

CLAIMS

What is claimed is:

1. An Fc-containing antibody that is specific for one or more of SIRP α and SIRP β 1, wherein binding of the antibody to one or more of SIRP α and SIRP β 1 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, 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: 55, 57-58 and 66-69;
 - ii. a CDR-H2 sequence selected from the group consisting of SEQ ID NOS: 71, 73-74 and 82-85; and
 - iii. a CDR-H3 sequence selected from the group consisting of SEQ ID NOS: 87, 90-91 and 100-103; and/orwherein the light chain variable region comprises:
 - i. a light chain CDR 1 (CDR-L1) sequence selected from the group consisting of SEQ ID NOS: 6, 9-10, and 19-22;
 - ii. a CDR-L2 sequence selected from the group consisting of SEQ ID NOS: 23, 25-26, 32 and 34-35; and
 - iii. a CDR-L3 sequence selected from the group consisting of SEQ ID NOS: 37, 40-41 and 50-53.
3. The antibody of claim 1 or 2, wherein the antibody comprises the heavy and light variable chain CDR sequence combination selected from the group consisting of:
 - a. SEQ ID NO: 6, SEQ ID NO: 23, SEQ ID NO: 37, SEQ ID NO: 55, SEQ ID NO: 71, and SEQ ID NO: 87;
 - b. SEQ ID NO: 9, SEQ ID NO: 25, SEQ ID NO: 40, SEQ ID NO: 57, SEQ ID NO: 73, and SEQ ID NO: 90;

- c. SEQ ID NO: 10, SEQ ID NO: 26, SEQ ID NO: 41, SEQ ID NO: 58, SEQ ID NO: 74, and SEQ ID NO: 91;
 - d. SEQ ID NO: 19, SEQ ID NO: 32, SEQ ID NO: 50, SEQ ID NO: 66, SEQ ID NO: 82, and SEQ ID NO: 100;
 - e. SEQ ID NO: 20, SEQ ID NO: 34, SEQ ID NO: 51, SEQ ID NO: 67, SEQ ID NO: 83, and SEQ ID NO: 101;
 - f. SEQ ID NO: 21, SEQ ID NO: 34, SEQ ID NO: 52, SEQ ID NO: 68, SEQ ID NO: 84, and SEQ ID NO: 102; and
 - g. SEQ ID NO: 22, SEQ ID NO: 35, SEQ ID NO: 53, SEQ ID NO: 69, SEQ ID NO: 85, and SEQ ID NO: 103.
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: 105, 108-109, 119-122.
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: 124, 127-128, 138-141.
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: 105 and SEQ ID NO: 124;
 - b. SEQ ID NO: 108 and SEQ ID NO: 127;
 - c. SEQ ID NO: 109 and SEQ ID NO: 128;
 - d. SEQ ID NO: 119 and SEQ ID NO: 138;
 - e. SEQ ID NO: 120 and SEQ ID NO: 139;
 - f. SEQ ID NO: 121 and SEQ ID NO: 140; and
 - g. SEQ ID NO: 122 and SEQ ID NO: 141.
7. 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: 105 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: 124, 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: 108 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: 127, 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: 109 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: 128, 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: 119 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: 138, 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: 120 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: 139, 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: 121 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: 140, 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: 122 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: 141, or an amino acid sequence with at least 80% sequence identity thereto.

14. The antibody of any one of claims 2-13, wherein the antibody comprises an Fc domain.
15. The antibody of any one of claims 1-14, wherein the antibody is an Fc-containing antibody, and the binding of the antibody to one or more of SIRP α and SIRP β 1, on a cell induces depletion of the cell.
16. The antibody of any one of claims 1-15, wherein the cell depletion involves antibody dependent cellular phagocytosis (ADCP).
17. The antibody of any one of claims 1-16, wherein the cell depletion involves antibody dependent cellular cytotoxicity (ADCC).
18. The antibody of any one of claims 1-17, wherein the cell depletion involves depletion of SIRP α positive cells.
19. The antibody of any one of claims 1-18, wherein the cell depletion involves depletion of SIRP β 1 positive cells.
20. The antibody of any one of claims 1-17, wherein the cell depletion involves depletion of SIRP α positive cells and depletion of SIRP β 1 positive cells.
21. The antibody of claim 18 or 20, wherein the SIRP α positive cells are myeloid cells or myeloid progenitor cells.
22. The antibody of claim 18 or 20, wherein the SIRP α positive cells are selected from the group consisting of monocytes, macrophages, dendritic cells, basophils, eosinophils, neutrophils, and mast cells.
23. The antibody of any one of claims 19-22, wherein the SIRP β 1 positive cells are myeloid cells.
24. The antibody of any one of claims 19-22, wherein the SIRP β 1 positive cells are selected from the group consisting of monocytes, macrophages, dendritic cells, eosinophils, basophils and neutrophils.
25. The antibody of any one of claims 1-24, wherein the antibody is a monoclonal antibody.
26. The antibody of any one of claims 1-24 wherein the antibody is an antibody fragment.

27. The antibody of any one of claims 1-24 wherein the antibody is a human antibody.
28. The antibody of any one of claims 1-24, wherein the antibody is a humanized antibody.
29. The antibody of any one of claims 1-24 wherein the antibody is a chimeric antibody.
30. The antibody of any one of claims 1-24 wherein the antibody is a full-length antibody.
31. The antibody of any one of claims 1 or 14-30, wherein the Fc domain is selected from the group consisting of human IgG1, IgG2, IgG3, and IgG4.
32. The antibody of claim 31, wherein the Fc domain comprises SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 16.
33. The antibody of claim 31, 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: 16.
34. The antibody of claim 31, wherein 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.
35. The antibody of claim 31, wherein the IgG1 Fc comprises a sequence selected from the group consisting of:
- a. SEQ ID NO: 11;
 - b. SEQ ID NO: 12, wherein X₁ is V or A;
 - c. SEQ ID NO: 13, 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: 14, wherein X₁ is V or A;
 - e. SEQ ID NO: 15, wherein X₁ is V or A; X₂ is M or L; and X₃ is N or S; and
 - f. SEQ ID NO: 16, wherein X₁ is K or R; X₂ is D or E; and X₃ is L or M.
36. The antibody of claim 31, wherein the IgG4 Fc comprises a sequence of SEQ ID NO: 17, 18 or 24, wherein X₁ in SEQ ID NO: 24 is S or P; and X₂ in SEQ ID NO: 24 is L or E.

37. The antibody of any one of claims 1-36, wherein the binding of the antibody does not disrupt the interaction between CD47 and SIRP α .
38. The antibody of any one of claims 1-36, wherein the binding of the antibody disrupts the interaction between CD47 and SIRP α .
39. The antibody of any one of claims 1-38, wherein the antibody binds SIRP α and exhibits little or no binding to SIRP β 1 and SIRP γ .
40. The antibody of any one of claims 1-38, wherein the antibody binds SIRP β 1 and exhibits little or no binding to SIRP α and SIRP γ .
41. The antibody of any one of claims 1-37, wherein antibody binds SIRP α and SIRP β 1, and exhibits little or no binding to SIRP γ .
42. The antibody of any one of claims 1-39 or 41, wherein the antibody comprises a binding affinity to SIRP α of about 100 pM, about 1 nM, about 5 nM, about 10 nM, about 50 nM, about 100 nM, about 500 nM, or about 1 μ M.
43. The antibody of any one of claims 1-38, or 40-41, 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, or about 1 μ M, or about 5 μ M .
44. A pharmaceutical composition comprising the antibody of any one of claims 1-43, and optionally a pharmaceutically acceptable carrier.
45. A nucleic acid encoding for the antibody of any one of claims 1-43.
46. The nucleic acid of claim 45, comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 143, 146-147, 157-160, 162, 165-166, and 176-179.
47. The nucleic acid of claim 45 or 46, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 143, 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: 162, or a nucleic acid sequence with at least 80% sequence identity thereto.
48. The nucleic acid of claim 45 or 46, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 146, 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: 165, or a nucleic acid sequence with at least 80% sequence identity thereto.

49. The nucleic acid of claim 45 or 46, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 147, 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: 166, or a nucleic acid sequence with at least 80% sequence identity thereto.

50. The nucleic acid of claim 45 or 46, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 157, 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: 176, or a nucleic acid sequence with at least 80% sequence identity thereto.

51. The nucleic acid of claim 45 or 46, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 158, 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: 177, or a nucleic acid sequence with at least 80% sequence identity thereto.

52. The nucleic acid of claim 45 or 46, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 159, 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: 178, or a nucleic acid sequence with at least 80% sequence identity thereto.

53. The nucleic acid of claim 45 or 46, wherein the heavy chain variable domain is encoded by the nucleic acid sequence of SEQ ID NO: 160, 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: 179, or a nucleic acid sequence with at least 80% sequence identity thereto.

54. A vector comprising the nucleic acid of any one of claims 45-53.

55. 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 1-43.
56. The method of claim 55, wherein at least a subset of the population of cells expresses SIRP α .
57. The method of claim 56, wherein the population of cells that express SIRP α comprise myeloid cells or myeloid progenitor cells.
58. The method of claim 55, wherein the population of cells that express SIRP α comprise monocytes, macrophages, dendritic cells, basophils, eosinophils, neutrophils, or mast cells.
59. The method of any one of claims 55-58, wherein at least a subset of the population of cells expresses SIRP β 1.
60. The method of claim 59, wherein the population of cells that express SIRP β 1 comprise myeloid cells or myeloid progenitor cells.
61. The method of claim 59, wherein the population of cells that express SIRP β 1 comprise monocytes, macrophages, dendritic cells, eosinophils, basophils, neutrophils or mast cells.
62. The method of any one of claims 55-61, wherein at least a subset of the population of cells expresses SIRP α and SIRP β 1.
63. The method of any one of claims 55-62, wherein the population of cells whose depletion is induced comprises a first population of cells expressing SIRP α and a second population of cells expressing SIRP β 1.
64. The method of any one of claims 55-63, wherein the method is *in vitro*.
65. The method of any one of claims 55-63, wherein the method is *in vivo*.
66. The method any one of claims 55-65, wherein the population of cells comprises tissue-resident cells.

67. The method any one of claims 55-66, wherein the population of cells comprises circulating cells.
68. The method of any one of claims 55-67, wherein the cell depletion involves ADCC.
69. The method of any one of claims 55-68, wherein the cell depletion involves ADCP.
70. The method of any one of claims 55-69, wherein the cell depletion involves ADCC and ADCP.
71. 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 1-43 or the pharmaceutical composition of claim 44.
72. The method of claim 71, wherein the disease or condition is characterized by overactivation and/or hyperproliferation of myeloid cells, and the antibody induces depletion of myeloid cells.
73. The method of claim 72, wherein the myeloid cells comprise monocytes, macrophages, dendritic cells, basophils, eosinophils, neutrophils, or mast cells.
74. The method of claim 73, wherein the myeloid cells comprise eosinophils, and wherein the disease or condition comprises acute eosinophilic pneumonia, chronic eosinophilic pneumonia, eosinophilic esophagitis, eosinophilic gastritis, eosinophilic gastroenteritis, eosinophilic enteritis, eosinophilic colitis, eosinophilic cardiomyopathy/Loeffler endocarditis, Löffler syndrome or episodic angioedema with eosinophilia/Gleich syndrome.
75. The method of claim 73, 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, or chronic urticaria.
76. The method of claim 73, 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.

77. The method of claim 73, wherein the disease or condition comprises an autoimmune disorder or an inflammatory disorder.
78. The method of claim 77, wherein the autoimmune disorder comprises presentation of self antigens by antigen presenting dendritic cells in germinal centers of secondary lymphoid tissue of the subject.
79. The method of claim 71, wherein the disease or condition comprises a hematological malignancy.
80. The method of claim 79, wherein the hematological malignancy comprises acute myelogenous leukemia, chronic myelogenous leukemia, chronic myelogenous leukemia, chronic myelomonocytic leukemia, juvenile myelomonocytic leukemia, chronic eosinophilic leukemia, or chronic neutrophilic leukemia.
81. The method of any one of claims 71-80 the subject is human.
82. The method of any one of claims 71-81, wherein the route of administration is intravenous.
83. The method of any one of claims 71-81, wherein the route of administration is subcutaneous.
84. A cell expressing SIRP α , wherein the cell bound is to an antibody of any one of claims 1-43, wherein the antibody is bound to the SIRP α .
85. A cell expressing SIRP β 1, wherein the cell bound is to an antibody of any one of claims 1-43, wherein the antibody is bound to the SIRP β 1.
86. A cell expressing SIRP α and SIRP β 1, wherein the cell bound is to an antibody of any one of claims 1-43, wherein the antibody is bound to the SIRP α and SIRP β 1.
87. A kit or article of manufacture comprising an antibody of any one claims 1-43, or the pharmaceutical composition of claim 44.
88. Use of the antibody of any one claims 1-43, or the pharmaceutical composition of claim 44 for the treatment of a disease or disorder in a subject in need thereof.

89. Use of the antibody of any one of claims 1-43, or the pharmaceutical composition of claim 44 for the manufacture of a medicament for the treatment of a disease or disorder in a subject in need thereof.