Claims

1. An antibody drug conjugate comprising an antibody or antigen binding fragment thereof which binds to a 158P1D7 protein, wherein the antibody or antigen binding fragment thereof is conjugated to one or more units of monomethyl auristatin E (MMAE), each being conjugated via a linker, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) consisting of the amino acid sequences of the CDRs in the heavy chain variable region sequence set forth in SEQ ID NO: 7, and a light chain variable region comprising CDRs consisting of the amino acid sequences of the CDRs in the light chain variable region sequence set forth in SEQ ID NO: 8.

2. The antibody drug conjugate of claim 1, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising CDR-H1 consisting of the amino acid sequence ranging from position 31 to 35 of SEQ ID NO:7, CDR-H2 consisting of the amino acid sequence ranging from position 50 to 66 of SEQ ID NO: 7, and CDR-H3 consisting of the amino acid sequence ranging from position 99 to 109 of SEQ ID NO: 7, and a light chain variable region comprising CDR-L1 consisting of the amino acid sequence ranging from position 24 to 39 of SEQ ID NO: 8, CDR-L2 consisting of the amino acid sequence ranging from position 55 to 61 of SEQ ID NO: 8, and CDR-L3 consisting of the amino acid sequence ranging from position 94 to 102 of SEQ ID NO: 8.

3. The antibody drug conjugate of claim 1, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region consisting of the amino acid sequence ranging from position 1 to position 120 of SEQ ID NO: 7, and a light chain variable region consisting of the amino acid sequence ranging from position 1 to position 113 of SEQ ID NO: 8.

4. The antibody drug conjugate of anyone of claims 1 to 3, wherein the antibody comprises a heavy chain consisting of the amino acid sequence ranging from position 1 to position 446 of SEQ ID NO: 7, and a light chain consisting of the amino acid sequence ranging from position 1 to position 219 of SEQ ID NO: 8.

5. An antibody drug conjugate comprising an antibody or antigen binding fragment thereof which binds to a 158P1D7 protein, wherein the antibody or antigen binding fragment thereof is conjugated to one or more units of monomethyl auristatin E (MMAE), each being conjugated via a linker, and wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) consisting of the amino acid sequences of the CDRs in the heavy chain variable region of an antibody produced by a Chinese Hamster Ovary (CHO) cell deposited under American Type Culture Collection (ATCC) Accession No. PTA-13102, and a light chain variable region comprising CDRs consisting of the amino acid sequences of the CDRs in the light chain variable region of an antibody produced by a Chinese Hamster Ovary (CHO) cell deposited under ATCC Accession No. PTA-13102.

6. The antibody drug conjugate of claim 5, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region consisting of the amino acid sequence of the heavy chain variable region of an antibody produced by a Chinese Hamster Ovary (CHO) cell deposited under ATCC Accession No. PTA-13102, and a light chain variable region consisting of the amino acid sequence of the light chain variable region of an antibody produced by a Chinese Hamster Ovary (CHO) cell deposited under ATCC Accession No. PTA-13102.

7. The antibody drug conjugate of claim 5, wherein the antibody or antigen binding fragment thereof comprises a heavy chain consisting of the amino acid sequence of the heavy chain of an antibody produced by a Chinese Hamster Ovary (CHO) cell deposited under ATCC Accession No. PTA-13102, and a light chain consisting of the amino acid sequence of the light chain of an antibody produced by a Chinese Hamster Ovary (CHO) cell deposited under ATCC Accession No. PTA-13102.

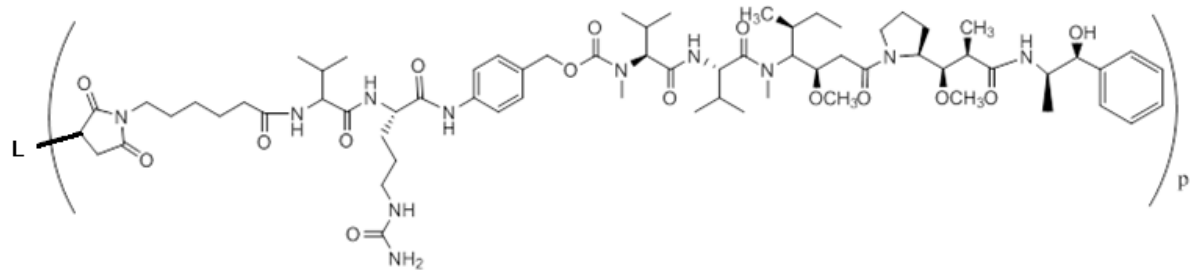
8. The antibody drug conjugate of any one of claims 1 to 3, 5 to 6, wherein the antigen binding fragment is an Fab, $F(ab')_2$, Fv or scFv.

9. The antibody drug conjugate of any one of claims 1 to 8, wherein the antibody is a fully human antibody.

10. The antibody drug conjugate of any one of claims 1 to 9, wherein the antibody or antigen binding fragment thereof is recombinantly produced.

11. The antibody drug conjugate of any one of claims 1 to 10, wherein the linker comprises valine-citrulline (Val-Cit).

12. The antibody drug conjugate of any one of claims 1 to 11, wherein the antibody drug conjugate has the following structure:

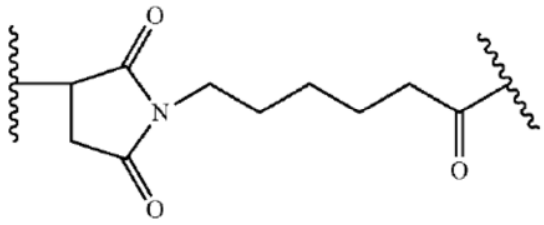


wherein L- represents the antibody or antigen binding fragment thereof and p ranges from 1 to about 10.

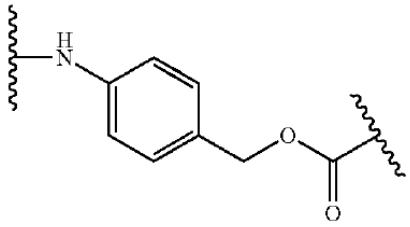
13. The antibody drug conjugate of claim 12, wherein p ranges from 2 to 5.

14. The antibody drug conjugate of any one of claims 1 to 10, wherein the linker has the formula: –Aa–Ww–Yy–; 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.

15. The antibody drug conjugate of claim 14, wherein the stretcher unit has the structure of Formula I below; the amino acid unit is Val-Cit; and the spacer unit is a PAB group having the structure of Formula II below;



Formula I;



Formula II.

16. The antibody drug conjugate of claim 15, wherein the stretcher unit forms a bond with a sulfur atom of the antibody or antigen binding fragment thereof; and wherein the spacer unit is linked to MMAE via a carbamate group.

17. A pharmaceutical composition that comprises a pharmaceutically effective amount of the antibody drug conjugate of any one of claims 1 to 16 and a pharmaceutically acceptable excipient in a human unit dose form.

18. The pharmaceutical composition of claim 17, wherein the composition is for treatment of glioblastoma cancer, lung cancer, bladder cancer, or breast cancer.

19. The pharmaceutical composition of claim 17 or claim 18, wherein the composition is to be administered in combination with radiation or a chemotherapeutic agent.

20. The pharmaceutical composition of claim 17 to claim 18, further comprising a chemotherapeutic agent.

21. Use of the antibody drug conjugate of any one of claims 1 to 16 in the manufacture of a medicament for the treatment of a cancer in a subject, wherein the cancer is selected from a group consisting of glioblastoma, lung cancer, bladder cancer, and breast cancer.

22. Use of a combination of the antibody drug conjugate of any one of claims 1 to 16 and a chemotherapeutic agent in the manufacture of a medicament for the treatment of a cancer in a subject, wherein the cancer is selected from a group consisting of glioblastoma, lung cancer, bladder cancer, and breast cancer.

23. The use of claim 21 or claim 22, wherein the cancer is glioblastoma.

24. The use of claim 21 or claim 22, wherein the cancer is lung cancer.

25. The use of claim 21 or claim 22, wherein the cancer is bladder cancer.

26. The use of claim 21 or claim 22, wherein the cancer is breast cancer.

27. An antibody or antigen binding fragment thereof that binds to a 158P1D7 protein, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) consisting of the amino acid sequences of the CDRs in the heavy chain variable region sequence set forth in SEQ ID NO: 7, and a light chain variable region comprising CDRs consisting of the amino acid sequences of the CDRs in the light chain variable region sequence set forth in SEQ ID NO: 8.

28. The antibody or antigen binding fragment thereof of claim 27, wherein the antibody or antigen binding fragment comprises a heavy chain variable region comprising CDR-H1 consisting of the amino acid sequence ranging from position 31 to 35 of SEQ ID NO:7, CDR-H2 consisting of the amino acid sequence ranging from position 50 to 66 of SEQ ID NO: 7, and CDR-H3 consisting of the amino acid sequence ranging from position 99 to 109 of SEQ

ID NO: 7, and a light chain variable region comprising CDR-L1 consisting of the amino acid sequence ranging from position 24 to 39 of SEQ ID NO: 8, CDR-L2 consisting of the amino acid sequence ranging from position 55 to 61 of SEQ ID NO: 8, and CDR-L3 consisting of the amino acid sequence ranging from position 94 to 102 of SEQ ID NO: 8.

29. The antibody or antigen binding fragment thereof of claim 27, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region consisting of the amino acid sequence ranging from position 1 to position 120 of SEQ ID NO: 7, and a light chain variable region consisting of the amino acid sequence ranging from position 1 to position 113 of SEQ ID NO: 8.

30. The antibody or antigen binding fragment thereof of claim 27, wherein the antibody comprises a heavy chain consisting of the amino acid sequence ranging from position 1 to position 446 of SEQ ID NO: 7, and a light chain consisting of the amino acid sequence ranging from position 1 to position 219 of SEQ ID NO: 8.

31. The antibody or antigen binding fragment thereof of any one of claims 27 to 30, wherein the fragment is an Fab, $F(ab')_2$, Fv or scFv.

32. The antibody or antigen binding fragment thereof of any one of claims 27 to 30 further comprises a human IgG constant region and a human light chain constant region.

33. The antibody or antigen binding fragment thereof of claim 32, wherein the IgG constant region is IgG2 and the light chain constant region is kappa.

34. The antibody or antigen binding fragment thereof of any one of claims 27 to 33, wherein the antibody is a fully human antibody.

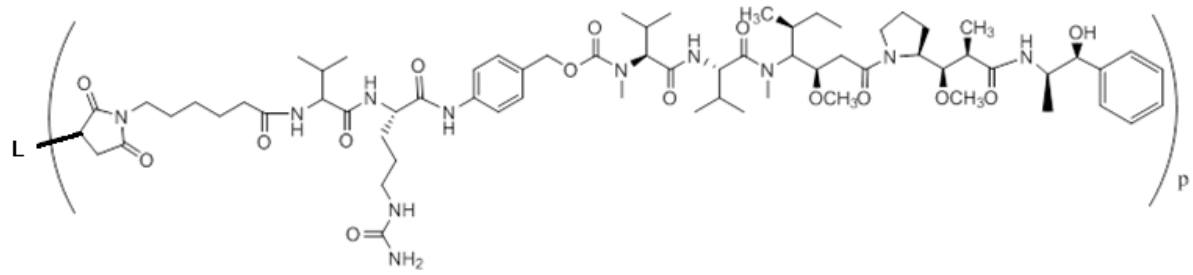
35. The antibody or antigen binding fragment thereof of any one of claims 27 to 34, wherein the antibody or antigen binding fragment thereof is recombinantly produced.

36. An antibody drug conjugate comprising the antibody or antigen binding fragment thereof of any one of claims 27 to 35 conjugated to a cytotoxic agent via a linker.

37. The antibody drug conjugate of claim 36, wherein the cytotoxic agent is monomethyl auristatin E (MMAE).

38. The antibody drug conjugate of claim 36 or claim 37, wherein the linker comprises valine-citrulline.

39. The antibody drug conjugate of any one of claims 36 to 38, wherein the antibody drug conjugate has the following structure:



wherein L- represents the antibody or antigen binding fragment thereof and p ranges from 1 to about 10.

40. A pharmaceutical composition that comprises a therapeutically effective amount of the antibody drug conjugate of any one of claims 36 to 39 and a pharmaceutically acceptable excipient in a human unit dosage form.

41. The pharmaceutical composition of claim 40, wherein the pharmaceutical composition is for treatment of a cancer, wherein the cancer is selected from a group consisting of glioblastoma cancer, lung cancer, bladder cancer, and breast cancer.

42. The pharmaceutical composition of claim 40 or claim 41, wherein the pharmaceutical composition is to be administered in combination with radiation or a chemotherapeutic agent.

43. The pharmaceutical composition of claim 40 or claim 41 further comprising a chemotherapeutic agent in a human unit dose form.

44. Use of the antibody drug conjugate of any one of claim 36 to 39 in the manufacture of a medicament for the treatment of a cancer, wherein the cancer is selected from a group consisting of glioblastoma cancer, lung cancer, bladder cancer, and breast cancer.

45. Use of a combination of the antibody drug conjugate of any one of claims 36 to 39 and a chemotherapeutic agent in the manufacture of a medicament for the treatment of a cancer, wherein the cancer is selected from a group consisting of glioblastoma cancer, lung cancer, bladder cancer, and breast cancer.

46. The use of claim 44 or claim 45, wherein the cancer is glioblastoma cancer.

47. The use of claim 44 or claim 45, wherein the cancer is lung cancer.

48. The use of claim 44 or claim 45, wherein the cancer is bladder cancer.

49. The use of claim 44 or claim 45, wherein the cancer is breast cancer.

50. An isolated polynucleotide encoding an antibody or antigen binding fragment thereof that binds to a 158P1D7 protein, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) consisting of the amino acid sequences of the CDRs in the heavy chain variable region sequence set forth in SEQ ID NO: 7, and a light chain variable region comprising CDRs

consisting of the amino acid sequences of the CDRs in the light chain variable region sequence set forth in SEQ ID NO: 8.

51. The polynucleotide of claim 50, wherein the antigen binding fragment is a Fab, $F(ab')_2$, Fv, or scFv.

52. An isolated vector comprising the polynucleotide of claim 50 or claim 51.

53. An isolated host cell comprising the vector of claim 52.

54. The host cell of 53, wherein the host cell is a Chinese Hamster Ovary (CHO) cell.

55. A method of making an antibody or antigen binding fragment thereof, wherein the method comprises:

a) culturing the host cell of claim 53 or claim 54 under conditions suitable for expression of the polynucleotide encoding the antibody or antigen binding fragment thereof; and

b) isolating the antibody or antigen binding fragment thereof.

56. The method of claim 55, wherein the antigen binding fragment is a Fab, $F(ab')_2$, Fv, or scFv.

57. An antibody or antigen binding fragment thereof produced by the method of claim 55 or claim 56.

58. A method of making an antibody drug conjugate, wherein the method comprises:

a) culturing the host cell of claim 53 or claim 54 under conditions suitable for expression of the polynucleotide encoding the antibody or antigen binding fragment thereof;

b) isolating the antibody or antigen binding fragment thereof; and

c) conjugating a drug to the antibody or antigen binding fragment thereof via a linker.

59. The method of claim 58, wherein the antigen binding fragment is a Fab, $F(ab')_2$, Fv, or scFv.

60. The method of claim 58 or claim 59, wherein the drug is a cytotoxin, a cytostatic agent, or an immunomodulatory agent.

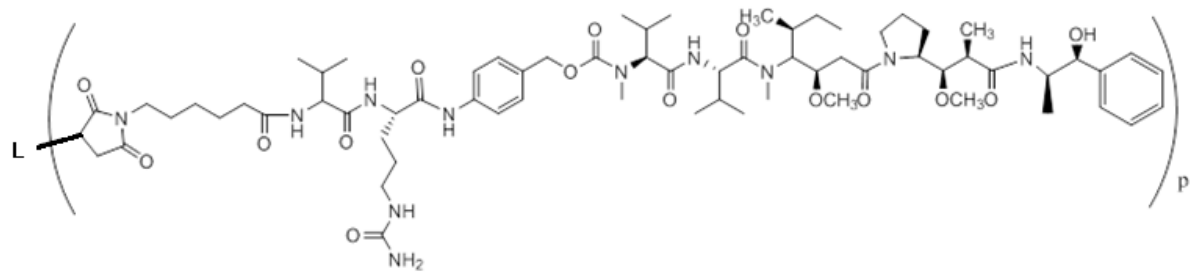
61. The method of claim 60, wherein the cytotoxin is an antitubulin agent.

62. The method of claim 61, wherein the antitubulin agent is selected from the group consisting of auristatin phenylalanine phenylenediamine (AFP), monomethyl auristatin phenylalanine (MMAF), and monomethyl auristatin E (MMAE).

63. The method of claim 62, wherein the antitubulin agent is monomethyl auristatin E (MMAE).

64. The method of any one of claims 58 to 63, wherein the linker comprises valine-citrulline (Val-Cit).

65. The method of any one of claims 58 to 63, wherein the antibody drug conjugate has the following structure:



wherein L- represents the antibody or antigen binding fragment thereof and p ranges from 1 to about 10.

66. An antibody drug conjugate produced by the method of any one of claims 58 to 65.

67. A host cell which is selected from the group consisting of the following:

(a) a host cell transformed with an expression vector comprising a polynucleotide comprising a sequence encoding a heavy chain variable region of an antibody or antigen binding fragment thereof, and a polynucleotide comprising a sequence encoding a light chain variable region of an antibody or antigen binding fragment thereof; and

(b) a host cell transformed with an expression vector comprising a polynucleotide comprising a sequence encoding a heavy chain variable region of an antibody or antigen binding fragment thereof, and an expression vector comprising a polynucleotide comprising a sequence encoding a light chain variable region of an antibody or antigen binding fragment thereof,

wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) consisting of the amino acid sequences of the CDRs in the heavy chain variable region sequence set forth in SEQ ID NO: 7, and a light chain variable region comprising CDRs consisting of the amino acid sequences of the CDRs in the light chain variable region sequence set forth in SEQ ID NO: 8.

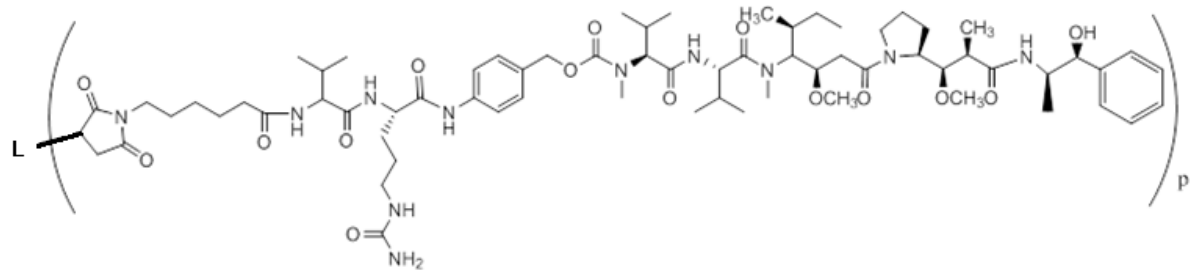
68. A method of producing the antibody or antigen binding fragment thereof, comprising culturing the host cell of claim 81 under conditions suitable for expression of the antibody or antigen binding fragment thereof.

69. An antibody or antigen binding fragment thereof produced by the method of claim 68.

70. An antibody drug conjugate comprising the antibody or antibody binding fragment thereof of claim 69 conjugated to a cytotoxin, a cytostatic agent, or an immunomodulatory agent.

71. The antibody drug conjugate of claim 70, wherein the cytotoxin is monomethyl auristatin E (MMAE).

72. The antibody drug conjugate of claim 70 or claim 71, wherein the antibody drug conjugate has the following structure:



wherein L- represents the antibody or antigen binding fragment thereof and p ranges from 1 to about 10.

73. A therapeutically effective amount of the antibody drug conjugate of any one of claims 1 to 16, for use as a medicament.