

CLAIMS

What is claimed is:

1. ~~A bispecific activatable antibody (BAA), wherein said BAA, when activated, specifically binds to two targets and comprises the following structure:~~
 - a. ~~an IgG antibody (AB1) that specifically binds to a first target wherein the AB1 comprises two heavy chains (AB1 HCs) and two light chains (AB1 LCs); and wherein the AB1 is linked to a first masking moiety (MM1) linked to a first cleavable moiety (CM1) to form a MM1-CM1 construct, wherein the carboxyl terminus of a MM1-CM1 construct is linked to each amino terminus of each light chain of the AB1, wherein~~
 - ~~the MM1 inhibits the binding of the AB1 to its target; and~~
 - ~~the CM1 is a polypeptide that functions as a substrate for a first protease;~~
 - b. ~~two scFvs (each an AB2) that each specifically binds to a second target wherein each AB2 comprises a light chain variable region linked to a heavy chain variable region, wherein the carboxyl terminus of each AB2 is linked to the amino terminus each of the AB1 heavy chains; and wherein each AB2 is linked to a second masking moiety (MM2) linked to a second cleavable moiety (CM2) to form a MM2-CM2 construct, wherein the carboxyl terminus of each MM2-CM2 construct is linked to the amino terminus of each AB2 wherein~~
 - ~~the MM2 inhibits the binding of the AB2 to its target; and~~
 - ~~the CM2 is a polypeptide that functions as a substrate for a second protease;~~

~~and wherein the BAA has at least one of the following characteristics:~~

 - i. ~~MM2 comprises amino acid sequence SEQ ID NO: 12;~~
 - ii. ~~MM1 comprises an amino acid sequence selected from the group consisting of sequences presented in Table 7;~~
 - iii. ~~AB2 comprises a heavy chain variable domain as set forth in SEQ ID NO: 2 or SEQ ID NO: 3 or a light chain variable domain as set forth in SEQ ID NO: 1 or SEQ ID NO: 4; and~~

- iv. ~~AB1 comprises an Fc region comprising an amino acid substitution in at least one of amino acid positions L234, L235, N297, and P331, as numbered by the EU index as set forth in Kabat, such that the BAA has reduced effector function.~~
2. ~~The BAA of claim 1, wherein AB2 comprises a heavy chain variable domain as set forth in SEQ ID NO: 2 or SEQ ID NO: 3 and a light chain variable domain as set forth in SEQ ID NO: 1 or SEQ ID NO: 4.~~
3. ~~The BAA of claim 1, wherein the AB1 binds a tumor target and the AB2 binds an immune effector target.~~
4. ~~The BAA of any one of claims 1 to 3, wherein the BAA is a T cell engaging bispecific (TCB)-AA (TCBAA).~~
5. ~~The BAA of any one of claims 1 to 4, wherein the AB1 binds EGFR and the AB2 binds CD3c.~~
6. ~~The BAA of any one of claims 1 to 5, wherein the MM1 comprises an amino acid sequence selected from the group consisting of sequences presented in Table 7.~~
7. ~~The BAA of any one of claims 1 to 5, wherein the MM1 comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 85 and SEQ ID NO: 78.~~
8. ~~The BAA of any one of claims 1 to 5, wherein the MM1 comprises SEQ ID NO: 78.~~
9. ~~The BAA of any one of claims 1 to 8, wherein the MM2 comprises the amino acid sequence SEQ ID NO: 12.~~
10. ~~The BAA of any one of claims 1 to 9, wherein the CM comprises the amino acid sequence of SEQ ID NO: 14.~~
11. ~~The BAA of any one of claims 1 to 9, wherein the CM comprises the amino acid sequence of SEQ ID NO: 17.~~

- ~~12. The BAA of any one of claims 1 to 9, wherein the CM comprises the amino acid sequence of SEQ ID NO: 16.~~
- ~~13. The BAA of any one of claims 1 to 9, wherein CM1 comprises an amino acid sequence selected from the group comprising SEQ ID NO: 14 and SEQ ID NO: 16.~~
- ~~14. The BAA of any one of claims 1 to 9, wherein CM2 comprises an amino acid sequence selected from the group comprising SEQ ID NO: 14 and SEQ ID NO: 17.~~
- ~~15. The BAA of any one of claims 1 to 14, wherein AB1 comprises amino acid substitutions in at least two of amino acid positions L234, L235, and P331.~~
- ~~16. The BAA of claim 15, wherein AB1 comprises amino acid substitutions at amino acid positions L234, L235, and P331.~~
- ~~17. The BAA of claim 15, wherein AB1 comprises L234F, L235E, and P331S amino acid substitutions.~~
- ~~18. The BAA of claim 15, wherein the AB1 comprises an Fc region comprising an amino acid substitution at N297.~~
- ~~19. The BAA of any one of claims 1 to 14, wherein AB1 comprises amino acid substitutions at amino acid positions L234F, L235E, P331S, and N297Q.~~
- ~~20. The BAA of claim 1, wherein the heavy chain of the AB1 comprises any one of SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75 and SEQ ID NO: 76, as set forth in Table 6.~~
- ~~21. The BAA CI106, comprising the layout and sequence as provided in Table 11 and Example 1.~~
- ~~22. The BAA CI107, comprising the layout and sequence as provided in Table 11 and Example 1.~~

- ~~23. The BAA CI079, comprising the layout and sequence as provided in Table 11 and Example 1.~~
- ~~24. The BAA CI090, comprising the layout and sequence as provided in Table 11 and Example 1.~~
- ~~25. An activatable antibody (AA) comprising:~~
- ~~a) an antibody or antigen binding fragment thereof (AB) that specifically binds to the epsilon chain of CD3 (CD3ε);~~
 - ~~b) a masking moiety (MM) coupled to the AB, wherein the MM reduces or inhibits the binding of the AB to the CD3ε when the AA is in an uncleaved state, wherein the MM comprises amino acid sequence SEQ ID NO: 12; and~~
 - ~~c) a cleavable moiety (CM) coupled to the AB, wherein the CM is a polypeptide that functions as a substrate for a protease.~~
- ~~26. The AA of claim 25, wherein the CM comprises any one of the sequences set forth in Table 4.~~
- ~~27. The AA of claim 25, wherein the CM comprises a substrate cleavable by a serine protease or an MMP.~~
- ~~28. The AA of claim 25, wherein the CM comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 18-56.~~
- ~~29. The AA of claim 25, wherein the protease is an MMP.~~
- ~~30. The AA of claim 25, wherein the protease is a serine protease.~~
- ~~31. The AA of claim 25, wherein the AB that specifically binds to CD3 is the antibody of any one of claims 38-47.~~
- ~~32. An activatable antibody (AA) comprising:~~
- ~~a. an antibody or an antigen binding fragment thereof (AB) that specifically binds to Epidermal Growth Factor Receptor (EGFR);~~

- b. ~~a masking moiety (MM) coupled to the AB, wherein the MM reduces or inhibits the binding of the AB to the EGFR when the AA is in an uncleaved state, and wherein the MM comprises an amino acid sequence selected from the group consisting of sequences presented in Table 7; and~~
 - c. ~~a cleavable moiety (CM) coupled to the AB, wherein the CM is a polypeptide that functions as a substrate for a protease.~~
- ~~33. The AA of claim 32, wherein the MM comprises the amino acid sequence of SEQ ID NO: 78.~~
- ~~34. The AA of any one of claims 32 to 33, wherein the CM comprises a substrate cleavable by a serine protease or an MMP.~~
- ~~35. The AA of any one of claims 32 to 33, wherein the CM comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 18-56.~~
- ~~36. The AA of claim 32, wherein the CM comprises the amino acid sequence of SEQ ID NO: 14.~~
- ~~37. The AA of claim 32, wherein the CM comprises the amino acid sequence of SEQ ID NO: 16.~~
- ~~38. An antibody or antigen binding fragment thereof (AB) that specifically binds to the epsilon chain of CD3 (CD3ε), wherein the antibody comprises a heavy chain variable domain as set forth in SEQ ID NO: 2 or SEQ ID NO: 3 or a light chain variable domain as set forth in SEQ ID NO: 1 or SEQ ID NO: 4.~~
- ~~39. The AB of claim 38, wherein, the antibody comprises a heavy chain variable domain as set forth in SEQ ID NO: 2 or SEQ ID NO: 3 and a light chain variable domain as set forth in SEQ ID NO: 1 or SEQ ID NO: 4.~~
- ~~40. The AB of claim 38, comprising a heavy chain variable domain as set forth in SEQ ID NO: 2.~~

- ~~41. The AB of claim 38, comprising a heavy chain variable domain as set forth in SEQ ID NO: 3.~~
- ~~42. The AB of claim 38, wherein the antibody comprises a light chain variable domain as set forth in SEQ ID NO: 1.~~
- ~~43. The AB of claim 38, comprising a light chain variable domain as set forth in SEQ ID NO: 4.~~
- ~~44. The AB of claim 38, comprising a heavy chain variable domain as set forth in SEQ ID NO: 2 and a light chain variable domain as set forth in SEQ ID NO: 1.~~
- ~~45. The AB of claim 38, comprising a heavy chain variable domain as set forth in SEQ ID NO: 3 and a light chain variable domain as set forth in SEQ ID NO: 1.~~
- ~~46. The AB of claim 38, comprising a heavy chain variable domain as set forth in SEQ ID NO: 3 and a light chain variable domain as set forth in SEQ ID NO: 4.~~
- ~~47. The AB of claim 38, comprising a heavy chain variable domain as set forth in SEQ ID NO: 2 and a light chain variable domain as set forth in SEQ ID NO: 4.~~
- ~~48. The AB of any one of claims 32 to 47, wherein the AB is a bispecific AB.~~
- ~~49. The AA of any one of claims 32 to 47, wherein the antibody is a scFv.~~
- ~~50. The AA of any one of claims 32 to 47, wherein the antibody is an IgG1 antibody.~~
- ~~51. An activatable antibody (AA) comprising:~~
- ~~a) an antibody or antigen-binding fragment thereof (AB) that specifically binds to the epsilon chain of CD3 (CD3 ϵ), wherein the antibody comprises a heavy chain variable domain as set forth in SEQ ID NO: 2 or SEQ ID NO: 3 or comprises a light chain variable domain as set forth in SEQ ID NO: 1 or SEQ ID NO: 4;~~
 - ~~b) a masking moiety (MM) coupled to the AB, wherein the MM reduces or inhibits the binding of the AB to the CD3 ϵ when the AA is in an uncleaved state; and~~

- e) ~~a cleavable moiety (CM) coupled to the AB, wherein the CM is a polypeptide that functions as a substrate for a protease.~~
- ~~52. The AA of claim 51, wherein the AB comprises a heavy chain variable domain as set forth in SEQ ID NO: 2.~~
- ~~53. The AA of claim 51, wherein the AB comprises a heavy chain variable domain as set forth in SEQ ID NO: 3.~~
- ~~54. The AA of claim 51, wherein the AB comprises a light chain variable domain as set forth in SEQ ID NO: 1.~~
- ~~55. The AA of claim 51, wherein the AB comprises a light chain variable domain as set forth in SEQ ID NO: 4.~~
- ~~56. The AA of claim 51, wherein the AB comprises a heavy chain variable domain as set forth in SEQ ID NO: 2 and a light chain variable domain as set forth in SEQ ID NO: 1.~~
- ~~57. The AA of claim 51, wherein the AB comprises a heavy chain variable domain as set forth in SEQ ID NO: 3 and a light chain variable domain as set forth in SEQ ID NO: 1.~~
- ~~58. The AA of claim 51, wherein the AB comprises a heavy chain variable domain as set forth in SEQ ID NO: 2 and a light chain variable domain as set forth in SEQ ID NO: 4.~~
- ~~59. The AA of claim 51, wherein the AB comprises a heavy chain variable domain as set forth in SEQ ID NO: 3 and a light chain variable domain as set forth in SEQ ID NO: 4.~~
- ~~60. The AA of any one of claims 51 to 59, wherein the MM comprises any one of the sequences set forth in Table 3.~~
- ~~61. The AA of any one of claims 51 to 59, wherein the CM comprises any one of the sequences set forth in Table 4.~~
- ~~62. A bispecific activatable antibody (BAA) comprising any one of the AAs of claims 51 to 61.~~

~~63. An activatable antibody (AA) comprising:~~

- ~~a. an antibody (AB) that specifically binds a target, wherein the antibody is an IgG1 antibody, and wherein the Fc region of the antibody comprises an amino acid substitution in amino acid positions L234, L235, and P331, as numbered by the EU index as set forth in Kabat, such that the AA has reduced effector function;~~
- ~~b. a masking moiety (MM) coupled to the AB, wherein the MM reduces or inhibits the binding of the AB to the target when the AA is in an uncleaved state; and~~
- ~~c. a cleavable moiety (CM) coupled to the AB, wherein the CM is a polypeptide that functions as a substrate for a protease.~~

~~64. The AA of claim 63, wherein the Fc region comprises amino acid substitutions in at least amino acid positions L234, L235, N297 and P331, as numbered by the EU index as set forth in Kabat, such that the AA has reduced effector function.~~

~~65. The AA of claim 63 or 64, wherein the target is selected from the group consisting of the targets presented in Table 9.~~

~~66. A bispecific activatable antibody (BAA) comprising:~~

- ~~a. an IgG antibody (AB1) that specifically binds to a first target wherein the AB1 comprises two heavy chains (AB1 HCs) and two light chains (AB1 LCs); and wherein the AB1 is linked to a first masking moiety (MM1) linked to a first cleavable moiety (CM1) to form a MM1-CM1 construct, wherein the carboxyl terminus of a MM1-CM1 construct is linked to each amino terminus of each light chain of the AB1, wherein
 - ~~the MM1 inhibits the binding of the AB1 to its target; and~~
 - ~~the CM1 is a polypeptide that functions as a substrate for a first protease;~~~~
- ~~b. two scFvs (each an AB2) that each specifically binds to a second target wherein each AB2 comprises a heavy chain variable region linked to a light chain variable region, wherein the carboxyl terminus of each AB2 is linked to the amino terminus each of the AB1 heavy chains; and wherein each AB2 is linked to a second masking moiety (MM2) linked to a second cleavable moiety (CM2) to form a MM2-CM2 construct,~~

wherein the carboxyl terminus of each MM2-CM2 construct is linked to the amino terminus of each AB2 wherein
the MM2 inhibits the binding of the AB2 to its target; and
the CM2 is a polypeptide that functions as a substrate for a second protease;
and wherein the AB1 comprises an Fc region comprises an amino acid substitution in at least one of amino acid positions L234, L235, N297, and P331, as numbered by the EU index as set forth in Kabat, such that the BAA has reduced effector function.

67. The BAA of claim 66, wherein the Fc region comprises amino acid substitutions in at least amino acid positions L234, L235, N297 and P331, as numbered by the EU index as set forth in Kabat, such that the BAA has reduced effector function.

68. The BAA of claim 66, wherein the Fc region comprises amino acid substitutions in at least amino acid positions L234, L235, and P331, as numbered by the EU index as set forth in Kabat, such that the BAA has reduced effector function.

69. The BAA of any one of claims 66 to 68, wherein the first target is selected from the group consisting of the targets presented in Table 9 and the second target is selected from the group consisting of the targets presented in Table 9.

70. The AA or BAA of any one of the above claims, wherein the antigen binding fragment thereof is selected from the group consisting of a Fab fragment, a F(ab')₂ fragment, a scFv, a scAb, a dAb, a single domain heavy chain antibody, and a single domain light chain antibody.

71. The AA or BAA of any one of the above claims wherein the antibody is a rodent antibody, a chimeric antibody, a humanized antibody, or a fully human monoclonal antibody.

72. The AA of any one of claims 32-37 and 51-71, wherein the AA is a BAA.

73. A pharmaceutical composition comprising the antibody, AA, or BAA of any one of claims 1-72 and optionally a carrier.

74. The pharmaceutical composition of claim 73 comprising an additional agent.

- ~~75. The pharmaceutical composition of claim 74, wherein the additional agent is a therapeutic agent.~~
- ~~76. An isolated nucleic acid molecule encoding the antibody, AA, or BAA of any one of claims 1-72.~~
- ~~77. A vector comprising the isolated nucleic acid molecule of claim 76.~~
- ~~78. A vector comprising the nucleic acid sequence of pLW289.~~
- ~~79. A vector comprising the nucleic acid sequence of pLW246.~~
- ~~80. A vector comprising the nucleic acid sequence of pLW307.~~
- ~~81. A vector comprising the nucleic acid sequence of pLW291.~~
- ~~82. A cell comprising any one of the vectors of claims 77-81.~~
- ~~83. A cell comprising pLW289 and pLW246.~~
- ~~84. A cell comprising pLW307 and pLW291.~~
- ~~85. A method of producing the antibody, AA, or BAA of any one of claims 1-72 by culturing a cell under conditions that lead to expression of the antibody, AA, or BAA, wherein the cell comprises the nucleic acid molecule of claim 76 or the vector of any one of claims 78-81.~~
- ~~86. A method of treating, alleviating a symptom of, or delaying the progression of a disorder or disease comprising administering a therapeutically effective amount of the antibody, AA, or BAA of any one of claims 1-72, or the pharmaceutical composition of any one of claims 73-75 to a subject in need thereof.~~
- ~~87. The method of claim 86, wherein the disorder or disease comprises disease cells expressing EGFR.~~
- ~~88. The method of claims 86 or 87, wherein the disorder or disease is cancer.~~

- ~~89. The method of claim 88, wherein the cancer is anal cancer, basal cell carcinoma, brain cancer, bladder cancer, breast cancer, bone cancer, cervical cancer, cholangiocarcinoma, colorectal cancer, endometrial cancer, esophageal cancer, gall bladder cancer, gastric cancer, glioblastoma, head and neck cancer, liver cancer, lung cancer, ovarian cancer, pancreatic cancer, prostate cancer, renal cancer, sarcoma, small bowel carcinoma, squamous cell cancer, skin cancer, testicular cancer, thyroid cancer or uterine cancer.~~
- ~~90. A method of inhibiting angiogenesis in a subject comprising administering a therapeutically effective amount of the antibody, AA, or BAA of any one of claims 1-72, or the pharmaceutical composition of any one of claims 73-75 to a subject in need thereof.~~
- ~~91. The method of any one of claims 86-90, wherein the method comprises administering an additional agent.~~
- ~~92. The method of claim 91 wherein the additional agent is a therapeutic agent.~~
- ~~93. A method of reducing damage to healthy tissue caused by an antibody binding to its target on healthy tissue as well as on diseased tissue, the method comprising administering to a subject in need thereof an AA or BAA or a pharmaceutical composition comprising an AA or BAA, wherein said AA or BAA is an AA or BAA of any one of the claims provided herein.~~
- ~~94. A method to improve tolerability of an antibody treatment comprising administering to a subject in need thereof an AA or BAA or a pharmaceutical composition comprising an AA or BAA, wherein said AA or BAA is an AA or BAA of any one of the claims provided herein.~~
- ~~95. A method to recruit T cells to tumor tissue comprising administering to a subject in need thereof an AA or BAA or a pharmaceutical composition comprising an AA or BAA, wherein said AA or BAA is an AA or BAA of any one of the claims provided herein.~~
- ~~96. An antibody, AA, or BAA of any one of claims 1-72, or the pharmaceutical composition of any one of claims 73-75, for use as a medicament.~~

- ~~97. An antibody, AA, or BAA of any one of claims 1-72, or the pharmaceutical composition of any one of claims 73-75, for use in a method of treating, alleviating a symptom of, or delaying the progression of a disorder or disease, wherein the disorder or disease comprises disease cells expressing EGFR.~~
- ~~98. An antibody, AA, or BAA of any one of claims 1-72, or the pharmaceutical composition of any one of claims 73-75, for use in a method of treating cancer; optionally wherein the cancer is anal cancer, basal cell carcinoma, brain cancer, bladder cancer, breast cancer, bone cancer, cervical cancer, cholangiocarcinoma, colorectal cancer, endometrial cancer, esophageal cancer, gall bladder cancer, gastric cancer, glioblastoma, head and neck cancer, liver cancer, lung cancer, ovarian cancer, pancreatic cancer, prostate cancer, renal cancer, sarcoma, small bowel carcinoma, squamous cell cancer, skin cancer testicular cancer, thyroid cancer or uterine cancer.~~
- ~~99. An antibody, AA, or BAA of any one of claims 1-72, or the pharmaceutical composition of any one of claims 73-75, for use in a method of treatment, wherein the method comprises inhibiting angiogenesis.~~
- ~~100. — The antibody, AA, or BAA, or the pharmaceutical composition, for use according to any of claims 96 to 99, wherein the use comprises administering an additional agent, optionally wherein the additional agent is a therapeutic agent.~~

CLAIMS

1. A bispecific activatable antibody (BAA) comprising the following structure:

- a. an IgG antibody (AB1) that specifically binds to an EGFR wherein the AB1 comprises two heavy chains (AB1 HCs) and two light chains (AB1 LCs), wherein the AB1 comprises a VH CDR1 amino acid sequence comprising NYGVH (SEQ ID NO:60), a VH CDR2 amino acid sequence comprising VIWSGGNTDYNTPFTS (SEQ ID NO:61), a VH CDR3 amino acid sequence comprising ALTYDYEFAY (SEQ ID NO:62), a VL CDR1 amino acid sequence comprising RASQSIGTNIH (SEQ ID NO:57), a VL CDR2 amino acid sequence comprising YASESIS (SEQ ID NO:58), and a VL CDR3 amino acid sequence comprising QQNNNWPTT (SEQ ID NO:59);

wherein the AB1 comprises an Fc region comprising an amino acid substitution in at least one of amino acid positions L234, L235, N297, and P331 as numbered by the EU index as set forth in Kabat, such that the BAA has reduced effector function; and

wherein the amino terminus of each of the two AB1 LCs is linked to the carboxyl terminus of a MM1-CM1 construct, wherein each MM1-CM1 construct comprises:

- i. a first masking moiety (MM1), the MM1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 78-84; and
ii. a first cleavable moiety (CM1), the CM1 being a substrate for a first protease;

wherein the MM1 is linked in an N- to C-terminal direction to the CM1, to form each MM1-CM1 construct; and

- b. two single chain variable antibody fragments (scFvs) (each an AB2), wherein each of the AB2s comprises a heavy chain variable domain as set forth in SEQ ID NO: 2 or SEQ ID NO: 3 and a light chain variable domain as set forth in SEQ ID NO: 1 or SEQ ID NO: 4; and

wherein the carboxyl terminus of each AB2 is linked to the amino terminus of a AB1 heavy chain; and

wherein each AB2 is linked to:

- i. a second masking moiety (MM2), the MM2 comprising the amino acid sequence SEQ ID NO: 12; and
- ii. a second cleavable moiety (CM2), the CM2 being a substrate for a second protease;

wherein the MM2 is linked to the CM2 to form a MM2-CM2 construct, wherein the carboxyl terminus of each MM2-CM2 construct is linked to the amino terminus of a corresponding AB2.

2. The BAA of claim 1, wherein the MM1 comprises an amino acid sequence of SEQ ID NO: 78.

3. The BAA of claim 1, wherein the CM1 or CM2 comprises one of the following characteristics:

- (a) amino acid sequence of SEQ ID NO: 14,
- (b) amino acid sequence of SEQ ID NO: 17, or
- (c) amino acid sequence of SEQ ID NO: 16.

4. The BAA of claim 1, wherein the CM1 comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 14 and SEQ ID NO: 16.

5. The BAA of claim 1, wherein the CM2 comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 14 and SEQ ID NO: 17.

6. The BAA of claim 1, wherein the AB1 comprises at least one of the following characteristics:

- (a) amino acid substitutions in at least two of amino acid positions L234, L235, N297 and P331.
- (b) amino acid substitutions in at least three of amino acid positions L234, L235, N297 and P331.

- (c) amino acid substitutions at amino acid positions L234, L235, N297 and P331.
- (d) amino acid substitutions at amino acid positions L234F, L235E, and P331S.
- (e) amino acid substitutions at amino acid positions L234F, L235E, N297Q and P331S.
- 7.** The BAA of claim 1, wherein the heavy chain of the AB1 comprises any one of SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75 and SEQ ID NO: 76.
- 8.** The BAA of claim 1, wherein the BAA is selected from the group consisting of:
- a) comprising a heavy chain amino acid sequence of SEQ ID NO: 130 and a light chain amino acid sequence of SEQ ID NO: 132 or a heavy chain amino acid sequence of SEQ ID NO: 197 and a light chain amino acid sequence of SEQ ID NO: 199,
 - b) comprising a heavy chain amino acid sequence of SEQ ID NO: 134 and a light chain amino acid sequence of SEQ ID NO: 136 or a heavy chain amino acid sequence of SEQ ID NO: 201 and a light chain amino acid sequence of SEQ ID NO: 203,
 - c) comprising a heavy chain amino acid sequence of SEQ ID NO: 121 and a light chain amino acid sequence of SEQ ID NO: 122 or a heavy chain amino acid sequence of SEQ ID NO: 192 and a light chain amino acid sequence of SEQ ID NO: 193, and
 - d) comprising a heavy chain amino acid sequence of SEQ ID NO: 124 and a light chain amino acid sequence of SEQ ID NO: 108 or a heavy chain amino acid sequence of SEQ ID NO: 195 and a light chain amino acid sequence of SEQ ID NO: 182.
- 9.** The BAA of claim 1, comprising the sequence of a heavy chain amino acid sequence of SEQ ID NO: 130 and a light chain amino acid sequence of SEQ ID NO: 132.
- 10.** The BAA of claim 1, comprising the sequence of a heavy chain amino acid sequence of SEQ ID NO: 134 and a light chain amino acid sequence of SEQ ID NO: 136.

11. The BAA of claim 1, comprising the sequence of a heavy chain amino acid sequence of SEQ ID NO: 121 and a light chain amino acid sequence of SEQ ID NO: 122.
12. The BAA of claim 1, comprising the sequence of a heavy chain amino acid sequence of SEQ ID NO: 124 and a light chain amino acid sequence of SEQ ID NO: 108.
13. The BAA of claim 1, wherein the antibody is a rodent antibody, a chimeric antibody, a humanized antibody, or a fully human monoclonal antibody.
14. A pharmaceutical composition comprising the BAA of claim 1 and a carrier.
15. The pharmaceutical composition of claim 14, comprising an additional agent.
16. The pharmaceutical composition of claim 15, wherein the additional agent is a therapeutic agent.
17. A method of producing the BAA of claim 1 by culturing a cell to express the BAA.
18. An activatable antibody (AA) comprising:
- a) an antibody or antigen binding fragment thereof (AB) that specifically binds to the epsilon chain of CD3 (CD3 ϵ);
 - b) a masking moiety (MM) coupled to the AB, wherein the MM reduces or inhibits the binding of the AB to the CD3 ϵ when the AA is in an uncleaved state, wherein the MM comprises amino acid sequence SEQ ID NO: 12; and
 - c) a cleavable moiety (CM) coupled to the AB, wherein the CM is a polypeptide that functions as a substrate for a protease.