

CLAIMS

1. An isolated anti- $\alpha\text{v}\beta 6$ antibody, or antigen-binding fragment thereof, comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises:

- (i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO:31;
- (ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO:32; and
- (iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO:33; and

wherein the light chain variable region comprises:

- (i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO:37;
- (ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO:42; and
- (iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO:39

wherein the CDRs are determined by Kabat.

2. An isolated anti- $\alpha\text{v}\beta 6$ antibody, or antigen-binding fragment thereof, comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises:

- (i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO:34;
- (ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO:35; and
- (iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO:36; and

wherein the light chain variable region comprises:

- (i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO:43;
- (ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO:44; and
- (iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO:45

wherein the CDRs are determined by IMGT.

3. The antibody or antigen-binding fragment of claim 1 or claim 2, wherein the antibody is humanized.

4. The antibody or antigen-binding fragment of any one of claims 1-3, wherein the heavy chain variable region comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 6 and the light chain variable region comprises an amino

acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 17.

5. The antibody or antigen-binding fragment of any one of claims 1-4, wherein the heavy chain variable region comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 6 and the light chain variable region comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 17.

6. The antibody or antigen-binding fragment of any one of claims 1-5, wherein the heavy chain variable region comprises an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 6 and the light chain variable region comprises an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 17.

7. The antibody or antigen-binding fragment of any one of claims 1-6, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 6 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 17.

8. The antibody or antigen-binding fragment of any of claims 4-7, wherein H2 is occupied by F, H28 is occupied by S, H48 is occupied by I, H67 is occupied by A, H69 is occupied by L, H71 is occupied by V, H73 is occupied by K, H78 is occupied by A, H93 is occupied by T, L69 is occupied by R, and L71 is occupied by Y, and wherein the numbering is via the Kabat numbering system.

9. The antibody or antigen-binding fragment of any of claims 1-8, wherein the heavy chain has an amino acid sequence comprising SEQ ID NO: 21 and the light chain has an amino acid sequence comprising SEQ ID NO: 29.

10. The antibody or antigen-binding fragment of any of claims 1-9, wherein the antibody or antigen-binding fragment is an antigen-binding fragment, and wherein the antigen-binding

fragment is selected from the group consisting of Fab, Fab', F(ab')₂, Fab'-SH, Fv, diabody, linear antibody, and single-chain antibody fragment.

11. The antibody or antigen-binding fragment of any of claims 1-10, wherein a heavy chain variable region of the antibody is fused to a heavy chain constant region and a light chain variable region is fused to a light chain constant region.

12. The antibody or antigen-binding fragment of claim 11, wherein the heavy chain constant region is of the IgG1 isotype.

13. An antibody-drug conjugate comprising the antibody or antigen-binding fragment of any one of claims 1-12 conjugated to a cytotoxic or cytostatic agent.

14. The antibody-drug conjugate of claim 13, wherein the antibody or antigen-binding fragment is conjugated to the cytotoxic or cytostatic agent via a linker.

15. The antibody-drug conjugate of any of claims 13-14, wherein the cytotoxic or cytostatic agent is a monomethyl auristatin.

16. The antibody-drug conjugate of any of claims 13-15, wherein the monomethyl auristatin is monomethyl auristatin E (MMAE).

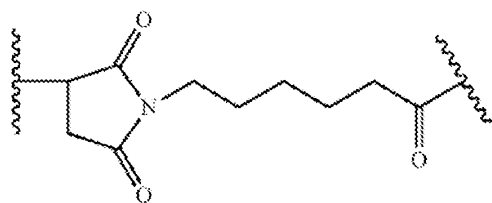
17. The antibody-drug conjugate of claim 16, wherein the antibody or antigen binding fragment thereof is conjugated to MMAE via an enzyme-cleavable linker unit.

18. The antibody-drug conjugate of claim 17, wherein the enzyme-cleavable linker unit comprises a Val-Cit linker.

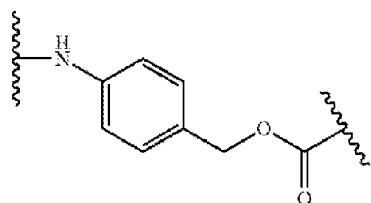
19. The antibody-drug conjugate of claim 18, wherein the antibody or antigen binding fragment thereof is conjugated to MMAE via a linker unit that has the formula: $-A_a-W_w-Y_y-$; wherein $-$

A— is a stretcher unit, a is 0 or 1; —W— is an amino acid unit, w is an integer ranging from 0 to 12; and —Y— is a spacer unit, y is 0, 1, or 2.

20. The antibody-drug conjugate of claim 19, wherein the stretcher unit has the structure of Formula I below; wherein the amino acid unit is Val-Cit; and wherein the spacer unit is a p-aminobenzyl alcohol (PAB) group having the structure of Formula II below;

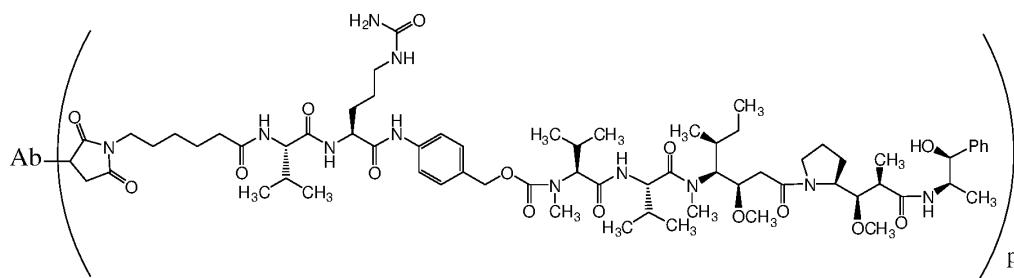


Formula I;



Formula II.

21. The antibody-drug conjugate of any of claims 14-20, wherein the linker is attached to monomethyl auristatin E forming an antibody-drug conjugate having the structure:

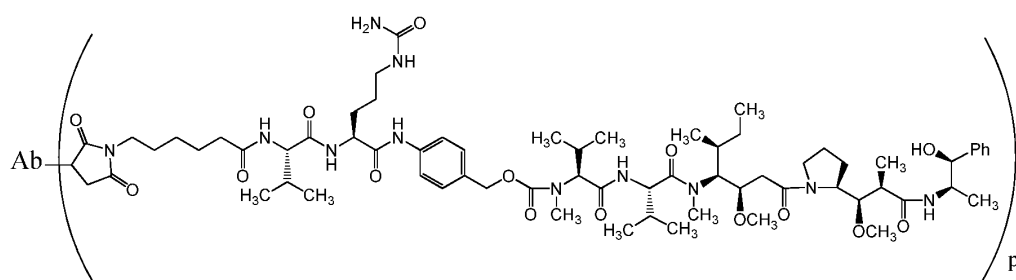


wherein Ab is the antibody h2A2 and p denotes a number from 1 to 16.

22. The antibody-drug conjugate of claim 21, wherein the average value of p in a population of the antibody-drug conjugate is about 4.
23. A nucleic acid encoding the heavy chain variable region and/or the light chain variable region as defined by any one of claims 1-12.
24. A vector comprising the nucleic acid of claim 23.
25. The vector of claim 24, wherein the vector is an expression vector.
26. A host cell comprising the nucleic acid of claim 25.
27. The host cell of claim 26, wherein the host cell is a Chinese hamster ovary (CHO) cell.
28. A method of producing an anti- $\alpha\nu\beta 6$ antibody or antigen-binding fragment thereof comprising culturing the host cell of claim 26 or 27 under a condition suitable for production of the anti- $\alpha\nu\beta 6$ antibody or antigen-binding fragment thereof.
29. The method of claim 28, further comprising isolating the anti- $\alpha\nu\beta 6$ antibody or antigen-binding fragment thereof produced by the host cell.
30. A method of producing an anti- $\alpha\nu\beta 6$ antibody-drug conjugate comprising culturing the host cell of claim 26 or 27 under a condition suitable for production of an anti- $\alpha\nu\beta 6$ antibody; isolating the anti- $\alpha\nu\beta 6$ antibody produced from the host cell; and conjugating the anti- $\alpha\nu\beta 6$ antibody to a cytotoxic or cytostatic agent.
31. The method of claim 30, wherein the anti- $\alpha\nu\beta 6$ antibody is conjugated to the cytotoxic or cytostatic agent via a linker.
32. The method of claim 31, wherein the linker is a Val-Cit linker.

33. The method of any of claims 30-32, wherein the cytotoxic or cytostatic agent is monomethyl auristatin E (MMAE).
34. A method of treating cancer in a subject, the method comprising administering to the subject the antibody or antigen-binding fragment of any one of claims 1-12 or the antibody-drug conjugate of any one of claims 13-22.
35. The method of claim 34, wherein the cancer is selected from the group consisting of non-small cell lung cancer (NSCLC), head and neck cancer, esophageal cancer, breast cancer, ovarian cancer, bladder cancer, skin cancer (SCC), ovarian cancer, cervical cancer, gastric cancer, and pancreatic cancer.
36. The method of claim 34, wherein the lung cancer is non-small cell lung cancer.
37. The method of claim 34, wherein the cancer is head and neck cancer.
38. The method of any one of claims 34-37, wherein the antibody or antigen-binding fragment or antibody-drug conjugate is in a pharmaceutical composition comprising the antibody or antigen-binding fragment or antibody-drug conjugate and a pharmaceutically acceptable carrier.
39. The method of any one of claims 34-38, wherein the subject is a human.
40. A pharmaceutical composition comprising the antibody or antigen-binding fragment of any one of claims 1-12 or the antibody-drug conjugate of any one of claims 13-22 and one or more agents selected from the group consisting of a physiologically acceptable carrier, a diluent, an excipient and an auxiliary.
41. The pharmaceutical composition of claim 40, wherein the composition is administered in combination with radiation or a chemotherapeutic agent.

42. An antibody-drug conjugate comprising isolated anti- $\alpha v \beta 6$ antibody conjugated to vcMMAE, wherein the antibody has a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 6 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 17, and wherein the antibody-drug conjugate has the structure:



wherein Ab is the antibody and p denotes a number from 1 to 16.