

therapies are useful for tumors that express HER2/neu; these tumors are the only class of breast cancer that is currently eligible for immunotherapy. For these patients, unconjugated antibodies, such as Herceptin or Perjeta, are generally used in combination with chemotherapy.

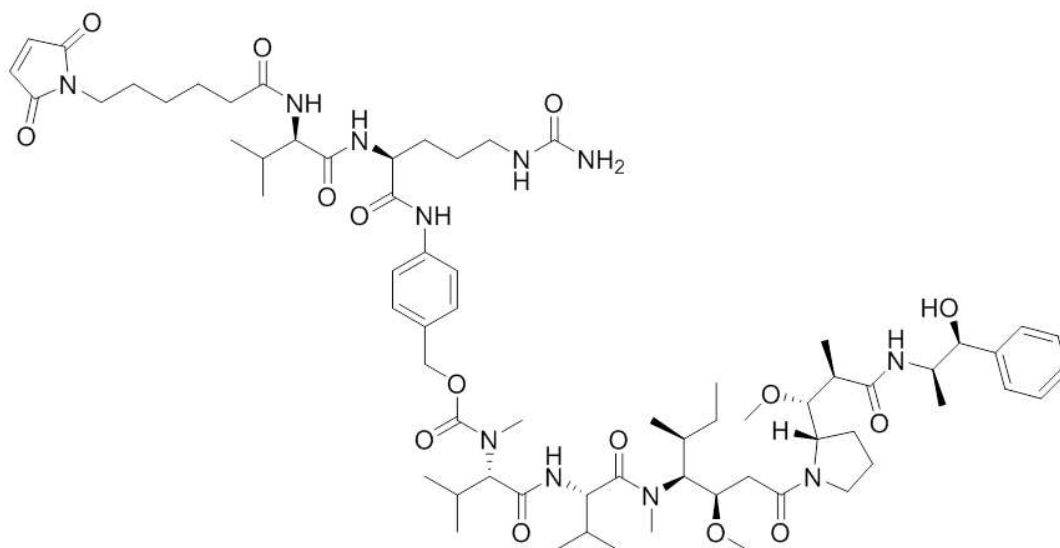
[0011] There is clearly a significant need for effective treatments for solid tumors, particularly locally advanced or metastatic solid tumors, and breast cancer, particularly late-stage breast cancer. The present invention meets the need for improved treatment of solid tumors, such as, e.g., locally advanced or metastatic solid tumors (e.g., small cell lung cancer, non-small cell lung cancer, head and neck squamous cell carcinoma, esophageal squamous cell carcinoma, and gastric and gastroesophageal junction adenocarcinoma), and breast cancer by providing a highly specific and effective anti-LIV1-antibody-drug conjugate.

[0012] All references cited herein, including patent applications, patent publications, and scientific literature, are herein incorporated by reference in their entirety, as if each individual reference were specifically and individually indicated to be incorporated by reference.

SUMMARY

[0013] In one aspect, the present disclosure provides a use of a therapeutically effective dose of an antibody or an antigen-binding fragment thereof that specifically binds human LIV1 in the formulation of a medicament for treating a subject having or at risk of having a LIV1-associated cancer, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (HCVR) having at least 95% identity to SEQ ID NO:1, and a light chain variable region (LCVR) having at least 95% identity to SEQ ID NO:2, wherein the cancer is a solid tumor.

[0013a] In another aspect, the present disclosure provides a use of therapeutically effective dose of a LIV1 antibody-drug conjugate (LIV1-ADC) in the formulation of a medicament for treating a subject having or at risk of having a LIV1-associated cancer, wherein the LIV1-ADC comprises a humanized hLIV22 antibody conjugated to a vcMMAE (valine-citruline-monomethyl auristating E), wherein the hLIV22 antibody comprises a heavy chain variable region comprising the sequence of SEQ ID NO:1 and a light chain variable region comprising the sequence of SEQ ID NO:2, wherein the vcMMAE has the structure:

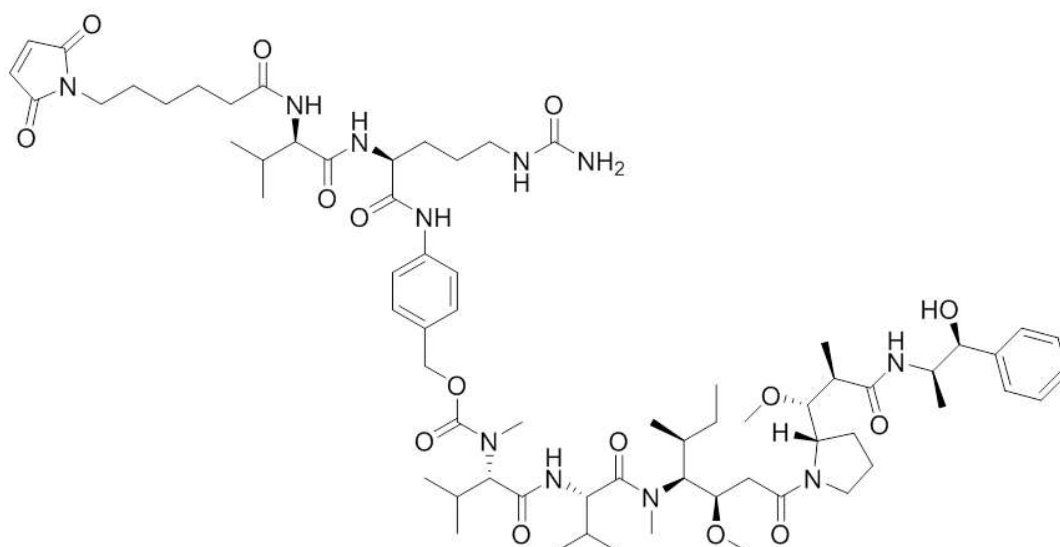


, wherein

the LIV1-ADC is to be administered about once per week.[0013b] In yet another aspect, the present disclosure provides a use of a therapeutically effective dose of a LIV1 antibody-drug conjugate (LIV1-ADC) in the formulation of a medicament for treating a subject having or at risk of having a LIV1-associated cancer

wherein the LIV1-ADC comprises a humanized hLIV22 antibody conjugated to a vcMMAE (valine-citruline-monomethyl auristating E), wherein the hLIV22 antibody comprises a heavy chain variable region comprising the sequence of SEQ ID NO:1 and a light chain variable region comprising the sequence of SEQ ID NO:2,

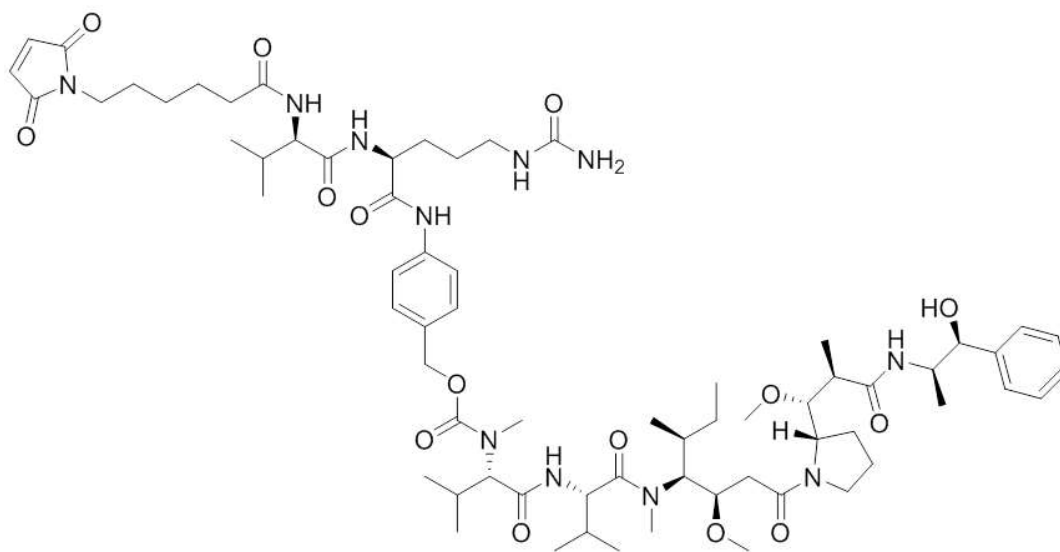
wherein the vcMMAE has the structure



, wherein

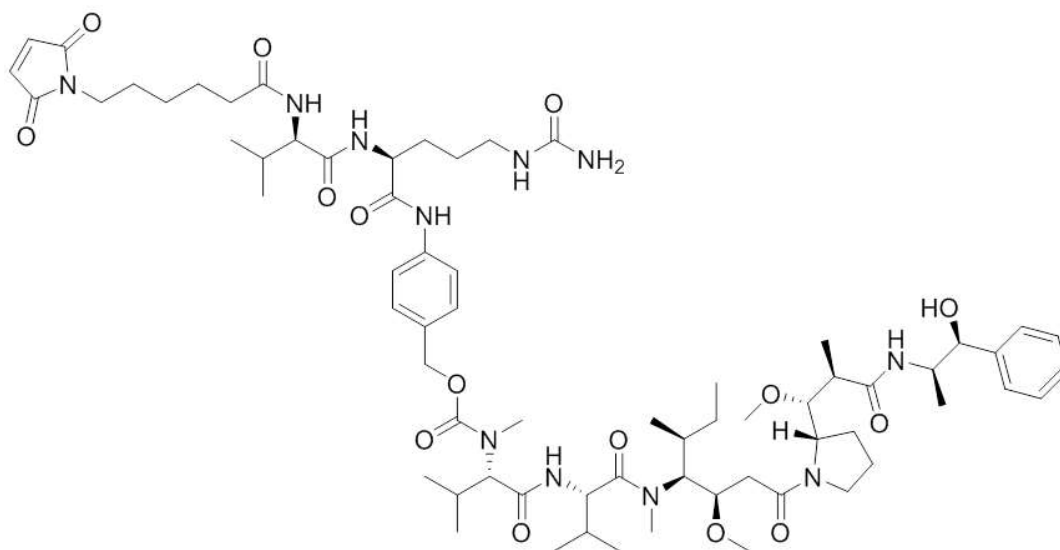
the LIV1-ADC is to be administered twice in a three week treatment cycle.

[0013c] Provided herein are methods of treating a subject having or at risk of having a LIV1-associated cancer, comprising administering to the subject a therapeutically effective dose of a LIV1 antibody-drug conjugate (LIV1-ADC), wherein the LIV1-ADC comprises a humanized hLIV22 antibody conjugated to a vcMMAE (valine-citruline-monomethyl auristating E), wherein the hLIV22 antibody comprises a heavy chain variable region comprising the sequence of SEQ ID NO:1 and a light chain variable region comprising the sequence of SEQ ID NO:2, wherein the vcMMAE has the structure:



wherein the LIV1-ADC is administered about once per week. In some examples, the LIV1-ADC is administered at a dose of about 0.5 mg/kg to about 2 mg/kg of body weight of the subject. In some examples, the LIV1-ADC is administered at a dose of about 0.75 mg/kg to about 1.67 mg/kg of body weight of the subject. In some examples, the LIV1-ADC is administered at a dose of about 0.75 mg/kg of body weight of the subject. In some examples, the LIV1-ADC is administered at a dose of about 1.0 mg/kg of body weight of the subject. In some examples, the LIV1-ADC is administered at a dose of about 1.25 mg/kg of body weight of the subject. In some examples, the LIV1-ADC is administered at a dose of about 1.5 mg/kg of body weight of the subject. In some examples, the LIV1-ADC is administered at a dose of about 1.75 mg/kg of body weight of the subject.

[0014] Also provided herein are methods of treating a subject having or at risk of having a LIV1-associated cancer, comprising administering to the subject a therapeutically effective dose of a LIV1 antibody-drug conjugate (LIV1-ADC), wherein the LIV1-ADC comprises a humanized hLIV22 antibody conjugated to a vcMMAE (valine-citrulline-monomethyl auristatin E), wherein the hLIV22 antibody comprises a heavy chain variable region comprising the sequence of SEQ ID NO:1 and a light chain variable region comprising the sequence of SEQ ID NO:2, wherein the vcMMAE has the structure:



wherein the LIV1-ADC is administered twice in a three week treatment cycle. In some examples, the LIV1-ADC is administered on day 1 and day 8 of the three week treatment cycle. In some examples, the LIV1-ADC is administered is administered at a dose of about 0.5 mg/kg to about 3.0 mg/kg of body weight of the subject. In some examples, the LIV1-ADC is administered is administered at a dose of about 1.0 mg/kg to about 2.5 mg/kg of body weight of the subject. In some examples, the LIV1-ADC is administered is administered at a dose of about 1.25 mg/kg of body weight of the subject. In some examples, the LIV1-ADC is administered is administered at a dose of about 1.5 mg/kg of body weight of the subject. In some examples, the LIV1-ADC is administered is administered at a dose of about 1.75 mg/kg of body weight of the subject. In some examples, the LIV1-ADC is administered is administered at a dose of about 2.0 mg/kg of body weight of the subject. In some examples, the LIV1-ADC is administered is administered at a dose of about 2.5 mg/kg of body weight of the subject.

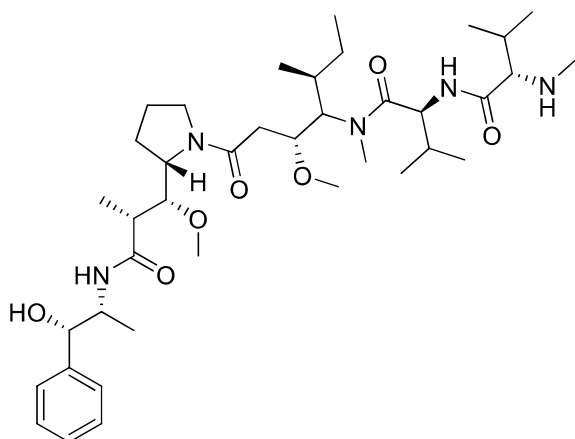
[0015] In some examples, a vcMMAE to hLIV22 ratio is from 1 to 8. In some examples, the average value of the vcMMAE to hLIV22 ratio in a population of the LIV1-ADC is about 4. In some examples, the LIV1-associated cancer is a breast cancer. In some examples, the breast cancer is estrogen receptor positive (ER+) breast cancer. In some examples, the breast cancer is progesterone receptor positive/human epidermal growth factor receptor 2 negative breast (PR+/HER2-) cancer. In some examples, the breast cancer is a triple negative breast cancer. In some examples, the breast cancer is hormone receptor

positive (HR+) breast cancer. In some examples, the breast cancer is HER2 positive breast cancer. In some examples, the breast cancer is HR+/HER2 negative breast cancer. In some examples, the cancer is an advanced stage cancer. In some examples, the advanced stage cancer is a stage 3 or stage 4 cancer. In some examples, the cancer is metastatic cancer. In some examples, the cancer is unresectable. In some examples, the cancer is locally advanced. In some examples, the cancer is recurrent cancer. In some examples, the subject received prior treatment with standard of care therapy for the cancer and failed the prior treatment. In some examples, the subject has been previously treated with one or more therapeutic agents and did not respond to the treatment, wherein the one or more therapeutic agents is not the LIV1-ADC. In some examples, the subject has been previously treated with one or more therapeutic agents and relapsed after the treatment, wherein the one or more therapeutic agents is not the LIV1-ADC. In some examples, the subject has been previously treated with one or more therapeutic agents and has experienced disease progression during treatment, wherein the one or more therapeutic agents is not the LIV1-ADC. In some examples, at least about 0.1%, at least about 1%, at least about 2%, at least about 3%, at least about 4%, at least about 5%, at least about 6%, at least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% of the cancer cells express LIV1. In some examples, one or more therapeutic effects in the subject is improved after administration of the LIV1-ADC relative to a baseline. In some examples, the one or more therapeutic effects is selected from the group consisting of: size of a tumor derived from the cancer, objective response rate, duration of response, time to response, progression free survival, and overall survival. In some examples, the route of administration for the LIV1-ADC is intravenous infusion. In some examples, the LIV1-ADC is administered as a monotherapy. In some examples, the LIV1-ADC is administered in combination with trastuzumab. In some examples, the LIV1-ADC is in a pharmaceutical composition comprising the LIV1-ADC and a pharmaceutically acceptable carrier. In some examples, the subject is a human.

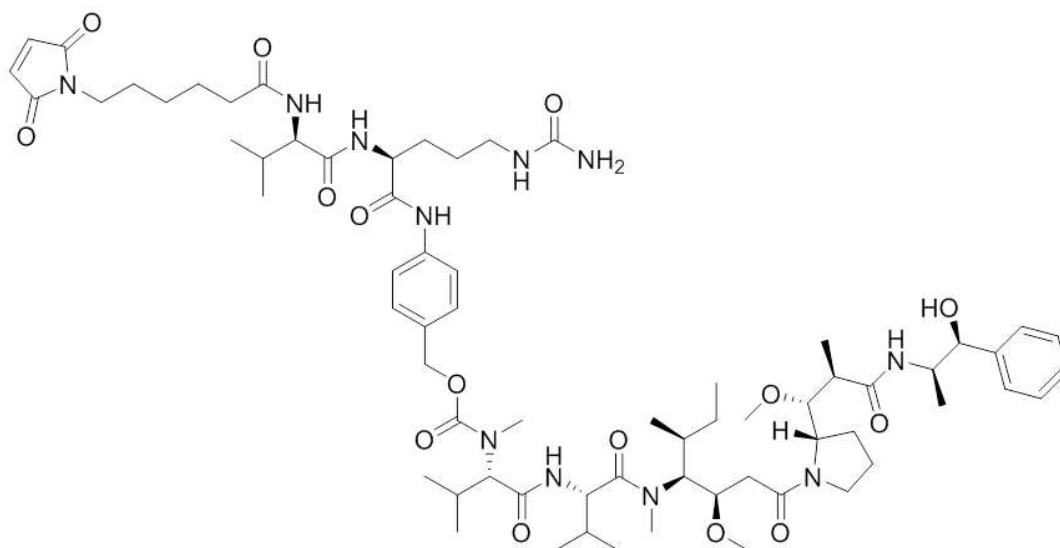
[0016] In another aspect, the present disclosure provides a kit comprising: (a) a dosage ranging from 0.5 mg/kg to 3.0 mg/kg of a LIV1-ADC; and (b) instructions for using the LIV1-ADC according to the use as described herein. Also provided here are kits comprising

(a) a dosage ranging from about 0.5 mg/kg to about 3.0 mg/kg of a LIV1-ADC; and

[0017] Also provided herein are methods of treating a subject having or at risk of having a LIV1-associated cancer, comprising administering to the subject a therapeutically effective dose of an antibody or an antigen-binding fragment thereof that specifically binds human LIV1, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (HCVR) having at least 95% identity to SEQ ID NO:1, and a light chain variable region (LCVR) having at least 95% identity to SEQ ID NO:2, wherein the cancer is a solid tumor. In some examples, the heavy chain variable region of the antibody or antigen-binding fragment thereof comprises the three complementarity determining regions (CDRs) of SEQ ID NO:1 and the light chain variable region of the antibody or antigen-binding fragment thereof comprises the three CDRs of SEQ ID NO:2. In some of the examples herein, the heavy chain variable region comprises the sequence of SEQ ID NO:1 and the light chain variable region comprises the sequence of SEQ ID NO:2. In some of the examples herein, the antibody or antigen-binding fragment thereof is conjugated to monomethyl auristatin E (MMAE):



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In some of the examples herein, the dose is about 2.5 mg/kg of body weight of the subject. In some of the examples herein, the dose administered is less than about 200 mg of the antibody or antigen-binding fragment thereof per treatment cycle. In some of the examples herein, the dose administered is less than about 250 mg of the antibody or antigen-binding fragment thereof per treatment cycle. In some of the examples herein, the treatment cycle is a Q3W treatment cycle. In some of the examples herein, the dose is about 1.0 mg/kg of body weight of the subject. In some of the examples herein, the dose administered is less than about 100 mg of the antibody or antigen-binding fragment thereof per treatment cycle. In some of the examples herein, the dose is about 1.25 mg/kg of body weight of the subject. In some of the examples herein, the dose administered is less than about 125 mg of the antibody or antigen-binding fragment thereof per treatment cycle. In some of the examples herein, the treatment cycle is a Q1W treatment cycle. In some of the examples herein, the subject has been previously treated with one or more therapeutic agents and did not respond to the treatment, wherein the one or more therapeutic agents is not the antibody or antigen-binding fragment thereof. In some of the examples herein, the subject has been previously treated with one or more therapeutic agents and relapsed after the treatment, wherein the one or more therapeutic agents is not the antibody or antigen-binding fragment thereof. In some of the examples herein, the subject has been previously treated with one or more therapeutic agents and has experienced disease progression during treatment, wherein the one or more therapeutic agents is not the antibody or antigen-binding fragment thereof. In some of the examples herein, the

solid tumor is selected from the group consisting of lung cancer, head and neck cancer, esophageal cancer, gastric cancer, and gastroesophageal junction cancer. In some of the examples herein, the solid tumor is lung cancer. In some of the examples herein, the lung cancer is small cell lung cancer. In some of the examples herein, the lung cancer is non-small cell lung cancer. In some of the examples herein, the non-small cell lung cancer is non-squamous cell carcinoma. In some of the examples herein, the non-small cell lung cancer is squamous cell carcinoma. In some of the examples herein, the solid tumor is head and neck cancer. In some of the examples herein, the head and neck cancer is squamous cell carcinoma. In some of the examples herein, the solid tumor is esophageal carcinoma. In some of the examples herein, the esophageal carcinoma is squamous cell carcinoma. In some of the examples herein, the solid tumor is gastric cancer. In some of the examples herein, the gastric cancer is gastric adenocarcinoma. In some of the examples herein, the solid tumor is gastroesophageal junction cancer. In some of the examples herein, the gastroesophageal junction cancer is gastroesophageal junction adenocarcinoma. In some of the examples herein, the cancer is an advanced stage cancer. In some of the examples herein, the advanced stage cancer is a stage 3 or stage 4 cancer. In some of the examples herein, the advanced stage cancer is metastatic cancer. In some of the examples herein, the cancer is recurrent cancer. In some of the examples herein, the cancer is unresectable. In some of the examples herein, the subject received prior treatment with standard of care therapy for the cancer and failed the prior treatment. In some of the examples herein, at least about 0.1%, at least about 1%, at least about 2%, at least about 3%, at least about 4%, at least about 5%, at least about 6%, at least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% of the cancer cells express LIV1. In some of the examples herein, one or more therapeutic effects in the subject is improved after administration of the antibody or antigen-binding fragment thereof relative to a baseline. In some of the examples herein, the one or more therapeutic effects is selected from the group consisting of: size of a tumor derived from the cancer, objective response rate, duration of response, time to response, progression free survival, and overall survival. In some of the examples herein, the route of administration for the antibody or antigen-binding fragment thereof is intravenous infusion. In some of the

examples herein, the antibody or antigen-binding fragment thereof is administered as a monotherapy. In some of the examples herein, the antibody or antigen-binding fragment thereof is administered in combination with a checkpoint inhibitor. In some of the examples herein, the checkpoint inhibitor is an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-CTLA4 antibody, B7-DC-Fc, LAG3, or TIM3. In some of the examples herein, the checkpoint inhibitor is selected from the group consisting of MEDI0680, AMP-224, nivolumab, pembrolizumab, pidilizumab, MEDI4736, MPDL3280A, ipilimumab and tremelimumab. In some of the examples herein, the checkpoint inhibitor is pembrolizumab. In some of the examples herein, the antibody or antigen-binding fragment thereof is in a pharmaceutical composition comprising the antibody or antigen-binding fragment thereof and a pharmaceutically acceptable carrier. In some of the examples herein, the subject is a human.

[0018] In a further aspect, the present disclosure provides a kit comprising: (a) a dosage ranging from 0.5 mg/kg to 2.8 mg/kg of an antibody or antigen-binding fragment thereof that binds LIV1; and (b) instructions for using the antibody or antigen-binding fragment thereof according to the use as described herein. Also provided herein are kits comprising:

(a) a dosage ranging from about 0.5 mg/kg to about 2.8 mg/kg of an antibody or antigen-binding fragment thereof that binds LIV1; and

(b) instructions for using the antibody or antigen-binding fragment thereof according to some of the methods provided herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

[0020] FIG.1 is a schematic displaying the dose finding (upper panel) and expansion (lower panel) protocol, where 1.25 mg/kg on a D1,8-Q3wk schedule was selected as the starting dose level. The total exposure per cycle (mg/kg/cycle) and the approximate relative exposure (x AUC) compared to the starting dose are also displayed.

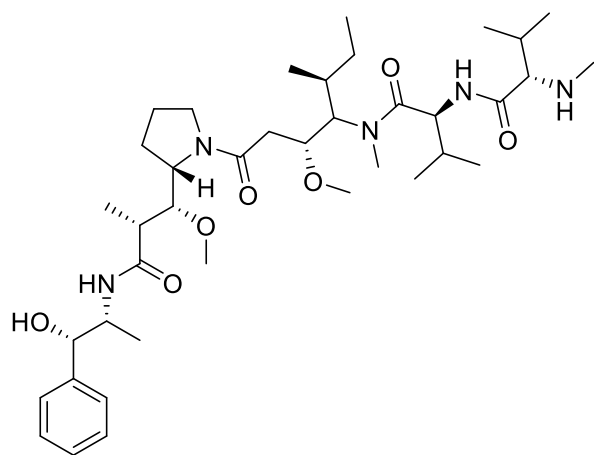
[0021] FIG. 2 is a table displaying total dose and relative exposure (relative AUC) under a weekly dosing schedule (Q1W) or a D1,8-Q3W dosing schedule at different dose levels.

[0022] FIG. 3A is a scatter plot showing the change of drug-antibody ratio (DAR) in blood ADC for subjects over 7 days after LV administration in Q3W dosing. FIG. 3B-C are graphs

CLAIMS

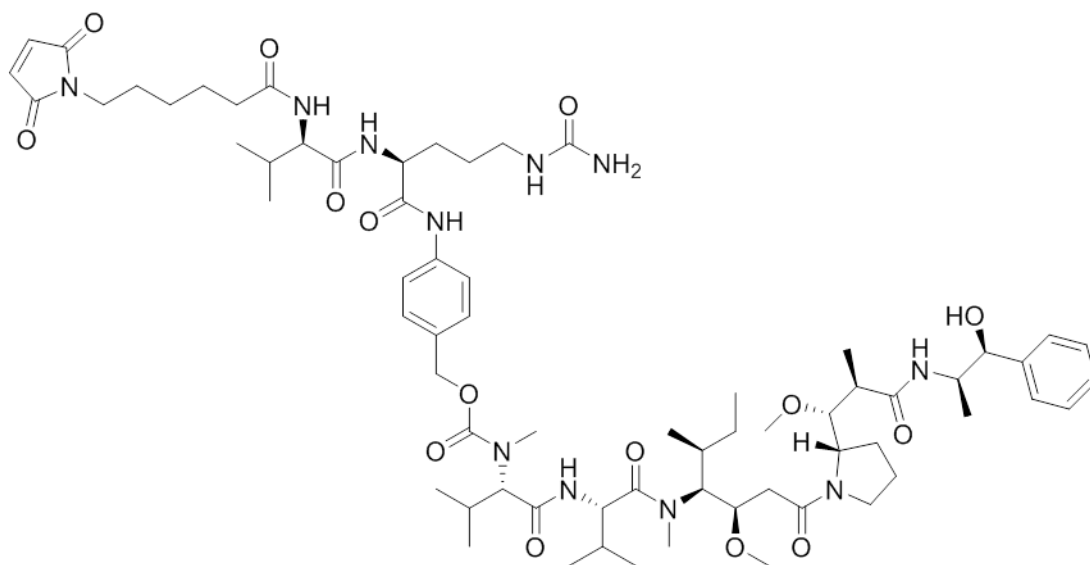
What is claimed:

1. Use of a therapeutically effective dose of an antibody or an antigen-binding fragment thereof that specifically binds human LIV1 in the formulation of a medicament for treating a subject having or at risk of having a LIV1-associated cancer,
wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (HCVR) having at least 95% identity to SEQ ID NO:1, and a light chain variable region (LCVR) having at least 95% identity to SEQ ID NO:2,
wherein the cancer is a solid tumor.
2. The use of claim 1, wherein the heavy chain variable region of the antibody or antigen-binding fragment thereof comprises the three complementarity determining regions (CDRs) of SEQ ID NO:1 and the light chain variable region of the antibody or antigen-binding fragment thereof comprises the three CDRs of SEQ ID NO:2.
3. The use of claim 1 or claim 2, wherein:
 - (a) the heavy chain variable region has at least 98% identity to SEQ ID NO:1 and the light chain variable region has at least 98% identity to SEQ ID NO:2; or
 - (b) the heavy chain variable region has at least 99% identity to SEQ ID NO:1 and the light chain variable region has at least 99% identity to SEQ ID NO:2; or
 - (c) the heavy chain variable region comprises the sequence of SEQ ID NO:1 and the light chain variable region comprises the sequence of SEQ ID NO:2.
4. The use of any one of claims 1-3, wherein the antibody or antigen-binding fragment thereof is conjugated to monomethyl auristatin E (MMAE):



MMAE.

5. The use of any one of claims 1-4, wherein the antibody or antigen-binding fragment thereof is conjugated to valine-citrulline-monomethyl auristatin E (vcMMAE):



vcMMAE.

6. The use of claim 5, wherein a vcMMAE to antibody or antigen-binding fragment thereof ratio is from 1 to 8.

7. The use of claim 6, wherein the vcMMAE to antibody or antigen-binding fragment thereof ratio is 4.

8. The use of any one of claims 1-7, wherein:

(a) the dose is about 2.5 mg/kg of body weight of the subject; and/or

(b) the dose is less than 200 mg of the antibody or antigen-binding fragment thereof per treatment cycle or the dose is less than 250 mg of the antibody or antigen-binding fragment thereof per treatment cycle; and/or

(c) the treatment cycle is a Q3W treatment cycle.

9. The use of any one of claims 1-7, wherein:

(a) the dose is about 1.0 mg/kg or about 1.25 mg/kg of body weight of the subject; and/or

(b) the treatment cycle is a Q1W treatment cycle.

10. The use of claim 9, wherein:

(a) the dose is about 1.0 mg/kg of body weight of the subject and wherein the dose is less than 100 mg of the antibody or antigen-binding fragment thereof per treatment cycle; or

(b) the dose is about 1.25 mg/kg of body weight of the subject and wherein the dose is less than 125 mg of the antibody or antigen-binding fragment thereof per treatment cycle.

11. The use of any one of claims 1-10, wherein:

(a) the subject has been previously treated with one or more therapeutic agents and did not respond to the treatment, wherein the one or more therapeutic agents is not the antibody or antigen-binding fragment thereof; or

(b) the subject has been previously treated with one or more therapeutic agents and relapsed after the treatment, wherein the one or more therapeutic agents is not the antibody or antigen-binding fragment thereof; or

(c) the subject has been previously treated with one or more therapeutic agents and has experienced disease progression during treatment, wherein the one or more therapeutic agents is not the antibody or antigen-binding fragment thereof.

12. The use of any one of claims 1-11, wherein the solid tumor is selected from the group consisting of lung cancer, head and neck cancer, esophageal cancer, gastric cancer, and gastroesophageal junction cancer.

13. The use of claim 12, wherein the solid tumor is lung cancer, wherein the lung cancer is small cell lung cancer or non-small cell lung cancer, wherein the lung cancer is small cell lung cancer.

14. The use of claim 13, wherein the lung cancer is small cell lung cancer, wherein the subject has received prior systemic therapy for the small cell lung cancer.

15. The use of claim 14, wherein:

- (a) the subject experienced disease progression on or after the prior systemic therapy for the small cell lung cancer; and/or
- (b) the subject received prior therapy with a cytotoxic chemotherapy; and/or
- (c) the subject received prior therapy with an inhibitor of PD-1 or PD-L1; and/or
- (d) the subject received 1 line of systemic therapy for the small cell lung cancer.

16. The use of claim 12, wherein the lung cancer is non-small cell lung cancer, wherein:

- (a) the non-small cell lung cancer is squamous cell carcinoma and/or the non-small cell lung cancer has predominant squamous histology; or
- (b) the non-small cell lung cancer is non-squamous cell carcinoma.

17. The use of claim 16, wherein the non-small cell lung cancer has predominant squamous histology, and wherein greater than 85% of the non-small cell lung cancer cells have squamous histology.

18. The use of claim 16, wherein the non-small cell lung cancer is non-squamous cell carcinoma, wherein the subject received prior systemic therapy for the non-small cell lung cancer.

19. The use of claim 28, wherein:

- (a) the subject experienced disease progression on or after the prior systemic therapy for the non-small cell lung cancer; and/or
- (b) the subject received prior therapy with a cytotoxic chemotherapy; and/or
- (c) the subject received prior therapy with a platinum-based therapy or platinum-based combination therapy; and/or

- (d) the subject received prior therapy with an inhibitor of PD-1 or PD-L1; and/or
- (e) the subject received 1 line of prior systemic therapy for the non-small cell lung cancer.

20. The use of claim 12, wherein the solid tumor is head and neck cancer, wherein:

- (a) the head and neck cancer is squamous cell carcinoma; and/or
- (b) the subject received prior systemic therapy for the head and neck cancer.

21. The use of claim 20, wherein the subject received prior systemic therapy for the head and neck cancer, wherein:

- (a) the subject experienced disease progression on or after the prior systemic therapy for the head and neck cancer; and/or
- (b) the subject received prior therapy with a cytotoxic chemotherapy; and/or
- (c) the subject received prior therapy with a platinum-based therapy or platinum-based combination therapy; and/or
- (d) the subject received prior therapy with an inhibitor of PD-1 or PD-L1; and/or
- (e) the subject received 1 line of prior systemic therapy for the head and neck cancer.

22. The use of claim 12, wherein the solid tumor is esophageal carcinoma, wherein:

- (a) the esophageal carcinoma is squamous cell carcinoma; and/or
- (b) the esophageal carcinoma has predominant squamous histology; and/or
- (c) greater than 85% of the esophageal cells have squamous histology; and/or
- (d) the subject received prior systemic therapy for the esophageal cancer.

23. The use of claim 22, wherein the subject received prior systemic therapy for the esophageal cancer, wherein:

- (a) the subject experienced disease progression on or after the prior systemic therapy for the esophageal cancer; and/or
- (b) the subject received prior therapy with a cytotoxic chemotherapy; and/or
- (c) the subject received 1 line of prior systemic therapy for the esophageal cancer.

24. The use of claim 12, wherein the solid tumor is gastric cancer, wherein:

- (a) the gastric cancer is gastric adenocarcinoma; and/or
- (b) the subject received prior systemic therapy for the gastric cancer.

25. The use of claim 24, wherein the subject received prior systemic therapy for the gastric cancer, wherein:

- (a) the subject experienced disease progression on or after the prior systemic therapy for the gastric cancer; and/or
- (b) the subject received prior therapy with a cytotoxic chemotherapy; and/or
- (c) the subject received prior therapy with a platinum-based therapy or platinum-based combination therapy; and/or
- (d) the subject overexpresses human epidermal growth factor receptor 2 (HER2); and/or
- (e) the subject received 1 line of prior systemic therapy for the gastric cancer.

26. The use of claim 25, wherein the subject overexpresses HER2, and wherein the subject received prior HER2-targeted therapy.

27. The use of claim 12, wherein the solid tumor is gastroesophageal junction cancer, wherein:

- (a) the gastroesophageal junction cancer is gastroesophageal junction adenocarcinoma; and/or
- (b) the subject received prior systemic therapy for the gastroesophageal junction cancer.

28. The use of claim 27, wherein the subject received prior systemic therapy for the gastroesophageal junction cancer, wherein:

- (a) the subject experienced disease progression on or after the prior systemic therapy for the gastroesophageal junction cancer; and/or
- (b) the subject received prior therapy with a cytotoxic chemotherapy; and/or
- (c) the subject received prior therapy with a platinum-based therapy or platinum-based combination therapy; and/or
- (d) the subject overexpresses human epidermal growth factor receptor 2 (HER2); and/or
- (e) the subject received 1 line of prior systemic therapy for the gastroesophageal junction cancer.

29. The use of claim 28, wherein the subject overexpresses HER2, and wherein the subject received prior HER2-targeted therapy.

30. The use of any one of claims 1-29, wherein:

- (a) the cancer is an advanced stage cancer; and/or
- (b) the cancer is recurrent cancer; and/or
- (c) the cancer is unresectable; and/or
- (d) the subject received prior treatment with standard of care therapy for the cancer and failed the prior treatment; and/or
- (e) at least 0.1%, at least 1%, at least 2%, at least 3%, at least 4%, at least 5%, at least 6%, at least 7%, at least 8%, at least 9%, at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 60%, at least 70%, or at least 80% of the cancer cells express LIV1; and/or
- (f) the subject is a human.

31. The use of claim 30, wherein the cancer is an advanced stage cancer, wherein:

- (a) the advanced stage cancer is a stage 3 or stage 4 cancer; and/or;
- (b) the advanced stage cancer is metastatic cancer.

32. The use of any one of claims 11-31, wherein:

- (a) one or more therapeutic effects in the subject is improved after administration of the antibody or antigen-binding fragment thereof relative to a baseline, optionally, wherein the one or more therapeutic effects in the subject is selected from the group consisting of: size of a tumor derived from the cancer, objective response rate, duration of response, time to response, progression free survival, and overall survival; and/or
- (b) the size of a tumor derived from the cancer is reduced by at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 60%, at least 70%, or at least 80% relative to the size of the tumor derived from the cancer before administration of the antibody or antigen-binding fragment thereof; and/or
- (c) the objective response rate is at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 60%, at least 70%, or at least 80%; and/or

- (d) the subject exhibits progression-free survival of at least 1 month, at least 2 months, at least 3 months, at least 4 months, at least 5 months, at least 6 months, at least 7 months, at least 8 months, at least 9 months, at least 10 months, at least 11 months, at least 12 months, at least eighteen months, at least two years, at least three years, at least four years, or at least five years after administration of the antibody or antigen-binding fragment thereof; and/or
- (e) the subject exhibits overall survival of at least 1 month, at least 2 months, at least 3 months, at least 4 months, at least 5 months, at least 6 months, at least 7 months, at least 8 months, at least 9 months, at least 10 months, at least 11 months, at least 12 months, at least eighteen months, at least two years, at least three years, at least four years, or at least five years after administration of the antibody or antigen-binding fragment thereof; and/or
- (f) the duration of response to the antibody-drug conjugate is at least 1 month, at least 2 months, at least 3 months, at least 4 months, at least 5 months, at least 6 months, at least 7 months, at least 8 months, at least 9 months, at least 10 months, at least 11 months, at least 12 months, at least eighteen months, at least two years, at least three years, at least four years, or at least five years after administration of the antibody or antigen-binding fragment thereof.

33. The use of any one of claims 1-32, wherein:

- (a) the subject has one or more adverse events and is to be further administered an additional therapeutic agent to eliminate or reduce the severity of the one or more adverse events; and/or
- (b) the subject is at risk of developing one or more adverse events and is to be further administered an additional therapeutic agent to prevent or reduce the severity of the one or more adverse events; and/or
- (c) the subject is at risk of developing one or more adverse events and the one or more adverse events is a grade 3 or greater adverse event; and/or
- (d) the subject is at risk of developing one or more adverse events and the one or more adverse events is a serious adverse event.

34. The use of any one of claims 1-33, wherein:

- (a) the route of administration for the antibody or antigen-binding fragment thereof is intravenous infusion; and/or

(b) the antibody or antigen-binding fragment thereof is to be administered as a monotherapy or the antibody or antigen-binding fragment thereof is to be administered in combination with a checkpoint inhibitor; and/or

(c) the antibody or antigen-binding fragment thereof is in a pharmaceutical composition comprising the antibody or antigen-binding fragment thereof and a pharmaceutically acceptable carrier.

35. The use of claim 34, wherein the antibody or antigen-binding fragment thereof is to be administered in combination with a checkpoint inhibitor, wherein the checkpoint inhibitor is an anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-CTLA4 antibody, B7-DC-Fc, LAG3, or TIM3.

36. The use of claim 35, wherein the checkpoint inhibitor is selected from the group consisting of MEDI0680, AMP-224, nivolumab, pembrolizumab, pidilizumab, MEDI4736, MPDL3280A, ipilimumab and tremelimumab.

37. The use of claim 36, wherein the checkpoint inhibitor is pembrolizumab.

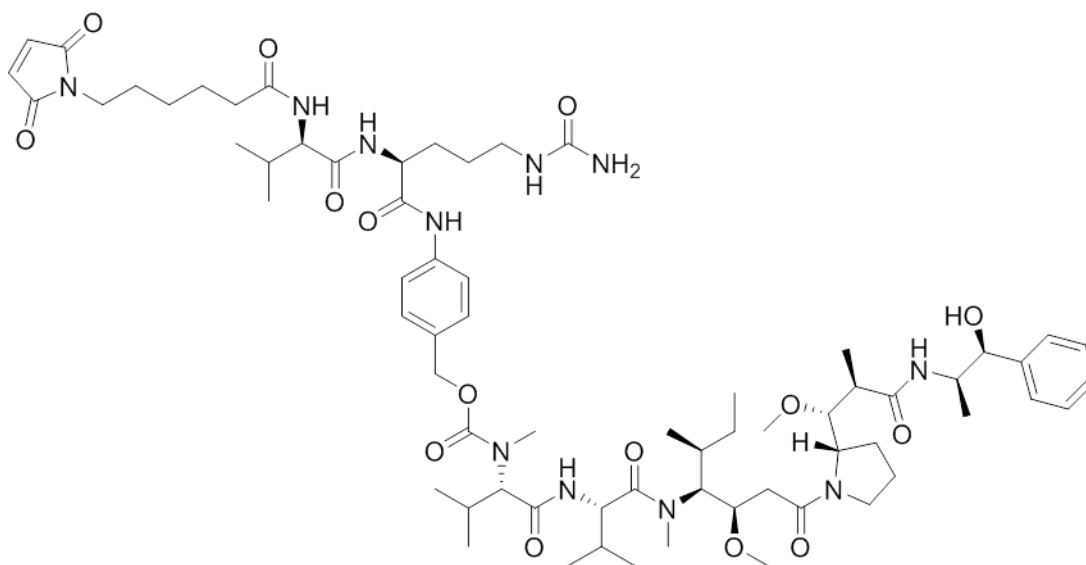
38. A kit comprising:

- (a) a dosage ranging from 0.5 mg/kg to 2.8 mg/kg of an antibody or antigen-binding fragment thereof that binds LIV1; and
- (b) instructions for using the antibody or antigen-binding fragment thereof according to the use of any one of claims 1-37.

39. Use of a therapeutically effective dose of a LIV1 antibody-drug conjugate (LIV1-ADC) in the formulation of a medicament for treating a subject having or at risk of having a LIV1-associated cancer,

wherein the LIV1-ADC comprises a humanized hLIV22 antibody conjugated to a vcMMAE (valine-citruline-monomethyl auristating E), wherein the hLIV22 antibody comprises a heavy chain variable region comprising the sequence of SEQ ID NO:1 and a light chain variable region comprising the sequence of SEQ ID NO:2,

wherein the vcMMAE has the structure:



wherein the LIV1-ADC is to be administered about once per week.

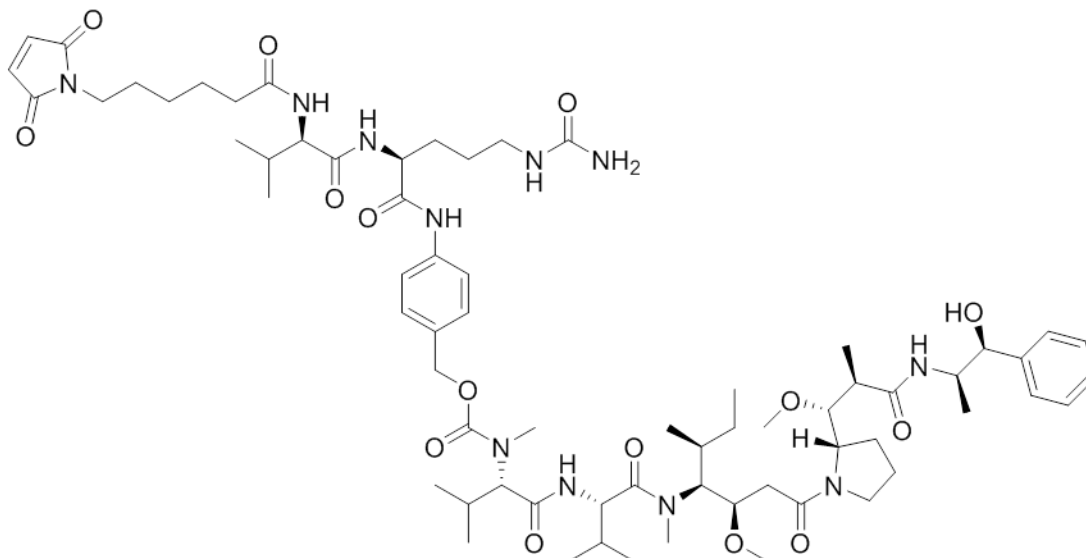
40. The use of claim 39, wherein the LIV1-ADC is to be administered at:
a dose of 0.5 mg/kg to 2 mg/kg of body weight of the subject, or a dose of 0.75 mg/kg to 1.67 mg/kg of body weight of the subject.

41. The use of claim 39, wherein the LIV1-ADC is to be administered at a dose of about any one of 0.75 mg/kg, 1.0 mg/kg, 1.25 mg/kg, 1.5 mg/kg or 1.75 mg/kg of body weight of the subject.

42. Use of a therapeutically effective dose of a LIV1 antibody-drug conjugate (LIV1-ADC) in the formulation of a medicament for treating a subject having or at risk of having a LIV1-associated cancer

wherein the LIV1-ADC comprises a humanized hLIV22 antibody conjugated to a vcMMAE (valine-citruline-monomethyl auristating E), wherein the hLIV22 antibody comprises a heavy chain variable region comprising the sequence of SEQ ID NO:1 and a light chain variable region comprising the sequence of SEQ ID NO:2,

wherein the vcMMAE has the structure:



wherein the LIV1-ADC is to be administered twice in a three week treatment cycle.

43. The use of claim 42, wherein:

(a) the LIV1-ADC is to be administered on day 1 and day 8 of the three week treatment cycle; and/or

(b) the LIV1-ADC is to be administered at a dose of 0.5 mg/kg to 3.0 mg/kg, or 1.0 mg/kg to 2.5 mg/kg of body weight of the subject.

44. The use of claim 42 or 43, wherein the LIV1-ADC is to be administered at a dose of about any one of 1.25 mg/kg, 1.5 mg/kg, 1.75 mg/kg, 2.0 mg/kg, 2.25 mg/kg, or 2.5 mg/kg.

45. The use of any one of claims 39-44, wherein a vcMMAE to hLIV22 ratio is from 1 to 8.

46. The use of claim 45, wherein the average value of the vcMMAE to hLIV22 ratio in a population of the LIV1-ADC is 4.

47. The use of any one of claims 39-46, wherein:

(a) the LIV1-associated cancer is a breast cancer; and/or

(b) the cancer is an advanced stage cancer; and/or

- (c) the cancer is metastatic cancer; and/or
- (d) the cancer is unresectable; and/or
- (e) the cancer is locally advanced; and/or
- (f) the cancer is recurrent cancer; and/or
- (g) the subject received prior treatment with standard of care therapy for the cancer and failed the prior treatment; and/or
- (h) the subject has been previously treated with one or more therapeutic agents and did not respond to the treatment, wherein the one or more therapeutic agents is not the LIV1-ADC; and/or
- (i) the subject has been previously treated with one or more therapeutic agents and relapsed after the treatment, wherein the one or more therapeutic agents is not the LIV1-ADC; and/or
- (j) the subject has been previously treated with one or more therapeutic agents and has experienced disease progression during treatment, wherein the one or more therapeutic agents is not the LIV1-ADC; and/or
- (k) at least 0.1%, at least 1%, at least 2%, at least 3%, at least 4%, at least 5%, at least 6%, at least 7%, at least 8%, at least 9%, at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 60%, at least 70%, or at least 80% of the cancer cells express LIV1; and/or
- (l) the subject is a human.

48. The use of claim 47, wherein the LIV1-associated cancer is a breast cancer, wherein:

- (a) the breast cancer is estrogen receptor positive (ER+) breast cancer; or
- (b) the breast cancer is a triple negative breast cancer; or
- (c) the breast cancer is hormone receptor positive (HR+) breast cancer; or
- (d) the breast cancer is HER2 positive breast cancer; or
- (e) the breast cancer is HR+/HER2 negative breast cancer.

49. The use of claim 47 or 48, wherein the breast cancer is ER+ breast cancer, wherein:

- (a) the breast cancer is progesterone receptor positive/human epidermal growth factor receptor 2 negative breast (PR+/HER2-) cancer; and/or
- (b) the subject is not a candidate for hormonal therapy.

50. The use of claim 48, wherein:

- (a) the breast cancer is a triple negative breast cancer, wherein the subject received one non-hormonally-directed prior therapy or the subject received one prior cytotoxic regimen; or
- (b) the subject received two or more prior cytotoxic regimens.

51. The use of claim 48, wherein the breast cancer is HR+/HER2 negative breast cancer, wherein:

- (a) the subject is eligible for chemotherapy; and/or
- (b) the subject is not a candidate for hormonal therapy.

52. The use of any one of claims 47-51, wherein the cancer is an advanced stage cancer, wherein the advanced stage cancer is a stage 3 or stage 4 cancer.

53. The use of any one of claims 39-52, wherein:

- (a) one or more therapeutic effects in the subject is improved after administration of the LIV1-ADC relative to a baseline, optionally, wherein the one or more therapeutic effects is selected from the group consisting of: size of a tumor derived from the cancer, objective response rate, duration of response, time to response, progression free survival, and overall survival; and/or
- (b) the size of a tumor derived from the cancer is reduced by at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 60%, at least 70%, or at least 80% relative to the size of the tumor derived from the cancer before administration of the LIV1-ADC; and/or
- (c) the objective response rate is at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 60%, at least 70%, or at least 80%; and/or
- (d) the subject exhibits progression-free survival of at least 1 month, at least 2 months, at least 3 months, at least 4 months, at least 5 months, at least 6 months, at least 7 months, at least 8 months, at least 9 months, at least 10 months, at least 11 months, at least 12 months, at least eighteen months, at least two years, at least three years, at least four years, or at least five years after administration of the LIV1-ADC; and/or
- (e) the subject exhibits overall survival of at least 1 month, at least 2 months, at least 3 months, at least 4 months, at least 5 months, at least 6 months, at least 7 months, at least 8 months, at least 9

months, at least 10 months, at least 11 months, at least 12 months, at least eighteen months, at least two years, at least three years, at least four years, or at least five years after administration of the LIV1-ADC; and/or

(f) the duration of response to the antibody-drug conjugate is at least 1 month, at least 2 months, at least 3 months, at least 4 months, at least 5 months, at least 6 months, at least 7 months, at least 8 months, at least 9 months, at least 10 months, at least 11 months, at least 12 months, at least eighteen months, at least two years, at least three years, at least four years, or at least five years after administration of the LIV1-ADC.

54. The use of claim any one of claims 39-53, wherein:

(a) the subject has one or more adverse events and is to be further administered an additional therapeutic agent to eliminate or reduce the severity of the one or more adverse events; and/or

(b) the subject is at risk of developing one or more adverse events and is to be further administered an additional therapeutic agent to prevent or reduce the severity of the one or more adverse events; and/or

(c) the subject is at risk of developing one or more adverse events and the one or more adverse events is a grade 3 or greater adverse event; and/or

(d) the subject is at risk of developing one or more adverse events and the one or more adverse events is a serious adverse event.

55. The use of any one of claims 39-54, wherein:

(a) the route of administration for the LIV1-ADC is intravenous infusion; and/or

(b) the LIV1-ADC is to be administered as a monotherapy, or the LIV1-ADC is to be administered in combination with trastuzumab; and/or

(c) the LIV1-ADC is in a pharmaceutical composition comprising the LIV1-ADC and a pharmaceutically acceptable carrier.

56. A kit comprising:

(a) a dosage ranging from 0.5 mg/kg to 3.0 mg/kg of a LIV1-ADC; and

(b) instructions for using the LIV1-ADC according to the use of any one of claims 39-55.