What Is Claimed Is:

1. A monoclonal antibody, or antigen-binding fragment thereof, that specifically binds human, rat, mouse, pig, and dog CD47 which comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein said LCVR and said HCVR comprise, respectively, amino acid sequences selected from the group consisting of:

SEQ ID NO:7 and SEQ ID NO:57;
SEQ ID NO:8 and SEQ ID NO:58;
SEQ ID NO:9 and SEQ ID NO:59;
SEQ ID NO:10 and SEQ ID NO:60;
SEQ ID NO:11 and SEQ ID NO:61;
SEQ ID NO:12 and SEQ ID NO:62;
SEQ ID NO:13 and SEQ ID NO:63;
SEQ ID NO:14 and SEQ ID NO:64;
SEQ ID NO:15 and SEQ ID NO:65;
SEQ ID NO:16 and SEQ ID NO:66;
SEQ ID NO:17 and SEQ ID NO:67;
SEQ ID NO:18 and SEQ ID NO:68;
SEQ ID NO:19 and SEQ ID NO:69;
SEQ ID NO:20 and SEQ ID NO:70;
SEQ ID NO:21 and SEQ ID NO:71;
SEQ ID NO:22 and SEQ ID NO:72;
SEQ ID NO:23 and SEQ ID NO:73;
SEQ ID NO:24 and SEQ ID NO:74;
SEQ ID NO:25 and SEQ ID NO:75;
SEQ ID NO:26 and SEQ ID NO:76;
SEQ ID NO:27 and SEQ ID NO:77;
SEQ ID NO:28 and SEQ ID NO:78;
SEQ ID NO:29 and SEQ ID NO:79;
SEQ ID NO:30 and SEQ ID NO:80; and
SEQ ID NO:31 and SEQ ID NO:81.

2. The monoclonal antibody or antigen-binding fragment thereof of claim 1, which is chimeric or humanized.

3. The monoclonal antibody, or antigen-binding fragment thereof, of claim 1 or 2, which comprises three light chain complementarity determining regions (LCDRs 1-3) and three heavy chain complementarity determining regions (HCDRs 1-3),wherein:

LCDR 1 comprises the amino acid sequence RSSQSLVHSNGNTYLH (SEQ ID NO:1);

LCDR 2 comprises the amino acid sequence KVSYRFS (SEQ ID NO:2); and

LCDR 3 comprises the amino acid sequence SQNTHVPRT (SEQ ID NO:3);

HCDR 1 comprises the amino acid sequence GYTFTNYYVF (SEQ ID NO:4);

HCDR 2 comprises the amino acid sequence DINPVNGDTNFNEKFKN (SEQ ID NO:5); and

HCDR 3 comprises the amino acid sequence GGYTMDY(SEQ ID NO:6).

~~4. The monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-3, which comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein said LCVR and said HCVR comprise, respectively, amino acid sequences selected from the group consisting of:~~

~~SEQ ID NO:7 and SEQ ID NO:57;~~

~~SEQ ID NO:8 and SEQ ID NO:58;~~

~~SEQ ID NO:9 and SEQ ID NO:59;~~

~~SEQ ID NO:10 and SEQ ID NO:60;~~

~~SEQ ID NO:11 and SEQ ID NO:61;~~

~~SEQ ID NO:12 and SEQ ID NO:62;~~

~~SEQ ID NO:13 and SEQ ID NO:63;~~

~~SEQ ID NO:14 and SEQ ID NO:64;~~

~~SEQ ID NO:15 and SEQ ID NO:65;~~

~~SEQ ID NO:16 and SEQ ID NO:66;~~

~~SEQ ID NO:17 and SEQ ID NO:67;~~

~~SEQ ID NO:18 and SEQ ID NO:68;~~

~~SEQ ID NO:19 and SEQ ID NO:69;~~

~~SEQ ID NO:20 and SEQ ID NO:70;~~

~~SEQ ID NO:21 and SEQ ID NO:71;~~

~~SEQ ID NO:22 and SEQ ID NO:72;~~

~~SEQ ID NO:23 and SEQ ID NO:73;~~

~~SEQ ID NO:24 and SEQ ID NO:74;~~

~~SEQ ID NO:25 and SEQ ID NO:75;~~

~~SEQ ID NO:26 and SEQ ID NO:76;~~

~~SEQ ID NO:27 and SEQ ID NO:77;~~

~~SEQ ID NO:28 and SEQ ID NO:78;~~

~~SEQ ID NO:29 and SEQ ID NO:79;~~

~~SEQ ID NO:30 and SEQ ID NO:80; and~~

~~SEQ ID NO:31 and SEQ ID NO:81.~~

~~5. A monoclonal antibody, or antigen-binding fragment thereof, that competes with said monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-4 for binding to CD47.~~

~~6~~4. A humanized or chimeric monoclonal antibody, or antigen-binding fragment thereof, that specifically binds human, rat, mouse, pig, ~~or~~ and dog CD47, blocks binding of SIRPalpha to CD47, and which exhibits the dual activities of:

i) inducing death of cancer cells, and

ii) increasing phagocytosis of said cancer cells;

which comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein said LCVR and said HCVR comprise, respectively, amino acid sequences selected from the group consisting of:

SEQ ID NO:7 and SEQ ID NO:57;

SEQ ID NO:8 and SEQ ID NO:58;

SEQ ID NO:11 and SEQ ID NO:61;

SEQ ID NO:14 and SEQ ID NO:64;

SEQ ID NO:16 and SEQ ID NO:66;

SEQ ID NO:18 and SEQ ID NO:68;

SEQ ID NO:19 and SEQ ID NO:69;

SEQ ID NO:25 and SEQ ID NO:75;

SEQ ID NO:27 and SEQ ID NO:77;

SEQ ID NO:28 and SEQ ID NO:78;

SEQ ID NO:29 and SEQ ID NO:79;

SEQ ID NO:30 and SEQ ID NO:80; and

SEQ ID NO:31 and SEQ ID NO:81.

~~7. A monoclonal antibody, or antigen-binding fragment thereof, that competes with said humanized or chimeric monoclonal antibody or antigen-binding fragment thereof of claim 6 for binding to human, rat, mouse, pig, or dog CD47, and which exhibits said dual activities.~~

~~8~~5. A pharmaceutical composition, comprising said monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-~~7~~4, and a pharmaceutically or physiologically acceptable carrier, diluent, or excipient.

~~9~~6. The monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-~~7~~ 4 for use in human therapy or therapy of companion/pet animals, working animals, sport animals, zoo animals, or therapy of other valuable animals kept in captivity.

~~10~~7. ~~The~~ Use of a monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-~~7~~ 4 in the manufacture of a medicament for use in treating ischemia-reperfusion injury, or an autoimmune or inflammatory disease, in a human or companion/pet animal, working animal, sport animal, zoo animal, or other valuable animal kept in captivity.

~~11~~8. The ~~monoclonal antibody, or antigen-binding fragment thereof,~~ use of claim ~~10~~7, which comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein said LCVR and said HCVR comprise, respectively, amino acid sequences selected from the group consisting of:

SEQ ID NO:7 and SEQ ID NO:57;
SEQ ID NO:8 and SEQ ID NO:58;
SEQ ID NO:11 and SEQ ID NO:61;
SEQ ID NO:14 and SEQ ID NO:64;
SEQ ID NO:16 and SEQ ID NO:66;
SEQ ID NO:18 and SEQ ID NO:68;
SEQ ID NO:19 and SEQ ID NO:69;
SEQ ID NO:25 and SEQ ID NO:75;
SEQ ID NO:27 and SEQ ID NO:77;
SEQ ID NO:28 and SEQ ID NO:78;
SEQ ID NO:29 and SEQ ID NO:79;

SEQ ID NO:30 and SEQ ID NO:80; and

SEQ ID NO:31 and SEQ ID NO:81.

~~12.~~9 The ~~monoclonal antibody, or antigen-binding fragment thereof,~~use of claim ~~10~~ 7 or ~~11~~8, wherein said ischemia-reperfusion injury occurs in organ transplantation, acute kidney injury, cardiopulmonary bypass surgery, pulmonary hypertension, sickle cell disease, myocardial infarction, stroke, surgical resections and reconstructive surgery, reattachment of an appendage or other body part, skin grafting, or trauma.

~~13~~10. The ~~monoclonal antibody, or antigen-binding fragment thereof,~~use of claim ~~10~~ 7 or ~~11~~8, wherein said autoimmune or inflammatory disease is selected from the group consisting of arthritis, multiple sclerosis, psoriasis, Crohn's disease, inflammatory bowel disease, lupus, Grave's disease and Hashimoto's thyroiditis, and ankylosing spondylitis.

~~14~~11. The use of any one of claims ~~9~~6-~~13~~10, further comprising ~~administering to said subject~~ an effective amount of a nitric oxide donor, precursor, or both; a nitric oxide generating topical agent; an agent that activates soluble guanylyl cyclase; an agent that inhibits cyclic nucleotide phosphodiesterases; or any combination of any of the foregoing.

~~15~~12. ~~The~~ Use of a monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-~~7~~4 in the manufacture of a medicament for use in treating leukemia, a lymphoma, ovarian cancer, breast cancer, endometrial cancer, colon cancer, rectal cancer, gastric cancer, bladder cancer, lung cancer, bronchial cancer, bone cancer, prostate cancer, pancreatic cancer, liver and bile duct cancer, esophageal cancer, renal cancer, thyroid cancer, head and neck cancer, testicular cancer, glioblastoma, astrocytoma, melanoma, myelodysplastic syndrome, and a sarcoma~~a susceptible cancer~~.

~~16~~13. The ~~monoclonal antibody, or antigen-binding fragment thereof,~~use of claim ~~15~~12, which comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein said LCVR and said HCVR comprise, respectively, amino acid sequences selected from the group consisting of:

SEQ ID NO:9 and SEQ ID NO:59;

SEQ ID NO:10 and SEQ ID NO:60;

SEQ ID NO:12 and SEQ ID NO:62;
SEQ ID NO:13 and SEQ ID NO:63;
SEQ ID NO:15 and SEQ ID NO:65;
SEQ ID NO:17 and SEQ ID NO:67;
SEQ ID NO:20 and SEQ ID NO:70;
SEQ ID NO:21 and SEQ ID NO:71;
SEQ ID NO:22 and SEQ ID NO:72;
SEQ ID NO:23 and SEQ ID NO:73;
SEQ ID NO:24 and SEQ ID NO:74; and
SEQ ID NO:26 and SEQ ID NO:76.

~~17~~14. The ~~monoclonal antibody, or antigen binding fragment thereof,~~use of claim ~~15~~ 12 or ~~16~~13, which promotes phagocytosis and/or killing of cells of said ~~susceptible~~ cancers.

~~18. The monoclonal antibody, or antigen binding fragment thereof, of any one of claims 15-17, wherein said susceptible cancer is selected from the group consisting of a leukemia, a lymphoma, ovarian cancer, breast cancer, endometrial cancer, colon cancer, rectal cancer, gastric cancer, bladder cancer, lung cancer, bronchial cancer, bone cancer, prostate cancer, pancreatic cancer, liver and bile duct cancer, esophageal cancer, renal cancer, thyroid cancer, head and neck cancer, testicular cancer, glioblastoma, astrocytoma, melanoma, myelodysplastic syndrome, and a sarcoma.~~

~~19~~15. The monoclonal antibody, or antigen binding fragment thereof, of claim ~~18~~17, wherein:

said leukemia is selected from the group consisting of acute lymphocytic (lymphoblastic) leukemia, acute myeloid leukemia, myelogenous leukemia, chronic lymphocytic leukemia, multiple myeloma, plasma cell leukemia, and chronic myeloid leukemia;

said lymphoma is selected from the group consisting of Hodgkin lymphoma and Non-Hodgkin lymphoma including B cell lymphoma, diffuse large B cell lymphoma, follicular lymphoma, mantle cell lymphoma, marginal zone B cell lymphoma, T cell lymphoma, and Waldenstrom macroglobulinemia; and

said sarcoma is selected from the group consisting of osteosarcoma, Ewing sarcoma, leiomyosarcoma, synovial sarcoma, alveolar soft part sarcoma, angiosarcoma, liposarcoma, fibrosarcoma, rhabdomyosarcoma, and chrondrosarcoma.

~~20~~16. The use of any one of claims ~~9~~ 6 or ~~15~~12-~~19~~15, further comprising ~~administering to said patient an anti-tumor therapeutic treatment selected from the group consisting of surgery, radiation,~~ an anti-tumor or anti-neoplastic agent, and combinations of any of the foregoing.

~~21~~17. ~~A~~ Use of a humanized or chimeric monoclonal antibody, or antigen-binding fragment thereof, that specifically binds human, rat, mouse, pig, ~~or~~ and dog CD47, blocks binding of SIRPalpha to CD47, and which exhibits the dual activities of:

i) inducing death of cancer cells, and

ii) increasing phagocytosis of said cancer cells, or

a monoclonal antibody, or antigen-binding fragment thereof, that competes with said humanized or chimeric monoclonal antibody, or antigen-binding fragment thereof, for binding to human, rat, mouse, pig, ~~or~~ and dog CD47, blocks binding of SIRPalpha to CD47, and which exhibits said dual activities, in the manufacture of a medicament for use in treating a leukemia, a lymphoma, ovarian cancer, breast cancer, endometrial cancer, colon cancer, rectal cancer, gastric cancer, bladder cancer, lung cancer, bronchial cancer, bone cancer, prostate cancer, pancreatic cancer, liver and bile duct cancer, esophageal cancer, renal cancer, thyroid cancer, head and neck cancer, testicular cancer, glioblastoma, astrocytoma, melanoma, myelodysplastic syndrome, and a sarcoma ~~susceptible cancer~~ in a human or companion/pet animal, working animal, sport animal, zoo animal, or other valuable animal kept in captivity in need thereof.

~~22. The humanized or chimeric monoclonal antibody, or antigen-binding fragment thereof, or competing monoclonal antibody, or antigen-binding fragment thereof, of claim 21, wherein said susceptible cancer is selected from the group consisting of a leukemia, a lymphoma, ovarian cancer, breast cancer, endometrial cancer, colon cancer, rectal cancer, gastric cancer, bladder cancer, lung cancer, bronchial cancer, bone cancer, prostate cancer, pancreatic cancer, liver and bile duct cancer, esophageal cancer, renal cancer, thyroid cancer, head and neck cancer, testicular cancer, glioblastoma, astrocytoma, melanoma, myelodysplastic syndrome, and a sarcoma.~~

What Is Claimed Is:

1. A monoclonal antibody, or antigen-binding fragment thereof, that specifically binds human, rat, mouse, pig, and dog CD47.

2. The monoclonal antibody or antigen-binding fragment thereof of claim 1, which is chimeric or humanized.

3. The monoclonal antibody, or antigen-binding fragment thereof, of claim 1 or 2, which comprises three light chain complementarity determining regions (LCDRs 1-3) and three heavy chain complementarity determining regions (HCDRs 1-3),wherein:

LCDR 1 comprises the amino acid sequence RSSQSLVHSNGNTYLH (SEQ ID NO:1);

LCDR 2 comprises the amino acid sequence KVSYRFS (SEQ ID NO:2); and

LCDR 3 comprises the amino acid sequence SQNTHVPRT (SEQ ID NO:3);

HCDR 1 comprises the amino acid sequence GYTFTNYYVF (SEQ ID NO:4);

HCDR 2 comprises the amino acid sequence DINPVNGDTNFNEKFKN (SEQ ID NO:5); and

HCDR 3 comprises the amino acid sequence GGYTMDY(SEQ ID NO:6).

4. The monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-3, which comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein said LCVR and said HCVR comprise, respectively, amino acid sequences selected from the group consisting of:

SEQ ID NO:7 and SEQ ID NO:57;
SEQ ID NO:8 and SEQ ID NO:58;
SEQ ID NO:9 and SEQ ID NO:59;
SEQ ID NO:10 and SEQ ID NO:60;
SEQ ID NO:11 and SEQ ID NO:61;
SEQ ID NO:12 and SEQ ID NO:62;
SEQ ID NO:13 and SEQ ID NO:63;
SEQ ID NO:14 and SEQ ID NO:64;
SEQ ID NO:15 and SEQ ID NO:65;
SEQ ID NO:16 and SEQ ID NO:66;

SEQ ID NO:17 and SEQ ID NO:67;
SEQ ID NO:18 and SEQ ID NO:68;
SEQ ID NO:19 and SEQ ID NO:69;
SEQ ID NO:20 and SEQ ID NO:70;
SEQ ID NO:21 and SEQ ID NO:71;
SEQ ID NO:22 and SEQ ID NO:72;
SEQ ID NO:23 and SEQ ID NO:73;
SEQ ID NO:24 and SEQ ID NO:74;
SEQ ID NO:25 and SEQ ID NO:75;
SEQ ID NO:26 and SEQ ID NO:76;
SEQ ID NO:27 and SEQ ID NO:77;
SEQ ID NO:28 and SEQ ID NO:78;
SEQ ID NO:29 and SEQ ID NO:79;
SEQ ID NO:30 and SEQ ID NO:80; and
SEQ ID NO:31 and SEQ ID NO:81.

5. A monoclonal antibody, or antigen-binding fragment thereof, that competes with said monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-4 for binding to CD47.

6. A humanized or chimeric monoclonal antibody, or antigen-binding fragment thereof, that specifically binds human, rat, mouse, pig, or dog CD47, blocks binding of SIRPalpha to CD47, and which exhibits the dual activities of:

i) inducing death of cancer cells, and

ii) increasing phagocytosis of said cancer cells.

7. A monoclonal antibody, or antigen-binding fragment thereof, that competes with said humanized or chimeric monoclonal antibody or antigen-binding fragment thereof of claim 6 for binding to human, rat, mouse, pig, or dog CD47, and which exhibits said dual activities.

8. A pharmaceutical composition, comprising said monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-7, and a pharmaceutically or physiologically acceptable carrier, diluent, or excipient.

9. The monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-7 for use in human therapy or therapy of companion/pet animals, working animals, sport animals, zoo animals, or therapy of other valuable animals kept in captivity.

10. The monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-7 for use in treating ischemia-reperfusion injury, or an autoimmune or inflammatory disease, in a human or companion/pet animal, working animal, sport animal, zoo animal, or other valuable animal kept in captivity.

11. The monoclonal antibody, or antigen-binding fragment thereof, of claim 10, which comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein said LCVR and said HCVR comprise, respectively, amino acid sequences selected from the group consisting of:

SEQ ID NO:7 and SEQ ID NO:57;
SEQ ID NO:8 and SEQ ID NO:58;
SEQ ID NO:11 and SEQ ID NO:61;
SEQ ID NO:14 and SEQ ID NO:64;
SEQ ID NO:16 and SEQ ID NO:66;
SEQ ID NO:18 and SEQ ID NO:68;
SEQ ID NO:19 and SEQ ID NO:69;
SEQ ID NO:25 and SEQ ID NO:75;
SEQ ID NO:27 and SEQ ID NO:77;
SEQ ID NO:28 and SEQ ID NO:78;
SEQ ID NO:29 and SEQ ID NO:79;
SEQ ID NO:30 and SEQ ID NO:80; and
SEQ ID NO:31 and SEQ ID NO:81.

12. The monoclonal antibody, or antigen-binding fragment thereof, of claim 10 or 11, wherein said ischemia-reperfusion injury occurs in organ transplantation, acute kidney injury, cardiopulmonary bypass surgery, pulmonary hypertension, sickle cell disease, myocardial infarction, stroke, surgical resections and reconstructive surgery, reattachment of an appendage or other body part, skin grafting, or trauma.

13. The monoclonal antibody, or antigen-binding fragment thereof, of claim 10 or 11, wherein said autoimmune or inflammatory disease is selected from the group consisting of arthritis, multiple sclerosis, psoriasis, Crohn's disease, inflammatory bowel disease, lupus, Grave's disease and Hashimoto's thyroiditis, and ankylosing spondylitis.

14. The use of any one of claims 9-13, further comprising administering to said subject an effective amount of a nitric oxide donor, precursor, or both; a nitric oxide generating topical agent; an agent that activates soluble guanylyl cyclase; an agent that inhibits cyclic nucleotide phosphodiesterases; or any combination of any of the foregoing.

15. The monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-7 for use in treating a susceptible cancer.

16. The monoclonal antibody, or antigen-binding fragment thereof, of claim 15, which comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein said LCVR and said HCVR comprise, respectively, amino acid sequences selected from the group consisting of:

SEQ ID NO:9 and SEQ ID NO:59;
SEQ ID NO:10 and SEQ ID NO:60;
SEQ ID NO:12 and SEQ ID NO:62;
SEQ ID NO:13 and SEQ ID NO:63;
SEQ ID NO:15 and SEQ ID NO:65;
SEQ ID NO:17 and SEQ ID NO:67;
SEQ ID NO:20 and SEQ ID NO:70;
SEQ ID NO:21 and SEQ ID NO:71;
SEQ ID NO:22 and SEQ ID NO:72;
SEQ ID NO:23 and SEQ ID NO:73;
SEQ ID NO:24 and SEQ ID NO:74; and
SEQ ID NO:26 and SEQ ID NO:76.

17. The monoclonal antibody, or antigen binding fragment thereof, of claim 15 or 16, which promotes phagocytosis and/or killing of cells of said susceptible cancer.

18. The monoclonal antibody, or antigen binding fragment thereof, of any one of claims 15-17, wherein said susceptible cancer is selected from the group consisting of a leukemia, a lymphoma, ovarian cancer, breast cancer, endometrial cancer, colon cancer, rectal cancer, gastric cancer, bladder cancer, lung cancer, bronchial cancer, bone cancer, prostate cancer, pancreatic cancer, liver and bile duct cancer, esophageal cancer, renal cancer, thyroid cancer, head and neck cancer, testicular cancer, glioblastoma, astrocytoma, melanoma, myelodysplastic syndrome, and a sarcoma.

19. The monoclonal antibody, or antigen binding fragment thereof, of claim 18, wherein:

said leukemia is selected from the group consisting of acute lymphocytic (lymphoblastic) leukemia, acute myeloid leukemia, myelogenous leukemia, chronic lymphocytic leukemia, multiple myeloma, plasma cell leukemia, and chronic myeloid leukemia;

said lymphoma is selected from the group consisting of Hodgkin lymphoma and Non-Hodgkin lymphoma including B cell lymphoma, diffuse large B cell lymphoma, follicular lymphoma, mantle cell lymphoma, marginal zone B cell lymphoma, T cell lymphoma, and Waldenstrom macroglobulinemia; and

said sarcoma is selected from the group consisting of osteosarcoma, Ewing sarcoma, leiomyosarcoma, synovial sarcoma, alveolar soft part sarcoma, angiosarcoma, liposarcoma, fibrosarcoma, rhabdomyosarcoma, and chrondrosarcoma.

20. The use of any one of claims 9 or 15-19, further comprising administering to said patient an anti-tumor therapeutic treatment selected from the group consisting of surgery, radiation, an anti-tumor or anti-neoplastic agent, and combinations of any of the foregoing.

21. A humanized or chimeric monoclonal antibody, or antigen-binding fragment thereof, that specifically binds human, rat, mouse, pig, or dog CD47, blocks binding of SIRPalpha to CD47, and which exhibits the dual activities of:

i) inducing death of cancer cells, and

ii) increasing phagocytosis of said cancer cells, or

a monoclonal antibody, or antigen-binding fragment thereof, that competes with said humanized or chimeric monoclonal antibody, or antigen-binding fragment thereof,

for binding to human, rat, mouse, pig, or dog CD47, blocks binding of SIRPalpha to CD47, and which exhibits said dual activities,

for use in treating a susceptible cancer in a human or companion/pet animal, working animal, sport animal, zoo animal, or other valuable animal kept in captivity in need thereof.

22. The humanized or chimeric monoclonal antibody, or antigen-binding fragment thereof, or competing monoclonal antibody, or antigen-binding fragment thereof, of claim 21, wherein said susceptible cancer is selected from the group consisting of a leukemia, a lymphoma, ovarian cancer, breast cancer, endometrial cancer, colon cancer, rectal cancer, gastric cancer, bladder cancer, lung cancer, bronchial cancer, bone cancer, prostate cancer, pancreatic cancer, liver and bile duct cancer, esophageal cancer, renal cancer, thyroid cancer, head and neck cancer, testicular cancer, glioblastoma, astrocytoma, melanoma, myelodysplastic syndrome, and a sarcoma.

What Is Claimed Is:

1. A monoclonal antibody, or antigen-binding fragment thereof, that specifically binds human, rat, mouse, pig, and dog CD47 which comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein said LCVR and said HCVR comprise, respectively, amino acid sequences selected from the group consisting of:

SEQ ID NO:7 and SEQ ID NO:57;
SEQ ID NO:8 and SEQ ID NO:58;
SEQ ID NO:9 and SEQ ID NO:59;
SEQ ID NO:10 and SEQ ID NO:60;
SEQ ID NO:11 and SEQ ID NO:61;
SEQ ID NO:12 and SEQ ID NO:62;
SEQ ID NO:13 and SEQ ID NO:63;
SEQ ID NO:14 and SEQ ID NO:64;
SEQ ID NO:15 and SEQ ID NO:65;
SEQ ID NO:16 and SEQ ID NO:66;
SEQ ID NO:17 and SEQ ID NO:67;
SEQ ID NO:18 and SEQ ID NO:68;
SEQ ID NO:19 and SEQ ID NO:69;
SEQ ID NO:20 and SEQ ID NO:70;
SEQ ID NO:21 and SEQ ID NO:71;
SEQ ID NO:22 and SEQ ID NO:72;
SEQ ID NO:23 and SEQ ID NO:73;
SEQ ID NO:24 and SEQ ID NO:74;
SEQ ID NO:25 and SEQ ID NO:75;
SEQ ID NO:26 and SEQ ID NO:76;
SEQ ID NO:27 and SEQ ID NO:77;
SEQ ID NO:28 and SEQ ID NO:78;
SEQ ID NO:29 and SEQ ID NO:79;
SEQ ID NO:30 and SEQ ID NO:80; and
SEQ ID NO:31 and SEQ ID NO:81.

2. The monoclonal antibody or antigen-binding fragment thereof of claim 1, which is chimeric or humanized.

3. The monoclonal antibody, or antigen-binding fragment thereof, of claim 1 or 2, which comprises three light chain complementarity determining regions (LCDRs 1-3) and three heavy chain complementarity determining regions (HCDRs 1-3),wherein:

LCDR 1 comprises the amino acid sequence RSSQSLVHSNGNTYLH (SEQ ID NO:1);

LCDR 2 comprises the amino acid sequence KVSYRFS (SEQ ID NO:2); and

LCDR 3 comprises the amino acid sequence SQNTHVPRT (SEQ ID NO:3);

HCDR 1 comprises the amino acid sequence GYTFTNYYVF (SEQ ID NO:4);

HCDR 2 comprises the amino acid sequence DINPVNGDTNFNEKFKN (SEQ ID NO:5); and

HCDR 3 comprises the amino acid sequence GGYTMDY(SEQ ID NO:6).

4. A humanized or chimeric monoclonal antibody, or antigen-binding fragment thereof, that specifically binds human, rat, mouse, pig, and dog CD47, blocks binding of SIRPalpha to CD47, and which exhibits the dual activities of:

i) inducing death of cancer cells, and

ii) increasing phagocytosis of said cancer cells;

which comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein said LCVR and said HCVR comprise, respectively, amino acid sequences selected from the group consisting of:

SEQ ID NO:7 and SEQ ID NO:57;

SEQ ID NO:8 and SEQ ID NO:58;

SEQ ID NO:11 and SEQ ID NO:61;

SEQ ID NO:14 and SEQ ID NO:64;

SEQ ID NO:16 and SEQ ID NO:66;

SEQ ID NO:18 and SEQ ID NO:68;

SEQ ID NO:19 and SEQ ID NO:69;

SEQ ID NO:25 and SEQ ID NO:75;

SEQ ID NO:27 and SEQ ID NO:77;

SEQ ID NO:28 and SEQ ID NO:78;

SEQ ID NO:29 and SEQ ID NO:79;

SEQ ID NO:30 and SEQ ID NO:80; and

SEQ ID NO:31 and SEQ ID NO:81.

5. A pharmaceutical composition, comprising said monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-4, and a pharmaceutically or physiologically acceptable carrier, diluent, or excipient.

6. The monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-4 for use in human therapy or therapy of companion/pet animals, working animals, sport animals, zoo animals, or therapy of other valuable animals kept in captivity.

7. Use of a monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-4 in the manufacture of a medicament for use in treating ischemia-reperfusion injury, or an autoimmune or inflammatory disease, in a human or companion/pet animal, working animal, sport animal, zoo animal, or other valuable animal kept in captivity.

8. The use of claim 7, which comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein said LCVR and said HCVR comprise, respectively, amino acid sequences selected from the group consisting of:

SEQ ID NO:7 and SEQ ID NO:57;
SEQ ID NO:8 and SEQ ID NO:58;
SEQ ID NO:11 and SEQ ID NO:61;
SEQ ID NO:14 and SEQ ID NO:64;
SEQ ID NO:16 and SEQ ID NO:66;
SEQ ID NO:18 and SEQ ID NO:68;
SEQ ID NO:19 and SEQ ID NO:69;
SEQ ID NO:25 and SEQ ID NO:75;
SEQ ID NO:27 and SEQ ID NO:77;
SEQ ID NO:28 and SEQ ID NO:78;
SEQ ID NO:29 and SEQ ID NO:79;
SEQ ID NO:30 and SEQ ID NO:80; and
SEQ ID NO:31 and SEQ ID NO:81.

9 The use of claim 7 or 8, wherein said ischemia-reperfusion injury occurs in organ transplantation, acute kidney injury, cardiopulmonary bypass surgery, pulmonary

hypertension, sickle cell disease, myocardial infarction, stroke, surgical resections and reconstructive surgery, reattachment of an appendage or other body part, skin grafting, or trauma.

10. The use of claim 7 or 8, wherein said autoimmune or inflammatory disease is selected from the group consisting of arthritis, multiple sclerosis, psoriasis, Crohn's disease, inflammatory bowel disease, lupus, Grave's disease and Hashimoto's thyroiditis, and ankylosing spondylitis.

11. The use of any one of claims 6-10, further comprising an effective amount of a nitric oxide donor, precursor, or both; a nitric oxide generating topical agent; an agent that activates soluble guanylyl cyclase; an agent that inhibits cyclic nucleotide phosphodiesterases; or any combination of any of the foregoing.

12. Use of a monoclonal antibody, or antigen-binding fragment thereof, of any one of claims 1-4 in the manufacture of a medicament for use in treating leukemia, a lymphoma, ovarian cancer, breast cancer, endometrial cancer, colon cancer, rectal cancer, gastric cancer, bladder cancer, lung cancer, bronchial cancer, bone cancer, prostate cancer, pancreatic cancer, liver and bile duct cancer, esophageal cancer, renal cancer, thyroid cancer, head and neck cancer, testicular cancer, glioblastoma, astrocytoma, melanoma, myelodysplastic syndrome, and a sarcoma.

13. The use of claim 12, which comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein said LCVR and said HCVR comprise, respectively, amino acid sequences selected from the group consisting of:

SEQ ID NO:9 and SEQ ID NO:59;
SEQ ID NO:10 and SEQ ID NO:60;
SEQ ID NO:12 and SEQ ID NO:62;
SEQ ID NO:13 and SEQ ID NO:63;
SEQ ID NO:15 and SEQ ID NO:65;
SEQ ID NO:17 and SEQ ID NO:67;
SEQ ID NO:20 and SEQ ID NO:70;
SEQ ID NO:21 and SEQ ID NO:71;

SEQ ID NO:22 and SEQ ID NO:72;
SEQ ID NO:23 and SEQ ID NO:73;
SEQ ID NO:24 and SEQ ID NO:74; and
SEQ ID NO:26 and SEQ ID NO:76.

14. The use of claim 12 or 13, which promotes phagocytosis and/or killing of cells of said cancers.

15. The monoclonal antibody, or antigen binding fragment thereof, of claim 17, wherein:

said leukemia is selected from the group consisting of acute lymphocytic (lymphoblastic) leukemia, acute myeloid leukemia, myelogenous leukemia, chronic lymphocytic leukemia, multiple myeloma, plasma cell leukemia, and chronic myeloid leukemia;

said lymphoma is selected from the group consisting of Hodgkin lymphoma and Non-Hodgkin lymphoma including B cell lymphoma, diffuse large B cell lymphoma, follicular lymphoma, mantle cell lymphoma, marginal zone B cell lymphoma, T cell lymphoma, and Waldenstrom macroglobulinemia; and

said sarcoma is selected from the group consisting of osteosarcoma, Ewing sarcoma, leiomyosarcoma, synovial sarcoma, alveolar soft part sarcoma, angiosarcoma, liposarcoma, fibrosarcoma, rhabdomyosarcoma, and chrondrosarcoma.

16. The use of any one of claims 6 or 12-15, further comprising an anti-tumor or anti-neoplastic agent, and combinations of any of the foregoing.

17. Use of a humanized or chimeric monoclonal antibody, or antigen-binding fragment thereof, that specifically binds human, rat, mouse, pig, and dog CD47, blocks binding of SIRPalpha to CD47, and which exhibits the dual activities of:

i) inducing death of cancer cells, and

ii) increasing phagocytosis of said cancer cells, or

a monoclonal antibody, or antigen-binding fragment thereof, that competes with said humanized or chimeric monoclonal antibody, or antigen-binding fragment thereof, for binding to human, rat, mouse, pig, and dog CD47, blocks binding of SIRPalpha to CD47, and which exhibits said dual activities, in the manufacture of a medicament for use in treating a leukemia, a lymphoma, ovarian cancer, breast cancer, endometrial cancer, colon cancer,

rectal cancer, gastric cancer, bladder cancer, lung cancer, bronchial cancer, bone cancer, prostate cancer, pancreatic cancer, liver and bile duct cancer, esophageal cancer, renal cancer, thyroid cancer, head and neck cancer, testicular cancer, glioblastoma, astrocytoma, melanoma, myelodysplastic syndrome, and a sarcoma in a human or companion/pet animal, working animal, sport animal, zoo animal, or other valuable animal kept in captivity in need thereof.