

What is claimed is:

1. ~~A polypeptide comprising an antibody heavy chain constant domain comprising an engineered cysteine residue at position 290, according to the numbering of the EU index of Kabat.~~
2. ~~The polypeptide of claim 1, wherein said constant domain comprises an IgG heavy chain CH₂ domain.~~
3. ~~A polypeptide comprising an antibody heavy chain constant domain comprising an engineered cysteine residue at a position corresponding to residue 60 of SEQ ID NO:61, when said constant domain is aligned with SEQ ID NO:61.~~
4. ~~The polypeptide of claim 3, wherein the substituted cysteine residue is located at position 290 of an IgG CH₂ domain, according to the numbering of the EU index of Kabat.~~
5. ~~The polypeptide of any one of claims 1-4, wherein said constant domain further comprises an engineered cysteine residue at a position selected from the group consisting of: 270, 276, 278, 283, 292, 293, 294, 300, 302, 303, 314, 315, 318, 320, 332, 333, 334, 336, 345, 347, 354, 355, 358, 360, 362, 370, 373, 375, 376, 378, 380, 382, 386, 388, 390, 392, 393, 401, 404, 411, 413, 414, 416, 418, 419, 421, 428, 431, 432, 437, 438, 439, 443, 444, and any combination thereof, according to the numbering of the EU index of Kabat.~~
6. ~~The polypeptide of any one of claims 1-5, wherein said constant domain further comprises an engineered cysteine residue at a position selected from the group consisting of: 118, 334, 347, 373, 375, 380, 388, 392, 421, 443, and any combination thereof, according to the numbering of the EU index of Kabat.~~
7. ~~The polypeptide of any one of claims 1-5, wherein said constant domain further comprises an engineered cysteine residue at position 334, according to the numbering of the EU index of Kabat.~~
8. ~~An antibody or antigen binding fragment thereof comprising a polypeptide of any one of claims 1-7.~~
19. An antibody that binds to HER2, or antigen binding fragment thereof comprising: heavy chain and light chain, wherein: (1) the heavy chain comprises a heavy chain constant region and a heavy chain variable region; and (2) the light chain comprises a light constant region and light chain variable region, and wherein:
 - (a) a polypeptide of one of claims 1-7, the heavy chain variable region comprises CDRs of SEQ ID NOs: 2, 3, and 4;
 - (b) the heavy chain constant region comprises SEQ ID NO: 17;
 - (c) the light chain variable region comprises CDRs of SEQ ID NO:8, 9, and 10; and
 - (d) an antibody the light chain constant region comprises SEQ ID NO:41, comprising
 - (i) an engineered cysteine residue at position 183, according to the numbering of Kabat; or
 - (ii) an engineered cysteine residue at a position corresponding to residue 76 of SEQ ID NO:63, when said constant domain is aligned with SEQ ID NO:63.
210. The antibody or antigen binding fragment thereof of claim 19, wherein the light chain comprises SEQ ID NO:42 wherein said light chain constant region comprises a kappa light chain constant domain (CL_K).
311. The antibody or antigen binding fragment thereof of claim 19 or claim 2, wherein the heavy chain comprises SEQ ID NO:18 wherein said light chain constant region comprises a lambda light chain constant domain (CL_λ).

412. ~~An antibody-drug conjugate (ADC) A compound comprising the polypeptide of any of claims 1-7, or the antibody or antigen binding fragment thereof of any one of claims 1-38-11,~~ wherein the ~~polypeptide or antibody~~ is conjugated to a therapeutic agent via ~~(1) said engineered cysteine site~~ the cysteine residue in the heavy chain constant region at position 173 of SEQ ID NO:17 and (2) the cysteine residue in the light chain constant region at position 76 of SEQ ID NO:41.

513. The ~~ADC compound~~ of claim 412, wherein the therapeutic agent is selected from the group consisting of: a cytotoxic agent, a cytostatic agent, a chemotherapeutic agent, a toxin, a radionuclide, a DNA, an RNA, an siRNA, a microRNA, a peptide nucleic acid, a non-natural amino acid, a peptide, an enzyme, a fluorescent tag, biotin, and any combination thereof.

614. The ~~ADC compound~~ of claim 412 or 513, wherein the therapeutic agent is conjugated to the ~~polypeptide or the antibody or antigen binding fragment thereof~~ via a linker.

715. The ~~ADC compound~~ of claim 614, wherein the linker is cleavable.

816. The ~~ADC compound~~ of claim 614 or 715, where the linker comprises vc, mc, MalPeg6, m(H2O)c, m(H2O)cvc, or a combination thereof.

917. The ~~ADC compound~~ of any one of claims 614-816, wherein the linker is vc.

1018. The ~~ADC compound~~ of any one of claims 412-917, wherein the therapeutic agent is an auristatin or tubulysin.

1119. The ~~ADC compound~~ of any one of claims 412-1018, wherein the therapeutic agent is an auristatin.

1220. The ~~ADC compound~~ of claim 1119, wherein the auristatin is selected from the group consisting of 0101, 8261, 6121, 8254, 6780, 0131, MMAD, MMAE, and MMAF.

1321. A pharmaceutical composition comprising the ~~ADC compound~~ of any one of claims 412-1220 and a pharmaceutically acceptable carrier.

1422. ~~A method of treating cancer, an autoimmune disease, an inflammatory disease, or an infectious disease, comprising administering to a subject in need thereof a therapeutically effective amount of the compound~~ The ADC of any one of claims 412-1220, or the composition of claim 1321, for use as a medicament.

15. The ADC of any one of claims 4-12, or the composition of claim 13, for use for the treatment of cancer.