

**[0005]** Therefore, there remains a need for novel anti-CD47 antibodies capable of blocking binding of CD47 to SIRP $\alpha$  without exhibiting the undesirable effects of binding to RBCs and other non-cancerous cells.

## SUMMARY

**[0006]** To provide anti-CD47 antibodies with powerful anti-tumor activity and reduced off-target effects, the inventors developed a suite of masked anti-CD47 antibodies (including activatable anti-CD47 antibodies), each comprising an N-terminal masking peptide and an IgG1 Fc region. The anti-tumor activity of the antibodies is two-fold: 1) blocking of the CD47-SIRP $\alpha$  interaction to allow recognition and phagocytosis of tumor cells by macrophages, and 2) tumor killing through IgG1 Fc-mediated effector functions such as ADCC and ADCP. The masking peptide is designed to compete with the anti-CD47 antibody moiety for target binding, thereby inhibiting on-target off-tumor activities in healthy tissues and allowing anti-tumor activities in the tumor microenvironment (TME).

**[0007]** A masked antibody is designed to mask its antigen-binding site with a masking moiety in the masking peptide, which prevents the antibody from binding to its target in healthy tissues. Masked antibodies may be activatable, also known as a SAFE BODY™, wherein the masking moiety is designed to be unmasked to activate the antibody in a TME having certain activation conditions, allowing the antigen-binding site to bind to its target. For example, the masking peptide of an activatable antibody may comprise a cleavable moiety that, upon cleavage by a protease, results in removal of the masking moiety from the antibody and activation of the antibody to bind CD47. In normal tissues and in circulation, the masking moiety in the activatable anti-CD47 antibody functions to block binding to CD47, reducing off-target effects associated with anti-CD47 antibodies, such as anemia. However, in the TME where protease activity has been reported to be elevated, the masking moiety is cleaved off, enabling the activated anti-CD47 antibody to bind CD47 on tumor cells. Thus, the activatable anti-CD47 antibodies described herein exhibit enhanced anti-tumor activity, both through blocking of the CD47-SIRP $\alpha$  interaction and ADCC/ADCP effector functions, with reduced toxicity on normal cells as compared to existing anti-CD47 antibodies.

**[0008]** Accordingly, in some examples, provided herein are antibodies (*e.g.*, isolated antibodies), antigen-binding fragments, and masked antibodies (*e.g.*, activatable antibodies) that bind to CD47 (*e.g.*, human CD47). In some examples, the antibodies (*e.g.*, isolated

antibodies), antigen-binding fragments, and masked antibodies (*e.g.*, activatable antibodies) have at least one (*e.g.*, at least one, at least two, at least three, at least four, at least five, or all six) of the following functional properties: (a) bind to human CD47 with a  $K_D$  of 500 nM or less; (b) are cross-reactive with monkey, rat, or dog CD47; (c) are capable of inhibiting tumor cell growth; (d) have therapeutic effect on a cancer; (e) block binding between CD47 and SIRP proteins (*e.g.*, SIRP $\alpha$ ); and (f) induce antibody-dependent cellular cytotoxicity (ADCC) and/or antibody-dependent cellular phagocytosis (ADCP) against CD47-expressing tumor cells.

**[0009]** Accordingly, in some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM. In some examples, 1) the VH comprises a first complementary-determining-region (CDR-H1), a second complementary-determining-region (CDR-H2), and a third complementary-determining-region (CDR-H3), wherein the CDR-H1 comprises the amino acid sequence of SEQ ID NO: 182 or 183; wherein the CDR-H2 comprises the amino acid sequence of SEQ ID NO: 184 or 185; and wherein the CDR-H3 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 186-189; and/or 2) the VL comprises a first complementary-determining-region (CDR-L1), a second complementary-determining-region (CDR-L2), and a third complementary-determining-region (CDR-L3), wherein the CDR-L1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 190-193; wherein the CDR-L2 comprises the amino acid sequence of SEQ ID NO: 194; and wherein the CDR-L3 comprises the amino acid sequence of SEQ ID NO: 195 or 196. In certain examples, the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 182, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 185, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 188; and b) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 191, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 194, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 195. In some examples, the masked antibody comprises a first polypeptide comprising, from N terminus to C terminus, the masking peptide and the VL, and a second polypeptide comprising the VH. In other examples, the masked antibody

comprises a first polypeptide comprising, from N terminus to C terminus, the masking peptide and the VH, and a second polypeptide comprising the VL. In additional examples, the masked antibody comprises a first polypeptide comprising, from N terminus to C terminus, the masking peptide, the VL, and the VH. In yet additional examples, the masked antibody comprises a first polypeptide comprising, from N terminus to C terminus the masking peptide, the VH, and the VL. In some examples, the masking moiety (MM) comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 197-200. In one example, the MM comprises the amino acid sequence of SEQ ID NO: 199. In certain examples, the MM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 137 and 167-181. In one, the MM comprises the amino acid sequence of SEQ ID NO: 137. In some examples, the masking peptide, or a part thereof (*e.g.*, the MM) has a masking efficiency of at least about 50 as determined by a Jurkat NFAT reporter assay. In some examples, the masking peptide, or a part thereof (*e.g.*, the MM) has a masking efficiency of at least about 100 as determined by a Jurkat NFAT reporter assay. In some examples, the masked antibody comprises a first polypeptide comprising, from N terminus to C terminus the masking peptide and the VL; and a second polypeptide comprising the VH. In certain examples, the masked antibody comprises a human IgG4 fragment crystallizable (Fc) region. In certain examples, the masked antibody comprises a human IgG1 Fc region. In some examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution). In some examples, the masked antibody binds to one or more amino acid residues of human CD47 selected from the group consisting of K39, W40, K41, F50, D51, G52, T99, E100, L101, and T102. In some examples, the masked antibody does not bind to one or more amino acid residues of human CD47 selected from the group consisting of L2, L3, F4, K6, N27, E29, A30, Q31, T34, E35, V36, Y37, D46, T49, A53, E97, R103, E104, G105, and E106. In certain examples, the masked antibody binds to amino acid residues K39, W40, K41, F50, D51, G52, T99, E100, L101, and T102 of human CD47 and/or does not bind to amino acid residues L2, L3, F4, K6, N27, E29, A30, Q31, T34, E35, V36, Y37, D46, T49, A53, E97, R103, E104, G105, and E106 of human CD47.

**[0010]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM); (b) a target binding moiety (TBM) comprising an antibody heavy chain

variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; and (c) an IgG1 Fc region (*e.g.*, a human IgG1 Fc region), or an IgG Fc region (*e.g.*, a human IgG Fc region) with enhanced antibody-dependent cellular cytotoxicity (ADCC) activity, wherein the masking peptide is linked to the N terminus of the VH or the VL, and wherein the MM competes with human CD47 to bind the TBM. In some examples, the masked antibody comprises an IgG1 Fc region. In some examples, the masked antibody comprises an IgG Fc region with enhanced ADCC activity. In some examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0011]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein (a) the VH comprises a CDR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 35-37 and 39-50, a CDR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 52-54 and 56-67, and a CDR-H3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 69-71 and 73-84; and (b) the VL comprises a CDR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 86-88 and 89-101, a CDR-L2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 103-105 and 106-118, and a CDR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 120-122 and 124-135.

**[0012]** In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises an amino acid sequence selected from the group consisting of SEQ ID

NOs: 1, 3, 5, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, and 31; and/or wherein the VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 4, 6, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, and 32.

**[0013]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 48, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 65, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 82; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 99, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 116, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 133. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 27, and/or the VL comprises the amino acid sequence of SEQ ID NO: 28. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0013a]** In one aspect, the present disclosure refers to a masked antibody, comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein: 1) the VH comprises: a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 48, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 65, a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 82; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 99, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 116, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 133.

**[0014]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 49, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 66, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 83; and 2) the VL comprises a CDR-L1

comprising the amino acid sequence of SEQ ID NO: 100, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 117, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 134. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 29, and/or the VL comprises the amino acid sequence of SEQ ID NO: 30. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0015]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 50, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 67, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 84; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 101, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 118, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 135. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 31, and/or the VL comprises the amino acid sequence of SEQ ID NO: 32. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0016]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 35, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 69; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 86, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 103, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 120. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 1, and/or the VL comprises the amino acid sequence of SEQ ID NO: 2. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0017]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 53, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 70; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 87, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 104, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 121. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM)

and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 3, and/or the VL comprises the amino acid sequence of SEQ ID NO: 4. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0018]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 37, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 54, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 71; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 88, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 105, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 122. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 5, and/or the VL comprises the amino acid sequence of SEQ ID NO: 6. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0019]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the

VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 39, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 56, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 73; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 107, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 124. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 9, and/or the VL comprises the amino acid sequence of SEQ ID NO: 10. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0020]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 40, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 57, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 74; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 91, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 108, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 125. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 11, and/or the VL comprises the

amino acid sequence of SEQ ID NO: 12. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0021]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 41, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 58, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 75; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 92, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 109, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 126. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 13, and/or the VL comprises the amino acid sequence of SEQ ID NO: 14. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0022]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 42, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 59, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 76; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 93, a CDR-L2 comprising the amino acid sequence

of SEQ ID NO: 110, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 127. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 15, and/or the VL comprises the amino acid sequence of SEQ ID NO: 16. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0023]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 43, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 60, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 77; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 94, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 111, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 128. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 17, and/or the VL comprises the amino acid sequence of SEQ ID NO: 18. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0024]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a

linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 44, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 61, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 78; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 95, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 112, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 129. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 19, and/or the VL comprises the amino acid sequence of SEQ ID NO: 20. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0025]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 45, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 62, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 79; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 96, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 113, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 130. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the

TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 21, and/or the VL comprises the amino acid sequence of SEQ ID NO: 22. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0026]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 46, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 63, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 80; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 97, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 114, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 131. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 23, and/or the VL comprises the amino acid sequence of SEQ ID NO: 24. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0027]** In some examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) a) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 47, a

CDR-H2 comprising the amino acid sequence of SEQ ID NO: 64, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 81; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 98, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 115, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 132. In certain examples, provided herein is a masked antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 25, and/or the VL comprises the amino acid sequence of SEQ ID NO: 26. In certain examples, the MM comprises the amino acid sequence of SEQ ID NO: 137.

**[0028]** In some examples according to any one of the masked antibodies described above, the LM does not comprise a cleavable moiety (CM) comprising at least one cleavage site.

**[0029]** In some examples according to any one of the masked antibodies described above, the masked antibody is an activatable antibody. Accordingly, in some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM. In preferred examples, the activatable antibody has a higher binding affinity to human CD47 *in vitro* upon cleavage of the CM than before the cleavage of the CM. In some examples, 1) the VH comprises a first complementary-determining-region (CDR-H1), a second complementary-determining-region (CDR-H2), and a third complementary-determining-region (CDR-H3), wherein the CDR-H1 comprises the amino acid sequence of SEQ ID NO: 182 or 183; wherein the CDR-H2 comprises the amino acid sequence of SEQ ID NO: 184 or 185; and wherein the CDR-H3 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 186-

189; and/or 2) the VL comprises a first complementary-determining-region (CDR-L1), a second complementary-determining-region (CDR-L2), and a third complementary-determining-region (CDR-L3), wherein the CDR-L1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 190-193; wherein the CDR-L2 comprises the amino acid sequence of SEQ ID NO: 194; and wherein the CDR-L3 comprises the amino acid sequence of SEQ ID NO: 195 or 196. In certain examples, the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 182, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 185, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 188; and b) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 191, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 194, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 195. In some examples, the activatable antibody comprises a first polypeptide comprising, from N terminus to C terminus, the masking peptide and the VL, and a second polypeptide comprising the VH. In other examples, the activatable antibody comprises a first polypeptide comprising, from N terminus to C terminus, the masking peptide and the VH, and a second polypeptide comprising the VL. In additional examples, the activatable antibody comprises a first polypeptide comprising, from N terminus to C terminus, the masking peptide, the VL, and the VH. In yet additional examples, the activatable antibody comprises a first polypeptide comprising, from N terminus to C terminus the masking peptide, the VH, and the VL. In some examples, the cleavage site of the cleavable moiety (CM) is a protease cleavage site for a protease selected from the group consisting of urokinase-type plasminogen activator (uPA), matrix metalloproteinase-1 (MMP-1), MMP-2, MMP-3, MMP-8, MMP-9, MMP-14, Tobacco Etch Virus (TEV) protease, plasmin, Thrombin, Factor X, PSA, PSMA, Cathepsin D, Cathepsin K, Cathepsin S, ADAM10, ADAM12, ADAMTS, Caspase-1, Caspase-2, Caspase-3, Caspase-4, Caspase-5, Caspase-6, Caspase-7, Caspase-8, Caspase-9, Caspase-10, Caspase-11, Caspase-12, Caspase-13, Caspase-14, and TACE. In certain examples, CM comprises an MMP-9 cleavage site that is cleavable by MMP-9. In some examples, the CM comprises the amino acid sequence of SEQ ID NO: 138. In some examples, the masking peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 139 and 152-166. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139. In some examples, the masking peptide, or a part thereof (*e.g.*, the MM) has a masking efficiency of at least about 50 as determined by a Jurkat NFAT reporter assay. In some examples, the masking peptide, or a part thereof (*e.g.*, the MM) has a masking

efficiency of at least about 100 as determined by a Jurkat NFAT reporter assay. In some examples, the activatable antibody comprises a first polypeptide comprising, from N terminus to C terminus the masking peptide and the VL; and a second polypeptide comprising the VH. In certain examples, the activatable antibody comprises a human IgG4 fragment crystallizable (Fc) region. In certain examples, the activatable antibody comprises a human IgG1 Fc region. In some examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0030]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein (a) the VH comprises a CDR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 35-37 and 39-50, a CDR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 52-54 and 56-67, and a CDR-H3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 69-71 and 73-84; and (b) the VL comprises a CDR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 86-88 and 89-101, a CDR-L2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 103-105 and 106-118, and a CDR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 120-122 and 124-135.

**[0031]** In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein

the VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 3, 5, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, and 31; and/or wherein the VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 4, 6, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, and 32.

**[0032]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 48, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 65, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 82; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 99, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 116, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 133. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 27, and/or the VL comprises the amino acid sequence of SEQ ID NO: 28. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138. In some examples, the activatable antibody comprises a first polypeptide comprising, from N terminus to C terminus the masking peptide and the VL; and a second polypeptide comprising the VH. In certain examples, the activatable antibody comprises a human IgG4 fragment crystallizable (Fc) region. In one example, the first polypeptide comprises a light chain comprising, from N terminus to C terminus, the masking peptide and the VL, wherein the first polypeptide comprises the amino

acid sequence of SEQ ID NO: 142; and wherein the second polypeptide comprises a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG4 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 143. In certain examples, the activatable antibody comprises a human IgG1 Fc region. In one example, wherein the first polypeptide comprises a light chain comprising, from N terminus to C terminus, the masking peptide and the VL, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 148; and wherein the second polypeptide comprises a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG1 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 149. In some examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution). In one example, the first polypeptide comprises a light chain comprising, from N terminus to C terminus, the masking peptide and the VL, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 150; and wherein the second polypeptide comprises a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG1 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 151.

**[0033]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 49, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 66, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 83; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 100, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 117, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 134. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM)

comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 29, and/or the VL comprises the amino acid sequence of SEQ ID NO: 30. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0034]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 50, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 67, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 84; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 101, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 118, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 135. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 31, and/or the VL comprises the amino acid sequence of SEQ ID NO: 32. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0035]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 35, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 69; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 86, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 103, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 120. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 1, and/or the VL comprises the amino acid sequence of SEQ ID NO: 2. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0036]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 53, and a CDR-H3 comprising

the amino acid sequence of SEQ ID NO: 70; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 87, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 104, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 121. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 3, and/or the VL comprises the amino acid sequence of SEQ ID NO: 4. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0037]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 37, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 54, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 71; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 88, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 105, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 122. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the

VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 5, and/or the VL comprises the amino acid sequence of SEQ ID NO: 6. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0038]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 39, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 56, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 73; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 107, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 124. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 9, and/or the VL comprises the amino acid sequence of SEQ ID NO: 10. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0039]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a

linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 40, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 57, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 74; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 91, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 108, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 125. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 11, and/or the VL comprises the amino acid sequence of SEQ ID NO: 12. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0040]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 41, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 58, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 75; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 92, a CDR-L2 comprising the amino acid sequence

of SEQ ID NO: 109, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 126. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 13, and/or the VL comprises the amino acid sequence of SEQ ID NO: 14. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0041]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 42, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 59, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 76; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 93, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 110, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 127. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 15, and/or the VL comprises the

amino acid sequence of SEQ ID NO: 16. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0042]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 43, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 60, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 77; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 94, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 111, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 128. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 17, and/or the VL comprises the amino acid sequence of SEQ ID NO: 18. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0043]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy

chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 44, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 61, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 78; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 95, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 112, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 129. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 19, and/or the VL comprises the amino acid sequence of SEQ ID NO: 20. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0044]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 45, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 62, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 79; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 96, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 113, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 130. In certain examples, provided herein is an activatable antibody comprising: (a) a

masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 21, and/or the VL comprises the amino acid sequence of SEQ ID NO: 22. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0045]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 46, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 63, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 80; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 97, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 114, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 131. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 23, and/or the VL comprises the amino acid sequence of SEQ ID NO: 24. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid

sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0046]** In some examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein 1) a) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 64, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 81; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 98, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 115, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 132. In certain examples, provided herein is an activatable antibody comprising: (a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site; and (b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47; wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein the MM competes with human CD47 to bind the TBM; wherein the VH comprises the amino acid sequence of SEQ ID NO: 25, and/or the VL comprises the amino acid sequence of SEQ ID NO: 26. In certain examples, the masking peptide comprises the amino acid sequence of SEQ ID NO: 139; the MM comprises the amino acid sequence of SEQ ID NO: 137; and/or the CM comprises the amino acid sequence of SEQ ID NO: 138.

**[0047]** In other examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL. In some examples, 1) the VH comprises a first complementary-determining-region (CDR-H1), a second complementary-determining-region (CDR-H2), and a third complementary-determining-region (CDR-H3), wherein the CDR-H1 comprises the amino acid sequence of SEQ ID NO: 182 or 183; wherein the CDR-H2 comprises the amino acid sequence of SEQ

ID NO: 184 or 185; and wherein the CDR-H3 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 186-189; and/or 2) the VL comprises a first complementary-determining-region (CDR-L1), a second complementary-determining-region (CDR-L2), and a third complementary-determining-region (CDR-L3), wherein the CDR-L1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 190-193; wherein the CDR-L2 comprises the amino acid sequence of SEQ ID NO: 194; and wherein the CDR-L3 comprises the amino acid sequence of SEQ ID NO: 195 or 196. In certain examples, the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 182, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 185, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 188; and b) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 191, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 194, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 195. In some examples, the isolated antibody comprises a human IgG4 Fc region. In other examples, the isolated antibody comprises a human IgG1 Fc region. In some examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution). In some examples, the antigen-binding fragment is selected from the group consisting of a Fab, a Fv, a scFab, and a scFv. In some examples, the antibody or antigen-binding fragment binds to one or more amino acid residues of human CD47 selected from the group consisting of K39, W40, K41, F50, D51, G52, T99, E100, L101, and T102. In some examples, the antibody or antigen-binding fragment does not bind to one or more amino acid residues of human CD47 selected from the group consisting of L2, L3, F4, K6, N27, E29, A30, Q31, T34, E35, V36, Y37, D46, T49, A53, E97, R103, E104, G105, and E106. In certain examples, the antibody or antigen-binding fragment binds to amino acid residues K39, W40, K41, F50, D51, G52, T99, E100, L101, and T102 of human CD47 and/or does not bind to amino acid residues L2, L3, F4, K6, N27, E29, A30, Q31, T34, E35, V36, Y37, D46, T49, A53, E97, R103, E104, G105, and E106 of human CD47.

**[0048]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein (a) the VH comprises a CDR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 35-37 and 39-50, a CDR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 52-54 and 56-67, and a CDR-H3 comprising an

amino acid sequence selected from the group consisting of SEQ ID NOs: 69-71 and 73-84; and (b) the VL comprises a CDR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 86-88 and 89-101, a CDR-L2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 103-105 and 106-118, and a CDR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 120-122 and 124-135. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 3, 5, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, and 31; and/or wherein the VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 4, 6, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, and 32.

**[0049]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 48, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 65, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 82; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 99, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 116, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 133. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 27, and/or the VL comprises the amino acid sequence of SEQ ID NO: 28. In some examples, the isolated antibody comprises a human IgG4 Fc region. In one example, the isolated antibody comprises a first polypeptide comprising a light chain comprising the VL, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 140; and a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG4 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 141. In other examples, the isolated antibody comprises a human IgG1 Fc region. In one example, the isolated antibody comprises a first polypeptide comprising a light chain comprising the VL, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 144; and a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG1 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 145. In certain examples,

the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution). In one example, wherein the isolated antibody comprises a first polypeptide comprising a light chain comprising the VL, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 146; and a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG1 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 147.

**[0049a]** In one aspect, the present disclosure refers to an antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a variable heavy chain (VH) and a variable light chain (VL), wherein: a) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 48, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 65, a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 82; and b) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 99, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 116, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 133.

**[0050]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 49, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 66, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 83; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 100, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 117, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 134. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 29, and/or the VL comprises the amino acid sequence of SEQ ID NO: 30. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0051]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 50, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 67, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 84; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 101, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 118, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 135. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 31, and/or the VL comprises the amino acid

sequence of SEQ ID NO: 32. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0052]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 35, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 69; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 86, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 103, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 120. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 1, and/or the VL comprises the amino acid sequence of SEQ ID NO: 2. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0053]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 53, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 70; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 87, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 104, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 121. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 3, and/or the VL comprises the amino acid sequence of SEQ ID NO: 4. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0054]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 37, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 54, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 71; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 88, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 105, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 122. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 5, and/or the VL comprises the amino acid sequence of SEQ ID NO: 6. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0055]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 39, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 56, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 73; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 107, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 124. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 9, and/or the VL comprises the amino acid sequence of SEQ ID NO: 10. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0056]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 40, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 57, and a CDR-H3 comprising the

amino acid sequence of SEQ ID NO: 74; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 91, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 108, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 125. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 11, and/or the VL comprises the amino acid sequence of SEQ ID NO: 12. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0057]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 41, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 58, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 75; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 92, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 109, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 126. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 13, and/or the VL comprises the amino acid sequence of SEQ ID NO: 14. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0058]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 42, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 59, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 76; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 93, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 110, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 127. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment

thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 15, and/or the VL comprises the amino acid sequence of SEQ ID NO: 16. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0059]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 43, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 60, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 77; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 94, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 111, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 128. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 17, and/or the VL comprises the amino acid sequence of SEQ ID NO: 18. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0060]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 44, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 61, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 78; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 95, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 112, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 129. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 19, and/or the VL comprises the amino acid sequence of SEQ ID NO: 20. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc

domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0061]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 45, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 62, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 79; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 96, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 113, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 130. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 21, and/or the VL comprises the amino acid sequence of SEQ ID NO: 22. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0062]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 46, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 63, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 80; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 97, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 114, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 131. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 23, and/or the VL comprises the amino acid sequence of SEQ ID NO: 24. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution).

**[0063]** In some examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein 1) a) the

VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 64, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 81; and 2) the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 98, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 115, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 132. In certain examples, provided herein is an isolated antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a VH and a VL, wherein the VH comprises the amino acid sequence of SEQ ID NO: 25, and/or the VL comprises the amino acid sequence of SEQ ID NO: 26. In some examples, the isolated antibody comprises a human IgG1 Fc region. In certain examples, the human IgG1 Fc region comprises two Fc domains, wherein each of the two Fc domains comprises a S239D substitution and/or an I332E substitution (*e.g.*, a S239D substitution and an I332E substitution). In some examples, the isolated antibody or antigen-binding fragment binds human CD47 with a KD of about 50 nM or less. In certain examples, the isolated antibody or antigen-binding fragment binds human CD47 with a KD of about 10 nM or less. In some examples, the isolated antibody or antigen-binding fragment has a half maximal inhibitory concentration (IC<sub>50</sub>) of about 100 nM or less for blocking binding of human CD47 to human SIRP $\alpha$  in vitro. In certain examples, the isolated antibody or antigen-binding fragment has a half maximal inhibitory concentration (IC<sub>50</sub>) of about 10 nM or less for blocking binding of human CD47 to human SIRP $\alpha$  in vitro. In some examples, the isolated antibody or antigen-binding fragment completely blocks binding of human CD47 to human SIRP $\alpha$  in vitro when the isolated antibody or antigen-binding fragment is provided at a concentration of about 1  $\mu$ M or greater. In some examples, the isolated antibody or antigen-binding fragment has a half maximal effective concentration (EC<sub>50</sub>) of about 10 nM or less for binding to tumor cells in vitro, wherein the tumor cells comprise a B cell lymphoma cell line, a T cell lymphoma cell line, or a combination thereof. In some examples, the isolated antibody or antigen-binding fragment has a half maximal effective concentration (EC<sub>50</sub>) of about 10 nM or less for increasing macrophage phagocytosis of tumor cells in vitro, wherein the tumor cells comprise a B cell lymphoma cell line, a T cell lymphoma cell line, or a combination thereof. In certain examples, the isolated antibody or antigen-binding fragment has a half maximal effective concentration (EC<sub>50</sub>) of about 1 nM or less for increasing macrophage phagocytosis of tumor cells in vitro, wherein the tumor cells comprise a B cell lymphoma cell line, a T cell lymphoma cell line, or a combination thereof.

**[0064]** In some examples which may be combined with any of the preceding examples, the masked antibody, activatable antibody, isolated antibody, or antigen-binding fragment thereof is cross-reactive with a CD47 polypeptide from at least one non-human species selected from the group consisting of cynomolgus monkey, rat, and dog. In certain examples which may be combined with any of the preceding examples, the masked antibody, activatable antibody, isolated antibody, or antigen-binding fragment thereof binds to cynomolgus monkey CD47.

**[0065]** In some examples, provided herein is an isolated polynucleotide encoding one or more polypeptide chains of any masked antibody, activatable antibody, isolated antibody, or antigen-binding fragment described herein.

**[0065a]** In one aspect, the present disclosure refers to an isolated polynucleotide encoding one or more polypeptide chains of the masked antibody disclosed herein or the antibody, or antigen-binding fragment thereof, disclosed herein.

**[0066]** In other examples, provided herein is a vector comprising a polynucleotide encoding one or more polypeptide chains of any masked antibody, activatable antibody, isolated antibody, or antigen-binding fragment described herein.

**[0066a]** In one aspect, the present disclosure refers to a vector comprising the polynucleotide disclosed herein.

**[0067]** In other examples, provided herein is a host cell comprising a vector comprising a polynucleotide encoding one or more polypeptide chains of any masked antibody, activatable antibody, isolated antibody, or antigen-binding fragment described herein.

**[0067a]** In one aspect, the present disclosure refers to a host cell comprising the vector disclosed herein.

**[0068]** In yet other examples, provided herein is a method of making a masked antibody, activatable antibody, isolated antibody, or antigen-binding fragment, comprising culturing a host cell under conditions suitable for producing the masked antibody, activatable antibody, isolated antibody, or antigen-binding fragment, wherein the host cell comprises a vector comprising a polynucleotide encoding one or more polypeptide chains of any masked antibody, activatable antibody, isolated antibody, or antigen-binding fragment described herein.

**[0068a]** In one aspect, the present disclosure refers to a method of making a masked antibody, or an antibody, or antigen-binding fragment thereof, comprising culturing the host cell disclosed herein under conditions suitable for producing the masked antibody, or the antibody or antigen-binding fragment thereof.

**[0069]** In some examples, provided herein is a pharmaceutical composition comprising any masked antibody, activatable antibody, isolated antibody, or antigen-binding fragment described herein and a pharmaceutically acceptable carrier.

**[0069a]** In one aspect, the present disclosure refers to a pharmaceutical composition comprising the masked antibody disclosed herein, or the antibody or antigen-binding fragment thereof disclosed herein, and a pharmaceutically acceptable carrier.

**[0070]** In other examples, provided herein is a method for treating a CD47-positive disease or condition in a subject in need thereof, comprising administering to the subject an effective amount of a pharmaceutical composition comprising any masked antibody, activatable antibody, isolated antibody, or antigen-binding fragment described herein, and a

pharmaceutically acceptable carrier. In some examples, the administering does not cause anemia in the subject. In some examples, the disease or condition is cancer. In certain examples, the cancer comprises B cell lymphoma, T cell lymphoma, or a combination thereof. In some examples, the cancer is selected from the group consisting of lymphoma, leukemia, head and neck cancer, gastric cancer, esophageal cancer, breast cancer, cervical cancer, cholangiocarcinoma, colon cancer, ovarian cancer, thyroid cancer, uterine cancer, endometrial cancer, lung cancer, mesothelioma, and pancreatic cancer. In certain examples, the cancer is selected from the group consisting of triple negative breast cancer (TNBC), Her2+ gastric-esophageal junction (GEJ) cancer, small cell lung cancer (SCLC), diffuse large B-cell lymphoma (DLBCL), acute myeloid leukemia (AML), Head and neck squamous cell carcinoma (HNSC), gastric carcinoma (GC), breast invasive carcinoma (BRCA), cervical squamous cell carcinoma and endocervical adenocarcinoma (CESC), cholangiocarcinoma (CHOL), colon adenocarcinoma (COAD), ovarian serous cystadenocarcinoma (OV), thyroid carcinoma (THCA), uterine corpus endometrial carcinoma (UCEC), HER2+ breast cancer, hormone receptor positive breast cancer, lymphoid neoplasm diffuse large B-cell lymphoma (DLBC), lung adenocarcinoma (LUAD), lung squamous cell carcinoma (LUSC), mesothelioma (MESO), and pancreatic adenocarcinoma (PAAD). In some examples, the masked antibody, or the antibody or antigen-binding fragment thereof, is administered at a dose of at least about 0.6 mg/kg. In some examples, the pharmaceutical compositions is administered at a frequency of at least once every three weeks or at least once every two weeks.

**[0070a]** In one aspect, the present disclosure refers to use of the pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating a CD47-positive disease or condition in a subject in need thereof.

**[0071]** In some examples according to any one of the methods for treating a CD47-positive disease or condition described above, the method further comprises administering to the subject an effective amount of one or more additional therapeutic agents. In some examples, the one or more therapeutic agents comprise viral gene therapy, an immune checkpoint inhibitor, a target therapy, a radiation therapy, a chemotherapy, or any combination thereof. In certain examples, the one or more additional therapeutic agents comprise pomalyst, revlimid, lenalidomide, pomalidomide, thalidomide, a DNA-alkylating platinum-containing derivative, cisplatin, 5-fluorouracil, cyclophosphamide, an anti-CD47 antibody, an anti-CTLA4 antibody, an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-CD20 antibody, an anti-CD40 antibody, an anti-DR5 antibody, an anti-CD1d antibody, an anti-TIM3 antibody, an anti-SLAMF7 antibody, an anti-KIR receptor antibody, an anti-OX40 antibody, an anti-HER2 antibody, an anti-ErbB-2 antibody, an anti-EGFR antibody,

cetuximab, rituximab, trastuzumab, pembrolizumab, radiotherapy, single dose radiation, fractionated radiation, focal radiation, whole organ radiation, IL-12, IFN $\alpha$ , GM-CSF, a chimeric antigen receptor, adoptively transferred T cells, an anti-cancer vaccine, an oncolytic virus, or any combination thereof.

**[0072]** In some examples, provided herein is a method of treating cancer comprising administering an anti-CD47 activatable antibody, wherein the anti-CD47 activatable antibody comprises a human IgG1 Fc or an IgG1 Fc with enhanced antibody-dependent cellular cytotoxicity (ADCC) activity, wherein the anti-CD47 activatable antibody comprises a masking peptide comprising a cleavable moiety (CM) comprising at least one cleavage site, wherein the activatable antibody has a higher binding affinity to human CD47 when the CM is cleaved at the site of the cancer (*e.g.*, in the tumor microenvironment (TME)) than when the CM is not cleaved.

#### DESCRIPTION OF THE FIGURES

**[0073]** The present application can be understood by reference to the following description taken in conjunction with the accompanying figures.

**[0074]** **FIG. 1** depicts the ability of the indicated antibodies to induce human RBC hemagglutination.

**[0075]** **FIG. 2** depicts the ADCC activity of human NK cells from different donors on Calcein-labeled CEM cells incubated with the indicated antibodies. Percent cell lysis is shown as percent cytotoxicity.

**[0076]** **FIG. 3A** and **FIG. 3B** depict the *in vivo* anti-tumor efficacy of the antibodies, or isotype control, in a B-NDG/Raji-Luc mouse systemic model in two independent experiments. Data points represent group mean; error bars represent standard deviation. **FIG. 3A** depicts the first independent experiment. **FIG. 3B** depicts the second independent experiment.

**[0077]** **FIG. 4A** and **FIG. 4B** depict the *in vivo* anti-tumor efficacy of the antibodies, or isotype control, in a B-NDG/Raji mouse subcutaneous tumor model. Data points represent group mean; error bars represent standard deviation. **FIG. 4A** depicts the first independent experiment. **FIG. 4B** depicts the second independent experiment.