

CLAIMS

What is claimed is:

1. An antibody or antigen-binding fragment thereof having binding specificity to a wild-type human signal regulatory protein alpha (SIRP α) protein, wherein the antibody or fragment thereof comprises a heavy chain variable region (VH) comprising heavy chain complementarity determining regions CDRH1, CDRH2, and CDRH3 having the amino acid sequences of VH CDR1, VH CDR2, and VH CDR3 of SEQ ID NO: 43 respectively, and a light chain variable region (VL) ~~light chain~~ comprising complementarity determining regions CDRL1, CDRL2, and CDRL3 having the amino acid sequences of VL CDR1, VL CDR2, and VL CDR3 of SEQ ID NO:45 respectively, ~~and wherein:~~

~~(a) the CDRH1 comprises the amino acid sequence of SEQ ID NO: 15, the CDRH2 comprises the amino acid sequence of SEQ ID NO: 16, 21 or 22, the CDRH3 comprises the amino acid sequence of SEQ ID NO: 17, the CDRL1 comprises the amino acid sequence of SEQ ID NO: 18, the CDRL2 comprises the amino acid sequence of SEQ ID NO: 19, and the CDRL3 comprises the amino acid sequence of SEQ ID NO: 20;~~

~~(b) the CDRH1 comprises the amino acid sequence of SEQ ID NO: 30, the CDRH2 comprises the amino acid sequence of SEQ ID NO: 31, 36, 37 or 38, the CDRH3 comprises the amino acid sequence of SEQ ID NO: 32, the CDRL1 comprises the amino acid sequence of SEQ ID NO: 33, the CDRL2 comprises the amino acid sequence of SEQ ID NO: 34, and the CDRL3 comprises the amino acid sequence of SEQ ID NO: 35;~~

~~(c) the CDRH1 comprises the amino acid sequence of SEQ ID NO: 47, the CDRH2 comprises the amino acid sequence of SEQ ID NO: 48, 53 or 54, the CDRH3 comprises the amino acid sequence of SEQ ID NO: 49, the CDRL1 comprises the amino acid sequence of SEQ ID NO: 50, the CDRL2 comprises the amino acid sequence of SEQ ID NO: 51, and the CDRL3 comprises the amino acid sequence of SEQ ID NO: 52;~~

- (d) ~~the CDRH1 comprises the amino acid sequence of SEQ ID NO: 63, the CDRH2 comprises the amino acid sequence of SEQ ID NO: 64, the CDRH3 comprises the amino acid sequence of SEQ ID NO: 65, the CDRL1 comprises the amino acid sequence of SEQ ID NO: 66, the CDRL2 comprises the amino acid sequence of SEQ ID NO: 67, and the CDRL3 comprises the amino acid sequence of SEQ ID NO: 68;~~
- (e) ~~the CDRH1 comprises the amino acid sequence of SEQ ID NO: 77, the CDRH2 comprises the amino acid sequence of SEQ ID NO: 78, the CDRH3 comprises the amino acid sequence of SEQ ID NO: 79, the CDRL1 comprises the amino acid sequence of SEQ ID NO: 80, the CDRL2 comprises the amino acid sequence of SEQ ID NO: 81, and the CDRL3 comprises the amino acid sequence of SEQ ID NO: 82;~~
- (f) ~~the CDRH1 comprises the amino acid sequence of SEQ ID NO: 91, the CDRH2 comprises the amino acid sequence of SEQ ID NO: 92, the CDRH3 comprises the amino acid sequence of SEQ ID NO: 93, the CDRL1 comprises the amino acid sequence of SEQ ID NO: 94, the CDRL2 comprises the amino acid sequence of SEQ ID NO: 95, and the CDRL3 comprises the amino acid sequence of SEQ ID NO: 96; or~~
- (g) ~~the CDRH1 comprises the amino acid sequence of SEQ ID NO: 103, the CDRH2 comprises the amino acid sequence of SEQ ID NO: 104, the CDRH3 comprises the amino acid sequence of SEQ ID NO: 105, the CDRL1 comprises the amino acid sequence of SEQ ID NO: 106, the CDRL2 comprises the amino acid sequence of SEQ ID NO: 107, and the CDRL3 comprises the amino acid sequence of SEQ ID NO: 108.~~

2. ~~An antibody or fragment thereof having binding specificity to a wild-type human signal regulatory protein alpha (SIRP α) protein, wherein the antibody or fragment thereof comprises a heavy chain variable region comprising heavy chain complementarity~~

determining regions CDRH1, CDRH2, and CDRH3 and a light chain variable region light chain comprising complementarity determining regions CDRL1, CDRL2, and CDRL3, and wherein the CDRH1 comprises the amino acid sequence of SEQ ID NO: 15, the CDRH2 comprises the amino acid sequence of SEQ ID NO: 16, 21 or 22, the CDRH3 comprises the amino acid sequence of SEQ ID NO: 17, the CDRL1 comprises the amino acid sequence of SEQ ID NO: 18, the CDRL2 comprises the amino acid sequence of SEQ ID NO: 19, and the CDRL3 comprises the amino acid sequence of SEQ ID NO: 20.

3. — The antibody or fragment thereof of claim 2, wherein the heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1 and 23-27, or a peptide having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1 and 23-27.

4. — The antibody or fragment thereof of claim 2 or 3, wherein the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO:2 and 28-29, or a peptide having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:2 and 28-29.

5. — The antibody or fragment thereof of claim 2, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:27 and the light chain variable region comprises the amino acid sequence of SEQ ID NO:29.

6. — An antibody or fragment thereof having binding specificity to a wild-type human signal regulatory protein alpha (SIRP α) protein, wherein the antibody or fragment thereof comprises a heavy chain variable region comprising heavy chain complementarity determining regions CDRH1, CDRH2, and CDRH3 and a light chain variable region light chain comprising complementarity determining regions CDRL1, CDRL2, and CDRL3, and wherein the CDRH1 comprises the amino acid sequence of SEQ ID NO: 30, the CDRH2

~~comprises the amino acid sequence of SEQ ID NO: 31, 36, 37 or 38, the CDRH3 comprises the amino acid sequence of SEQ ID NO: 32, the CDRL1 comprises the amino acid sequence of SEQ ID NO: 33, the CDRL2 comprises the amino acid sequence of SEQ ID NO: 34, and the CDRL3 comprises the amino acid sequence of SEQ ID NO: 35.~~

~~7. The antibody or fragment thereof of claim 6, wherein the heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO:3 and 39-44, or a peptide having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:3 and 39-44.~~

~~8. The antibody or fragment thereof of claim 6 or 7, wherein the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4 and 45-46, or a peptide having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:4 and 45-46.~~

2. The antibody or antigen-binding fragment thereof of claim 1, wherein the VH CDR1, VH CDR2, and VH CDR3 of SEQ ID NO:43 and the VL CDR1, VL CDR2, and VL CDR3 of SEQ ID NO:45 are defined according to the Kabat system.

3. The antibody or antigen-binding fragment thereof of claim 1, wherein the VH CDR1, VH CDR2, and VH CDR3 of SEQ ID NO:43 and the VL CDR1, VL CDR2, and VL CDR3 of SEQ ID NO:45 are defined according to the Chothia system.

49. The antibody or antigen-binding fragment thereof of claim 16, wherein the heavy chain variable region comprises~~has~~ the amino acid sequence of SEQ ID NO:43 and the light chain variable region comprises~~has~~ the amino acid sequence of SEQ ID NO:45.

~~10. — An antibody or fragment thereof having binding specificity to a wild type human signal regulatory protein alpha (SIRP α) protein, wherein the antibody or fragment thereof comprises a heavy chain variable region comprising heavy chain complementarity determining regions CDRH1, CDRH2, and CDRH3 and a light chain variable region light chain comprising complementarity determining regions CDRL1, CDRL2, and CDRL3, and wherein the CDRH1 comprises the amino acid sequence of SEQ ID NO: 47, the CDRH2 comprises the amino acid sequence of SEQ ID NO: 48, 53 or 54, the CDRH3 comprises the amino acid sequence of SEQ ID NO: 49, the CDRL1 comprises the amino acid sequence of SEQ ID NO: 50, the CDRL2 comprises the amino acid sequence of SEQ ID NO: 51, and the CDRL3 comprises the amino acid sequence of SEQ ID NO: 52;~~

~~11. — The antibody or fragment thereof of claim 10, wherein the heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO:5 and 55-60, or a peptide having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:5 and 55-60.~~

~~12. — The antibody or fragment thereof of claim 10 or 11, wherein the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO:6 and 61-62, or a peptide having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO: 6 and 61-62.~~

~~13. — The antibody or fragment thereof of any one of claims 1-12, which can bind to SIRP α variant 1 and variant 2.~~

~~14. — The antibody or fragment thereof of any one of claims 1-13, which is humanized.~~

515. The antibody or fragment thereof of any one of claims 1-~~4~~24, which further has a binding specificity to a second target protein.

616. A composition comprising the antibody or fragment thereof of any one of claims 1-
515 and a pharmaceutically acceptable carrier.

717. The composition of claim 616, further comprising a second antibody having specificity to a tumor antigen.

818. The composition of claim 717, wherein the second antibody is a tumor-opsonizing antibody.

919. Use of the antibody or antigen-binding fragment thereof of any one of claims 1-5 in the manufacture of a medicament for~~A method of treating cancer in a patient in need thereof, comprising administering to the patient the antibody or fragment thereof of any one of claims 1-15.~~

1020. The ~~method-use~~ of claim 919, wherein the cancer is selected from the group consisting of bladder cancer, liver cancer, colon cancer, rectal cancer, endometrial cancer, leukemia, lymphoma, pancreatic cancer, small cell lung cancer, non-small cell lung cancer, breast cancer, urethral cancer, head and neck cancer, gastrointestinal cancer, stomach cancer, oesophageal cancer, ovarian cancer, renal cancer, melanoma, prostate cancer and thyroid cancer.

1121. The ~~use method~~ of claim 9 or claim 1019, wherein the medicament is to be administered with~~further comprising administering to the patient~~ a second antibody targeting a protein that triggers tumor opsonizing.

1222. The ~~method-use~~ of claim 1121, wherein the protein is selected from the group consisting of CD19, CD20, EGFR, HER2, CD3, CD16, PD1, PD-L1, LAG3, TIM3, CTLA4,

VISTA, CSFR1, A2AR, CD73, CD39, CD40, CEA, HER2, VEGFR, TIGIT, claudin18.2, CD24, GPC3, IL13RA2, 4-1BB, CCR8, and CMET.