

What is claimed is:

1. An isolated antibody that specifically binds B7-H4 comprising a variable heavy chain complementarity determining region 1 (CDRH1) comprising the amino acid sequence GFIVSRNY (SEQ ID NO: 2), a variable heavy chain complementarity determining region 2 (CDRH2) comprising the amino acid sequence IYGSGRT (SEQ ID NO: 3), a variable heavy chain complementarity determining region 3 (CDRH3) comprising the amino acid sequence ARDADYGLDV (SEQ ID NO: 16) or the amino acid sequence ARDADYGMDV (SEQ ID NO: 10), a variable light chain complementarity determining region 1 (CDRL1) comprising the amino acid sequence QSVSSSY (SEQ ID NO: 53), a variable light chain complementarity determining region 2 (CDRL2) comprising the amino acid sequence GAS (SEQ ID NO: 54), and a variable light chain complementarity determining region 3 (CDRL3) comprising the amino acid sequence QQYGSSPLYT (SEQ ID NO: 55).

2. The isolated antibody of claim 1, wherein the isolated antibody comprises a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO: 44 and a light chain variable sequence comprising the amino acid sequence of SEQ ID NO: 50.

3. The isolated antibody of claim 1 or claim 2, wherein the isolated antibody comprises a heavy chain comprising a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO: 44 and a heavy chain constant region comprising the amino acid sequence:
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS
GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG
PSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
DELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG; and

a light chain comprising a light chain variable sequence comprising the amino acid sequence of SEQ ID NO: 50 and a light chain constant region comprising the amino acid sequence of SEQ ID NO: 51.

4. The isolated antibody of any one of claims 1-3, wherein the isolated antibody comprises a heavy chain comprising a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO: 22 and a heavy chain constant region comprising the amino acid sequence:

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS
GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG
PSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
DELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG; and

a light chain comprising a light chain variable sequence comprising the amino acid sequence of SEQ ID NO: 50 and a light chain constant region comprising the amino acid sequence of SEQ ID NO: 51.

5. The isolated antibody of any one of claims 1-4, wherein the isolated antibody comprises: (i) a heavy chain comprising the amino acid sequence of SEQ ID NO: 45 and a light chain comprising the amino acid sequence of SEQ ID NO: 52; (ii) a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO: 22 and a light chain variable sequence comprising the amino acid sequence of SEQ ID NO: 50; or (iii) a heavy chain comprising the amino acid sequence of SEQ ID NO: 23 and a light chain comprising the amino acid sequence of SEQ ID NO: 52.

6. The isolated antibody of any one of the preceding claims, wherein the isolated antibody is a monoclonal antibody.

7. The isolated antibody of any one of the preceding claims, wherein the isolated antibody is a rabbit, mouse, chimeric, humanized or fully human monoclonal antibody.

8. The isolated antibody of any one of the preceding claims, wherein the isolated antibody is an IgG isotype or an IgG1 isotype antibody.

9. The isolated antibody of any one of the preceding claims, wherein the isolated antibody competes for specific binding to human B7-H4 with an isolated antibody comprising a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO: 44 and a light chain variable sequence comprising the amino acid sequence of SEQ ID NO: 50 or with an isolated antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 45 and a light chain comprising the amino acid sequence of SEQ ID NO: 52.

10. A B7-H4 antibody-drug conjugate comprising the isolated antibody of any one of the preceding claims.

11. The antibody-drug conjugate of claim 10, comprising one or more Linker-Drug moieties covalently linked to the antibody, wherein:

each Linker-Drug moiety comprises a Multifunctional Linker that connects the antibody to one or more Drug Units (e.g., one or more therapeutic agents (D)) through intermediacy of a Releasable Assembly Unit for each Drug Unit, and connects a hydrophilic group to the Drug Unit of each Linker-Drug moiety;

the Releasable Assembly unit is capable of releasing free drug in proximity to a target site targeted by the antibody; and

the Multifunctional Linker comprises a peptide moiety between the targeting moiety and the hydrophilic group, wherein the peptide moiety comprises at least two amino acids.

12. The B7-H4 antibody-drug conjugate of claim 10, wherein the B7-H4 antibody-drug conjugate is selected from any one of the conjugates of Table A1, Table A2, Table B1 or Table B2.

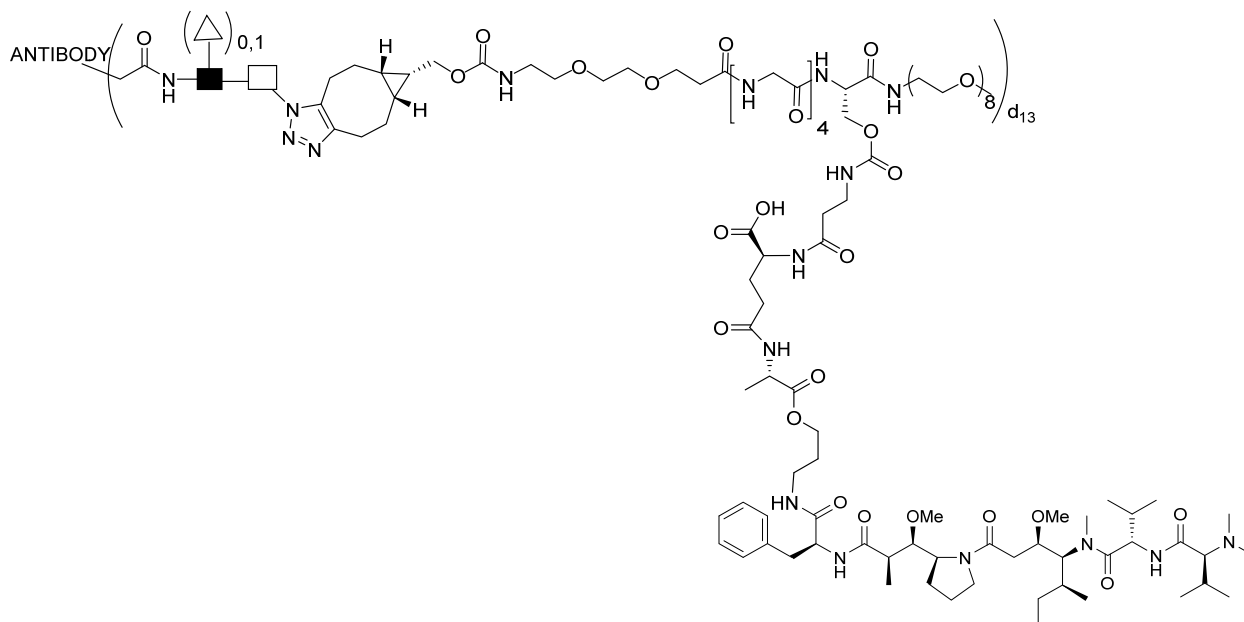
13. The B7-H4 antibody-drug conjugate of any one of claims 10-12, wherein the B7-H4 antibody-drug conjugate comprises Formula (XXXVII):



d_{13} is about 2;

■ is GlcNAc; △ is Fuc; and □ is GalNAc.

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(XXXVIII)

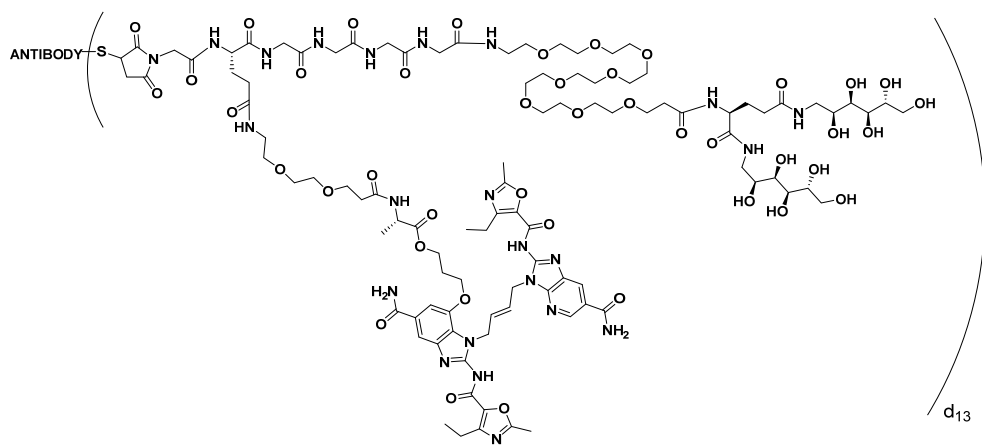
wherein

d_{13} is about 2;

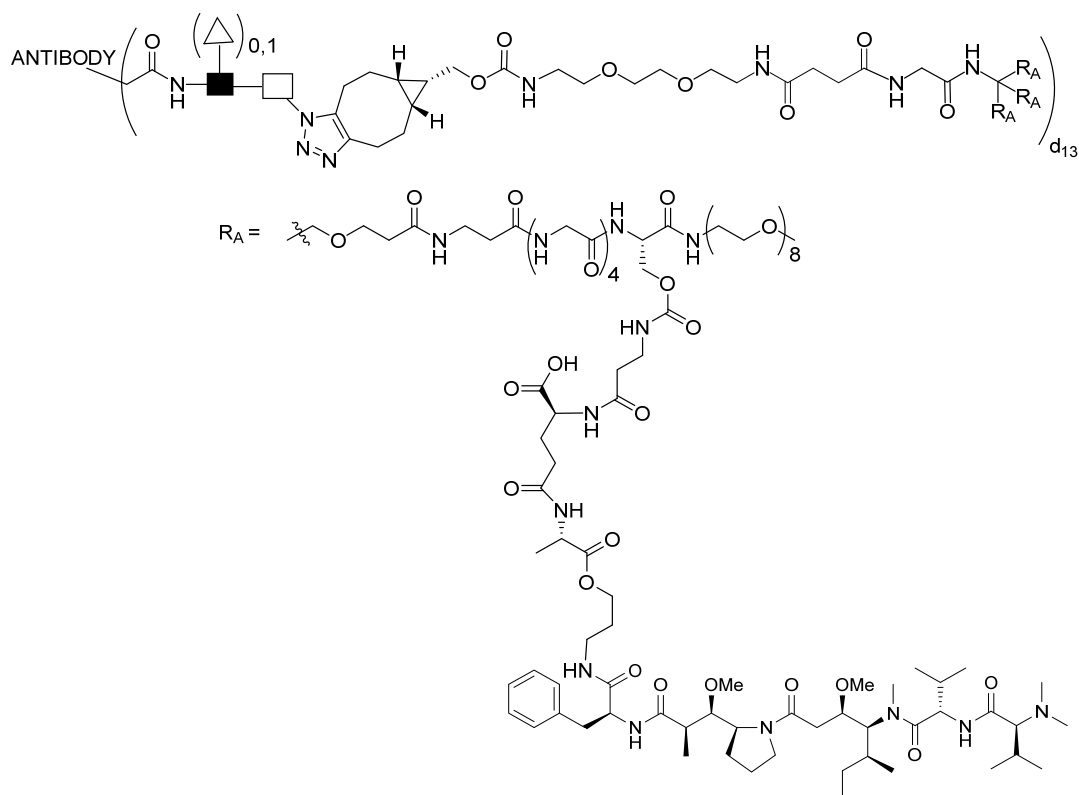
the drug is attached to a heavy chain of the antibody via a linker moiety at an asparagine residue at position 297 when numbered in accordance with EU numbering; and

■ is GlcNAc; $\triangle$ is Fuc; and □ is GalNAc.

15. The B7-H4 antibody-drug conjugate of any one of claims 10-12, wherein the B7-H4 antibody-drug conjugate comprises:



19. The use of claim 18, wherein said conjugate releases one or more therapeutic agents upon biodegradation.
20. The use of claims 18 or 19, wherein the disease or disorder is cancer.
21. The use of claim 20, wherein the cancer is a B7-H4 positive cancer.
22. The use of claim 21, wherein the B7-H4 positive cancer is bile duct carcinoma, breast cancer, endometrial cancer, ovarian cancer, non-small cell lung cancer, small cell lung cancer, uterine cancer, thyroid cancer, kidney cancer, head and neck cancer, gastric cancer, melanoma, bile duct carcinoma, cholangial carcinoma, pancreatic cancer, colon cancer or bladder cancer.
23. The use of claim 22, wherein the B7-H4 positive cancer is breast cancer, endometrial cancer, ovarian cancer, or cholangial carcinoma.
24. The use of any one of claims 18-23, wherein the subject is human.
25. The use of any one of claims 18-24, wherein the medicament is to be administered to the subject with a therapeutic agent.
26. The isolated antibody of any one of claims 1-9, wherein the antibody is a cysteine engineered antibody.
27. A B7-H4 antibody-drug conjugate comprising Formula (XXXVII):



(XXXVII)

wherein

ANTIBODY binds B7-H4 and comprises a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 44 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 50;

d₁₃ is about 2;

the drug is attached to a heavy chain of the antibody via a linker moiety at position N297 when numbered in accordance EU numbering;

■ is GlcNAc; △ is Fuc; and □ is GalNAc.

28. A nucleic acid molecule comprising a sequence encoding a light chain variable sequence, a heavy chain variable sequence, or both a light chain variable sequence and a heavy chain variable sequence of the antibody of any one of claims 1-9.

29. A nucleic acid molecule comprising: a sequence encoding SEQ ID NO: 44; a sequence encoding SEQ ID NO: 50; a sequence encoding both SEQ ID NO: 44 and SEQ ID NO: 50; a

sequence encoding SEQ ID NO: 44 and a sequence encoding

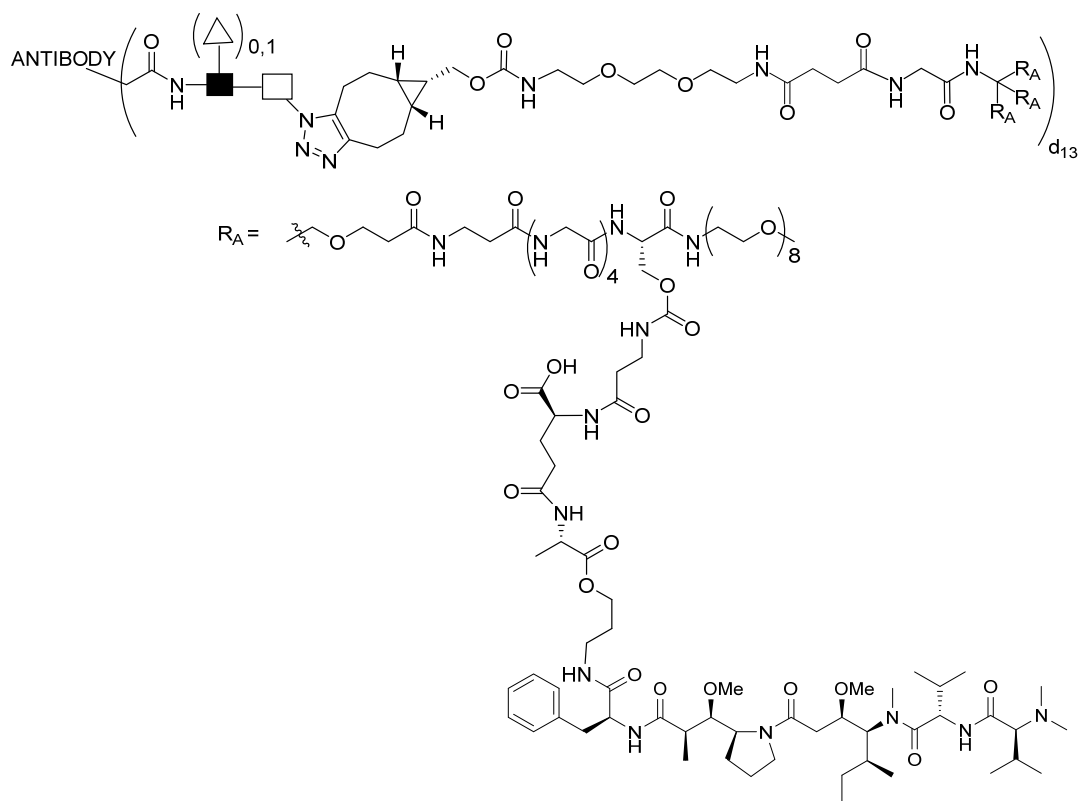
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS
GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG
PSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
DELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG; a sequence encoding SEQ ID NO: 52; or

a sequence encoding SEQ ID NO: 44,

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS
GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG
PSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
DELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG; and SEQ ID NO: 52.

30. A pharmaceutical composition comprising the B7-H4 antibody-drug conjugate of claim 27 and a pharmaceutically acceptable carrier.

31. A B7-H4 antibody-drug conjugate being of Formula (XXXVII):



(XXXVII)

wherein

ANTIBODY binds B7-H4 and comprises a heavy chain comprising a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO: 44 and a heavy chain constant region comprising the amino acid sequence:

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS
GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG
PSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
DELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG; and

a light chain comprising a light chain variable sequence comprising the amino acid sequence of SEQ ID NO: 50 and a light chain constant region comprising the amino acid sequence of SEQ ID NO: 51;

d_{13} is about 2;

the drug is attached to said heavy chain of the antibody via a linker moiety at an asparagine residue at position 296 according to SEQ ID NO: 45;

■ is GlcNAc; △ is Fuc; and □ is GalNAc.

32. A pharmaceutical composition comprising the antibody-drug conjugate of claim 31 and a pharmaceutically acceptable carrier.

33. A cell comprising the nucleic acid molecule of claim 28 or 29.

34. Use of the nucleic acid molecule of claim 28 or 29 or the cell of claim 35, in the manufacture of a medicament for the treatment or prevention of a disease or disorder in a subject in need thereof.