) an HCDR3 amino acid sequence of SEQ ID NO: 841, (d) an LCDR1 amino acid sequence of SEQ ID NO: 842, (e) an LCDR2 amino acid sequence of SEQ ID NO: 843, and (f) an LCDR3 amino acid sequence of SEQ ID NO: 844.

9. The antibody or antigen-binding fragment of claim 8, which comprises an HCVR amino acid sequence of SEQ ID NO: 1017 and an LCVR amino acid sequence of SEQ ID NO: 1018.

10. The antibody or antigen-binding fragment of claim 8 or claim 9, which comprises an HC amino acid sequence of SEQ ID NO: 1125 or SEQ ID NO: 1237 and an LC amino acid sequence of SEQ ID NO: 1126.

11. The antibody or antigen-binding fragment of any one of claims 8-10, which comprises two HCs and two LCs, wherein both HCs comprise an amino acid sequence of SEQ ID NO: 1125 or SEQ ID NO: 1227, and both LCs comprise an amino acid sequence of SEQ ID NO: 1126.

12. An antibody that binds to human CCR8, or an antigen-binding fragment thereof, wherein the antibody comprises:

(a) an HCDR1 amino acid sequence of $X_1X_2GX_4H$, (SEQ ID NO: 1233), wherein (i) X_1 is N, S, D, G, T, or R, (ii) X_2 is C, N, Y, S, or F, and (iii) X_4 is M or F;

(b) an HCDR2 amino acid sequence of SEQ ID NOs: 648, 654, 660, 666, 672, 678, 684, 690, 696, 702, 708, 714, 720, 726, 732, 738, 744, 750, 756, 762, 768, 774,

780, 786, 792, 798, 804, 810, 816, 822, 828, 834, 840, 846, 852, 858, 867, 873, 879, 885, 891, 897, 903, 909, 915, 921, 927, 933, 939, or 945, or a variant thereof that comprises 1-4 amino acid substitutions or is at least 90% identical to any one of the foregoing HCDR2 amino acid sequences;

(c) an HCDR3 amino acid sequence of SEQ ID NOs: 649, 655, 661, 667, 673, 679, 685, 691, 697, 703, 709, 715, 721, 727, 733, 739, 745, 751, 757, 763, 769, 775, 781, 787, 793, 799, 805, 811, 817, 823, 829, 835, 847, 853, 859, 868, 874, 880, 886, 892, 898, 904, 910, 916, 922, 928, 934, 940, or 946 or a variant thereof that comprises 1-4 amino acid substitutions or is at least 90% identical to any one of the foregoing HCDR3 amino acid sequences;

(d) an LCDR1 amino acid sequence of SEQ ID NOs: 650, 656, 662, 668, 674, 680, 686, 692, 698, 704, 710, 716, 722, 728, 734, 740, 746, 752, 758, 764, 770, 776, 782, 788, 794, 800, 806, 812, 818, 824, 830, 836, 848, 854, 860, 863, 869, 875, 881, 887, 893, 899, 905, 911, 917, 923, 929, 935, or 941 or a variant thereof that comprises 1-4 amino acid substitutions or is at least 90% identical to any one of the foregoing LCDR1 amino acid sequences;

(e) an LCDR2 amino acid sequence of $RX_2X_3X_4RPS$ (SEQ ID NO: 1234), wherein (i) X_2 is A, N, D, S, or Q, (ii) X_3 is S, T, N, I, F, or A, and (iii) X_4 is N or V; and

(f) an LCDR3 amino acid sequence of SEQ ID NOs: 652, 658, 664, 670, 676, 682, 688, 694, 700, 706, 712, 718, 724, 730, 736, 742, 748, 754, 760, 766, 772, 778, 784, 790, 796, 802, 808, 814, 820, 826, 832, 838, 850, 856, 862, 865, 871, 877, 883, 889, 895, 901, 907, 913, 919, 925, 931, 937, or 943 or a variant thereof that comprises 1-4 amino acid substitutions or is at least 90% identical to any one of the foregoing LCDR3 amino acid sequences.

13. The antibody or antigen-binding fragment of claim 12, which comprises an HCDR1 amino acid sequence of SEQ ID NOs: 647, 653, 659, 665, 671, 677, 683, 689, 695, 701, 707, 713, 719, 725, 731, 737, 743, 749, 755, 761, 767, 773, 779, 785, 791, 797, 803, 809, 815, 821, 827, 833, 845, 851, 857, 866, 872, 878, 884, 890, 896, 902, 908, 914, 920, 926, 932, 938, or 944.

14. The antibody or antigen-binding fragment of claim 12 or claim 13, which comprises an LCDR2 amino acid sequence of SEQ ID NOs: 651, 657, 663, 669, 675, 681,

687, 693, 699, 705, 711, 717, 723, 729, 735, 741, 747, 753, 759, 765, 771, 777, 783, 789, 795, 801, 807, 813, 819, 825, 831, 837 849, 855, 861, 864, 870, 876, 882, 888, 894, 900, 906, 912, 918, 924, 930, 936, or 942

15. The antibody or antigen-binding fragment of any one of claims 12-14, which comprises a HCVR amino acid sequence comprising any one of SEQ ID NOs: 953, 955, 957, 959, 961, 963, 965, 967, 969, 971, 973, 975, 977, 979, 981, 983, 985, 987, 989, 991, 993, 995, 997, 999, 1001, 1003, 1005, 1007, 1009, 1011, 1013, 1015, 1019, 1021, 1023, 1026, 1028, 1030, 1032, 1034, 1036, 1038, 1040, 1042, 1044, 1046, 1048, 1050, or 1052, or an amino acid sequence that is at least 90% identical to any one of the foregoing HCVR amino acid sequences.

16. The antibody or antigen-binding fragment of any one of claims 12-15, which comprises a LCVR amino acid sequence comprising any one of SEQ ID NOs: 964, 966, 968, 970, 972, 974, 976, 978, 980, 982, 984, 986, 988, 990, 992, 994, 996, 998, 1000, 1002, 1004, 1006, 1008, 1010, 1012, 1014, 1016, 1020, 1022, 1024, 1025, 1027, 1029, 1031, 1033, 1035, 1037, 1039, 1041, 1043, 1045, 1047, 1049, or 1051, or an amino acid sequence that is at least 90% identical to any one of the foregoing LCVR amino acid sequences.

17. The antibody of or antigen-binding fragment claim 15 or claim 16, which comprises:

(a) a HCVR comprising an amino acid sequence of SEQ ID NO: 1019 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1020;

(b) a HCVR comprising an amino acid sequence of SEQ ID NO: 1021 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1022;

(c) a HCVR comprising an amino acid sequence of SEQ ID NO: 1023 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1024;

(d) a HCVR comprising an amino acid sequence of SEQ ID NO: 1026 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1025;

(e) a HCVR comprising an amino acid sequence of SEQ ID NO: 1028 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1027;

(f) a HCVR comprising an amino acid sequence of SEQ ID NO: 1030 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1029;

(g) a HCVR comprising an amino acid sequence of SEQ ID NO: 1032 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1031;

(h) a HCVR comprising an amino acid sequence of SEQ ID NO: 1034 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1033;

(i) a HCVR comprising an amino acid sequence of SEQ ID NO: 1036 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1035;

(j) a HCVR comprising an amino acid sequence of SEQ ID NO: 1038 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1037;

(k) a HCVR comprising an amino acid sequence of SEQ ID NO: 1040 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1039;

(l) a HCVR comprising an amino acid sequence of SEQ ID NO: 1042 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1041;

(m) a HCVR comprising an amino acid sequence of SEQ ID NO: 1044 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1043;

(n) a HCVR comprising an amino acid sequence of SEQ ID NO: 1046 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1045;

(o) a HCVR comprising an amino acid sequence of SEQ ID NO: 1048 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1047;

(p) a HCVR comprising an amino acid sequence of SEQ ID NO: 1050 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1049; or

(q) a HCVR comprising an amino acid sequence of SEQ ID NO: 1052 and a LCVR comprising an amino acid sequence of SEQ ID NO: 1051.

18. The antibody or antigen-binding fragment of any one of claims 12-17, which comprises a HC amino acid sequence of SEQ ID NOs: 1127, 1129, 1131, 1134, 1136, 1138, 1140, 1142, 1144, 1146, 1148, 1150, 1152, 1154, 1156, 1158, 1160, 1238-1254, or an amino acid sequence that is at least 90% identical to any one of the foregoing HC amino acid sequences.

19. The antibody or antigen-binding fragment of any one of claims 12-18, which comprises a LC amino acid sequence of SEQ ID NOs: 1128, 1130, 1132, 1133, 1135, 1137, 1139, 1141, 1143, 1145, 1147, 1149, 1151, 1153, 1155, 1157, or 1159, or an amino acid sequence that is at least 90% identical to any one of the foregoing LC amino acid sequences.

20. The antibody or antigen-binding fragment of claim 18 or claim 19, which comprises:

(a) an HC amino acid sequence of SEQ ID NO: 1127 or SEQ ID NO: 1238 and a LC amino acid sequence of SEQ ID NO: 1128;

(b) an HC amino acid sequence of SEQ ID NO: 1129 or SEQ ID NO: 1239 and a LC amino acid sequence of SEQ ID NO: 1130;

(c) an HC amino acid sequence of SEQ ID NO: 1131 or SEQ ID NO: 1240 and a LC amino acid sequence of SEQ ID NO: 1132;

(d) an HC amino acid sequence of SEQ ID NO: 1134 or SEQ ID NO: 1241 and a LC amino acid sequence of SEQ ID NO: 1133;

(e) an HC amino acid sequence of SEQ ID NO: 1136 or SEQ ID NO: 1242 and a LC amino acid sequence of SEQ ID NO: 1135;

(f) an HC amino acid sequence of SEQ ID NO: 1138 or SEQ ID NO: 1243 and a LC amino acid sequence of SEQ ID NO: 1137;

(g) an HC amino acid sequence of SEQ ID NO: 1140 or SEQ ID NO: 1244 and a LC amino acid sequence of SEQ ID NO: 1139;

(h) an HC amino acid sequence of SEQ ID NO: 1142 or SEQ ID NO: 1245 and a LC amino acid sequence of SEQ ID NO: 1141;

(i) an HC amino acid sequence of SEQ ID NO: 1144 or SEQ ID NO: 1246 and a LC amino acid sequence of SEQ ID NO: 1143;

(j) an HC amino acid sequence of SEQ ID NO: 1146 or SEQ ID NO: 1247 and a LC amino acid sequence of SEQ ID NO: 1145;

(k) an HC amino acid sequence of SEQ ID NO: 1148 or SEQ ID NO: 1248 and a LC amino acid sequence of SEQ ID NO: 1147;

(l) an HC amino acid sequence of SEQ ID NO: 1150 or SEQ ID NO: 1249 and a LC amino acid sequence of SEQ ID NO: 1149;

(m) an HC amino acid sequence of SEQ ID NO: 1152 or SEQ ID NO: 1250 and a LC amino acid sequence of SEQ ID NO: 1151;

(n) an HC amino acid sequence of SEQ ID NO: 1154 or SEQ ID NO: 1251 and a LC amino acid sequence of SEQ ID NO: 1153;

(o) an HC amino acid sequence of SEQ ID NO: 1156 or SEQ ID NO: 1252 and a LC amino acid sequence of SEQ ID NO: 1155;

(p) an HC amino acid sequence of SEQ ID NO: 1158 or SEQ ID NO: 1253 and a LC amino acid sequence of SEQ ID NO: 1157; or

(q) an HC amino acid sequence of SEQ ID NO: 1160 or SEQ ID NO: 1254 and a LC amino acid sequence of SEQ ID NO: 1159.

21. The antibody of or antigen-binding fragment claim 15 or claim 16, which is a single chain variable fragment (scFv) comprising an amino acid sequence of any one of SEQ ID NOs: 1093-1124.

22. The antibody or antigen-binding fragment of any one of claims 1-21, which is an antibody.

23. The antibody or antigen-binding fragment of any one of claims 1-21, which is an antigen-binding fragment of an antibody.

24. A nucleic acid sequence encoding the antibody or antigen-binding fragment of any one of claims 1-23.

25. A nucleic acid sequence encoding a heavy chain amino acid sequence of SEQ ID NOs: 1127, 1129, 1131, 1134, 1136, 1138, 1140, 1142, 1144, 1146, 1148, 1150, 1152, 1154, 1156, 1158, 1160, or 1238-1254.

26. A nucleic acid sequence encoding a light chain amino acid sequence of SEQ ID NOs: 1128, 1130, 1132, 1133, 1135, 1137, 1139, 1141, 1143, 1145, 1147, 1149, 1151, 1153, 1155, 1157, or 1159.

27. A vector comprising the nucleic acid sequence of any one of claims 24-26.

28. A mammalian cell comprising the nucleic acid sequence of any one of claims 24-26 or the vector of claim 27.

29. A pharmaceutical composition comprising the antibody or antigen-binding fragment of any one of claims 1-23 and a pharmaceutically acceptable carrier.

30. Use of the antibody of any one of claims 1-23, or the composition of claim 29 in the manufacture of a medicament for treating cancer in a patient.

31. The use of claim 30, wherein the cancer is a solid tumor.

32. The use of claim 30, wherein the cancer is non-small cell lung cancer, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, triple-negative breast cancer, colorectal cancer, pancreatic cancer, or metastatic castrate-resistant prostate cancer.

33. The use of any one of claims 30-32, which further comprises that a PD-1 antagonist antibody is to be administered to the patient.

34. The use of claim 33, wherein the PD-1 antagonist antibody is a monoclonal antibody.

35. The use of claim 33 or 34, wherein the PD-1 antagonist antibody is pembrolizumab, nivolumab, or zeluvalimab.

36. A process for producing an antibody comprising two HCs and two LCs, wherein the process comprises cultivating the mammalian cell of claim 28 under conditions such that the antibody is expressed and recovering the expressed antibody, and wherein:

(a) both HCs comprise an amino acid sequence of SEQ ID NOs: 15, 573, 1125, 1127, 1129, 1131, 1134, 1136, 1138, 1140, 1142, 1144, 1146, 1148, 1150, 1152, 1154, 1156, 1158, 1160, 1238-1254, or an amino acid sequence that is at least 90% identical to any one of the foregoing HC amino acid sequences; and

(b) both LCs comprise an amino acid sequence of SEQ ID NOs: 16, 365, 1126, 1128, 1130, 1132, 1133, 1135, 1137, 1139, 1141, 1143, 1145, 1147, 1149, 1151, 1153, 1155, 1157, or 1159, or an amino acid sequence that is at least 90% identical to any one of the foregoing LC amino acid sequences.

37. An antibody obtainable by the process of claim 36.

38. The antibody of any one of claims 1-23 or 37, which is afucosylated.

39. The antibody of any one of claims 1-23 or 37 for use in treating cancer.

40. The antibody of claim 39, wherein the cancer is a solid tumor.

41. The antibody of 39 or 40, wherein the cancer is non-small cell lung cancer, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, triple-negative breast cancer, colorectal cancer, pancreatic cancer, or metastatic castrate-resistant prostate cancer.

42. The antibody of claim 40, wherein the cancer is non-small cell lung cancer, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, or triple-negative breast cancer.

43. Use of the antibody of any one of claims 1-23 or 37 in the manufacture of a medicament for treating cancer.

44. The use of claim 43, wherein the cancer is a solid tumor.

45. The use of claim 43, wherein the cancer is non-small cell lung cancer, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, triple-negative breast cancer, colorectal cancer, pancreatic cancer, or metastatic castrate-resistant prostate cancer.

46. The use of claim 43, wherein the cancer is non-small cell lung cancer, gastric cancer, head and neck squamous cell carcinoma, hepatocellular carcinoma, or triple-negative breast cancer.

47. Use of a Treg depleting antibody and one or more of a bispecific T-cell engager molecule, an agonist of a T cell co-stimulatory receptor, and an antagonist of the PD-1/PD-L1 pathway in the manufacture of a medicament for treating cancer in a patient.

48. The use of claim 47, comprising that a Treg depleting antibody and a bispecific T-cell engager molecule are to be administered.

49. The use of claim 48, further comprising that an antagonist of the PD-1/PD-L1 pathway is to be administered.

50. The use of claim 48 or 49, further comprising that an agonist of a T cell co-stimulatory receptor is to be administered.

51. The use of any one of claims 47-50, wherein the Treg depleting antibody is an anti-CCR8 antibody.

52. The use of any one of claims 47-50, wherein the Treg depleting antibody is the anti-CCR8 antibody of any one of claims 1-23 or 37.

53. The use of any one of claims 47-50, wherein the Treg depleting antibody is an anti-CTLA-4 antibody.

54. The use of any one of claims 47 or 49-53, wherein the antagonist of the PD-1/PD-L1 pathway is an PD-1 antagonist antibody.

55. The use of claim 54, wherein the PD-1 antagonist antibody is pembrolizumab, nivolumab, or zeluvalimab.

56. The use of any one of claims 47 or 50-55, wherein the agonist of an immune cell co-stimulatory receptor is a 4-1BB agonist antibody.

57. Use of an antibody or antigen-binding fragment thereof that binds human CCR8 at an epitope in the manufacture of a medicament for treating cancer in a patient, wherein the epitope comprises at least one residue of SEQ ID NO: 82.

58. The use of claim 57, wherein the epitope comprises at least two residues of SEQ ID NO: 82.

59. The use of claim 57 or claim 58, wherein the epitope comprises at least three residues of SEQ ID NO: 82.

60. The use of any one of claims 57-59, wherein the epitope comprises at least four residues of SEQ ID NO: 82.

61. The use of any one of claims 57-60, wherein the epitope comprises a threonine at position 4 of SEQ ID NO: 82.

62. The use of any one of claims 57-61, wherein the antibody does not block ligand binding to CCR8.

63. Use of an antibody or antigen-binding fragment thereof that binds human CCR8 at an epitope in the manufacture of a medicament for treating cancer in a patient, wherein the epitope consists of threonine at position 4 of SEQ ID NO: 82.

64. The use of any one of Claims 57-63, wherein the epitope is determined by anti-CCR8 antibody or antigen-binding fragment thereof binding to the T4R mutation in cynomolgus monkey CCR8.

65. The use of Claim 64, wherein the epitope is determined in a cell-based affinity assay, wherein antibody binding to cells expressing cynomolgus monkey CCR8 containing a T4R mutation is compared to antibody binding to cells expressing wild-type cynomolgus monkey CCR8.

66. The use of any one of Claims 57-63, wherein the epitope is determined by epitope binning, binding to CCR8 peptide-nanobody complexes, and/or by screening binding to CCR8 by phage display.

67. The use of any one of claims 63-67, wherein the antibody does not block ligand binding to CCR8.

68. An anti-CCR8 antibody or antigen-binding fragment thereof, that binds human CCR8 at an epitope, wherein the epitope comprises at least one residue of SEQ ID NO: 82.

69. The anti-CCR8 antibody or antigen-binding fragment thereof of Claim 68, wherein the epitope comprises at least two residues of SEQ ID NO: 82.

70. The anti-CCR8 antibody or antigen-binding fragment thereof of Claim 68 or 69, wherein the epitope comprises at least three residues of SEQ ID NO: 82.

71. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-70, wherein the epitope comprises at least four residues of SEQ ID NO: 82.

72. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-71, wherein the epitope comprises at least five residues of SEQ ID NO: 82.

73. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-72, wherein the epitope comprises at least six residues of SEQ ID NO: 82.

74. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-73, wherein the epitope comprises at least seven residues of SEQ ID NO: 82.

75. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-74, wherein the epitope comprises at least eight residues of SEQ ID NO: 82.

76. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-75, wherein the epitope comprises at least nine residues of SEQ ID NO: 82.

77. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-76, wherein the epitope comprises at least ten residues of SEQ ID NO: 82.

78. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-77, wherein the epitope comprises at least eleven residues of SEQ ID NO: 82.

79. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-78, wherein the epitope comprises twelve residues of SEQ ID NO: 82.

80. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-79, wherein the epitope comprises a threonine at position 4 of SEQ ID NO: 82.

81. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-80, wherein the anti-CCR8 antibody does not block the binding of CCL1 to CCR8.

82. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-81, wherein the epitope is determined by epitope binning.

83. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-81, wherein the epitope is determined by binding to CCR8 peptide-nanobody complexes.

84. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-81, wherein the epitope is determined by screening antibody binding to CCR8 by phage display.

85. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-80, wherein the epitope is determined by anti-CCR8 antibody or antigen-binding fragment thereof binding to the T4R mutation in cynomolgus monkey CCR8.

86. The anti-CCR8 antibody or antigen-binding fragment thereof of Claim 85, wherein the epitope is determined in a cell based affinity assay, wherein antibody binding to cells expressing cynomolgus monkey CCR8 containing a T4R mutation is compared to antibody binding to cells expressing wild-type cynomolgus monkey CCR8.

87. The anti-CCR8 antibody or antigen-binding fragment thereof of Claim 85 or Claim 86, wherein the antibody or antigen-binding fragment demonstrates reduced or no detectable binding to CCR8 comprising a T4R mutation.

88. The anti-CCR8 antibody or antigen-binding fragment thereof of any one of Claims 68-84, wherein the antibody or antigen-binding fragment thereof does not block ligand binding to CCR8.

89. The anti-CCR8 antibody or antigen-binding fragment thereof of Claim 88, wherein the ligand is CCL1.

90. The anti-CCR8 antibody or antigen-binding fragment thereof, or the use of any one of Claims 57-89, wherein the anti-CCR8 antibody or antigen-binding fragment thereof is an antibody.