

CLAIMS

What is claimed is:

1. An ~~Fe-containing~~ antibody that is specific for one or more of SIRP α and SIRP β 1, and is also specific for SIRP γ , wherein binding of the antibody to one or more of SIRP α , SIRP β 1, and SIRP γ does not disrupt the interaction between CD47 and SIRP α , and/or the interaction between CD47 and SIRP γ on a cell induces depletion of the cell.
- ~~2. An antibody that is specific for one or more of SIRP α and SIRP β 1, and is specific for SIRP γ , wherein the antibody comprises a heavy chain variable region and a light chain variable region, and~~
~~wherein the heavy chain variable region comprises:~~
 - ~~i. a complementarity determining region 1 (CDR-H1) sequence selected from the group consisting of SEQ ID NOS: 54, 56, and 59-65;~~
 - ~~ii. a CDR-H2 sequence selected from the group consisting of SEQ ID NOS: 70, 72, and 75-81; and~~
 - ~~iii. a CDR-H3 sequence selected from the group consisting of SEQ ID NOS: 86, 88-89, and 92-99; and/or~~
~~wherein the light chain variable region comprises:~~
 - ~~i. a light chain CDR 1 (CDR-L1) sequence selected from the group consisting of SEQ ID NOS: 5, 7-8, and 11-18;~~
 - ~~ii. a CDR-L2 sequence selected from the group consisting of SEQ ID NOS: 23-24, and 27-33; and~~
 - ~~iii. a CDR-H3 sequence selected from the group consisting of SEQ ID NOS: 36, 38-39, and 42-49.~~
- ~~3.2.~~ The antibody of claim 1 ~~or 2~~, wherein the antibody comprises a heavy variable domain and a light variable domain, and wherein the heavy and light variable domains comprise a complementarity determining region ~~chain~~ (CDR) sequence combination selected from the group consisting of:

- a. SEQ ID NO: 5, SEQ ID NO: 23, SEQ ID NO: 36, SEQ ID NO: 54, SEQ ID NO: 70, and SEQ ID NO: 86;
- ~~b. SEQ ID NO: 7, SEQ ID NO: 24, SEQ ID NO: 38, SEQ ID NO: 54, SEQ ID NO: 72, and SEQ ID NO: 88;~~
- ~~c. SEQ ID NO: 8, SEQ ID NO: 24, SEQ ID NO: 39, SEQ ID NO: 56, SEQ ID NO: 72, and SEQ ID NO: 89;~~
- ~~d. SEQ ID NO: 11, SEQ ID NO: 27, SEQ ID NO: 42, SEQ ID NO: 59, SEQ ID NO: 75, and SEQ ID NO: 92;~~
- ~~e. SEQ ID NO: 12, SEQ ID NO: 28, SEQ ID NO: 43, SEQ ID NO: 60, SEQ ID NO: 76, and SEQ ID NO: 93;~~
- ~~f. SEQ ID NO: 13, SEQ ID NO: 29, SEQ ID NO: 44, SEQ ID NO: 61, SEQ ID NO: 76, and SEQ ID NO: 94;~~
- ~~g. SEQ ID NO: 13, SEQ ID NO: 30, SEQ ID NO: 45, SEQ ID NO: 62, SEQ ID NO: 77, and SEQ ID NO: 95;~~
- ~~h. SEQ ID NO: 14, SEQ ID NO: 31, SEQ ID NO: 46, SEQ ID NO: 63, SEQ ID NO: 78, and SEQ ID NO: 96;~~
- ~~i.b.~~ SEQ ID NO: 15, SEQ ID NO: 31, SEQ ID NO: 47, SEQ ID NO: 62, SEQ ID NO: 79, and SEQ ID NO: 97;
- ~~j.c.~~ SEQ ID NO: 16, SEQ ID NO: 31, SEQ ID NO: 47, SEQ ID NO: 62, SEQ ID NO: 79, and SEQ ID NO: 97; and
- ~~k. SEQ ID NO: 17, SEQ ID NO: 32, SEQ ID NO: 48, SEQ ID NO: 64, SEQ ID NO: 80, and SEQ ID NO: 98; and~~
- ~~l.d.~~ SEQ ID NO: 18, SEQ ID NO: 33, SEQ ID NO: 49, SEQ ID NO: 65, SEQ ID NO: 81, and SEQ ID NO: 99.

- ~~4. The antibody of any one of claims 1-3, wherein the heavy chain variable region comprises a sequence selected from the group consisting of SEQ ID NOS: 104, 106-107, and 110-118.~~
- ~~5. The antibody of any one of claims 1-4, wherein the light chain variable region comprises a sequence selected from the group consisting of SEQ ID NOS: 123, 125-126, and 129-137.~~
- ~~6. The antibody of any one of claims 1-5, wherein the heavy chain variable region sequence and the light chain variable region sequence are selected from the group consisting of:~~

- ~~a. SEQ ID NO: 104 and SEQ ID NO: 123;~~
- ~~b. SEQ ID NO: 106 and SEQ ID NO: 125;~~
- ~~c. SEQ ID NO: 107 and SEQ ID NO: 126;~~
- ~~d. SEQ ID NO: 110 and SEQ ID NO: 129;~~
- ~~e. SEQ ID NO: 111 and SEQ ID NO: 130;~~
- ~~f. SEQ ID NO: 112 and SEQ ID NO: 131;~~
- ~~g. SEQ ID NO: 113 and SEQ ID NO: 132;~~
- ~~h. SEQ ID NO: 114 and SEQ ID NO: 133;~~
- ~~i. SEQ ID NO: 115 and SEQ ID NO: 134;~~
- ~~j. SEQ ID NO: 116 and SEQ ID NO: 135;~~
- ~~k. SEQ ID NO: 117 and SEQ ID NO: 136; and~~
- ~~l.e. SEQ ID NO: 118 and SEQ ID NO: 137.~~

7.3. The antibody of claim 1 or 2~~any one of claims 1-5~~, wherein the antibody comprises a heavy variable domain and a light variable domain, wherein:

- a. the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 104 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 123, or an amino acid sequence with at least 80% sequence identity thereto;
- b. the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 115 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 134, or an amino acid sequence with at least 80% sequence identity thereto;
- c. the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 116 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the

amino acid sequence of SEQ ID NO: 135, or an amino acid sequence with at least 80% sequence identity thereto; or

d. the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 118 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 137, or an amino acid sequence with at least 80% sequence identity thereto.

- ~~8. The antibody of any one of claims 1-5, wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 106 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 125, or an amino acid sequence with at least 80% sequence identity thereto.~~
- ~~9. The antibody of any one of claims 1-5, wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 107 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 126, or an amino acid sequence with at least 80% sequence identity thereto.~~
- ~~10. The antibody of any one of claims 1-5, wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 110 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 129, or an amino acid sequence with at least 80% sequence identity thereto.~~
- ~~11. The antibody of any one of claims 1-5, wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 111 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 130, or an amino acid sequence with at least 80% sequence identity thereto.~~
- ~~12. The antibody of any one of claims 1-5, wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 112 or an amino acid~~

~~sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 131, or an amino acid sequence with at least 80% sequence identity thereto.~~

~~13. The antibody of any one of claims 1-5, wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 113 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 132, or an amino acid sequence with at least 80% sequence identity thereto.~~

~~14. The antibody of any one of claims 1-5, wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 114 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 133, or an amino acid sequence with at least 80% sequence identity thereto.~~

~~15. The antibody of any one of claims 1-5, wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 115 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 134, or an amino acid sequence with at least 80% sequence identity thereto.~~

~~16. The antibody of any one of claims 1-5, wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 116 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 135, or an amino acid sequence with at least 80% sequence identity thereto.~~

~~17. The antibody of any one of claims 1-5, wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 117 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 136, or an amino acid sequence with at least 80% sequence identity thereto.~~

- ~~18. The antibody of any one of claims 1-5, wherein the heavy chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 118 or an amino acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain of the antibody comprises the amino acid sequence of SEQ ID NO: 137, or an amino acid sequence with at least 80% sequence identity thereto.~~
- 19.4.** The antibody of any one of claims 12-318, wherein the antibody comprises an Fc domain, optionally wherein the Fc domain is selected from the group consisting of human IgG1, IgG2, IgG3, and IgG4.
- ~~20. The antibody of any one of claims 1-19, wherein the antibody is an Fc-containing antibody, and the binding of the antibody to one or more of SIRP α , SIRP β 1, and SIRP γ on a cell induces depletion of the cell.~~
- ~~21. The antibody of any one of claims 1-20, wherein the cell depletion involves antibody dependent cellular phagocytosis (ADCP).~~
- ~~22. The antibody of any one of claims 1-21, wherein the cell depletion involves antibody dependent cellular cytotoxicity (ADCC).~~
- ~~23. The method of any one of claims 1-22, wherein the cell depletion involves depletion of SIRP γ positive cells.~~
- ~~24. The antibody of any one of claims 1-23 wherein the SIRP γ cells are lymphocytes.~~
- ~~25. The antibody of claim 24, wherein the lymphocytes are T cells or NK cells.~~
- ~~26. The antibody of claim 25, wherein the T cells are cytotoxic T cells, helper T cells, memory T cells, regulatory T cells, natural killer T cells, mucosal associated invariant T cells, gamma delta T cells, or a combination thereof.~~
- ~~27. The antibody of any one of claims 1-22, wherein the cell depletion involves depletion of SIRP γ positive cells and SIRP α and/or SIRP β 1 positive cells.~~
- ~~28. The antibody of claim 27, wherein the SIRP α and/or SIRP β 1 cells are myeloid cells or myeloid progenitor cells.~~
- 29.** The antibody of claim 27 or 28, wherein the SIRP α and/or SIRP β 1 cells are selected from the group consisting of myeloid cell progenitors, monocytes, macrophages, dendritic cells, basophils, eosinophils, neutrophils, and mast cells.

30.5. The antibody of any one of claims 1-~~429~~, wherein the antibody is a monoclonal antibody, an antibody fragment, a human antibody, a humanized antibody, a chimeric antibody, or a full-length antibody.

~~31. The antibody of any one of claims 1-29, wherein the antibody is an antibody fragment.~~

~~32. The antibody of any one of claims 1-29, wherein the antibody is a human antibody.~~

~~33. The antibody of any one of claims 1-29, wherein the antibody is a humanized antibody.~~

~~34. The antibody of any one of claims 1-29, wherein the antibody is a chimeric antibody.~~

~~35. The antibody of any one of claims 1-29, wherein the antibody is a full-length antibody.~~

~~36. The antibody of any one of claims 1 or 19-35, wherein the Fc domain is selected from the group consisting of human IgG1, IgG2, IgG3, and IgG4.~~

~~37. The antibody of claim 36, wherein the Fc domain comprises SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 26.~~

~~38. -The antibody of claim 36, wherein the Fc domain comprises one or more amino acid substitutions relative to SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 26.~~

39.6. The antibody of claim 4 or 536, wherein:

a. the Fc domain of the antibody is human IgG1 and comprises at least one amino acid substitution at a position selected from the group consisting of: 214, 215, 221, 222, 228, 234, 235, 236, 239, 240, 241, 243, 244, 245, 247, 250, 252, 254, 256, 262, 263, 264, 265, 266, 267, 268, 269, 270, 292, 296, 297, 298, 299, 300, 305, 313, 324, 325, 326, 327, 328, 329, 330, 332, 333, 334, 345, 356, 358, 396, 428, 430, 433, 434, and 440 wherein the position numbers of the amino acid residues are of the EU numbering scheme;

b. the IgG1 Fc comprises a sequence selected from the group consisting of:

i. SEQ ID NO: 19;

ii. SEQ ID NO: 20, wherein X1 is V or A;

iii. SEQ ID NO: 21, wherein X1 is V or A; X2 is G or A; X3 is S or D; and X4 is I or E;

iv. SEQ ID NO: 22, wherein X1 is V or A;

v. SEQ ID NO: 25, wherein X1 is V or A; X2 is M or L; and X3 is N or S;

and

- vi. SEQ ID NO: 26, wherein X1 is K or R; X2 is D or E; and X3 is L or M;
or
c. the IgG4 Fc comprises a sequence of SEQ ID NO: 34, 35 or 37, wherein X1 in
SEQ ID NO: 37 is S or P; and X2 in SEQ ID NO: 37 is L or E.
- ~~40. The antibody of claim 36, wherein the IgG1 Fc comprises a sequence selected from the group consisting of:~~
- ~~a. SEQ ID NO: 19;~~
 - ~~b. SEQ ID NO: 20, wherein X₁ is V or A;~~
 - ~~c. SEQ ID NO: 21, wherein X₁ is V or A; X₂ is G or A; X₃ is S or D; and X₄ is I or E;~~
 - ~~d. SEQ ID NO: 22, wherein X₁ is V or A;~~
 - ~~e. SEQ ID NO: 25, wherein X₁ is V or A; X₂ is M or L; and X₃ is N or S; and~~
 - ~~f. SEQ ID NO: 26, wherein X₁ is K or R; X₂ is D or E; and X₃ is L or M.~~
- ~~41. The antibody of claim 36, wherein the IgG4 Fc comprises a sequence of SEQ ID NO: 34, 35 or 37, wherein X₁ in SEQ ID NO: 37 is S or P; and X₂ in SEQ ID NO: 37 is L or E.~~
- ~~42. The antibody of any one of claims 1-41, wherein the binding of the antibody does not disrupt the interaction between CD47 and SIRP α , and/or the interaction between CD47 and SIRP γ .~~
- ~~43. The antibody of any one of claims 1-41, wherein the binding of the antibody disrupts the the interaction between CD47 and SIRP α , and/or between CD47 and SIRP γ .~~
- ~~44.7. _____~~ The antibody of any one of claims 1-~~643~~, wherein the antibody binds SIRP α , SIRP β 1 and SIRP γ .
- ~~45.8. _____~~ The antibody of any one of claims 1-~~643~~, wherein the antibody binds SIRP α and SIRP γ and exhibits little or no binding to SIRP β 1.
- ~~46.9. _____~~ The antibody of any one of claims 1-~~643~~, wherein the antibody binds SIRP β 1 and SIRP γ and exhibits little or no binding to SIRP α .
- ~~47. The antibody of any one of claims 1-45, wherein the antibody comprises a binding affinity to SIRP α of about 100pm, about 1nM, about 5nM, about 10nM, about 50nM, about 100nM, about 500nM, or about 1 μ M.~~

- ~~48.~~ The antibody of any one of claims 1-47, wherein the antibody comprises a binding affinity for ~~SIRP β 1~~ of about 0.05 nM, about 0.1 nM, about 5 nM, about 10 nM, about 50 nM, about 100 nM, about 500 nM, about 1 μ M, about 5 μ M, or about 10 μ M.
- ~~49.~~ The antibody of any one of claims 1-47, wherein the antibody comprises a binding affinity for ~~SIRP γ~~ of about 0.0001 nM, about 0.0005 nM, about 0.001 nM, about 0.005 nM, about 0.1 nM, about 0.05 nM, about 0.1 nM, about 0.5 nM, about 1 nM, about 5 nM, about 10 nM, about 50 nM, about 100 nM, about 500 nM, about 1 μ M, about 2 μ M or about 3 μ M.
- ~~50.10.~~ A pharmaceutical composition comprising any one of the antibodies of claims 1-49, and optionally a pharmaceutically acceptable carrier.
- ~~51.11.~~ A nucleic acid encoding for the antibody of any one of claims 1-49, optionally wherein:
- a. the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 142, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 161, or a nucleic acid sequence with at least 80% sequence identity thereto;
 - b. the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 153, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 172, or a nucleic acid sequence with at least 80% sequence identity thereto;
 - c. the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 154, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 173, or a nucleic acid sequence with at least 80% sequence identity thereto; or
 - d. the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 156, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic

acid sequence of SEQ ID NO: 175, or a nucleic acid sequence with at least 80% sequence identity thereto.

- ~~52. The nucleic acid of claim 51, comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 142, 144-145, 148-156, 161, 163-164, and 167-175.~~
- ~~53. The nucleic acid of claim 51 or 52, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 142, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 161, or a nucleic acid sequence with at least 80% sequence identity thereto.~~
- ~~54. The nucleic acid of claim 51 or 52, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 144, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 163, or a nucleic acid sequence with at least 80% sequence identity thereto.~~
- ~~55. The nucleic acid of claim 51 or 52, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 145, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 164, or a nucleic acid sequence with at least 80% sequence identity thereto.~~
- ~~56. The nucleic acid of claim 51 or 52, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 148, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 167, or a nucleic acid sequence with at least 80% sequence identity thereto.~~
- ~~57. The nucleic acid of claim 51 or 52, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 149, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 168, or a nucleic acid sequence with at least 80% sequence identity thereto.~~

- ~~58. The nucleic acid of claim 51 or 52, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 150, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 169, or a nucleic acid sequence with at least 80% sequence identity thereto.~~
- ~~59. The nucleic acid of claim 51 or 52, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 151, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 170, or a nucleic acid sequence with at least 80% sequence identity thereto.~~
- ~~60. The nucleic acid of claim 51 or 52, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 152, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 171, or a nucleic acid sequence with at least 80% sequence identity thereto.~~
- ~~61. The nucleic acid of claim 51 or 52, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 153, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 172, or a nucleic acid sequence with at least 80% sequence identity thereto.~~
- ~~62. The nucleic acid of claim 51 or 52, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 154, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 173, or a nucleic acid sequence with at least 80% sequence identity thereto.~~
- ~~63. The nucleic acid of claim 51 or 52, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 155, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded~~

~~by the nucleic acid sequence of SEQ ID NO: 174, or a nucleic acid sequence with at least 80% sequence identity thereto.~~

~~64. The nucleic acid of claim 51 or 52, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 156, or a nucleic acid sequence with at least 80% sequence identity thereto; and/or wherein the light chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 175, or a nucleic acid sequence with at least 80% sequence identity thereto.~~

~~65.12. A vector comprising the nucleic acid of claim 11 any one of claims 51-64.~~

~~66. A method of inducing the depletion of a population of cells, the method comprising contacting the population of cells with the antibody of any one of claims 1-49.~~

~~67. The method of claim 66, wherein at least a subset of the population of cells expresses SIRP γ .~~

~~68. The method of claim 66, wherein the population of cells that express SIRP γ comprise lymphocytes.~~

~~69. The method of claim 68, wherein the lymphocytes comprise T cells or NK cells.~~

~~70. The method of any one of claims 66-69, wherein at least a subset of the population of cells expresses SIRP α and/or SIRP β 1.~~

~~71. The method of claim 70, wherein the population of cells that express SIRP α and/or SIRP β 1 comprise myeloid cells or myeloid progenitor cells.~~

~~72. The method of claim 70, wherein the population of cells that express SIRP α and/or SIRP β 1 comprise monocytes, macrophages, dendritic cells, basophils, eosinophils, neutrophils, or mast cells.~~

~~73. The method of any one of claims 66-72, wherein the method is *in vitro*.~~

~~74. The method of any one of claims 66-72, wherein the method is *in vivo*.~~

~~75. The method any one of claims 66-74, wherein the population of cells comprises tissue-resident cells.~~

~~76. The method any one of claims 66-75, wherein the population of cells comprises circulating cells.~~

~~77. The method of any one of claims 66-76, wherein the cell depletion involves ADCC.~~

~~78. The method of any one of claims 66-77, wherein the cell depletion involves ADCP.~~

~~79. The method of any one of claims 66-78, wherein the cell depletion involves ADCC and ADCP.~~

~~80.13. A method of treating a disease or condition in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of the antibody of any one of claims 1-49 or the pharmaceutical composition of claim 1050, for use in therapy.~~

~~14. Use of the antibody of any one of claims 1-9 or the pharmaceutical composition of claim 10, in the manufacture of a medicament for treating a disease or condition in a subject in need thereof.~~

~~81.15. The method-use of claim 1480, wherein the disease or condition is characterized by overactivation and/or hyperproliferation of lymphocytes, and the antibody induces depletion of lymphocytes, optionally wherein the lymphocytes are T cells, optionally wherein the disease or condition comprises aplastic anemia, cell mediated rejection of solid organ transplant, graft failure post-HSCT (hematopoietic stem cell transplant), lymphocyte-variant hypereosinophilia, atopic dermatitis, lymphocytic myocarditis, axial spondyloarthritis, celiac disease, or Rasmussen's encephalitis.~~

~~82. The method of claim 81, wherein the lymphocytes are T cells.~~

~~83. The method of claim 82 or 83, wherein the disease or condition comprises aplastic anemia, cell mediated rejection of solid organ transplant, graft failure post HSCT (hematopoietic stem cell transplant), lymphocyte-variant hypereosinophilia, atopic dermatitis, lymphocytic myocarditis, axial spondyloarthritis, celiac disease, or Rasmussen's encephalitis.~~

84.16. ~~The method-use~~ of claim ~~1480~~, wherein the disease or condition is characterized by overactivation and/or hyperproliferation of myeloid cells, and the antibody induces depletion of myeloid cells, optionally wherein the myeloid cells comprise monocytes, macrophages, dendritic cells, basophils, eosinophils, neutrophils, or mast cells, optionally wherein the myeloid cells comprise:

- a. eosinophils, and the disease or condition comprises acute eosinophilic pneumonia, chronic eosinophilic pneumonia, eosinophilic esophagitis, eosinophilic gastritis, eosinophilic gastroenteritis, eosinophilic enteritis, eosinophilic colitis, lymphocyte-variant hypereosinophilia, eosinophilic cardiomyopathy/Loeffler endocarditis, Löffler syndrome or episodic angioedema with eosinophilia/Gleich syndrome;
- b. mast cells, and wherein the disease or condition comprises cutaneous mastocytosis, mastocytic enterocolitis, systemic mastocytosis, mast cell activation syndrome, hereditary alpha tryptasemia syndrome, chronic urticaria or severe allergic conjunctivitis; or
- c. neutrophils, and wherein the disease or condition comprises neutrophilic dermatoses, psoriatic arthritis, generalized pustular psoriasis, pyoderma gangrenosum, Sweet's syndrome, subcorneal pustular dermatosis, neutrophilic eccrine hidradenitis, bowel-associated dermatosis-arthritis syndrome (BADAS), rheumatoid neutrophilic dermatitis, or Behçet's disease.

85. ~~The method of claim 84, wherein the myeloid cells comprise monocytes, macrophages, dendritic cells, basophils, eosinophils, neutrophils, or mast cells.~~

86. ~~The method of claim 85, wherein the myeloid cells comprise eosinophils, and the disease or condition comprises acute eosinophilic pneumonia, chronic eosinophilic pneumonia, eosinophilic esophagitis, eosinophilic gastritis, eosinophilic gastroenteritis, eosinophilic enteritis, eosinophilic colitis, lymphocyte-variant hypereosinophilia, eosinophilic cardiomyopathy/Loeffler endocarditis, Löffler syndrome or episodic angioedema with eosinophilia/Gleich syndrome.~~

87. ~~The method of claim 85, wherein the myeloid cells comprise mast cells, and wherein the disease or condition comprises cutaneous mastocytosis, mastocytic enterocolitis, systemic mastocytosis, mast cell activation syndrome, hereditary alpha tryptasemia syndrome, chronic urticaria or severe allergic conjunctivitis.~~

- 88.** ~~The method of claim 85, wherein the myeloid cells comprise neutrophils, and wherein the disease or condition comprises neutrophilic dermatoses, psoriatic arthritis, generalized pustular psoriasis, pyoderma gangrenosum, Sweet's syndrome, subcorneal pustular dermatosis, neutrophilic eccrine hidradenitis, bowel-associated dermatosis-arthritis syndrome (BADAS), rheumatoid neutrophilic dermatitis, or Behçet's disease.~~
- 89.17.** ~~The method-use of claim 1480, wherein the disease or condition comprises a disease or disorder associated with both lymphocytes and myeloid cells, optionally wherein the disease or disorder comprises histiocytosis.~~
- 90.** ~~The method of claim 89, wherein the disease or disorder comprises histiocytosis.~~
- 91.18.** ~~The method-use of claim 1490, wherein:~~
- ~~a. the histiocytosis comprises hemophagocytic lymphohistiocytosis (HLH) (including primary and secondary HLH), macrophage activation syndrome, Langerhans cell histiocytosis (LCH), indeterminate cell histiocytosis, Erdheim-Chester disease (ECD), mixed LCH/ECD, Rosai Dorfman disease, malignant histiocytosis, cutaneous non-LCH histiocytoses, juvenile xanthogranuloma, virus-associated HLH, bacteria-associated HLH, parasite-associated HLH, fungal-associated (fungal induced) HLH, autoimmune disease mediated HLH, or malignancy-triggered HLH, optionally wherein the malignancy-triggered HLH includes an HLH triggered by a hematological malignancy or solid tumor; or~~
 - ~~b. the disease or disorder comprises a non-mendelian secondary HLH (secondary HLH, or sHLH) and wherein the secondary HLH~~
 - ~~i. comprises an infection-associated HLH;~~
 - ~~ii. is associated with a rheumatologic condition; or~~
 - ~~iii. is associated with a kidney transplant or hematologic stem cell transplant.~~
- 92.** ~~The method of claim 91, wherein the malignancy-triggered HLH includes an HLH triggered by a hematological malignancy or solid tumor.~~
- 93.** ~~The method of claim 89, wherein the disease or disorder comprises a non-mendelian secondary HLH (secondary HLH, or sHLH).~~
- 94.** ~~The method of claim 93, wherein the secondary HLH comprises an infection-associated HLH.~~
- 95.** ~~The method of claim 93, wherein the sHLH is associated with a rheumatologic condition.~~

- 96.** ~~The method of claim 93, wherein the sHLH is associated with a kidney transplant or hematologic stem cell transplant.~~
- 97.19.** ~~The method use~~ of claim ~~1480~~, wherein the disease or condition:
- ~~a. comprises cytokine release syndrome (CRS), optionally wherein the CRS is associated with iatrogenic immune activation, infection, T cell therapy, or T cell activating bispecific antibody therapy;~~
 - ~~b. comprises sHLH or CRS associated with iatrogenic immune activation, infection, T cell therapy, chimeric antigen receptor T cell (CAR-T) therapy, T cell receptor T cell therapy (TCR-T), T cell activating bispecific antibody therapy, or iatrogenic immune suppression;~~
 - ~~c. comprises a granulomatous disease or condition, or a disease characterized by the presence of multinucleated giant cells, optionally wherein the disease or condition comprises sarcoidosis, Crohn's disease, Takayasu arteritis, giant cell arteritis, psoriatic arthritis, granulomatosis with polyangiitis (Wegener's Granulomatosis), giant cell myocarditis, chronic granulomatous disease, eosinophilic granulomatosis with polyangiitis (Churg-Strauss Syndrome), or chronic beryllium disease (berylliosis);~~
 - ~~d. comprises an autoimmune disorder or an inflammatory disorder, optionally wherein the autoimmune disorder comprises presentation of self antigens by antigen presenting dendritic cells in germinal centers of secondary lymphoid tissue of the subject;~~
 - ~~e. is associated with pathological alloantibodies or autoantibodies; or~~
 - ~~f. comprises a hematological malignancy.~~
- 98.** ~~The method of claim 97, wherein the CRS is associated with iatrogenic immune activation, infection, T cell therapy, or T cell activating bispecific antibody therapy.~~
- 99.** ~~The method of claim 80, wherein the disease or condition comprises sHLH or CRS associated with iatrogenic immune activation, infection, T cell therapy, chimeric antigen receptor T cell (CAR-T) therapy, T cell receptor T cell therapy (TCR-T), T cell activating bispecific antibody therapy, or iatrogenic immune suppression.~~
- 100.** ~~The method of claim 80, wherein the disease or disorder comprises a granulomatous disease or condition, or a disease characterized by the presence of multinucleated giant cells.~~

- 101.** ~~—The method of claim 100, wherein the disease or condition comprises sarcoidosis, Crohn's disease, Takayasu arteritis, giant cell arteritis, psoriatic arthritis, granulomatosis with polyangiitis (Wegener's Granulomatosis), giant cell myocarditis, chronic granulomatous disease, eosinophilic granulomatosis with polyangiitis (Churg-Strauss Syndrome), or chronic beryllium disease (berylliosis).~~
- 102.** ~~—The method of claim 80, wherein the disease or condition comprises an autoimmune disorder or an inflammatory disorder.~~
- 103.** ~~—The method of claim 102, wherein the autoimmune disorder comprises presentation of self antigens by antigen presenting dendritic cells in germinal centers of secondary lymphoid tissue of the subject.~~
- 104.** ~~—The method of claim 80, wherein th disease or condition is associated with pathological alloantibodies or autoantibodies.~~
- 105.** ~~—The method of claim 80, wherein the disease or disorder comprises a hematological malignancy.~~
- 106.20.** ~~—The method-use of any one of claims 1480-19105 wherein the subject is human.~~
- 107.21.** ~~—The method-use of any one of claims 1480-20106, wherein the antibody or pharmaceutical composition is to be administered intravenously or subcutaneously.~~
- 108.** ~~—The method of any one of claims 80-106, wherein the antibody or pharmaceutical composition is administered subcutaneously.~~
- 109.** ~~—A cell expressing SIRP γ , wherein the cell bound is to an antibody of any one of claims 1-49, wherein the antibody is bound to the SIRP γ .~~
- 110.** ~~—A kit or article of manufacture comprising an antibody of any one claims 1-49, or the pharmaceutical composition of claim 50.~~
- 111.** ~~—Use of the antibody of any one claims 1-49, or the pharmaceutical composition of claim 50 for the treatment of a disease or disorder in a subject in need thereof.~~
- 112.** ~~—Use of the antibody of any one claims 1-49, or the pharmaceutical composition of claim 50 for the manufacture of a medicament for the treatment of a disease or disorder in a subject in need thereof.~~