

What is Claimed is:

1. A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate,

wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and

wherein the subject has hormone receptor positive and human epidermal growth factor receptor 2 negative (HR+/HER2-) breast cancer.

2. The method of claim 1, wherein the HR+/HER2- breast cancer is estrogen receptor (ER) positive and/or progesterone receptor (PR) positive, and HER2 negative.

3. The method of claim 1 or claim 2, wherein the subject has locally advanced or metastatic cancer.

4. The method of any one of claims 1 to 3, wherein the subject has previously received at least one line of an endocrine therapy and a cyclin-dependent kinase (CDK) 4/6 inhibitor in metastatic or locally advanced setting.

5. The method of any one of claims 1 to 4, wherein the subject has previously received a treatment with a taxane or anthracycline.

6. The method of any one of claims 1 to 5, wherein the subject has a deleterious germline mutation in breast cancer susceptibility gene (BRCA)1 or BRCA2, and wherein the subject has previously been treated with a poly ADP ribose polymerase (PARP) inhibitor.

7. A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate,

wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E

(MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and

wherein the subject has ER negative, PR negative, and HER2 negative (ER-/PR-/HER2-) breast cancer (Triple Negative Breast Cancer - TNBC).

8. The method of claim 7, wherein the subject has locally advanced or metastatic cancer.

9. The method of claim 7 or claim 8, wherein the subject has previously received at least two lines of systemic therapies.

10. The method of claim 9, wherein the subject has previously received a treatment with a taxane.

11. The method of any one of claims 7 to 10, wherein the subject has a deleterious germline mutation in breast cancer susceptibility gene (BRCA)1 or BRCA2, and wherein the subject has previously been treated with a poly ADP ribose polymerase (PARP) inhibitor.

12. A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate,

wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and

wherein the subject has squamous non-small cell lung cancer (NSCLC).

13. The method of claim 12, wherein the subject has locally advanced or metastatic cancer.

14. The method of claim 12 or claim 13, wherein the subject has progressed or relapsed following a platinum-based therapy.

15. The method of claim 14, wherein the subject has progressed or relapsed within 12 months after a platinum-based therapy.

16. The method of any one of claims 12 to 15, wherein the subject has previously received a therapy with an inhibitor of programmed cell death protein-1 (PD-1) or an inhibitor of programmed cell death-ligand 1 (PD-L1), wherein optionally the inhibitor of PD-1 is nivolumab and wherein optionally the inhibitor of PD-L1 is selected from a group consisting of atezolizumab, avelumab, and durvalumab.

17. A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate,

wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and

wherein the subject has non-squamous NSCLC.

18. The method of claim 17, wherein the subject has wild-type epidermal growth factor receptor (EGFR) and wild-type anaplastic lymphoma kinase (ALK).

19. The method of claim 17 or claim 18, wherein the subject has locally advanced or metastatic cancer.

20. The method of any one of claims 17 to 19, wherein the subject has progressed or relapsed following a platinum-based therapy.

21. The method of claim 20, wherein the subject has progressed or relapsed within 12 months after a platinum-based therapy.

22. The method of any one of claims 17 to 21, wherein the subject has previously received a therapy with an inhibitor of programmed cell death protein-1 (PD-1) or an inhibitor of programmed cell death-ligand 1 (PD-L1), wherein optionally the inhibitor of PD-1 is nivolumab and wherein optionally the inhibitor of PD-L1 is selected from a group consisting of atezolizumab, avelumab, and durvalumab.

23. A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate,

wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and

wherein the subject has locally advanced or metastatic head and neck cancer.

24. The method of claim 23, wherein the subject has progressed or relapsed following a platinum-based therapy.

25. The method of claim 24, wherein the subject has progressed or relapsed within 6 months after a platinum-based therapy.

26. The method of any one of claims 23 to 25, wherein the subject has previously received a therapy with an inhibitor of programmed cell death protein-1 (PD-1) or an inhibitor of programmed cell death-ligand 1 (PD-L1), wherein optionally the inhibitor of PD-1 is nivolumab and wherein optionally the inhibitor of PD-L1 is selected from a group consisting of atezolizumab, avelumab, and durvalumab.

27. A method of preventing or treating cancer in a subject, comprising administering to the subject an effective amount of an antibody drug conjugate,

wherein the antibody drug conjugate comprises an antibody or antigen binding fragment thereof that binds to 191P4D12 conjugated to one or more units of monomethyl auristatin E (MMAE), wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising complementarity determining regions (CDRs) comprising the amino acid sequences of the CDRs of the heavy chain variable region set forth in SEQ ID NO:22 and a light chain variable region comprising CDRs comprising the amino acid sequences of the CDRs of the light chain variable region set forth in SEQ ID NO:23; and

wherein the subject has gastric or esophageal cancer.

28. The method of claim 27, wherein the subject has locally advanced or metastatic cancer.

29. The method of claim 27 or claim 28, wherein the subject has progressed or relapsed following a platinum-based therapy and/or a chemotherapy that included a fluoropyrimidine.

30. The method of claim 29, wherein the subject has progressed or relapsed within 6 months after the platinum-based therapy or the chemotherapy that included a fluoropyrimidine.

31. The method of any one of claims 27 to 30, wherein the gastric or esophageal cancer is HER2 positive cancer, and wherein the subject has previously received a HER2 directed therapy.

32. The method of any one of claims 1 to 31, wherein the antibody or antigen binding fragment thereof comprises CDR H1 comprising the amino acid sequence of SEQ ID NO:9, CDR H2 comprising the amino acid sequence of SEQ ID NO:10, CDR H3 comprising the amino acid sequence of SEQ ID NO:11; CDR L1 comprising the amino acid sequence of SEQ ID NO:12, CDR L2 comprising the amino acid sequence of SEQ ID NO:13, and CDR L3 comprising the amino acid sequence of SEQ ID NO:14, or

wherein the antibody or antigen binding fragment thereof comprises CDR H1 comprising the amino acid sequence of SEQ ID NO:16, CDR H2 comprising the amino acid sequence of SEQ ID NO:17, CDR H3 comprising the amino acid sequence of SEQ ID NO:18; CDR L1 comprising the amino acid sequence of SEQ ID NO:19, CDR L2 comprising the amino

acid sequence of SEQ ID NO:20, and CDR L3 comprising the amino acid sequence of SEQ ID NO:21.

33. The method of any one of claims 1 to 31, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:22 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:23.

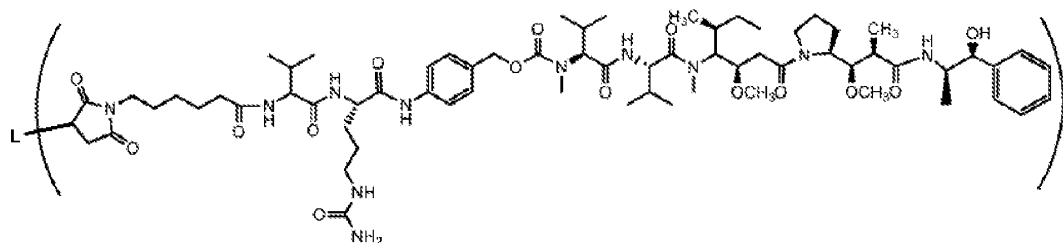
34. The method of any one of claims 1 to 31, wherein the antibody comprises a heavy chain comprising the amino acid sequence ranging from the 20th amino acid (glutamic acid) to the 466th amino acid (lysine) of SEQ ID NO:7 and a light chain comprising the amino acid sequence ranging from the 23rd amino acid (aspartic acid) to the 236th amino acid (cysteine) of SEQ ID NO:8.

35. The method of any one of claims 1 to 34, wherein the antigen binding fragment is an Fab, F(ab')₂, Fv or scFv fragment.

36. The method of any one of claims 1 to 35, wherein the antibody is a fully human antibody.

37. The method of any one of claims 1 to 36, wherein the antibody or antigen binding fragment thereof is recombinantly produced.

38. The method of any one of claims 1 to 37, wherein the antibody drug conjugate has the following structure:



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

39. The method of claim 38, wherein p is from 2 to 8.

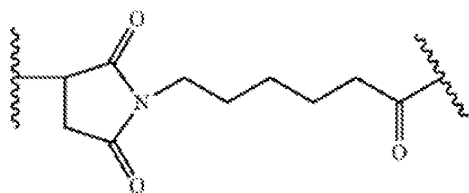
40. The method of claim 38, wherein p is from 3 to 5.

41. The method of any one of claims 1 to 40, wherein the antibody or antigen binding fragment is linked to each unit of monomethyl auristatin E (MMAE) via a linker.

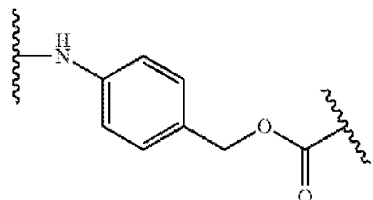
42. The method of claim 41, wherein the linker is an enzyme-cleavable linker, and wherein the linker forms a bond with a sulfur atom of the antibody or antigen binding fragment thereof.

43. The method of claim 41, wherein the linker has a formula of: $-A_a-W_w-Y_y-$; 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.

44. The method of claim 43, wherein the stretcher unit has the structure of Formula (1) below; the amino acid unit is valine citrulline; and the spacer unit is a PAB group comprising the structure of Formula (2) below:



Formula (1)



Formula (2).

45. The method of claim 43, 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.

46. The method of any one of claims 1 to 37, wherein the antibody drug conjugate comprises from 1 to 10 units of MMAE per antibody or antigen binding fragment thereof.

47. The method of any one of claims 1 to 37, wherein the antibody drug conjugate comprises from 2 to 8 units of MMAE per antibody or antigen binding fragment thereof.

48. The method of any one of claims 1 to 37, wherein the antibody drug conjugate comprises from 3 to 5 units of MMAE per antibody or antigen binding fragment thereof.

49. The method of any one of claims 1 to 48, wherein the antibody drug conjugate is administered at a dose of 1 to 10 mg/kg of the subject's body weight, 1 to 5 mg/kg of the subject's body weight, 1 to 2.5 mg/kg of the subject's body weight, or 1 to 1.25 mg/kg of the subject's body weight.

50. The method of claim 49, wherein the antibody drug conjugate is administered at a dose of about 1 mg/kg of the subject's body weight.

51. The method of claim 49, wherein the antibody drug conjugate is administered at a dose of about 1.25 mg/kg of the subject's body weight.

52. The method of any one of claims 1 to 51, wherein the antibody drug conjugate is administered by an intravenous (IV) injection or infusion.

53. The method of any one of claims 1 to 51, wherein the antibody drug conjugate is administered by an intravenous (IV) injection or infusion over about 30 minutes twice every three-week cycle.

54. The method of any one of claims 1 to 51, wherein the antibody drug conjugate is administered by an intravenous (IV) injection or infusion over about 30 minutes on Days 1 and 8 of every three-week cycle.

55. The method of any one of claims 1 to 51, wherein the antibody drug conjugate is administered by an intravenous (IV) injection or infusion over about 30 minutes three times every four-week cycle.

56. The method of any one of claims 1 to 51, wherein the antibody drug conjugate formulated in the pharmaceutical composition is administered by an intravenous (IV) injection or infusion over about 30 minutes on Days 1, 8 and 15 of every four-week cycle.