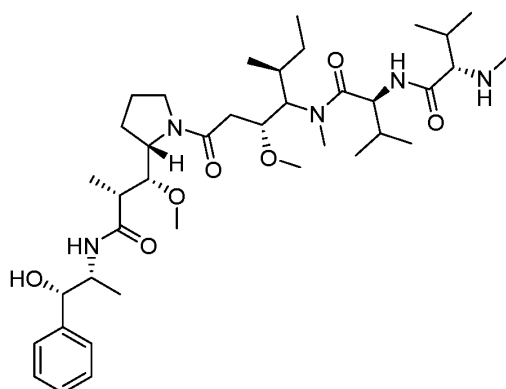


## CLAIMS

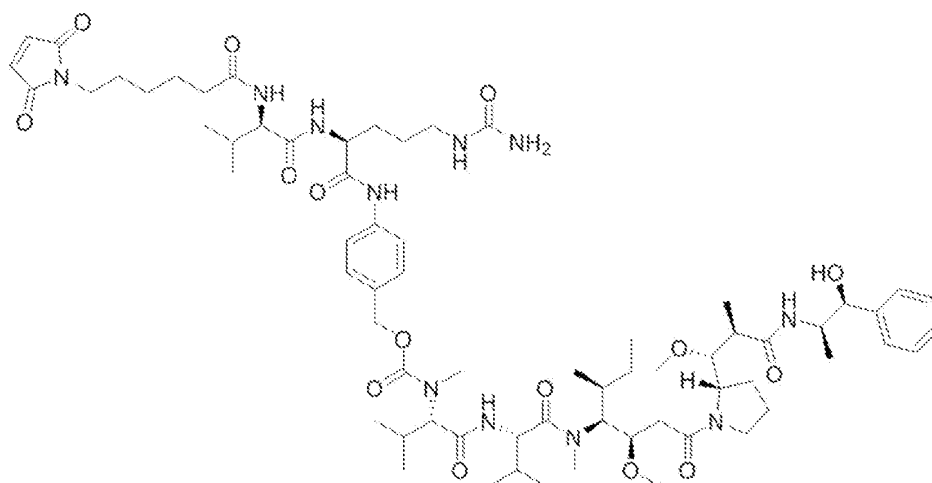
What is claimed:

1. A method 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.
2. The method 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 method of claim 1 or claim 2, wherein 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.
4. The method of claim 1 or claim 2, wherein 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.
5. The method of claim 1, wherein 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.
6. The method of any one of claims 1-5, wherein the antibody or antigen-binding fragment thereof is conjugated to monomethyl auristatin E (MMAE):



MMAE.

7. The method of any one of claims 1-6, wherein the antibody or antigen-binding fragment thereof is conjugated to valine-citrulline-monomethyl auristatin E (vcMMAE):



vcMMAE.

8. The method of claim 7, wherein a vcMMAE to antibody or antigen-binding fragment thereof ratio is from about 1 to about 8.

9. The method of claim 8, wherein the vcMMAE to antibody or antigen-binding fragment thereof ratio is about 4.

10. The method of any one of claims 1-9, wherein the dose is about 2.5 mg/kg of body weight of the subject.
11. The method of any one of claims 1-10, wherein the dose administered is less than about 200 mg of the antibody or antigen-binding fragment thereof per treatment cycle.
12. The method of any one of claims 1-10, wherein the dose administered is less than about 250 mg of the antibody or antigen-binding fragment thereof per treatment cycle.
13. The method of any one of claims 1-12, wherein the treatment cycle is a Q3W treatment cycle.
14. The method of any one of claims 1-9, wherein the dose is about 1.0 mg/kg of body weight of the subject.
15. The method of claim 14, wherein the dose administered is less than about 100 mg of the antibody or antigen-binding fragment thereof per treatment cycle.
16. The method of any one of claims 1-9, wherein the dose is about 1.25 mg/kg of body weight of the subject.
17. The method of claim 16, wherein the dose administered is less than about 125 mg of the antibody or antigen-binding fragment thereof per treatment cycle.
18. The method of any one of claims 14-17, wherein the treatment cycle is a Q1W treatment cycle.
19. The method of any one of claims 1-18, wherein 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.

20. The method of any one of claims 1-18, wherein 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.
21. The method of any one of claims 1-18, wherein 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.
22. The method of any one of claims 1-21, 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.
23. The method of claim 22, wherein the solid tumor is lung cancer.
24. The method of claim 23, wherein the lung cancer is small cell lung cancer.
25. The method of claim 24, wherein the subject has received prior systemic therapy for the small cell lung cancer.
26. The method of claim 25, wherein the subject experienced disease progression on or after the prior systemic therapy for the small cell lung cancer.
27. The method of claim 25 or 26, wherein the subject received prior therapy with a cytotoxic chemotherapy.
28. The method of any one of claims 25-27, wherein the subject received prior therapy with an inhibitor of PD-1 or PD-L1.
29. The method of any one of claims 25-28, wherein the subject received 1 line of systemic therapy for the small cell lung cancer.

30. The method of claim 23, wherein the lung cancer is non-small cell lung cancer.
31. The method of claim 30, wherein the non-small cell lung cancer is squamous cell carcinoma.
32. The method of claim 30 or 31, wherein the non-small cell lung cancer has predominant squamous histology.
33. The method of claim 32, wherein greater than 85% of the non-small cell lung cancer cells have squamous histology.
34. The method of claim 30, wherein the non-small cell lung cancer is non-squamous cell carcinoma.
35. The method of claim 34, wherein the subject received prior systemic therapy for the non-small cell lung cancer.
36. The method of claim 35, wherein the subject experienced disease progression on or after the prior systemic therapy for the non-small cell lung cancer.
37. The method of claim 35 or claim 36, wherein the subject received prior therapy with a cytotoxic chemotherapy.
38. The method of any one of claims 35-37, wherein the subject received prior therapy with a platinum-based therapy or platinum-based combination therapy.
39. The method of any one of claims 35-38, wherein the subject received prior therapy with an inhibitor of PD-1 or PD-L1.
40. The method of any one of claims 35-39, wherein the subject received 1 line of prior systemic therapy for the non-small cell lung cancer.

41. The method of claim 22, wherein the solid tumor is head and neck cancer.
42. The method of claim 41, wherein the head and neck cancer is squamous cell carcinoma.
43. The method of claim 41 or 42, wherein the subject received prior systemic therapy for the head and neck cancer.
44. The method of claim 43, wherein the subject experienced disease progression on or after the prior systemic therapy for the head and neck cancer.
45. The method of claim 43 or claim 44, wherein the subject received prior therapy with a cytotoxic chemotherapy.
46. The method of any one of claims 43-45 wherein the subject received prior therapy with a platinum-based therapy or platinum-based combination therapy.
47. The method of any one of claims 43-46, wherein the subject received prior therapy with an inhibitor of PD-1 or PD-L1.
48. The method of any one of claims 43-47, wherein the subject received 1 line of prior systemic therapy for the head and neck cancer.
49. The method of claim 22, wherein the solid tumor is esophageal carcinoma.
50. The method of claim 49, wherein the esophageal carcinoma is squamous cell carcinoma.
51. The method of claim 49 or claim 50, wherein the esophageal carcinoma has predominant squamous histology.

52. The method of claim 51, wherein greater than 85% of the esophageal cells have squamous histology.
53. The method of claim 49-52, wherein the subject received prior systemic therapy for the esophageal cancer.
54. The method of claim 53, wherein the subject experienced disease progression on or after the prior systemic therapy for the esophageal cancer.
55. The method of claim 53 or claim 54, wherein the subject received prior therapy with a cytotoxic chemotherapy.
56. The method of any one of claims 53-55, wherein the subject received 1 line of prior systemic therapy for the esophageal cancer.
57. The method of claim 22, wherein the solid tumor is gastric cancer.
58. The method of claim 57, wherein the gastric cancer is gastric adenocarcinoma.
59. The method of claim 57 or claim 58, wherein the subject received prior systemic therapy for the gastric cancer.
60. The method of claim 59, wherein the subject experienced disease progression on or after the prior systemic therapy for the gastric cancer.
61. The method of claim 59 or claim 60, wherein the subject received prior therapy with a cytotoxic chemotherapy.
62. The method of any one of claims 59-61, wherein the subject received prior therapy with a platinum-based therapy or platinum-based combination therapy.

63. The method of any one of claims 59-62, wherein the subject overexpresses human epidermal growth factor receptor 2 (HER2).
64. The method of claim 63, wherein the subject received prior HER2-targeted therapy.
65. The method of any one of claims 59-64, wherein the subject received 1 line of prior systemic therapy for the gastric cancer.
66. The method of claim 22, wherein the solid tumor is gastroesophageal junction cancer.
67. The method of claim 66, wherein the gastroesophageal junction cancer is gastroesophageal junction adenocarcinoma.
68. The method of claim 66 or claim 67, wherein the subject received prior systemic therapy for the gastroesophageal junction cancer.
69. The method of claim 68, wherein the subject experienced disease progression on or after the prior systemic therapy for the gastroesophageal junction cancer.
70. The method of claim 68 or claim 69, wherein the subject received prior therapy with a cytotoxic chemotherapy.
71. The method of any one of claims 68-70, wherein the subject received prior therapy with a platinum-based therapy or platinum-based combination therapy.
72. The method of any one of claims 68-71, wherein the subject overexpresses human epidermal growth factor receptor 2 (HER2).
73. The method of claim 72, wherein the subject received prior HER2-targeted therapy.

74. The method of any one of claims 68-73, wherein the subject received 1 line of prior systemic therapy for the gastroesophageal junction cancer.

75. The method of any one of claims 1-74, wherein the cancer is an advanced stage cancer.

76. The method of claim 75, wherein the advanced stage cancer is a stage 3 or stage 4 cancer.

77. The method of claim 75 or 76, wherein the advanced stage cancer is metastatic cancer.

78. The method of any one of claims 1-77, wherein the cancer is recurrent cancer.

79. The method of any one of claims 1-78, wherein the cancer is unresectable.

80. The method of any one of claims 1-79, wherein the subject received prior treatment with standard of care therapy for the cancer and failed the prior treatment.

81. The method of any one of claims 1-80, wherein 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.

82. The method of any one of claims 1-81, wherein one or more therapeutic effects in the subject is improved after administration of the antibody or antigen-binding fragment thereof relative to a baseline.

83. The method of claim 82, 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.

84. The method of any one of claims 1-83, wherein the size of a tumor derived from the cancer is reduced by 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% relative to the size of the tumor derived from the cancer before administration of the antibody or antigen-binding fragment thereof.

85. The method of any one of claims 1-84, wherein the objective response rate is 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%.

86. The method of any one of claims 1-85, wherein the subject exhibits progression-free survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the antibody or antigen-binding fragment thereof.

87. The method of any one of claims 1-86, wherein the subject exhibits overall survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the antibody or antigen-binding fragment thereof.

88. The method of any one of claims 1-87, wherein the duration of response to the antibody-drug conjugate is at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at

least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the antibody or antigen-binding fragment thereof.

89. The method of any one of claims 1-88, wherein the subject has one or more adverse events and is further administered an additional therapeutic agent to eliminate or reduce the severity of the one or more adverse events.

90. The method of any one of claims 1-89, wherein the subject is at risk of developing one or more adverse events and is further administered an additional therapeutic agent to prevent or reduce the severity of the one or more adverse events.

91. The method of claim 89 or claim 90, wherein the one or more adverse events is a grade 3 or greater adverse event.

92. The method of claim 89 or claim 90, wherein the one or more adverse events is a serious adverse event.

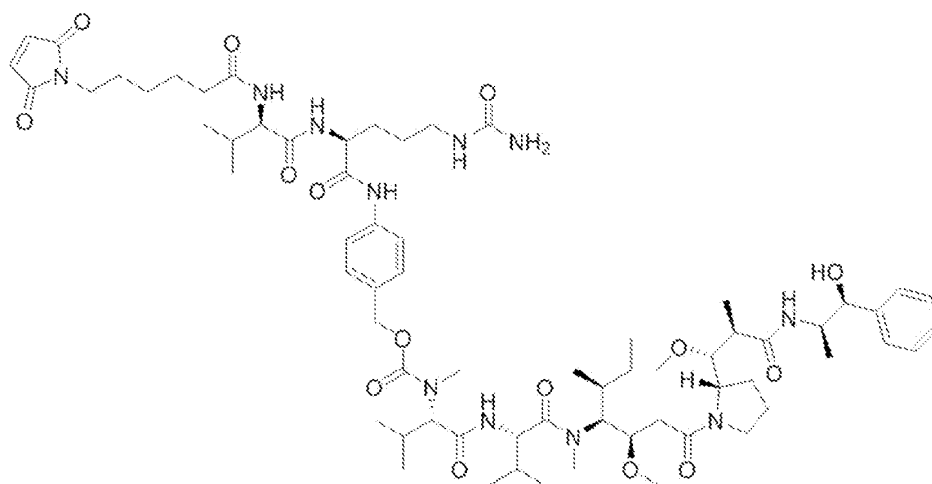
93. The method of any one of claims 1-92, wherein the route of administration for the antibody or antigen-binding fragment thereof is intravenous infusion.

94. The method of any one of claims 1-93, wherein the antibody or antigen-binding fragment thereof is administered as a monotherapy.

95. The method of any one of claims 1-93, wherein the antibody or antigen-binding fragment thereof is administered in combination with a checkpoint inhibitor.

96. The method of claim 95, 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.

97. The method of claim 96, wherein the checkpoint inhibitor is selected from the group consisting of MEDI0680, AMP-224, nivolumab, pembrolizumab, pidilizumab, MEDI4736, MPDL3280A, ipilimumab and tremelimumab.
98. The method of claim 97, wherein the checkpoint inhibitor is pembrolizumab.
99. The method of any one of claims 1-98, wherein 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.
100. The method of any one of claims 1-99, wherein the subject is a human.
101. A kit 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 the method of any one of claims 1-100.
102. A method 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.

103. The method of claim 102, wherein 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.

104. The method of claim 102, wherein 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.

105. The method of claim 102, wherein the LIV1-ADC is administered at a dose of about 0.75 mg/kg of body weight of the subject.

106. The method of claim 102, wherein the LIV1-ADC is administered at a dose of about 1.0 mg/kg of body weight of the subject.

107. The method of claim 102, wherein the LIV1-ADC is administered at a dose of about 1.25 mg/kg of body weight of the subject.

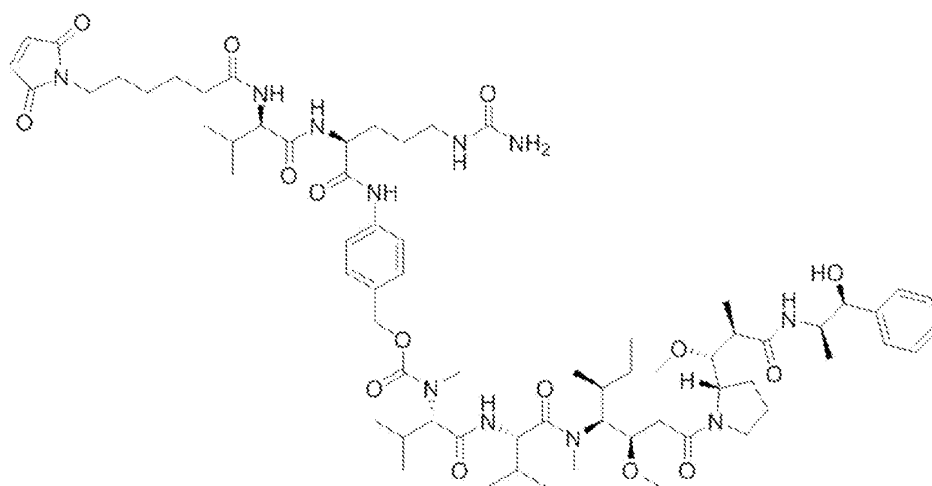
108. The method of claim 102, wherein the LIV1-ADC is administered at a dose of about 1.5 mg/kg of body weight of the subject.

109. The method of claim 102, wherein the LIV1-ADC is administered at a dose of about 1.75 mg/kg of body weight of the subject.

110. A method 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 twice in a three week treatment cycle.

111. The method of claim 110, wherein the LIV1-ADC is administered on day 1 and day 8 of the three week treatment cycle.

112. The method of claim 110 or 111, wherein 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.

113. The method of claim 110 or 111, wherein 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.

114. The method of claim 110 or 111, wherein the LIV1-ADC is administered is administered at a dose of about 1.25 mg/kg of body weight of the subject.

115. The method of claim 110 or 111, wherein the LIV1-ADC is administered is administered at a dose of about 1.5 mg/kg of body weight of the subject.

116. The method of claim 110 or 111, wherein the LIV1-ADC is administered is administered at a dose of about 1.75 mg/kg of body weight of the subject.

117. The method of claim 110 or 111, wherein the LIV1-ADC is administered is administered at a dose of about 2.0 mg/kg of body weight of the subject.

118. The method of claim 110 or 111, wherein the LIV1-ADC is administered is administered at a dose of about 2.25 mg/kg of body weight of the subject.

119. The method of claim 110 or 111, wherein the LIV1-ADC is administered is administered at a dose of about 2.5 mg/kg of body weight of the subject.

120. The method of any one of claims 102-119, wherein a vcMMAE to hLIV22 ratio is from 1 to 8.

121. The method of claim 120, wherein the average value of the vcMMAE to hLIV22 ratio in a population of the LIV1-ADC is about 4.

122. The method of any one of claims 102-121, wherein the LIV1-associated cancer is a breast cancer.

123. The method of claim 122, wherein the breast cancer is estrogen receptor positive (ER+) breast cancer.

124. The method of claim 122 or 123, wherein the breast cancer is progesterone receptor positive/human epidermal growth factor receptor 2 negative breast (PR+/HER2-) cancer.

125. The method of claim 123 or 124, wherein the subject is not a candidate for hormonal therapy.

126. The method of claim 122, wherein the breast cancer is a triple negative breast cancer.

127. The method of claim 126, wherein the subject received one non-hormonally-directed prior therapy.

128. The method of claim 126, wherein the subject received one prior cytotoxic regimen.

129. The method of any one of claims 123-126, wherein the subject received two or more prior cytotoxic regimens.

130. The method of claim 122, wherein the breast cancer is hormone receptor positive (HR+) breast cancer.

131. The method of claim 122, wherein the breast cancer is HER2 positive breast cancer.

132. The method of claim 131, wherein the subject received two or more prior cytotoxic regimens.

133. The method of claim 122, wherein the breast cancer is HR+/HER2 negative breast cancer.

134. The method of claim 133, wherein the subject is eligible for chemotherapy.

135. The method of claim 133 or 134, wherein the subject is not a candidate for hormonal therapy.
136. The method of any one of claims 102-135, wherein the cancer is an advanced stage cancer.
137. The method of claim 136, wherein the advanced stage cancer is a stage 3 or stage 4 cancer.
138. The method of any one of claims 102-137, wherein the cancer is metastatic cancer.
139. The method of any one of claims 102-138, wherein the cancer is unresectable.
140. The method of any one of claims 102-139, wherein the cancer is locally advanced.
141. The method of any one of claims 102-140, wherein the cancer is recurrent cancer.
142. The method of any one of claims 102-141, wherein the subject received prior treatment with standard of care therapy for the cancer and failed the prior treatment.
143. The method of any one of claims 102-142, wherein 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.
144. The method of any one of claims 102-142, wherein 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.
145. The method of any one of claims 102-142, wherein 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.

146. The method of any one of claims 102-145, wherein 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.

147. The method of any one of claims 102-146, wherein one or more therapeutic effects in the subject is improved after administration of the LIV1-ADC relative to a baseline.

148. The method of claim 147, 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.

149. The method of any one of claims 102-148, wherein the size of a tumor derived from the cancer is reduced by 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% relative to the size of the tumor derived from the cancer before administration of the LIV1-ADC.

150. The method of any one of claims 102-149, wherein the objective response rate is 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%.

151. The method of any one of claims 102-150, wherein the subject exhibits progression-free survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the LIV1-ADC.

152. The method of any one of claims 102-151, wherein the subject exhibits overall survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the LIV1-ADC.

153. The method of any one of claims 102-152, wherein the duration of response to the antibody-drug conjugate is at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the LIV1-ADC.

154. The method of any one of claims 102-153, wherein the subject has one or more adverse events and is further administered an additional therapeutic agent to eliminate or reduce the severity of the one or more adverse events.

155. The method of any one of claims 102-154, wherein the subject is at risk of developing one or more adverse events and is further administered an additional therapeutic agent to prevent or reduce the severity of the one or more adverse events.

156. The method of claim 154 or claim 155, wherein the one or more adverse events is a grade 3 or greater adverse event.

157. The method of claim 154 or claim 155, wherein the one or more adverse events is a serious adverse event.

158. The method of any one of claims 102-157, wherein the route of administration for the LIV1-ADC is intravenous infusion.
159. The method of any one of claims 102-158, wherein the LIV1-ADC is administered as a monotherapy.
160. The method of any one of claims 102-158, wherein the LIV1-ADC is administered in combination with trastuzumab.
161. The method of any one of claims 102-160, wherein the LIV1-ADC is in a pharmaceutical composition comprising the LIV1-ADC and a pharmaceutically acceptable carrier.
162. The method of any one of claims 102-161, wherein the subject is a human.
163. A kit comprising:
- (a) a dosage ranging from about 0.5 mg/kg to about 3.0 mg/kg of a LIV1-ADC; and
  - (b) instructions for using the LIV1-ADC according to the method of any one of claims 102-162.