CLAIMS

1. An antibody conjugate comprising an isolated antibody or antigen-binding fragment thereof, and a payload molecule covalently linked by a cleavable linker to the isolated antibody or antigen-binding fragment thereof,

wherein the cleavable linker is a protease-sensitive linker comprising a valine-citrulline dipeptide, and the payload molecule is a therapeutic agent, a detectable indicator, or a combination thereof,

wherein the isolated antibody or antigen-binding fragment thereof comprises:

(a) an immunoglobulin heavy chain variable region (VH) comprising

a complementarity determining region 1 (VH CDR1) comprising the amino acid sequence set forth in SEQ ID NO: 2 or a variant thereof, wherein the variant consists of a Y to A substitution at position 33 of SEQ ID NO: 35,

a complementarity determining region 2 (VH CDR2) comprising the amino acid sequence set forth in SEQ ID NO: 3 or a variant thereof, wherein the variant consists of a T to S substitution at position 55 of SEQ ID NO: 35,

a complementarity determining region 3 (VH CDR3) comprising the amino acid sequence set forth in SEQ ID NO: 4 or a variant thereof, wherein the variant consists of a Y to A substitution at position 104 of SEQ ID NO: 35, a A to H substitution at position 106 of SEQ ID NO: 35, or both; and

(b) an immunoglobulin light chain variable region (VL) comprising

a complementarity determining region 1 (VL CDR1) comprising the amino acid sequence set forth in SEQ ID NO: 6 or a variant thereof, wherein the variant consists of a Y to A substitution at position 30 of SEQ ID NO: 5,

a complementarity determining region 2 (VL CDR2) comprising the amino acid sequence set forth in SEQ ID NO: 7 or a variant thereof, wherein the variant consists of a G to A substitution at position 50 of SEQ ID NO: 5, and

a complementarity determining region 3 (VL CDR3) comprising the amino acid sequence set forth in SEQ ID NO: 8 or a variant thereof, wherein the variant consists of a T to S substitution at position 93 of SEQ ID NO: 5.

2. The antibody conjugate of claim 1, wherein the isolated antibody or antigen-binding fragment thereof comprises: the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 2, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 3, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 4, the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 6, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 7, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 8.

3. The antibody conjugate of claim 1 or claim 2, wherein the antibody or antigen-binding fragment thereof binds specifically to at least one of (a)-(d):

(a) a biantennary Le^B/Le^B antigen comprising $Fuc_4(Gal\beta1\rightarrow3GlcNAc)_2$ **[I]** or $[Fuc\alpha1\text{-}2Gal\beta1\text{-}3(Fuc\alpha1\text{-}4)GlcNAc]_2$ **[II]**,

(b) a biantennary Le^Y/Le^Y antigen comprising $Fuc_4(Gal\beta1\rightarrow4GlcNAc)_2$ **[III]** or $[Fuc\alpha1\text{-}2Gal\beta1\text{-}4(Fuc\alpha1\text{-}3)GlcNAc]_2$ **[IV]**,

(c) a biantennary Le^B/Le^Y antigen comprising $Fuc_2(Gal\beta1\rightarrow3GlcNAc)[Fuc_2(Gal\beta1\rightarrow4GlcNAc)]$ **[V]**, or [Fucα1-2Galβ1-3(Fucα1-4)GlcNAc][Fucα1-2Galβ1-4(Fucα1-3)GlcNAc] **[VI]**, and

(d) a biantennary Le^Y/Le^B antigen comprising $Fuc_2(Gal\beta1\text{-}4GlcNAc)[Fuc_2(Gal\beta1\text{-}3GlcNAc)]$ **[VII]** or [Fucα1-2Galβ1-4(Fucα1-3)GlcNAc][Fucα1-2Galβ1-3(Fucα1-4)GlcNAc] **[VIII]**.

4. The antibody conjugate of any one of claims 1 to 3, wherein the antibody or antigen-binding fragment thereof binds specifically to:

the biantennary Le^B/Le^B antigen **[I]** or **[II]**, the biantennary Le^Y/Le^Y antigen **[III]** or **[IV]**, the biantennary Le^B/Le^Y antigen **[V]** or **[VI]**, and the biantennary Le^Y/Le^B antigen **[VII]** or **[VIII]**.

5. The antibody conjugate of any one of claims 1 to 4, wherein the antibody or antigen-binding fragment thereof does not bind specifically to a monoantennary Le^x antigen that comprises $Gal\beta1\rightarrow4(Fuc\alpha1\rightarrow3)GlcNAc$ **[IX]**, or to a biantennary Le^x

antigen that comprises [Galβ1→4(Fucα1→3)GlcNAc]$_2$ **[X]**, or to a monoantennary Le^A antigen that comprises Galβ1-3(Fucα1-4)GlcNAc **[XI]**, or to a monoantennary H antigen type 2 that comprises Fucα1-2Galβ1-4GlcNAc **[XII]**, or to a biantennary H antigen type 2 that comprises (Fucα1-2Galβ1-4GlcNAc)$_2$ **[XIII]** or to a monoantennary H antigen type 1 that comprises Fucα1-2Galβ1-3GlcNAc **[XIV]**.

6. The antibody conjugate of any one of claims 1 to 5, wherein:

the VH comprises an amino acid sequence that has at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99 percent identity to the amino acid sequence set forth in SEQ ID NO: 35, and

the VL comprises an amino acid sequence that has at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99 percent identity to the amino acid sequence set forth in SEQ ID NO: 5.

7. The antibody conjugate of claim 6, wherein the VH comprises an amino acid sequence that has at least 97 percent identity to the amino acid sequence set forth in SEQ ID NO: 35, and the VL comprises an amino acid sequence that has at least 97 percent identity to the amino acid sequence set forth in SEQ ID NO: 5.

8. The antibody conjugate of claim 6, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO: 35, and the VL comprises the amino acid sequence set forth in SEQ ID NO: 5.

9. The antibody conjugate of any one of claims 1 to 8, wherein the antibody or antigen-binding fragment thereof further comprises an Fc fragment comprising CH2 and CH3 domains of a human IgG1 subclass or CH2 and CH3 domains of a human IgG4 subclass.

10. The antibody conjugate of claim 9, wherein the Fc fragment comprises the CH2 and CH3 domains of human IgG1 subclass.

11. The antibody conjugate of any one of claims 1 to 10, wherein the antibody comprises: an immunoglobulin heavy chain having the amino acid sequence set forth in SEQ ID NO: 10 and an immunoglobulin light chain having the amino acid sequence set forth in SEQ ID NO: 11.

12. The antibody conjugate of any one of claims 1 to 11, wherein the payload molecule is a cytotoxic agent or an anti-proliferative agent.

13. The antibody conjugate of any one of claims 1 to 12, wherein the payload molecule is selected from the group consisting of a tubulin-targeting anti-mitotic agent, a peptide-based toxin, a PBD dimer, an antibiotic, a pyrimidine synthesis inhibitor, an antimetabolite, a DNA alkylating agent, and a topoisomerase inhibitor.

14. The antibody conjugate of any one of claims 1 to 13, wherein the therapeutic agent is selected from the group consisting of a maytansinoid, an auristatin, doxorubicin, calicheamicin, and a PBD dimer.

15. The antibody conjugate of claim 14, wherein the auristatin is monomethylauristatin E (MMAE) or monomethylauristatin F (MMAF).

16. The antibody conjugate of claim 14, wherein the therapeutic agent is monomethylauristatin E (MMAE).

17. An antibody conjugate comprising an isolated antibody or antigen-binding fragment thereof linked to a payload molecule by a cleavable linker, wherein:
(i) the isolated antibody or antigen-binding fragment thereof comprises:

(a) in an immunoglobulin heavy chain variable region, a complementarity determining region 1 (VH CDR1) comprising the amino acid sequence set forth in SEQ ID NO: 2 or a variant thereof, wherein the variant consists of a Y to A substitution at position 33 of SEQ ID NO: 35, a VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 3 or a variant thereof, wherein

the variant consists of a T to S substitution at position 55 of SEQ ID NO: 35, a VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 4 or a variant thereof, wherein the variant consists of a Y to A substitution at position 104 of SEQ ID NO: 35, a A to H substitution at position 106 of SEQ ID NO: 35, or both;

(b) in an immunoglobulin light chain variable region (VL), a complementarity determining region 1 (VL CDR1) comprising the amino acid sequence set forth in SEQ ID NO: 6 or a variant thereof, wherein the variant consists of a Y to A substitution at position 30 of SEQ ID NO: 5, a VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 7 or a variant thereof, wherein the variant consists of a G to A substitution at position 50 of SEQ ID NO: 5, and a VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 8 or a variant thereof, wherein the variant consists of a T to S substitution at position 93 of SEQ ID NO: 5, and

(c) means for coupling to the linker;

(ii) the cleavable linker is a protease-sensitive linker comprising a valine-citrulline dipeptide; and

(iii) the payload molecule is a therapeutic agent.

18. The antibody conjugate of claim 17, wherein the payload molecule is a cytotoxic agent or an anti-proliferative agent.

19. The antibody conjugate of claim 17 or claim 18, wherein the payload molecule is selected from the group consisting of a tubulin-targeting anti-mitotic agent, a peptide-based toxin, a PBD dimer, an antibiotic, a pyrimidine synthesis inhibitor, an antimetabolite, a DNA alkylating agent, and a topoisomerase inhibitor.

20. The antibody conjugate of any one of claims 17 to 19, wherein the antibody or antigen-binding fragment thereof binds specifically to at least one of (a)-(d):

(a) a biantennary Le^B/Le^B antigen comprising $Fuc_4(Gal\beta1\rightarrow3GlcNAc)_2$ **[I]** or $[Fuc\alpha1\text{-}2Gal\beta1\text{-}3(Fuc\alpha1\text{-}4)GlcNAc]_2$ **[II]**,

(b) a biantennary Le^Y/Le^Y antigen comprising $Fuc_4(Gal\beta1\rightarrow4GlcNAc)_2$ **[III]** or $[Fuc\alpha1\text{-}2Gal\beta1\text{-}4(Fuc\alpha1\text{-}3)GlcNAc]_2$ **[IV]**,

(c) a biantennary Le^B/Le^Y antigen comprising $Fuc_2(Gal\beta1\rightarrow3GlcNAc)[Fuc_2(Gal\beta1\rightarrow4GlcNAc)]$ **[V]**, or [Fucα1-2Galβ1-3(Fucα1-4)GlcNAc][Fucα1-2Galβ1-4(Fucα1-3)GlcNAc] **[VI]**, and

(d) a biantennary Le^Y/Le^B antigen comprising $Fuc_2(Gal\beta1\text{-}4GlcNAc)[Fuc_2(Gal\beta1\text{-}3GlcNAc)]$ **[VII]** or [Fucα1-2Galβ1-4(Fucα1-3)GlcNAc][Fucα1-2Galβ1-3(Fucα1-4)GlcNAc] **[VIII]**.

21. The antibody conjugate of any one of claims 17 to 20, wherein the isolated antibody or antigen-binding fragment thereof comprises: the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 2, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 3, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 4, the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 6, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 7, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 8.

22. A pharmaceutical composition, comprising the antibody conjugate of any one of claims 1 to 21 and a pharmaceutical carrier.

23. The pharmaceutical composition of claim 22 for use in treating a cancer that expresses one or more biantennary Lewis antigens selected from the group consisting of biantennary Le^B/Le^B, biantennary Le^Y/Le^Y, biantennary Le^B/Le^Y, and biantennary Le^Y/Le^B in a subject in need thereof, wherein the payload molecule is a therapeutic agent.

24. The pharmaceutical composition for use according to claim 23, wherein the cancer is colorectal adenocarcinoma, gastric adenocarcinoma, or lung cancer.

25. Use of the antibody conjugate of any one of claims 1 to 21 in the manufacture of a medicament for detecting cancer that expresses one or more biantennary Lewis antigens selected from the group consisting of biantennary Le^B/Le^B, biantennary Le^Y/Le^Y, biantennary Le^B/Le^Y, and biantennary Le^Y/Le^B, wherein the payload molecule is a detectable indicator.