humanized, or fully human. In some embodiments, the antibody binds to human CD47. In some embodiments, the antibody or immunologically active fragment thereof prevents CD47 from interacting with SIRPα. In some embodiments, the antibody or immunologically active fragment thereof is an IgG isotype selected from the group consisting of IgG1 isotype, IgG2 isotype, IgG3 isotype, and IgG4 isotype. In some embodiments, the antibody or immunologically active fragment thereof is an IgG isotype selected from IgG4P and IgGPE.

[0038] In some embodiments, the CD47 antibodies described herein are used in conjunction with one or more additional agents or a combination of additional agents. Suitable additional agents include current pharmaceutical and/or surgical therapies for an intended application, such as, for example, cancer. For example, the CD47 antibodies can be used in conjunction with one or more additional chemotherapeutic or anti-neoplastic agents. Alternatively, the additional chemotherapeutic agent is radiotherapy. In some embodiments, the chemotherapeutic agent is a cell death-inducing agent. In some embodiments, the chemotherapeutic agent induces a loss of phospholipid asymmetry across the plasma membrane, for example causes cell surface exposure of phosphatidylserine (PS). In some embodiments, the chemotherapeutic agent induces endoplasmic reticulum (ER) stress. In some embodiments, the chemotherapeutic agent is a proteasome inhibitor. In some embodiments, the chemotherapeutic agent induces the translocation of ER proteins to the cell surface. In some embodiments, the chemotherapeutic agent induces the translocation and cell surface exposure of calreticulin.

[0039] In some embodiments, the CD47 antibody and additional agent are formulated into a single therapeutic composition, and the CD47 antibody and additional agent are administered simultaneously. Alternatively, the CD47 antibody and additional agent are separate from each other, *e.g.*, each is formulated into a separate therapeutic composition, and the CD47 antibody and the additional agent are administered simultaneously, or the CD47 antibody and the additional agent are administered at different times during a treatment regimen. For example, the CD47 antibody is administered prior to the administration of the additional agent, the CD47 antibody is administered subsequent to the administration of the additional agent, or the CD47 antibody and the additional agent are administered in an alternating fashion. As described herein, the CD47 antibody and additional agent are administered in single doses or in multiple doses.

[0040] One skilled in the art will appreciate that the antibodies of the invention have a variety of uses. For example, the antibodies of the invention are used as therapeutic

available antibodies used in these assays were the SIRPα blocking antibodies, BRC126 and CC2C6, and the non-SIRPα blocking antibody, 2D3.

[0045] Figure 5 is a graph showing 2A1 and B6H12 binding to cynomolgus (cyno) monkey B-cells and Raji, as assessed by flow cytometry. 2A1 binds human and cyno CD47 with equivalent affinity, as does B6H12, albeit with lower affinity to both human and cyno CD47 than 2A1.

[0046] Figure 6 is a graph depicting the binding of 2A1, 2A1-xi, and B6H12 to Raji cells, as assessed by flow cytometry. Importantly, the graph shows that the variable region sequences of the heavy (VH) and light (VL) chains were correctly elucidated in the chimeric version of 2A1.

[0047] Figure 7A-7J is a series of graphs showing binding of humanized variants of 2A1 to Raji cells. 2A1-xi was used as an internal control on most graphs. Numerous combinations of heavy and light chains were tested as described in Example 8.

[0048] Figure 8A is image of the trace from size exclusion chromatography using an AKTA FLPC with a superdex200 column. Shown are the IgG1, IgG4P, and IgGPE variants of the AB6.12 antibody. All three variant are over 97% monomeric. Figure 8B is a photograph of a coomassie blue stained SDS-PAGE gel of numerous humanized variants of 2A1 under reducing (R) and non-reducing (NR) conditions.

[0049] Figure 9 is a series of graphs depicting the ability of CD47 antibodies to promote phagocytosis of human tumor cell lines by human monocyte derived macrophages (MDM). Figure 9A is a graph showing the phagocytic index, wherein antibodies used were the commercial antibody B6H12, the murine 2A1 antibody, a humanized variant AB2.05 antibody, and the non-blocking commercial antibody 2D3. Figure 9B is a graph showing the phagocytic index, wherein the antibodies used were the commercial antibody B6H12, humanized antibody AB2.05 (human IgG1), and the IgG1, IgG4P, and IgG4PE variants of the humanized antibody AB6.12. CCRF-CEM cells were used as the CD47 target cell line in these experiments.

[0050] Figure 10 is a series of graphs showing the anti-tumor effects of CD47 antibodies in a Raji tumor model. Figure 10A is a graph that shows the efficacy of the murine antibodies 9E4, 1B4, 2A1, and the commercial antibody B6H12. Figure 10B is a graph that shows the efficacy of the IgG1, IgG4P, and IgG4PE isotypes of the humanized antibody AB6.12, along with the murine 2A1 antibody. In both models, mice were treated with 200μg antibody doses three times a week.

[00262] An image of the trace from size exclusion chromatography using an AKTA FLPC with a superdex200 column is shown in Figure 8A. The IgG1, IgG4P, and IgGPE variants of the AB6.12 antibody are shown. All three variant are over 98% monomeric. Figure 8B is a photograph of a coomassie blue stained SDS-PAGE gel of numerous humanized variants of 2A1 under reducing (R) and non-reducing (NR) conditions.

EXAMPLE 9: CD47 Antibodies Promote Phagocytosis of Tumor Cell Lines

[00263] CD47 is a cell surface receptor that is upregulated on tumor cells and is also thought to contribute to immune evasion through its interaction with its natural ligand SIRPα. Ligation of CD47 to SIRPα on macrophages results in decreased phagocytic activity. As described in detail below, it was determined if the CD47 binding and SIRPα blocking activity of the 2A1 antibody, and variations thereof, promote tumor cell phagocytosis in the presence of human macrophages.

[00264] PBMCs were isolated from human blood, and the monocytes were differentiated into macrophages by incubating them in AIM-V media (Life Technologies) for 7 days. These monocyte derived macrophages (MDMs) become adherent allowing other cells to be washed away. MDMs were scraped and re-plated in 12-well dishes and allowed to adhere for 24 hours. The human tumor cell line CCRF-CEM was chosen as a target cell type because of its high CD47 expression. CCRF-CEM cells were labeled with 0.3 μM CFSE at 37°C for 15 minutes, then washed and added to MDMs at a ratio of 4:1 tumor cells per phagocyte, and CD47 antibody was added at various concentrations. Phagocytosis of target cells was allowed for 3 hours. Subsequently, non-phagocytosed target cells were washed away with PBS. The remaining phagocytes were scraped off, stained with an antibody to the macrophage marker CD14 conjugated to DyLite 649 (Biolegend), and analyzed by flow cytometry. Phagocytosis was measured by gating on live cells that were FL4 positive (CD14+), and then assessing the percent of FL1 (CFSE+) positive cells.

[00265] Figure 9 shows that the CD47 antibody 2A1 and its humanized variants demonstrated a dose-dependent increase in phagocytosis of tumor cells by MDMs. Antibody 2A1 and the humanized variant AB2.05 were unique in their ability to induce phagocytosis of tumor cells at 66.7 pM, whereas B6H12 had no activity at that concentration(Figure 9A). Figure 9B shows how 2A1, and the humanized variants AB2.05, AB6.12-IgG1, AB6.12-IgG4P, and AB6.12-IgG4PE all induce maximal phagocytosis at 0.3 μg/ml or 2 nM, while B6H12 requires higher concentrations. This data demonstrates that the CD47 antibody, 2A1 (and humanized variants derived from it), induce macrophage-

What is claimed is:

1. An isolated monoclonal antibody that binds to CD47 or an immunologically active fragment thereof, wherein the antibody does not cause a significant level of agglutination of cells after administration.

2. The antibody of claim 1, wherein the antibody is chimeric, humanized, or fully human.

3. The antibody of claim 1, wherein the CD47 is human CD47.

4. The antibody of claim 1, wherein the antibody or immunologically active fragment thereof prevents CD47 from interacting with signal-regulatory-protein α (SIRPα).

5. The antibody of claim 4, wherein the antibody or immunologically active fragment thereof promotes macrophage-mediated phagocytosis of a CD47-expressing cell.

6. The antibody of claim 1, wherein the antibody or immunologically active fragment thereof is an IgG isotype selected from the group consisting of IgG1 isotype, IgG2 isotype, IgG3 isotype, and IgG4 isotype.

7. The antibody of claim 1, wherein the antibody or immunologically active fragment thereof comprises a variable heavy (VH) chain region selected from the group consisting of SEQ ID NOs: 5-30.

8. The antibody of claim 1, wherein the antibody or immunologically active fragment thereof comprises a variable light (VL) chain region selected from the group consisting of SEQ ID NOs: 31-47.

9. The antibody of claim 1, wherein the antibody or immunologically active fragment thereof comprises a VH region provided in any one of SEQ ID NOs: 5-30 and a VL region provided in any one of SEQ ID NOs: 31-47.

10. The antibody of claim 9, wherein the antibody or immunologically active fragment thereof comprises a VH region provided in any one of SEQ ID NOs: 5, 7, 8, 11, 12, 15-17, 20-22, and 27-30 paired with a VL region provided in any one of SEQ ID NOs: 31, 32, 35, 40, 41, 42, 43, 44, and 47.

11. The antibody of claim 9, wherein the antibody comprises a combination of a VH chain region and a VL chain region selected from the combinations listed in Table 1.

12. The antibody of claim 1, wherein the antibody or immunologically active fragment thereof comprises a VH complementarity determining region 1 (CDR1) sequence set forth in SEQ ID NO: 50, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, or SEQ ID NO: 66, a VH CDR2 sequence set forth in SEQ ID NO: 51, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, or SEQ ID NO: 76, a VH CDR3 sequence set forth in SEQ ID NO: 52 or SEQ ID NO: 77, a VL CDR1 sequence set forth in SEQ ID NO: 53, SEQ ID NO: 67, or SEQ ID NO: 68, a VL CDR2 sequence set forth in SEQ ID NO: 54, SEQ ID NO: 69, SEQ ID NO: 70, or SEQ ID NO: 71 and a VL CDR3 sequence set forth in SEQ ID NO: 55.

13. The antibody of claim 12, wherein the antibody or immunologically active fragment thereof comprises a VH CDR1 sequence set forth in SEQ ID NO: 50, a VH CDR2 sequence set forth in SEQ ID NO: 51, a VH CDR3 sequence set forth in SEQ ID NO: 52, a VL CDR1 sequence set forth in SEQ ID NO: 53, a VL CDR2 sequence set forth in SEQ ID NO: 54, and a VL CDR3 sequence set forth in SEQ ID NO: 55.

14. The antibody of claim 12, wherein the antibody or immunologically active fragment thereof comprises a VH CDR1 sequence set forth in SEQ ID NO: 50, a VH CDR2 sequence set forth in SEQ ID NO: 72, a VH CDR3 sequence set forth in SEQ ID NO: 52, a VL CDR1 set forth in SEQ ID NO: 53, a VL CDR2 sequence set forth in SEQ ID NO: 71, and a VL CDR3 sequence set forth in SEQ ID NO: 55.

15. The antibody of claim 1, wherein the antibody binds to CD47 in a head to side orientation, wherein a VH chain of the antibody is positioned near the membrane of a CD47

expressing cell, and wherein a VL chain of the antibody occludes a SIRPα binding site on CD47.

16. The antibody of claim 1, wherein the antibody binds to CD47 in a head to side orientation, wherein a VL chain of the antibody is positioned near the membrane of a CD47 expressing cell, and wherein a VH chain of the antibody occludes a SIRPα binding site on CD47.

17. The antibody of claim 1, wherein the antibody binds to a discontinuous epitope on CD47.

18. The antibody of claim 17, wherein the antibody binds to a CD47 loop comprising SEQ ID NO: 56.

19. The antibody of claim 17, wherein the discontinuous epitope comprises amino acids residues Y37, K39, K41, K43, G44, R45, D46, D51, H90, N93, E97, T99, E104, or E106 of CD47 when numbered in accordance with SEQ ID NO: 147.

20. The antibody of claim 1, wherein the antibody does not cause a significant level of hemagglutination of red blood cells after administration.

21. The antibody of claim 1, wherein the antibody or immunologically active fragment thereof is an IgG isotype selected from IgG4P and IgGPE.

22. An isolated antibody or an immunologically active fragment thereof, wherein the antibody competes with the antibody of any of the preceding claims for preventing CD47 from interacting with SIRPα.

23. A polypeptide comprising amino acids residues Y37, K39, K41, K43, G44, R45, D46, D51, H90, N93, E97, T99, E104, and E106 of CD47 when numbered in accordance with SEQ ID NO: 147.

24. A pharmaceutical composition comprising the antibody of claim 1 or an immunologically active fragment thereof and a carrier.

25. A method of alleviating a symptom of a cancer or other neoplastic condition, the method comprising administering the antibody of claim 1 or an immunologically active fragment thereof to a subject in need thereof in an amount sufficient to alleviate the symptom of the cancer or other neoplastic condition in the subject.

26. The method of claim 25, wherein the subject is a human.

27. The method of claim 25, wherein the antibody is chimeric, humanized, or fully human.

28. The method of claim 25, wherein the CD47 is human CD47.

29. The method of claim 25, wherein the antibody or immunologically active fragment thereof prevents CD47 from interacting with SIRPα.

30. The method of claim 25, wherein the antibody or immunologically active fragment thereof is an IgG isotype selected from the group consisting of IgG1 isotype, IgG2 isotype, IgG3 isotype, and IgG4 isotype.

31. The method of claim 25, wherein the antibody or immunologically active fragment thereof is an IgG isotype selected from IgG4P and IgGPE.

32. The method of claim 25, further comprising administering chemotherapy.

33. The method of claim 32, wherein said chemotherapy is radiotherapy.

humanized, or fully human. In some embodiments, the antibody binds to human CD47. In some embodiments, the antibody or immunologically active fragment thereof prevents CD47 from interacting with SIRPα. In some embodiments, the antibody or immunologically active fragment thereof is an IgG isotype selected from the group consisting of IgG1 isotype, IgG2 isotype, IgG3 isotype, and IgG4 isotype. In some embodiments, the antibody or immunologically active fragment thereof is an IgG isotype selected from IgG4P and IgG4PE.

[0038] In some embodiments, the CD47 antibodies described herein are used in conjunction with one or more additional agents or a combination of additional agents. Suitable additional agents include current pharmaceutical and/or surgical therapies for an intended application, such as, for example, cancer. For example, the CD47 antibodies can be used in conjunction with one or more additional chemotherapeutic or anti-neoplastic agents. Alternatively, the additional chemotherapeutic agent is radiotherapy. In some embodiments, the chemotherapeutic agent is a cell death-inducing agent. In some embodiments, the chemotherapeutic agent induces a loss of phospholipid asymmetry across the plasma membrane, for example causes cell surface exposure of phosphatidylserine (PS). In some embodiments, the chemotherapeutic agent induces endoplasmic reticulum (ER) stress. In some embodiments, the chemotherapeutic agent is a proteasome inhibitor. In some embodiments, the chemotherapeutic agent induces the translocation of ER proteins to the cell surface. In some embodiments, the chemotherapeutic agent induces the translocation and cell surface exposure of calreticulin.

[0039] In some embodiments, the CD47 antibody and additional agent are formulated into a single therapeutic composition, and the CD47 antibody and additional agent are administered simultaneously. Alternatively, the CD47 antibody and additional agent are separate from each other, *e.g.*, each is formulated into a separate therapeutic composition, and the CD47 antibody and the additional agent are administered simultaneously, or the CD47 antibody and the additional agent are administered at different times during a treatment regimen. For example, the CD47 antibody is administered prior to the administration of the additional agent, the CD47 antibody is administered subsequent to the administration of the additional agent, or the CD47 antibody and the additional agent are administered in an alternating fashion. As described herein, the CD47 antibody and additional agent are administered in single doses or in multiple doses.

[0040] One skilled in the art will appreciate that the antibodies of the invention have a variety of uses. For example, the antibodies of the invention are used as therapeutic

available antibodies used in these assays were the SIRPα blocking antibodies, BRC126 and CC2C6, and the non-SIRPα blocking antibody, 2D3.

[0045] Figure 5 is a graph showing 2A1 and B6H12 binding to cynomolgus (cyno) monkey B-cells and Raji, as assessed by flow cytometry. 2A1 binds human and cyno CD47 with equivalent affinity, as does B6H12, albeit with lower affinity to both human and cyno CD47 than 2A1.

[0046] Figure 6 is a graph depicting the binding of 2A1, 2A1-xi, and B6H12 to Raji cells, as assessed by flow cytometry. Importantly, the graph shows that the variable region sequences of the heavy (VH) and light (VL) chains were correctly elucidated in the chimeric version of 2A1.

[0047] Figure 7A-7J is a series of graphs showing binding of humanized variants of 2A1 to Raji cells. 2A1-xi was used as an internal control on most graphs. Numerous combinations of heavy and light chains were tested as described in Example 8.

[0048] Figure 8A is image of the trace from size exclusion chromatography using an AKTA FLPC with a superdex200 column. Shown are the IgG1, IgG4P, and IgG4PE variants of the AB6.12 antibody. All three variant are over 97% monomeric. Figure 8B is a photograph of a coomassie blue stained SDS-PAGE gel of numerous humanized variants of 2A1 under reducing (R) and non-reducing (NR) conditions.

[0049] Figure 9 is a series of graphs depicting the ability of CD47 antibodies to promote phagocytosis of human tumor cell lines by human monocyte derived macrophages (MDM). Figure 9A is a graph showing the phagocytic index, wherein antibodies used were the commercial antibody B6H12, the murine 2A1 antibody, a humanized variant AB2.05 antibody, and the non-blocking commercial antibody 2D3. Figure 9B is a graph showing the phagocytic index, wherein the antibodies used were the commercial antibody B6H12, humanized antibody AB2.05 (human IgG1), and the IgG1, IgG4P, and IgG4PE variants of the humanized antibody AB6.12. CCRF-CEM cells were used as the CD47 target cell line in these experiments.

[0050] Figure 10 is a series of graphs showing the anti-tumor effects of CD47 antibodies in a Raji tumor model. Figure 10A is a graph that shows the efficacy of the murine antibodies 9E4, 1B4, 2A1, and the commercial antibody B6H12. Figure 10B is a graph that shows the efficacy of the IgG1, IgG4P, and IgG4PE isotypes of the humanized antibody AB6.12, along with the murine 2A1 antibody. In both models, mice were treated with 200μg antibody doses three times a week.

[00262] An image of the trace from size exclusion chromatography using an AKTA FLPC with a superdex200 column is shown in Figure 8A. The IgG1, IgG4P, and IgG4PE variants of the AB6.12 antibody are shown. All three variant are over 98% monomeric. Figure 8B is a photograph of a coomassie blue stained SDS-PAGE gel of numerous humanized variants of 2A1 under reducing (R) and non-reducing (NR) conditions.

EXAMPLE 9: CD47 Antibodies Promote Phagocytosis of Tumor Cell Lines

[00263] CD47 is a cell surface receptor that is upregulated on tumor cells and is also thought to contribute to immune evasion through its interaction with its natural ligand SIRPα. Ligation of CD47 to SIRPα on macrophages results in decreased phagocytic activity. As described in detail below, it was determined if the CD47 binding and SIRPα blocking activity of the 2A1 antibody, and variations thereof, promote tumor cell phagocytosis in the presence of human macrophages.

[00264] PBMCs were isolated from human blood, and the monocytes were differentiated into macrophages by incubating them in AIM-V media (Life Technologies) for 7 days. These monocyte derived macrophages (MDMs) become adherent allowing other cells to be washed away. MDMs were scraped and re-plated in 12-well dishes and allowed to adhere for 24 hours. The human tumor cell line CCRF-CEM was chosen as a target cell type because of its high CD47 expression. CCRF-CEM cells were labeled with 0.3 μM CFSE at 37°C for 15 minutes, then washed and added to MDMs at a ratio of 4:1 tumor cells per phagocyte, and CD47 antibody was added at various concentrations. Phagocytosis of target cells was allowed for 3 hours. Subsequently, non-phagocytosed target cells were washed away with PBS. The remaining phagocytes were scraped off, stained with an antibody to the macrophage marker CD14 conjugated to DyLite 649 (Biolegend), and analyzed by flow cytometry. Phagocytosis was measured by gating on live cells that were FL4 positive (CD14+), and then assessing the percent of FL1 (CFSE+) positive cells.

[00265] Figure 9 shows that the CD47 antibody 2A1 and its humanized variants demonstrated a dose-dependent increase in phagocytosis of tumor cells by MDMs. Antibody 2A1 and the humanized variant AB2.05 were unique in their ability to induce phagocytosis of tumor cells at 66.7 pM, whereas B6H12 had no activity at that concentration(Figure 9A). Figure 9B shows how 2A1, and the humanized variants AB2.05, AB6.12-IgG1, AB6.12-IgG4P, and AB6.12-IgG4PE all induce maximal phagocytosis at 0.3 μg/ml or 2 nM, while B6H12 requires higher concentrations. This data demonstrates that the CD47 antibody, 2A1 (and humanized variants derived from it), induce macrophage-

What is claimed is:

1. An isolated monoclonal antibody or immunologically active fragment thereof that binds to human CD47, said antibody or immunologically active fragment thereof comprising:

a variable heavy (VH) chain CDR1 amino acid sequence set forth in SEQ ID NO: 50, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, or SEQ ID NO: 66;

a VH chain CDR2 amino acid sequence set forth in SEQ ID NO: 51, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, or SEQ ID NO: 76;

a VH chain CDR3 amino acid sequence set forth in SEQ ID NO: 52 or SEQ ID NO: 77;

a variable light (VL) chain CDR1 amino acid sequence set forth in SEQ ID NO: 53, SEQ ID NO: 67, or SEQ ID NO: 68;

a VL chain CDR2 amino acid sequence set forth in SEQ ID NO: 54, SEQ ID NO: 69, SEQ ID NO: 70, or SEQ ID NO: 71; and

a VL CDR3 sequence set forth in SEQ ID NO: 55.

2. The antibody or immunologically active fragment thereof of claim 1, wherein the antibody is chimeric or humanized.

3. The antibody or immunologically active fragment thereof of claim 1, wherein the antibody or immunologically active fragment thereof prevents the human CD47 from interacting with signal-regulatory-protein α (SIRPα).

4. The antibody or immunologically active fragment thereof of claim 3, wherein the antibody or immunologically active fragment thereof promotes macrophage-mediated phagocytosis of a CD47-expressing cell.

5. The antibody or immunologically active fragment thereof of claim 1, wherein the antibody or immunologically active fragment thereof is of an IgG isotype selected from the group consisting of IgG1 isotype, IgG2 isotype, IgG3 isotype, and IgG4 isotype.

6. The antibody or immunologically active fragment thereof of claim 1, wherein the antibody or immunologically active fragment thereof comprises a variable heavy (VH) chain region sequence selected from the group consisting of SEQ ID NOs: 5-30.

7. The antibody or immunologically active fragment thereof of claim 1, wherein the antibody or immunologically active fragment thereof comprises a variable light (VL) chain region sequence selected from the group consisting of SEQ ID NOs: 31-47.

8. The antibody or immunologically active fragment thereof of claim 1, wherein the antibody or immunologically active fragment thereof comprises a VH region sequence provided in any one of SEQ ID NOs: 5-30 and a VL region sequence provided in any one of SEQ ID NOs: 31-47.

9. The antibody or immunologically active fragment thereof of claim 8, wherein the antibody or immunologically active fragment thereof comprises a VH region sequence provided in any one of SEQ ID NOs: 5, 7, 8, 11, 12, 15-17, 20-22, and 27-30 and a VL region sequence provided in any one of SEQ ID NOs: 31, 32, 35, 40, 41, 42, 43, 44, and 47.

10. The antibody or immunologically active fragment thereof of claim 8, wherein the antibody comprises a combination of a VH chain region sequence and a VL chain region sequence, said combination selected from the combinations listed in Table 1.

11. The antibody or immunologically active fragment thereof of claim 1, wherein the antibody or immunologically active fragment thereof comprises the VH CDR1 sequence set forth in SEQ ID NO: 50, the VH CDR2 sequence set forth in SEQ ID NO: 51, the VH CDR3 sequence set forth in SEQ ID NO: 52, the VL CDR1 sequence set forth in SEQ ID NO: 53, the VL CDR2 sequence set forth in SEQ ID NO: 54, and the VL CDR3 sequence set forth in SEQ ID NO: 55.

12. The antibody or immunologically active fragment thereof of claim 1, wherein the antibody or immunologically active fragment thereof comprises the VH CDR1 sequence set forth in SEQ ID NO: 50, the VH CDR2 sequence set forth in SEQ ID NO: 72, the VH CDR3 sequence set forth in SEQ ID NO: 52, the VL CDR1 sequence set forth in SEQ ID NO: 53, the VL CDR2 sequence set forth in SEQ ID NO: 71, and the VL CDR3 sequence set forth in SEQ ID NO: 55.

13. The antibody or immunologically active fragment thereof of claim 1, wherein the antibody binds to CD47 in a head to side orientation, wherein a VH chain of the antibody is positioned near the membrane of a CD47 expressing cell, and wherein a VL chain of the antibody occludes a SIRPα binding site on CD47.

14. The antibody or immunologically active fragment thereof of claim 1, wherein the antibody binds to a discontinuous epitope on CD47.

15. The antibody or immunologically active fragment thereof of claim 14, wherein the antibody binds to a CD47 loop comprising SEQ ID NO: 56.

16. The antibody or immunologically active fragment thereof of claim 14, wherein the discontinuous epitope comprises amino acid residues Y37, K39, K41, K43, G44, R45, D46, D51, H90, N93, E97, T99, E104, or E106 of CD47 when numbered in accordance with SEQ ID NO: 147.

17. The antibody or immunologically active fragment thereof of claim 1, wherein the antibody does not cause a significant level of hemagglutination of red blood cells, as measured by an in vitro hemagglutination assay.

18. The antibody or immunologically active fragment thereof of claim 1, wherein the antibody or immunologically active fragment thereof is of an IgG isotype selected from IgG4P and Ig4GPE.

19. A pharmaceutical composition comprising the antibody or immunologically active fragment thereof of claim 1 and a carrier.

20. An isolated monoclonal antibody or immunologically active fragment thereof that binds to human CD47, said antibody or immunologically active fragment thereof comprising:
a VH CDR1, a VH CDR2, and a VH CDR3, respectively comprising the amino acid sequences of a CDR1, a CDR2, and a CDR3 within a VH chain region having the sequence set forth in any of SEQ ID NOs: 5-30; and

a VL CDR1, a VL CDR2, and a VLCDR3, respectively comprising the amino acid sequences of a CDR1, a CDR2, and a CDR3 within a VL chain region having the sequence set forth in any of SEQ ID NOs: 31-47.

21. A pharmaceutical composition comprising the antibody or immunologically active fragment thereof of claim 20.