

CLAIMS

1. An antibody-drug conjugate comprising (a) an antibody, or antigen binding fragment thereof, that binds to extra domain B of fibronectin, wherein the antibody, or antigen binding fragment, comprises a heavy chain variable region comprising three complementarity determining regions (CDRs) comprising SEQ ID NOs: 3, 5, and 7, and a light chain variable region comprising three CDRs comprising SEQ ID NOs: 12, 13, and 14, wherein the heavy chain constant region comprises an engineered cysteine residue at position 290 (K290C), according to the numbering of the EU index of Kabat, and wherein the light chain constant region comprises an engineered cysteine residue at position 183 (κ K183C), according to the numbering of Kabat, (b) a linker, and (c) a drug.
2. The antibody-drug conjugate of claim 1, wherein the antibody, or antigen binding fragment, comprises:
a heavy chain variable region comprising SEQ ID NO: 1, and a light chain variable region comprising SEQ ID NO: 10; or
a heavy chain variable region comprising SEQ ID NO: 21, and a light chain variable region comprising SEQ ID NO: 10.
3. The antibody-drug conjugate of claim 1 or 2, wherein the antibody, or antigen binding fragment, comprises:
a heavy chain comprising SEQ ID NO: 19 and a light chain comprising SEQ ID NO: 31; or
a heavy chain comprising SEQ ID NO: 25 and a light chain comprising SEQ ID NO: 31.

4. The antibody-drug conjugate of any one of claims 1 to 3, wherein the antibody, or antigen binding fragment, comprises a heavy chain constant region comprising an engineered glutamine-containing tag inserted in the antibody at position E294 - N297, wherein the glutamine-containing tag comprises an amino acid sequence LLQG (SEQ ID NO: 40) according to the numbering of the EU index of Kabat.
5. The antibody-drug conjugate of claim 4, wherein the heavy chain constant region further comprises an arginine (R) substituting a lysine (K) at position 222 (K222R), according to the numbering of the EU index of Kabat.
6. The antibody-drug conjugate of any one of claims 1 to 5, wherein the antibody, or antigen binding fragment, comprises a heavy chain variable region comprising an arginine (R) substituting a lysine (K) at position 94 (K94R), according to the numbering of Kabat.
7. The antibody-drug conjugate of any one of claims 1 to 6, wherein the linker is a cleavable linker, and the cleavable linker is selected from the group consisting of vc, diS, diS-C2OCO and AcLys-vc.
8. The antibody-drug conjugate of any one of claims 1 to 7, wherein the drug is a cytotoxic agent.
9. The antibody-drug conjugate of claim 8, wherein the cytotoxic agent is an auristatin or a CPI dimer.
10. An antibody-drug conjugate comprising (a) an antibody, or antigen binding fragment thereof, that binds to extra domain B of fibronectin, that comprises a heavy chain comprising SEQ ID NO: 19 or 25, and a light chain comprising SEQ ID NO: 31, (b) a vc linker, and (c) a drug; or
(a) an antibody, or antigen binding fragment thereof, that binds to extra domain

B of fibronectin, that comprises a heavy chain comprising SEQ ID NO: 25, and a light chain comprising SEQ ID NO: 31, (b) a vc linker, and (c) a drug.

11. An antibody-drug conjugate comprising (a) an antibody, or antigen binding fragment thereof, that binds to extra domain B of fibronectin, that comprises a heavy chain variable region comprising SEQ ID NO: 21 and a light chain variable region comprising SEQ ID NO: 10; or (a heavy chain variable region comprising SEQ ID NO: 1 and a light chain variable region comprising SEQ ID NO: 10; wherein the heavy chain constant region comprises an engineered cysteine residue at position 290 (K290C), according to the numbering of the EU index of Kabat, and wherein the light chain constant region comprises an engineered cysteine residue at position 183 (κK183C), according to the numbering of Kabat, (b) a vc linker, and (c) an auristatin.
12. An antibody-drug conjugate comprising (a) an antibody, or antigen binding fragment thereof, that binds to extra domain B of fibronectin, that comprises a heavy chain comprising SEQ ID NO: 19 and a light chain comprising SEQ ID NO: 31, (b) a vc linker, and (c) an auristatin.
13. An antibody-drug conjugate comprising (a) an antibody, or antigen binding fragment thereof, that binds to extra domain B of fibronectin, that comprises a heavy chain comprising SEQ ID NO: 25 and a light chain comprising SEQ ID NO: 31, (b) a vc linker, and (c) an auristatin.
14. A pharmaceutical composition comprising the antibody-drug conjugate of any one of claims 1 to 13 and a pharmaceutically acceptable carrier.
15. A pharmaceutical composition comprising a plurality of the antibody-drug conjugates of any one of claims 1 to 13 and a pharmaceutically acceptable carrier, wherein the composition has an average DAR ranging from 3 to 5.

16. A pharmaceutical composition comprising a plurality of the antibody-drug conjugates of any one of claims 1 to 13 and a pharmaceutically acceptable carrier, wherein the composition has an average DAR ranging from 1 to 3.
17. A nucleic acid encoding a heavy chain and a light chain of the antibody of any one of claims 1 to 13, a vector comprising the nucleic acid, or a host cell comprising the nucleic acid or the vector.
18. A process for producing the antibody-drug conjugate of any one of claims 1 to 13 comprising:
 - (a) linking the linker to the drug;
 - (b) conjugating the linker and drug to the antibody; and
 - (c) purifying the antibody-drug conjugate,wherein the conjugating is site-specific on one or more engineered cysteine residues and/or engineered glutamine residues on the antibody.
19. The antibody-drug conjugate of any one of claims 1 to 13 or the pharmaceutical composition of any one of claims 14 to 16, wherein the antibody-drug conjugate or the pharmaceutical composition is for treating an EDB+ FN-expressing disorder or disease.
20. The antibody-drug conjugate or the pharmaceutical composition of claim 19, wherein the EDB+ FN-expressing disorder or disease is a solid tumor or blood cancer.