

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:7 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:8; and (b) a pharmaceutically acceptable excipient comprising L-histidine, polysorbate-20 (TWEEN-20), and at least one of trehalose dihydrate and sucrose.

[0005] In some examples, the antibody or antigen binding fragment thereof comprises CDR H1 comprising an amino acid sequence of SEQ ID NO:9, CDR H2 comprising an amino acid sequence of SEQ ID NO:10, CDR H3 comprising an amino acid sequence of SEQ ID NO:11; CDR L1 comprising an amino acid sequence of SEQ ID NO:12, CDR L2 comprising an amino acid sequence of SEQ ID NO:13, and CDR L3 comprising an amino acid sequence of SEQ ID NO:14.

[0006] In some examples, the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence ranging from the 20th amino acid (glutamic acid) to the 136th amino acid (serine) of SEQ ID NO:7 and a light chain variable region comprising the amino acid sequence ranging from the 23rd amino acid (aspartic acid) to the 130th amino acid (arginine) of SEQ ID NO:8.

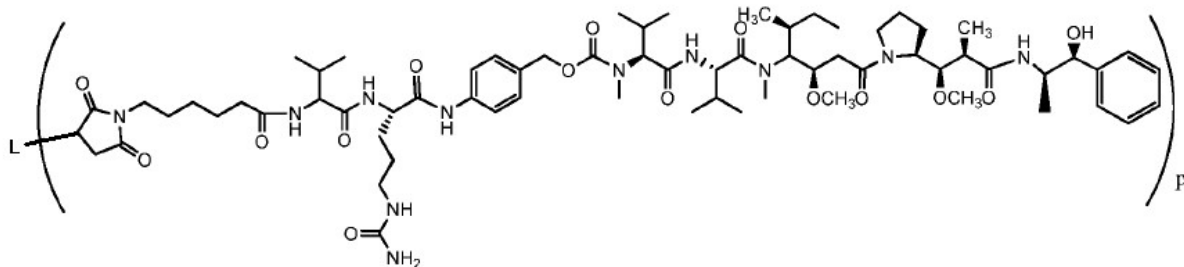
[0007] In some examples, the antibody comprises a heavy chain comprising the amino acid sequence ranging from the 20th amino acid (glutamic acid) to the 466th amino acid (lysine) of SEQ ID NO:7 and a light chain comprising the amino acid sequence ranging from the 23rd amino acid (aspartic acid) to the 236th amino acid (cysteine) of SEQ ID NO:8.

[0008] In some examples, the antigen binding fragment is an Fab, F(ab')₂, Fv or scFv fragment.

[0009] In some examples, the antibody is a fully human antibody.

[0010] In some examples, the antibody or antigen binding fragment thereof is recombinantly produced.

[0011] In some examples, 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.

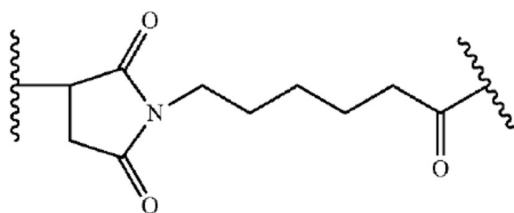
[0012] In some examples, p is from 2 to 8.

[0013] In some examples, the antibody or antigen binding fragment is linked to each unit of monomethyl auristatin E (MMAE) via a linker.

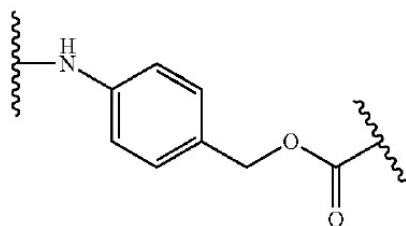
[0014] In some examples, the linker is an enzyme-cleavable linker, and in one example, the linker forms a bond with a sulfur atom of the antibody or antigen binding fragment thereof.

[0015] In some examples, 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.

[0016] In some examples, 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 having the structure of Formula (2) below:



Formula (1)



Formula (2).

[0017] In some examples, 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.

[0018] In some examples, the antibody drug conjugate comprises from 1 to 10 units of MMAE per antibody or antigen binding fragment thereof.

[0019] In some examples, the antibody drug conjugate comprises from 2 to 8 units of MMAE per antibody or antigen binding fragment thereof.

[0020] In some examples, the pharmaceutical composition comprises the antibody drug conjugate at a concentration of from about 1 to about 20 mg/mL. In some examples, the pharmaceutical composition comprises the antibody drug conjugate at a concentration of from about 5 to about 15 mg/mL. In other examples, the pharmaceutical composition comprises the antibody drug conjugate at a concentration of from about 8 to about 12 mg/mL. In yet other examples, the pharmaceutical composition comprises the antibody drug conjugate at a concentration of about 10 mg/mL.

[0021] In some examples, L-histidine is present in the range of about 5 to about 50 mM. In other examples, L-histidine is present in the range of about 10 to about 40 mM. In other examples, L-histidine is present in the range of about 15 to about 35 mM. In other examples, L-histidine is present in the range of about 15 to about 30 mM. In other examples, L-histidine is present in the range of about 15 to about 25 mM. In yet other examples, L-histidine is present at about 20 mM.

[0022] In some examples, the concentration of TWEEN-20 is in the range of from about 0.001 to about 0.1% (v/v). In other examples, the concentration of TWEEN-20 is in the range of from about 0.0025 to about 0.075% (v/v). In other examples, the concentration of TWEEN-20 is in the range of from about 0.005 to about 0.05% (v/v). In other examples, the concentration of TWEEN-20 is in the range of from about 0.01 to about 0.03% (v/v). In yet other examples, the concentration of TWEEN-20 is in the range of about 0.02% (v/v).

[0023] In some examples, the pharmaceutical composition provided herein comprises trehalose dihydrate. In some examples, the trehalose dihydrate is present in the range of about 1 to about 20% (w/v). In some examples, the trehalose dihydrate is present in the range of about 2 to about 15% (w/v). In other examples, the trehalose dihydrate is present in the range of about 3 to about 10% (w/v). In yet other examples, the trehalose dihydrate is present in the range of

about 4 to about 6% (w/v). In yet other examples, the trehalose dihydrate is present at about 5.5% (w/v).

[0024] In some examples, the trehalose dihydrate is present in the range of about 50 mM to about 300 mM. In some examples, the trehalose dihydrate is present in the range of about 75 mM to about 250 mM. In other examples, the trehalose dihydrate is present in the range of about 100 mM to about 200 mM. In yet other examples, the trehalose dihydrate is present in the range of about 130 mM to about 150 mM. In yet other examples, the trehalose dihydrate is present at about 146 mM.

[0025] In some examples, the pharmaceutical composition comprises sucrose. In some examples, the sucrose is present in the range of about 1 to about 20% (w/v). In some examples, the sucrose is present in the range of about 2 to about 15% (w/v). In other examples, the sucrose is present in the range of about 3 to about 10% (w/v). In other examples, the sucrose is present in the range of about 4 to about 6% (w/v). In yet other examples, the sucrose is present at about 5.5% (w/v).

[0026] In some examples, the sucrose is present in the range of about 50 mM to about 300 mM. In other examples, the sucrose is present in the range of about 75 mM to about 250 mM. In other examples, the sucrose is present in the range of about 100 mM to about 200 mM. In yet other examples, the sucrose is present in the range of about 130 mM to about 150 mM. In yet other examples, the sucrose is present at about 146 mM.

[0027] In some examples, the pharmaceutical composition has a pH in a range of about 5.5 to about 6.5. In some examples, the pharmaceutical composition has a pH in a range of about 5.7 to about 6.3. In other examples, the pharmaceutical composition has a pH of about 6.0.

[0028] In some examples, the pH is taken at room temperature. In some examples, the pH is taken at about 15°C to about 27°C. In other examples, the pH is taken at about 4°C. In other examples, the pH is taken at about 25°C.

[0029] In some examples, the pharmaceutical composition provided herein comprises hydrochloric acid (HCl). In some examples, the pH is adjusted by HCl.

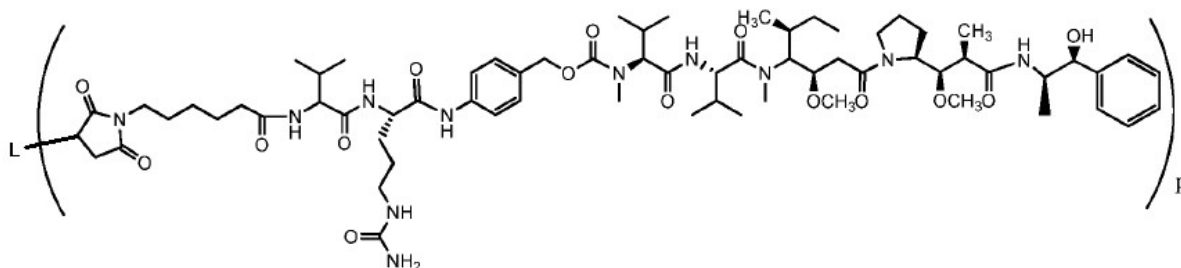
[0030] In other examples, the pharmaceutical composition provided herein comprises succinic acid. In some examples, the pH is adjusted by succinic acid.

[0031] In some examples, the pharmaceutical composition provided herein comprises about 20 mM L-histidine, about 0.02% (w/v) TWEEN-20, and at least one of about 5.5% (w/v)

trehalose dihydrate or about 5% (w/v) sucrose. In some examples, the pharmaceutical composition provided herein further comprises HCl or succinic acid. In some examples, the pH is about 6.0 at room temperature. In other examples, the pH is about 6.0 at 25°C.

[0032] In some specific examples, the pharmaceutical composition provided herein comprises:

(a) an antibody drug conjugate having the following structure:



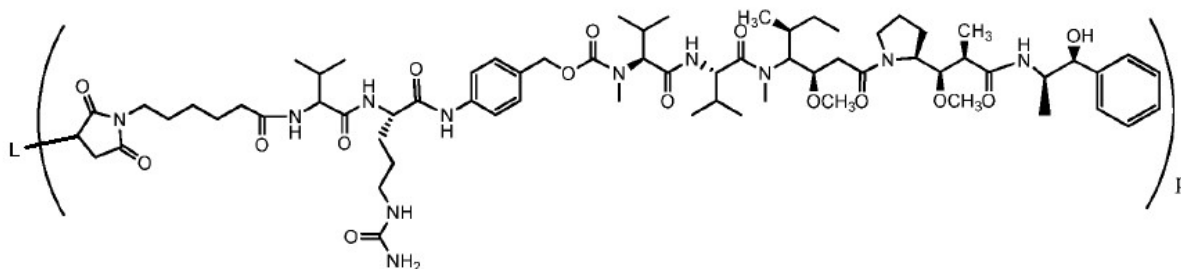
wherein L- represents the antibody or antigen binding fragment thereof and p is from 1 to 10;

and (b) a pharmaceutically acceptable excipient comprising about 20 mM L-histidine, about 0.02% (w/v) TWEEN-20, about 5.5% (w/v) trehalose dihydrate, and HCl, wherein the pH is about 6.0 at 25°C.

[0033] In some examples, the antibody drug conjugate is at the concentration of about 10 mg/mL.

[0034] In other specific examples, the pharmaceutical composition provided herein comprises:

(a) an antibody drug conjugate comprising the following structure:



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

and

(b) a pharmaceutically acceptable excipient comprising about 20 mM L-histidine, about 0.02% (w/v) TWEEN-20, about 5.5% (w/v) trehalose dihydrate, and succinic acid, wherein the

[0042b] In another aspect, provided herein is a use of a pharmaceutical composition as provided herein in the manufacture of a medicament for treating cancer in a subject; wherein

- (a) optionally the subject is a human subject;
- (b) optionally the cancer is colon cancer, pancreatic cancer, ovarian cancer, lung cancer, bladder cancer, urothelial cancer, breast cancer, esophageal cancer, head cancer, or neck cancer;
- (c) optionally the lung cancer is non-small cell lung cancer;
- (d) optionally the bladder cancer or urothelial cancer is advanced or metastatic; and
- (e) optionally the cancer has tumor cells expressing 191P4D12.

[0043] In some examples, the subject is a human subject.

[0044] In some examples, the cancer is a solid tumor. In some examples, the cancer is colon cancer, pancreatic cancer, ovarian cancer, lung cancer, bladder cancer, breast cancer, esophageal cancer, head cancer, or neck cancer.

[0045] In a specific example, the cancer is colon cancer. In a specific example, the cancer is pancreatic cancer. In a specific example, the cancer is ovarian cancer. In a specific example, the cancer is lung cancer. In some examples, the lung cancer is non-small cell lung cancer. In a specific example, the cancer is bladder cancer. In a specific example, the cancer is advanced bladder cancer. In a specific example, the cancer is metastatic bladder cancer. In a specific example, the cancer is breast cancer. In a specific example, the cancer is esophageal cancer. In a specific example, the cancer is head cancer. In a specific example, the cancer is neck cancer. In a specific example, the cancer has tumor cells expressing 191P4D12.

[0046] In some examples, the method provided herein further comprises administering to the subject a second therapeutic agent. In some examples, the second therapeutic agent is an immune checkpoint inhibitor. In some examples, the immune checkpoint inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor. In other examples, the immune checkpoint inhibitor is a PD-1 inhibitor. In yet other examples, the PD-1 inhibitor is pembrolizumab or nivolumab. In other examples, the immune checkpoint inhibitor is a PD-L1 inhibitor. In other examples, the PD-L1 inhibitor is selected from a group consisting of atezolizumab, avelumab, and durvalumab.

[0047] In some examples, the antibody drug conjugate formulated in the pharmaceutical composition is administered at a dose of 1 to 10 mg/kg of the subject's body weight. In other

examples, the antibody drug conjugate formulated in the pharmaceutical composition is administered at a dose of 1 to 5 mg/kg of the subject's body weight. In yet other examples, the antibody drug conjugate formulated in the pharmaceutical composition is administered at a dose of 1 to 2.5 mg/kg of the subject's body weight. In some examples, the antibody drug conjugate formulated in the pharmaceutical composition is administered at a dose of 1 to 1.25 mg/kg of the subject's body weight. In some examples, the antibody drug conjugate formulated in the pharmaceutical composition is administered at a dose of about 1 mg/kg of the subject's body weight. In some examples, the antibody drug conjugate formulated in the pharmaceutical composition is administered at a dose of about 1.25 mg/kg of the subject's body weight.

[0048] In some examples, the antibody drug conjugate formulated in the pharmaceutical composition is administered by an intravenous (IV) injection or infusion.

[0049] In some examples, the antibody drug conjugate formulated in the pharmaceutical composition is administered by an intravenous (IV) injection or infusion over about 30 minutes twice every three-week cycle. In some examples, 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 and 8 of every three-week cycle. In some examples, the method further comprises administering an immune checkpoint inhibitor by an intravenous (IV) injection or infusion on Day 1 of every three-week cycle. In some examples, the immune checkpoint inhibitor is pembrolizumab, and wherein pembrolizumab is administered at amount of about 200 mg over about 30 minutes. In other examples, the immune checkpoint inhibitor is atezolizumab, and wherein atezolizumab is administered at amount of about 1200 mg over about 60 minutes or 30 minutes.

[0050] In other examples, the antibody drug conjugate formulated in the pharmaceutical composition is administered by an intravenous (IV) injection or infusion over about 30 minutes three times every four-week cycle. In some examples, 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. In some examples, the method further comprises administering an immune checkpoint inhibitor by an intravenous (IV) injection or infusion. In some examples, the immune checkpoint inhibitor is pembrolizumab. In other examples, the immune checkpoint inhibitor is atezolizumab.

4. Description of the Drawings

[0051] **FIG. 1A, 1B, 1C, and 1D** depict the results of SDS-PAGE analysis for the 14-day stability study for the formulations F1-F14 at 40°C.

[0052] **FIG. 1E** depicts the summary of the PR-HPLC study described in Section 6.1.

[0053] **FIG. 1F, 1G, and 1H** depicts the results of the SE-HPLC analysis for the formulations F1- F14 at 40°C.

[0054] **FIG. 2A** depicts the results of the shade study for the formulations F4, F9 and F14 at T0.

[0055] **FIG. 2B** depicts the SDS-PAGE results of the cycle freeze-thaw study for the formulations F4, F9, and F14.

[0056] **FIG. 2C** depicts the total cumulative counts per mL as measured by HIAC for the formulations F4, F9, and F14.

[0057] **FIG. 3A** depicts the results of the residual moisture analysis for the formulations F4, F9, and F14.

[0058] **FIG. 3B** depicts the A280 (concentration) results in the 12 week concurrent BDS and DP formulation study.

[0059] **FIG. 3C** depicts the A330 (turbidity) results in the 12 week concurrent BDS and DP formulation study.

[0060] **FIG. 3D** depicts the results of the SDS-PAGE analysis of the BDS (before lyophilization) at T0.

[0061] **FIG. 3E** depicts the results of the SDS-PAGE analysis of the BDS stored at -70°C or 2-8°C for 12 weeks.

[0062] **FIG. 3F** depicts the results of the SDS-PAGE analysis of the DP after lyophilization and reconstitution at T0.

[0063] **FIG. 3G** depicts the results of the SDS-PAGE analysis of the DP (after lyophilization and reconstitution) stored at 25°C or 40°C for 12 weeks.

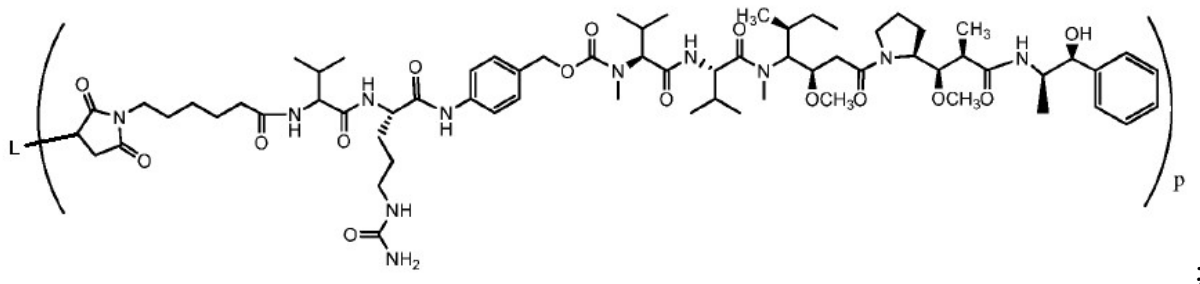
[0064] **FIG. 3H** depicts the results of the SDS-PAGE analysis of the DP (after lyophilization and reconstitution) stored at 2-8°C for 12 weeks.

What is Claimed is:

1. A pharmaceutical composition comprising
 - (a) an antibody drug conjugate comprising 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:7 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:8; and
 - (b) a pharmaceutically acceptable excipient comprising L-histidine, polysorbate-20 (TWEEN-20), and at least one of trehalose dihydrate and sucrose.
2. The pharmaceutical composition of claim 1, wherein
 - (a) the antibody or antigen binding fragment thereof comprises CDR H1 comprising an amino acid sequence of SEQ ID NO:9, CDR H2 comprising an amino acid sequence of SEQ ID NO:10, CDR H3 comprising an amino acid sequence of SEQ ID NO:11; CDR L1 comprising an amino acid sequence of SEQ ID NO:12, CDR L2 comprising an amino acid sequence of SEQ ID NO:13, and CDR L3 comprising an amino acid sequence of SEQ ID NO:14;
 - (b) the antibody or antigen binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence ranging from the 20th amino acid (glutamic acid) to the 136th amino acid (serine) of SEQ ID NO:7 and a light chain variable region comprising the amino acid sequence ranging from the 23rd amino acid (aspartic acid) to the 130th amino acid (arginine) of SEQ ID NO:8; or
 - (c) 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.
3. The pharmaceutical composition of claim 1 or 2, wherein
 - (a) the antigen binding fragment is an Fab, F(ab')₂, Fv or scFv fragment;
 - (b) the antibody is a fully human antibody; or

(c) the antibody or antigen binding fragment thereof is recombinantly produced.

4. The pharmaceutical composition of any one of claims 1 to 3, wherein the antibody drug conjugate has the following structure:



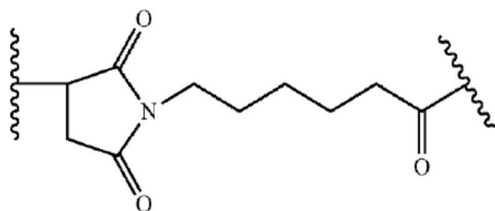
wherein L- represents the antibody or antigen binding fragment thereof and p is from 1 to 10;
wherein optionally p is from 2 to 8.

5. The pharmaceutical composition of claim 1, wherein the antibody or antigen binding fragment thereof is linked to each unit of monomethyl auristatin E (MMAE) via a linker;
wherein

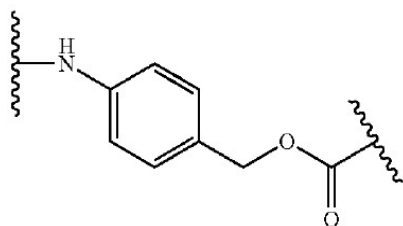
(a) optionally the linker is an enzyme-cleavable linker, and the linker forms a bond with a sulfur atom of the antibody or antigen binding fragment thereof; or

(b) optionally 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; wherein

(i) optionally 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); or

(ii) optionally the stretcher unit forms a bond with a sulfur atom of the antibody or antigen binding fragment thereof, and the spacer unit is linked to MMAE via a carbamate group.

6. The pharmaceutical composition of any one of claims 1 to 5, comprising the antibody drug conjugate at a concentration of (i) from 1 to 20 mg/mL; (ii) from 5 to 15 mg/mL; (iii) from 8 to 12 mg/mL; or (iv) about 10 mg/mL.

7. The pharmaceutical composition of any one of claims 1 to 6, wherein the L-histidine is present (i) in the range of 5 to 50 mM; (ii) in the range of 10 to 40 mM; (iii) in the range of 15 to 35 mM; (iv) in the range of 15 to 30 mM; (v) in the range of 15 to 25 mM; or (vi) at about 20 mM.

8. The pharmaceutical composition of any one of claims 1 to 7, wherein the concentration of TWEEN-20 is (i) in the range of from 0.001 to 0.1% (v/v); (ii) in the range of from 0.0025 to 0.075% (v/v); (iii) in the range of from 0.005 to 0.05% (v/v); (iv) in the range of from 0.01 to 0.03% (v/v); or (v) about 0.02% (v/v).

9. The pharmaceutical composition of any one of claims 1 to 8, wherein the pharmaceutical composition comprises trehalose dihydrate; wherein optionally the trehalose dihydrate is present (i) in the range of 1 to 20% (w/v); (ii) in the range of 2 to 15% (w/v); (iii) in the range of 3 to 10% (w/v); (iv) in the range of 4 to 6% (w/v); (v) at about 5.5% (w/v); (vi) in the range of 50 mM to 300 mM; (vii) in the range of 75 mM to 250 mM; (viii) in the range of 100 mM to 200 mM; (ix) in the range of 130 mM to 150 mM; or (x) at about 146 mM.

10. The pharmaceutical composition of any one of claims 1 to 8, wherein the pharmaceutical composition comprises sucrose; wherein optionally the sucrose is present (i) in

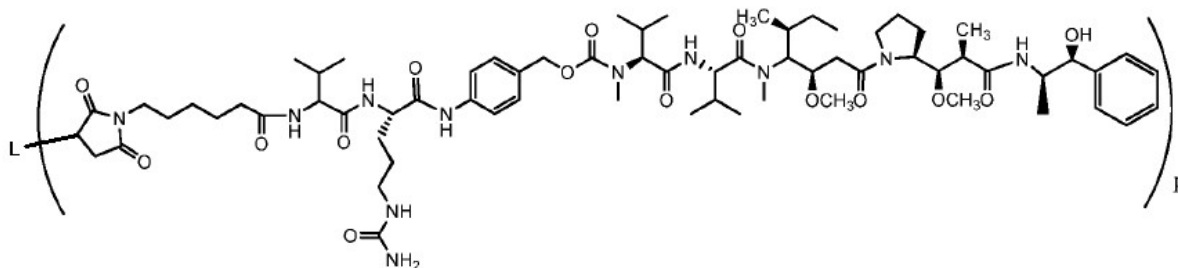
the range of 1 to 20% (w/v); (ii) in the range of 2 to 15% (w/v); (iii) in the range of 3 to 10% (w/v); (iv) in the range of 4 to 6% (w/v); (v) at about 5.5% (w/v); (vi) in the range of 50 mM to 300 mM; (vii) in the range of 75 mM to 250 mM; (viii) in the range of 100 mM to 200 mM; (ix) in the range of 130 mM to 150 mM; or (x) at about 146 mM.

11. The pharmaceutical composition of any one of claims 1 to 10, wherein the pharmaceutical composition has a pH (i) in the range of 5.5 to 6.5, (ii) in the range of 5.7 to 6.3, or (iii) of about 6.0; wherein optionally the pH is taken at (i) room temperature, (ii) 15°C to 27°C, (iii) 4°C, or (iv) 25°C.

12. The pharmaceutical composition of any one of claims 1 to 11, wherein
- (a) the pharmaceutical composition further comprises hydrochloric acid (HCl);
 - (b) the pH is adjusted by HCl;
 - (c) the pharmaceutical composition further comprises succinic acid; or
 - (d) the pH is adjusted by succinic acid.

13. The pharmaceutical composition of any one of claims 1 to 5, comprising about 20 mM L-histidine, about 0.02% (w/v) TWEEN-20, and at least one of about 5.5% (w/v) trehalose dihydrate or about 5 % (w/v) sucrose; wherein

- (a) optionally the pharmaceutical composition further comprises HCl or succinic acid;



- (b) optionally the pH is 6.0 at room temperature or at 25°C; and
- (c) optionally the antibody drug conjugate is at a concentration of about 10 mg/mL.

18. The use of claim 17, wherein the pharmaceutical composition is adapted to be administrable with a second therapeutic agent; wherein

- (a) optionally the second therapeutic agent is an immune checkpoint inhibitor;
- (b) optionally the immune checkpoint inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor;
- (c) optionally the PD-1 inhibitor is nivolumab; and
- (d) optionally the PD-L1 inhibitor is selected from a group consisting of atezolizumab, avelumab, and durvalumab.

19. The use of claim 17 or 18, wherein the antibody drug conjugate formulated in the pharmaceutical composition is to be administered at a dose of (i) 1 to 10 mg/kg of the subject's body weight; (ii) 1 to 5 mg/kg of the subject's body weight; (iii) 1 to 2.5 mg/kg of the subject's body weight; (iv) 1 to 1.25 mg/kg of the subject's body weight; or (v) about 1 mg/kg or 1.25 mg/kg of the subject's body weight.

20. The use of claim 19, wherein the antibody drug conjugate formulated in the pharmaceutical composition is to be administered by an intravenous (IV) injection or infusion;

21. The use of claim 20, wherein the antibody drug conjugate formulated in the pharmaceutical composition is to be administered by an intravenous (IV) injection or infusion over about 30 minutes twice every three-week cycle; wherein

- (a) optionally the antibody drug conjugate formulated in the pharmaceutical composition is to be administered by an intravenous (IV) injection or infusion over about 30 minutes on Days 1 and 8 of every three-week cycle;
- (b) optionally the pharmaceutical composition is adapted to be administrable with an immune checkpoint inhibitor by an intravenous (IV) injection or infusion on Day 1 of every three-week cycle; and
- (c) optionally the immune checkpoint inhibitor is to be administered at an amount of about 100 mg to about 1500 over about 30 minutes or 60 minutes.

22. The use of claim 20, wherein the antibody drug conjugate formulated in the pharmaceutical composition is to be administered by an intravenous (IV) injection or infusion over about 30 minutes three times every four-week cycle; wherein

(a) optionally the antibody drug conjugate formulated in the pharmaceutical composition is to be administered by an intravenous (IV) injection or infusion over about 30 minutes on Days 1, 8 and 15 of every four-week cycle; and

(b) optionally the pharmaceutical composition is adapted to be administrable with an immune checkpoint inhibitor by an intravenous (IV) injection or infusion.