CLAIMS

1. An isolated antibody or an antigen binding fragment thereof (AB) that specifically binds human CD71 and cynomolgus monkey CD71,

wherein the AB comprises the VH CDR1 sequence GYTFTSYWMH (SEQ ID NO: 9); the VH CDR2 sequence AIYPGNSETG (SEQ ID NO: 10); the VH CDR3 sequence ENWDPGFAF (SEQ ID NO: 11); the VL CDR1 sequence SASSSVYYMY (SEQ ID NO: 12) or CRASSSVYYMY (SEQ ID NO: 13); the VL CDR2 sequence STSNLAS (SEQ ID NO: 14); and the VL CDR3 sequence QQRRNYPYT (SEQ ID NO: 15).

2. The AB of claim 1, wherein the AB comprises a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 3-5, and a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-8.

3. An activatable antibody that, in an activated state, specifically binds to human CD71 and cynomolgus CD71 comprising:

an antibody or antigen binding fragment thereof (AB) that specifically binds human CD71 and cynomolgus monkey CD71;

a masking moiety (MM) coupled to the AB that inhibits the binding of the AB to CD71 when the activatable antibody is in an uncleaved state; and

a cleavable moiety (CM) coupled to the AB, wherein the CM is a polypeptide that functions as a substrate for a protease,

wherein the AB comprises the VH CDR1 sequence GYTFTSYWMH (SEQ ID NO: 9); the VH CDR2 sequence AIYPGNSETG (SEQ ID NO: 10); the VH CDR3 sequence ENWDPGFAF (SEQ ID NO: 11); the VL CDR1 sequence SASSSVYYMY (SEQ ID NO: 12) or CRASSSVYYMY (SEQ ID NO: 13); the VL CDR2 sequence STSNLAS (SEQ ID NO: 14); and the VL CDR3 sequence QQRRNYPYT (SEQ ID NO: 15).

4. The activatable antibody of claim 3, wherein the MM has one or more of the characteristics selected from the group consisting of:

(i) the MM has a dissociation constant for binding to the AB that is greater than the dissociation constant of the AB to CD71;

(ii) the MM does not interfere or compete with the AB for binding to CD71 when the activatable antibody is in a cleaved state;

(iii) the MM is a polypeptide of no more than 40 amino acids in length;

(iv) the MM polypeptide sequence is different that of human CD71;

(v) the MM polypeptide sequence is no more than 50% identical to any natural binding partner of the AB; and

(vi) the MM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 16-295 and 297-314.

5. The activatable antibody of claim 3, wherein the CM has one or more of the characteristics selected from the group consisting of:

(i) the CM is a substrate for a protease that is active in diseased tissue; and

(ii) the CM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 356-423, 680-698, 713, 714, and 789-808.

6. The activatable antibody of claim 3, wherein the antigen binding fragment thereof is selected from the group consisting of a Fab fragment, a $F(ab')_2$ fragment, a scFv, and a scAb.

7. The activatable antibody of claim 3, wherein the AB comprises a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 3-5, and a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-8.

8. The activatable antibody of claim 3, wherein the AB is linked to the CM.

9. The activatable antibody of claim 3, wherein the AB is linked directly to the CM.

10. The activatable antibody of claim 3, wherein the AB is linked to the CM via a linking peptide.

11. The activatable antibody of claim 3, wherein the MM is linked to the CM such that the activatable antibody in an uncleaved state comprises the structural arrangement from N-terminus to C-terminus as follows: MM-CM-AB or AB-CM-MM.

12. The activatable antibody of claim 3, wherein the activatable antibody comprises a linking peptide between the MM and the CM, a linking peptide between the CM and the AB, or both a linking peptide between the MM and the CM and a linking peptide between the CM and the AB.

13. The activatable antibody of claim 3, wherein the activatable antibody comprises a first linking peptide (LP1) and a second linking peptide (LP2), and wherein the activatable antibody in the uncleaved state has the structural arrangement from N-terminus to C-terminus as follows: MM-LP1-CM-LP2-AB or AB-LP2-CM-LP1-MM.

14. The activatable antibody of claim 13, wherein the two linking peptides are not identical to each other.

15. The activatable antibody of claim 13, wherein each of LP1 and LP2 is a peptide of about 1 to 20 amino acids in length.

16. The activatable antibody of claim 3, wherein the activatable antibody has one or more of the characteristics selected from the group consisting of:

(a) the activatable antibody comprises the heavy chain sequence of SEQ ID NO: 325 or 699 and a light chain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 327, 329, 331, 333, 335, 337, 650, 652, 654, 656, 658, 660, 670-673, 701-712, and 721-788;

(b) the activatable antibody comprises a combination of amino acid sequences, wherein the combination of amino acid sequences is selected from a single row in Table D, wherein for a given combination,

(i) the heavy chain of the AB comprises the amino acid sequences of the VH CDR sequences corresponding to the given combination in the single row listed in Table D,

(ii) the light chain of the AB comprises the amino acid sequences of the VL CDR sequences corresponding to the given combination in the single row listed in Table D,

(iii) the MM comprises the amino acid sequence of the mask sequence (MM) corresponding to the given combination in the single row listed in Table D, and

(iv) the CM comprises the amino acid sequence of the substrate sequence (CM) corresponding to the given combination in the single row listed in Table D;

(c) the activatable antibody comprises a combination of amino acid sequences, wherein for a given combination of amino acid sequences,

(i) the heavy chain of the AB comprises the amino acid sequences of the VH sequence or VH CDR sequences selected from the group consisting of: the VH sequence or VH CDR sequences listed in the corresponding column of Table E,

(ii) the light chain of the AB comprises the amino acid sequences of the VL sequence or VL CDR sequences selected from the group consisting of: the VL sequence or VL CDR sequences listed in the corresponding column of Table E,

(iii) the MM comprises the amino acid sequence of the mask sequence (MM) selected from the group consisting of: the MM sequences listed in the corresponding column of Table E, and

(iv) the CM comprises the amino acid sequence of the substrate sequence (CM) selected from the group consisting of: the CM sequences listed in the corresponding column of Table E; and

(d) the activatable antibody comprises a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 3-5, and a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-8, 809-836, and 841-908.

17. An activatable antibody comprising an antibody or an antigen binding fragment thereof (AB) that specifically binds to human CD71 and cynomolgus CD71, a masking moiety (MM), and a cleavable moiety (CM),

wherein the AB comprises the VH CDR1 sequence GYTFTSYWMH (SEQ ID NO: 9), the VH CDR2 sequence AIYPGNSETG (SEQ ID NO: 10), the VH CDR3 sequence ENWDPGFAF (SEQ ID NO: 11), the VL CDR1 sequence SASSSVYYMY (SEQ ID NO: 12) or CRASSSVYYMY (SEQ ID NO: 13), the VL CDR2 sequence STSNLAS (SEQ ID NO: 14), and the VL CDR3 sequence QQRRNYPYT (SEQ ID NO: 15); and

wherein the activatable antibody has one or more of the following characteristics selected from the group consisting of:

(i) the activatable antibody comprises a heavy chain sequence of SEQ ID NOs: 325 or 699; and a light chain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 327, 329, 331, 333, 335, 337, 650, 652, 654, 656, 658, 660, 670-673, 701-712, and 721-788;

(ii) the MM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 16-295 and 297-314, and the CM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 356-423, 680-698, 713, 714, and 789-808; and

(iii) the activatable antibody comprises a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 3-5, and a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-8, 809-836, and 841-908.

18. A conjugated activatable antibody comprising the activatable antibody of claim 3 conjugated to an agent.

19. The conjugated activatable antibody of claim 18, wherein the agent has one or more of the characteristics selected from the group consisting of:

(a) the agent is a toxin or fragment thereof;

(b) the agent is a microtubule inhibitor;

(c) the agent is a nucleic acid damaging agent;

(d) the agent is a dolastatin or a derivative thereof;

(e) the agent is an auristatin or a derivative thereof;

(1) the agent is a maytansinoid or a derivative thereof;

(g) the agent is a duocarmycin or a derivative thereof;

(h) the agent is a calicheamicin or a derivative thereof;

(i) the agent is a pyrrolobenzodiazepine or a derivative thereof;

(j) the agent is auristatin E or a derivative thereof;

(k) the agent is monomethyl auristatin E (MMAE);

(l) the agent is monomethyl auristatin D (MMAD);

(m) the agent is the maytansinoid DM1;

(n) the agent is the maytansinoid DM4;

(o) the agent is a detectable moiety; and

(p) the agent is a diagnostic agent.

20. The conjugated activatable antibody of claim 18, wherein the agent is conjugated to the AB via a linker.

21. The conjugated activatable antibody of claim 20, wherein the linker with which the agent is conjugated to the AB comprises an SPDB moiety, a vc moiety, or a PEG2-vc moiety.

22. The conjugated activatable antibody of claim 18, wherein the agent is a toxin conjugated to the AB via a linker, and wherein the linker and the toxin conjugated to the AB comprise a moiety selected from the group consisting of: an SPDB-DM4 moiety, a vc-MMAD moiety, a vc-MMAE moiety, a vc-duocarmycin moiety, or a PEG2-vc-MMAD moiety.

23. The conjugated activatable antibody of claim 20, wherein the linker is a cleavable linker.

24. The conjugated activatable antibody of claim 20, wherein the linker is a non-cleavable linker.

25. A conjugated activatable antibody that, in an activated state, binds human CD71 and cynomolgus CD71 comprising:

(a) an activatable antibody comprising:

(i) an antibody or an antigen binding fragment thereof (AB) that specifically binds to human CD71 and cynomolgus CD71, wherein the AB specifically binds human CD71 and cynomolgus monkey CD71, wherein the AB comprises the VH CDR1 sequence GYTFTSYWMH (SEQ ID NO: 9), the VH CDR2 sequence AIYPGNSETG (SEQ ID NO: 10), the VH CDR3 sequence ENWDPGFAF (SEQ ID NO: 11), the VL CDR1 sequence SASSSVYYMY (SEQ ID NO: 12) or CRASSSVYYMY (SEQ ID NO: 13), the VL CDR2 sequence STSNLAS (SEQ ID NO: 14), and the VL CDR3 sequence QQRRNYPYT (SEQ ID NO. 15);

(ii) a masking moiety (MM) coupled to the AB that inhibits the binding of the AB to CD71 when the activatable antibody is in an uncleaved state; and

(iii) a cleavable moiety (CM) coupled to the AB, wherein the CM is a polypeptide that functions as a substrate for a protease; and

(b) an agent conjugated to the AB.

26. The conjugated activatable antibody of claim 25, wherein the agent is selected from the group consisting of a dolastatin or a derivative thereof, an auristatin or a derivative thereof, a maytansinoid or a derivative thereof, a duocarmycin or a derivative thereof, a

calicheamicin or a derivative thereof, a pyrrolobenzodiazepine or a derivative thereof, auristatin E, monomethyl auristatin F (MMAF), monomethyl auristatin E (MMAE), monomethyl auristatin D (MMAD), maytansinoid DM4, maytansinoid DM1, a duocarmycin, a calicheamicin, a pyrrolobenzodiazepine, and a pyrrolobenzodiazepine dimer.

27. The conjugated activatable antibody of claim 25, wherein the agent is conjugated to the AB via a linker.

28. The conjugated activatable antibody of claim 27, wherein the linker with which the agent is conjugated to the AB comprises an SPDB moiety, a vc moiety, or a PEG2-vc moiety.

29. The conjugated activatable antibody of claim 25, wherein the agent is a toxin conjugated to the AB via a linker, and wherein the linker and the toxin conjugated to the AB comprise a moiety selected from the group consisting of: an SPDB-DM4 moiety, a vc-MMAD moiety, a vc-MMAE moiety, a vc-duocarmycin moiety, or a PEG2-vc-MMAD moiety.

30. The conjugated activatable antibody of claim 25, wherein the activatable antibody has one or more of the characteristics selected from the group consisting of:

(i) the activatable antibody comprises a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 3-5, and a light

chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-8, 809-836, and 841-908; and

(ii) the activatable antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NOs: 325 or 699, and a light chain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 327, 329, 331, 333, 335, 337, 650, 652, 654, 656, 658, 660, 670-673, 701-712, and 721-788.

31. The conjugated activatable antibody of claim 25, wherein the MM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 16-295 and 297-314.

32. The conjugated activatable antibody of claim 25, wherein the CM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 356-423, 680-698, 713, 714, and 789-808.

33. The conjugated activatable antibody of claim 25, wherein the activatable antibody has one or more of the following characteristics selected from the group consisting of:

(i) the activatable antibody comprises a combination of amino acid sequences, wherein the combination of amino acid sequences is selected from a single row in Table D, wherein for a given combination,

(a) the heavy chain of the AB comprises the amino acid sequences of the VH CDR sequences corresponding to the given combination in the single row listed in Table D,

(b) the light chain of the AB comprises the amino acid sequences of the VL CDR sequences corresponding to the given combination in the single row listed in Table D,

(c) the MM comprises the amino acid sequence of the mask sequence (MM) corresponding to the given combination in the single row listed in Table D, and

(d) the CM comprises the amino acid sequence of the substrate sequence (CM) corresponding to the given combination in the single row listed in Table D; and

(ii) the activatable antibody comprises a combination of amino acid sequences, wherein for a given combination of amino acid sequences,

(a) the heavy chain of the AB comprises the amino acid sequences of the VH sequence or VH CDR sequences selected from the group consisting of: the VH sequence or VH CDR sequences listed in the corresponding column of Table E,

(b) the light chain of the AB comprises the amino acid sequences of the VL sequence or VL CDR sequences selected from the group consisting of: the VL sequence or VL CDR sequences listed in the corresponding column of Table E,

(c) the MM comprises the amino acid sequence of the mask sequence (MM) selected from the group consisting of: the MM sequences listed in the corresponding column of Table E, and

(d) the CM comprises the amino acid sequence of the substrate sequence (CM) selected from the group consisting of: the CM sequences listed in the corresponding column of Table E.

34. A conjugated antibody comprising:

(a) an antibody or an antigen binding fragment thereof (AB) that specifically binds to human CD71 and cynomolgus CD71, wherein the AB comprises:

(i) the VH CDR1 sequence GYTFTSYWMH (SEQ ID NO: 9); the VH CDR2 sequence AIYPGNSETG (SEQ ID NO: 10); the VH CDR3 sequence ENWDPGFAF (SEQ ID NO: 11); the VL CDR1 sequence SASSSVYYMY (SEQ ID NO: 12) or CRASSSVYYMY (SEQ ID NO: 13); the VL CDR2 sequence STSNLAS (SEQ ID NO: 14); and the VL CDR3 sequence QQRRNYPYT (SEQ ID NO: 15), or

(ii) a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 3-5, and a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-8; and

(b) an agent conjugated to the AB, wherein the agent is selected from the group consisting of auristatin E, monomethyl auristatin F (MMAF), monomethyl auristatin E (MMAE), monomethyl auristatin D (MMAD), maytansinoid DM4, maytansinoid DM1, a calicheamicin, a pyrrolobenzodiazepine, a pyrrolobenzodiazepine dimer, and a duocarmycin.

35. A conjugated activatable antibody that, in an activated state, specifically binds to human CD71 and cynomolgus CD71, comprising:

(a) an activatable antibody comprising:

(i) an antibody or an antigen binding fragment thereof (AB) that specifically binds human CD71 and cynomolgus monkey CD71, wherein the AB comprises the VH CDR1 sequence GYTFTSYWMH (SEQ ID NO: 9); the VH CDR2 sequence AIYPGNSETG (SEQ ID NO: 10); the VH CDR3 sequence ENWDPGFAF (SEQ ID NO: 11); the VL CDR1 sequence SASSSVYYMY (SEQ ID NO: 12) or CRASSSVYYMY (SEQ ID NO: 13); the VL CDR2 sequence STSNLAS (SEQ ID NO: 14); and the VL CDR3 sequence QQRRNYPYT (SEQ ID NO: 15);

(ii) a masking moiety (MM) coupled to the AB that to inhibits the binding of the AB to CD71 when the activatable antibody is in an uncleaved state;

(iii) a cleavable moiety (CM) coupled to the AB, wherein the CM is a polypeptide that functions as a substrate for a protease; and

(b) an agent conjugated to the AB, wherein the activatable antibody comprises:

(i) a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 3-5, and a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-8, 809-836, and 841-908, or

(ii) a heavy chain comprising the amino acid sequence of SEQ ID NOs: 325 or 699, and a light chain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 327, 329, 331, 333, 335, 337, 650, 652, 654, 656, 658, 660, 670-673, 701-712, and 721-788; and

wherein the agent is selected from the group consisting of auristatin E, monomethyl auristatin F (MMAF), monomethyl auristatin E (MMAE), monomethyl auristatin D (MMAD), maytansinoid DM4, maytansinoid DM1, a calicheamicin, a pyrrolobenzodiazepine, a pyrrolobenzodiazepine dimer, and a duocarmycin.

36. The conjugated activatable antibody of claim 35, wherein the MM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 16-295 and 297-314.

37. The conjugated activatable antibody of claim 35, wherein the CM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 356-423, 680-698, 713, 714, and 789-808.

38. The conjugated activatable antibody of claim 35, wherein the agent is conjugated to the AB via a linker, and wherein the linker to which the agent is conjugated to the AB comprises an SPDB moiety, a vc moiety, or a PEG2-vc moiety.

39. The conjugated activatable antibody of claim 35, wherein the agent is a toxin conjugated to the AB via a linker, and wherein the linker and the toxin conjugated to the AB comprise a moiety selected from the group consisting of: an SPDB-DM4 moiety, a vc-MMAD moiety, a vc-MMAE moiety, a vc-duocarmycin moiety, or a PEG2-vc-MMAD moiety.

40. A conjugated activatable antibody or conjugated antibody comprising:

an antibody or antigen binding fragment thereof (AB) that, in an activated state, binds human CD71 and cynomolgus CD71; and

a toxin conjugated to the AB via a linker,

wherein the conjugated activatable antibody or the conjugated antibody comprises amino acid sequences, a linker, and a toxin selected from a single row in Table F, wherein for the given combination:

(a) the AB comprises a heavy chain comprising the amino acid sequence of the heavy chain sequence or heavy chain variable domain sequence corresponding to the given combination in the single row listed in Table F,

(b) the AB comprises a light chain comprising the amino acid sequence of the light chain sequence or light chain variable domain sequence corresponding to the given combination in the single row listed in Table F, and

(c) the linker and the toxin comprise the linker and the toxin corresponding to the given combination in the single row listed in Table F.

41. A pharmaceutical composition comprising the activatable antibody of claim 3; and a carrier.

42. The pharmaceutical composition of claim 41 comprising an additional agent.

43. The pharmaceutical composition of claim 42, wherein the additional agent is a therapeutic agent.

44. A pharmaceutical composition comprising the conjugated activatable antibody of claim 18; and a carrier.

45. The pharmaceutical composition of claim 44 comprising an additional agent.

46. The activatable antibody of claim 3, wherein the MM is linked to the CM.

47. The activatable antibody of claim 3, wherein the MM is linked directly to the CM.

48. The activatable antibody of claim 3, wherein the MM is linked to the CM via a linking peptide.