

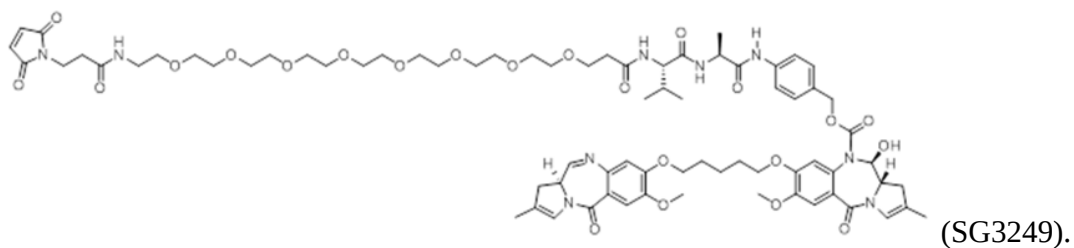
CLAIMS

1. An antibody or antigen binding fragment thereof which binds to B7-H4, comprising:
 - i. a heavy chain CDR1 (HCDR1), a heavy chain CDR2 (HCDR2), a heavy chain CDR3 (HCDR3), a light chain CDR1 (LCDR1), a light chain CDR2 (LCDR2), and a light chain CDR3 (LCDR3) comprising the amino acid sequence of SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, and SEQ ID NO: 12, respectively, or a functional variant thereof;
 - ii. a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2, and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6, respectively, or a functional variant thereof;
 - iii. a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2, and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, and SEQ ID NO: 18, respectively, or a functional variant thereof;
 - iv. a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2, and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, and SEQ ID NO: 24, respectively, or a functional variant thereof; or
 - v. a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2, and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, and SEQ ID NO: 30, respectively, or a functional variant thereof.
2. The antibody or antigen binding fragment thereof according to claim 1, wherein the antibody or antigen binding fragment thereof comprises:
 - i. a variable heavy (VH) chain and a variable light (VL) chain comprising the amino acid sequence of SEQ ID NO: 45 and SEQ ID NO: 34, respectively, or a functional variant thereof;

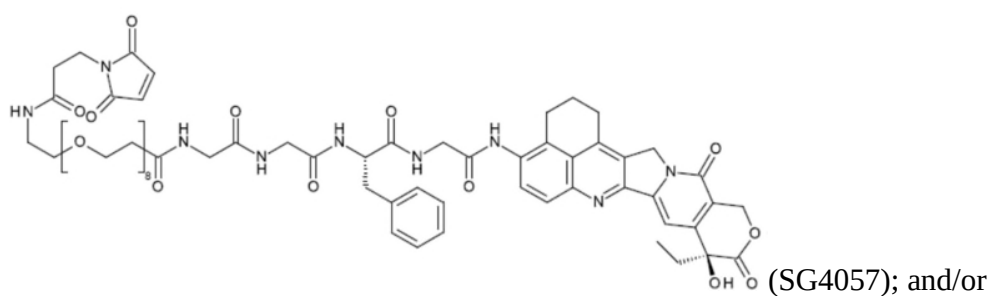
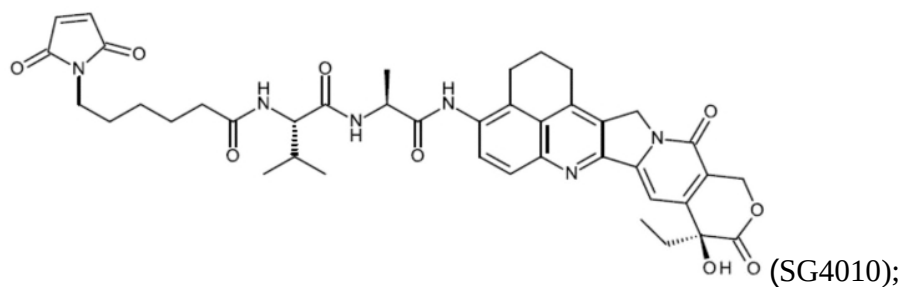
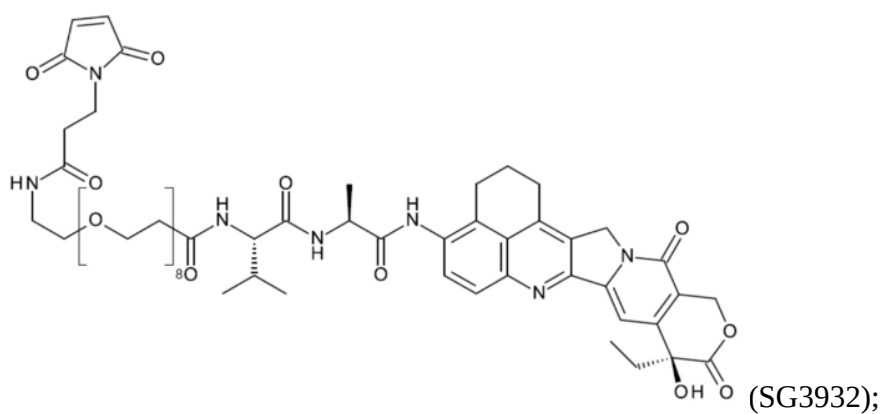
- ii. a variable heavy (VH) chain and a variable light (VL) chain comprising the amino acid sequence of SEQ ID NO: 33 and SEQ ID NO: 34, respectively, or a functional variant thereof;
 - iii. a variable heavy (VH) chain and a variable light (VL) chain comprising the amino acid sequence of SEQ ID NO: 43 and SEQ ID NO: 34, respectively, or a functional variant thereof;
 - iv. a variable heavy (VH) chain and a variable light (VL) chain comprising the amino acid sequence of SEQ ID NO: 46 and SEQ ID NO: 34, respectively, or a functional variant thereof;
 - v. a variable heavy (VH) chain and a variable light (VL) chain comprising the amino acid sequence of SEQ ID NO: 47 and SEQ ID NO: 34, respectively, or a functional variant thereof;
 - vi. a VH chain and a VL chain comprising the amino acid sequence of SEQ ID NO: 31, and SEQ ID NO: 32, respectively, or a functional variant thereof;
 - vii. a VH chain and a VL chain comprising the amino acid sequence of SEQ ID NO: 35 and SEQ ID NO: 36, respectively, or a functional variant thereof;
 - viii. a VH chain and a VL chain comprising the amino acid sequence of SEQ ID NO: 37 and SEQ ID NO: 38, respectively, or a functional variant thereof; or
 - ix. a VH chain and a VL chain comprising the amino acid sequence of SEQ ID NO: 39 and SEQ ID NO: 40, respectively, or a functional variant thereof.
- 3. The antibody or antigen binding fragment thereof according to claim 1 or claim 2, wherein the antibody or antigen binding fragment thereof comprises:
 - i. a HCDR1, a HCDR2, a HCDR3, a LCDR1, a LCDR2, and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, and SEQ ID NO: 12, respectively, or a functional variant thereof.
- 4. The antibody or antigen binding fragment thereof according to any one of the preceding claims, wherein the antibody or antigen binding fragment thereof comprises:

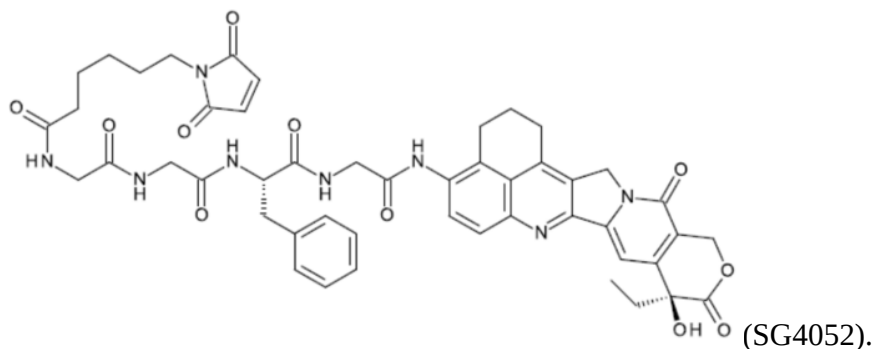
- i. a VH chain and a VL chain comprising the amino acid sequence of SEQ ID NO: 45 and SEQ ID NO: 34, respectively, or a functional variant thereof.
5. The antibody or antigen binding fragment thereof according any one of the preceding claims, wherein the antibody or antigen binding fragment thereof binds an OVCAR4 cell line.
6. The antibody or antigen binding fragment thereof according to any one of the preceding claims, wherein the antibody or antigen binding fragment thereof comprises a heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 41.
7. The antibody or antigen binding fragment thereof according to any one of claims 1-5, wherein the antibody or antigen binding fragment thereof comprises a heavy chain constant region comprising the amino acid sequence of SEQ ID NO: 52.
8. The antibody or antigen binding fragment thereof according to any one of the preceding claims, wherein the antibody or antigen binding fragment thereof comprises a light constant region comprising the amino acid sequence of SEQ ID NO: 42.
9. The antibody or antigen binding fragment thereof according to any one of claims 1-5, wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 51; and a light chain comprising the amino acid sequence of SEQ ID NO: 44.
10. The antibody or antigen binding fragment thereof according to any one of claims 1-5, wherein the antibody or antigen binding fragment thereof comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 48; and a light chain comprising the amino acid sequence of SEQ ID NO: 44.

11. The antibody or antigen binding fragment thereof according to any one of the preceding claims, wherein the antibody or antigen binding fragment thereof is conjugated to a heterologous agent.
12. The antibody or antigen binding fragment thereof according to any one of the preceding claims, wherein the antibody or antigen binding fragment thereof is conjugated to one or more heterologous agent selected from the group consisting of a topoisomerase I inhibitor, a tubulysin derivative, a pyrrolobenzodiazepine, an antimicrobial agent, a therapeutic agent, a prodrug, a peptide, a protein, an enzyme, a lipid, a biological response modifier, a pharmaceutical agent, a lymphokine, a heterologous antibody, a fragment of a heterologous antibody, a detectable label, a polyethylene glycol (PEG), a radioisotope, or a combination thereof.
13. The antibody or antigen binding fragment thereof according to any one of the preceding claims, wherein the antibody or antigen binding fragment thereof is conjugated to one or more heterologous agent selected from a topoisomerase I inhibitor, tubulysin derivative, a pyrrolobenzodiazepine, or a combination thereof.
14. The antibody or antigen binding fragment thereof according to any one of the preceding claims, wherein the antibody or antigen binding fragment thereof is conjugated to a heterologous agent selected from the group consisting of tubulysin AZ1508, pyrrolobenzodiazepine SG3315, pyrrolobenzodiazepine SG3249, or a combination thereof.
15. The antibody or antigen binding fragment thereof according to any one of the preceding claims, wherein the antibody or antigen binding fragment thereof is conjugated to a pyrrolobenzodiazepine SG3249 cytotoxin:

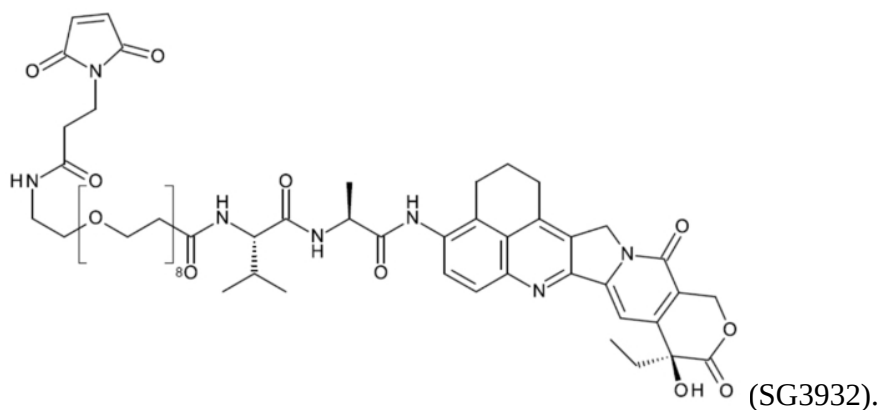


16. The antibody or antigen binding fragment thereof according to any one claims 1-14, wherein the antibody or antigen binding fragment thereof is conjugated to:





17. The antibody or antigen binding fragment thereof according to any one of claims 1-14 or 16, wherein the antibody or antigen binding fragment thereof is conjugated to:



18. The antibody or antigen binding fragment thereof according to any one of the preceding claims, wherein said antibody or antigen binding fragment thereof is a monoclonal antibody.
19. The antibody or antigen binding fragment thereof according to any one of the preceding claims, wherein said antibody or antigen binding fragment thereof is a humanised monoclonal antibody.
20. A pharmaceutical composition comprising an antibody or antigen binding fragment thereof according to any one of the preceding claims.

21. A polynucleotide encoding the antibody or antigen binding fragment thereof according to any one of claims 1-19.
22. A host cell comprising the polynucleotide of claim 21.
23. A method for producing an antibody or antigen binding fragment thereof that binds to B7-H4, comprising expressing a polynucleotide according to claim 22 in a host cell.
24. An antibody or antigen binding fragment thereof obtainable by the method of claim 23.
25. Use of the antibody or antigen binding fragment of any one of claims 1-19 or 24, the pharmaceutical composition of claim 20, or a combination thereof in the manufacture of a medicament for the treatment of ~~A method of treating~~ a cancer comprising a cancer cell which expresses B7-H4, ~~the method comprising administering to a subject the antibody or antigen binding fragment of any one of claims 1-19 or 24, the pharmaceutical composition of claim 20, or a combination thereof.~~
26. An antibody or antigen binding fragment thereof according to any one of claims 1-19 or 24, or the pharmaceutical composition of claim 20, for use in treating a cancer, wherein said cancer comprises a cancer cell which expresses B7-H4.
27. The use method ~~method~~ according to claim 25, or antibody or antigen binding fragment thereof or pharmaceutical composition for use according to claim 26, where said cancer is selected from breast cancer, ovarian cancer, endometrial cancer, cholangiocarcinoma, NSCLC (squamous and/or adenocarcinoma), pancreatic cancer, and gastric cancer.
28. The use method ~~method~~, or antibody or antigen binding fragment thereof or pharmaceutical composition for use according to any one of claims 25-27, wherein said cancer is selected from breast cancer, ovarian cancer, endometrial cancer, and cholangiocarcinoma.

29. The ~~use~~method, or antibody or antigen binding fragment thereof or pharmaceutical composition for use according to any one of claims 25-28, wherein said cancer is a breast cancer selected from hormone receptor-positive (HR+) breast cancer, human epidermal growth factor receptor 2 positive (HER2+) breast cancer, and triple negative breast cancer (TNBC).
30. A method for detecting the presence or absence of a B7-H4 polypeptide in a sample, comprising:
 - i. contacting a sample with an antibody or antigen binding fragment thereof according to any one of claims 1-19 or 24, or a pharmaceutical composition according to claim 20, to provide an antibody-antigen complex;
 - ii. detecting the presence or absence of said antibody-antigen complex;
 - iii. wherein the presence of the antibody-antigen complex confirms the presence of a B7-H4 polypeptide;
 - iv. wherein the absence of the antibody-antigen complex confirms the absence of B7-H4 polypeptide.
31. The method according to claim 30, wherein the presence of said antibody-antigen complex is indicative of the presence of a cancer cell, and wherein the absence of said antibody-antigen complex is indicative of the absence of a cancer cell.
32. The method according to claim 30 or claim 31, wherein the sample is an isolated sample obtainable from a subject.
33. The method according to any one of claims 30-32, wherein the B7-H4 polypeptide is an integral component of a cancer cell.
34. An antibody-drug conjugate (ADC) comprising:

(i) antibody or antigen binding fragment thereof which binds to a B7-H4 polypeptide comprising: a HCDR1 comprising the amino acid sequence of SEQ ID NO: 7; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 8; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 9; and a LCDR1 comprising the amino acid sequence of SEQ ID NO: 10; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 11; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 12;

(ii) a cleavable mp-PEG8-val-ala linker; and

(iii) a cytotoxic agent wherein the cytotoxic agent is SG3932,

and wherein the ADC has a drug to antibody ratio (DAR) of about 8.

35. The ADC of claim 34, wherein the antibody or antigen binding fragment thereof comprises a variable heavy (VH) chain comprising the amino acid sequence of SEQ ID NO: 45 and a variable light (VL) chain comprising the amino acid sequence of SEQ ID NO: 34.

36. The ADC of claim 34 or 35 comprising a heavy chain (HC) comprising the amino acid sequence of SEQ ID NO: 51, and light chain (LC) comprising the amino acid sequence of SEQ ID NO: 44.

37. A pharmaceutical composition comprising the ADC of any one of claims 34-37.

38. Use of the ADC of any one of claims 34-37, or the pharmaceutical composition of claim 37, or a combination thereof in the manufacture of a medicament for the treatment of ~~A method of treating a cancer comprising a cancer cell which expresses B7-H4, the method comprising administering to a subject the ADC of any one of claims 34-37, or the pharmaceutical composition of claim 37, or a combination thereof.~~

39. ~~The use method~~ of claim 25 or claim 38, wherein the cancer cell has a homologous DNA repair defect.

40. The ~~use method~~ of claim 39, wherein the homologous DNA repair defect is defined by the presence of a BRCA1 mutation.
41. The ~~use method~~ of claim 39 or claim 40, wherein the homologous DNA repair defect is defined by a negative score in a RAD51 foci formation assay.
42. Use of the antibody or antigen binding fragment of any one of claims 1-19 or 24, the pharmaceutical composition of claim 20, the ADC of of any one of claims 34-37, the pharmaceutical composition of claim 37, or a combination thereof in the manufacture of a medicament ~~A method for reducing the volume of a tumor which expresses B7-H4, the method comprising administering to a subject the the antibody or antigen binding fragment of any one of claims 1-19 or 24, the pharmaceutical composition of claim 20, the ADC of of any one of claims 34-37, the pharmaceutical composition of claim 37, or a combination thereof.~~
43. The ~~use method~~ of claim 42, wherein the tumor has a homologous DNA repair defect.
44. The ~~use method~~ of claim 43, wherein the homologous DNA repair defect is defined by the presence of a BRCA1 mutation.
45. ~~The use method~~ of claim 43 or 44, wherein the homologous DNA repair defect is defined by a negative score in a RAD51 foci formation assay.
46. The antibody or antigen binding fragment of any one of claims 1-19 or 24, the pharmaceutical composition of claim 20, the ADC of of any one of claims 34-37, the pharmaceutical composition of claim 37, or a combination thereof for use in therapy.