response has been proposed. Antibodies capable of specifically binding to PD-1 and PD-L1 have been reported.

[0005] However, an unmet need remains to develop antibody compositions for patients whose tumors express PD-L1, including those whose tumors express low levels of PD-L1 or who have failed on other PD-1 therapies. The present disclosure directly addresses this need and others, as described below.

SUMMARY

[0006] In one example, the present disclosure provides pharmaceutical compositions, for storage and administration, comprising an anti-human PD-1 ("hPD-1") antibody ("retifanlimab") and buffering agents. The disclosure further provides containers and kits comprising such pharmaceutical compositions. The disclosure further provides the use of such pharmaceutical compositions, containers, and kits containing retifanlimab for the treatment of a cancer, and in certain examples treatment of a cancer expressing PD-L1, for example with a therapeutically effective amount or prophylactically effective amount of retinfanlimab.

[0007] In one example, the disclosure provides a pharmaceutical composition comprising retifanlimab, acetate, sucrose, polysorbate 80 ("PS80"), and water. In one aspect, the present disclosure refers to a pharmaceutical composition comprising: (a) about 10 mg/mL to about 100 mg/mL retifanlimab; (b) acetate; (c) sucrose; (d) polysorbate 80 ("PS80"); and (e) water. In certain examples, the disclosure provides an example of such pharmaceutical compositions, wherein the acetate is present at a concentration of about 5 mM to about 30 mM. The disclosure further provides an example of such pharmaceutical compositions, wherein the acetate comprises sodium acetate, or wherein the acetate comprises glacial acetic acid and sodium acetate.

[0008] The disclosure additionally provides an example of such pharmaceutical compositions, wherein the composition comprises:

a) about 5 mM to about 30 mM acetate, about 50 mg/mL to about 130 mg/mL of sucrose, about 0.02 mg/mL to about 0.6 mg/mL of PS80, and water, wherein the composition has a pH of about 4.0 to about 6.5; or

b) about 7.5 mM to about 20 mM acetate, about 50 mg/mL to about 130 mg/mL of sucrose, about 0.05 mg/mL to about 0.6 mg/mL of PS80, and water, wherein the composition has a pH of about 4.0 to about 6.5; or

c) about 9 mM to about 11 mM acetate, about 76 mg/mL to about 104 mg/mL of sucrose, about 0.08 mg/mL to about 0.53 mg/mL of PS80, and water, wherein the

composition has a pH of about 4.5 to about 5.7; or

d) about 9 mM to about 11 mM acetate, about 80 mg/mL to about 100 mg/mL of sucrose, about 0.08 mg/mL to about 0.15 mg/mL of PS80, and water, wherein the composition has a pH of about 4.5 to about 5.7.

[0009] The disclosure provides an example of such pharmaceutical compositions, wherein retifanlimab is present at a concentration of about 10 mg/mL to about 100 mg/mL. The disclosure further provides an example of such pharmaceutical compositions, wherein retifanlimab is present at a concentration of about 20 mg/mL to about 30 mg/mL. The disclosure further provides an example of such pharmaceutical compositions, wherein retifanlimab is present at a concentration of about 25 mg/mL.

[0010] The disclosure provides an example of such pharmaceutical composition, wherein the acetate comprises glacial acetic acid at a concentration of about 0.05 mg/mL to about 0.35 mg/mL and sodium acetate trihydrate at a concentration of about 0.80 mg/mL to about 2.0 mg/mL. The disclosure further provides an example of pharmaceutical compositions, wherein the acetate comprises glacial acetic acid at a concentration of about 0.18 mg/mL and sodium acetate trihydrate at a concentration of about 0.95 mg/mL.

[0011] The disclosure provides an example of such pharmaceutical compositions, wherein the sucrose is present at a concentration of about 80 mg/mL to about 100 mg/mL. The disclosure further provides an example of such pharmaceutical compositions, wherein the sucrose is present at a concentration of about 90 mg/mL.

[0012] The disclosure provides an example of such pharmaceutical compositions, wherein the PS80 is present at a concentration of about 0.08 mg/mL to about 0.15 mg/mL. The disclosure further provides an example of such pharmaceutical compositions, wherein the concentration of PS80 is about 0.1 mg/mL.

[0013] The disclosure provides an example of such pharmaceutical compositions, wherein the composition has a pH of about 4.5 to about 5.7. The disclosure further provides an example of such pharmaceutical compositions, wherein the composition has a pH of about 5.1.

[0014] The disclosure provides an example of such pharmaceutical compositions, wherein the composition comprises about 25 mg/mL of retifanlimab, about 0.18 mg/mL of glacial acetic acid, about 0.95 mg/mL of sodium acetate trihydrate, about 90 mg/mL of

sucrose, about 0.1 mg/mL of PS80, and water, wherein the composition has a pH of about 4.8 to about 5.4.

[0015] The disclosure provides an example of such pharmaceutical compositions, wherein the composition has a shelf-life of at least about 18 months at about 2°C to about 8°C. The disclosure further provides an example of such pharmaceutical compositions, wherein the composition has a shelf-life of about 24 months at about 2°C to about 8°C. The disclosure further provides an example of such pharmaceutical compositions, wherein the composition has a shelf-life of about 36 months at about 2°C to about 8°C. The disclosure further provides an example of such pharmaceutical compositions, wherein the composition has a shelf-life of about 48 months at about 2°C to about 8°C. The disclosure further provides an example of such pharmaceutical compositions, wherein the composition has a shelf-life of about 60 months at about 2°C to about 8°C.

[0016] The disclosure provides an example of such pharmaceutical compositions, wherein the composition has an osmolality of about 200 to about 400 mOsm/kg H_2O. The disclosure further provides an example of such pharmaceutical compositions, wherein the composition has an osmolality of about 225 to about 400 mOsm/kg H_2O. The disclosure further provides an example of such pharmaceutical compositions, wherein the composition has an osmolality of about 250 to about 375 mOsm/kg H_2O. The disclosure further provides an example of such pharmaceutical compositions, wherein the composition has an osmolality of about 260 to about 340 mOsm/kg H_2O.

[0017] The disclosure provides an example of such pharmaceutical compositions, wherein the composition maintains monomeric purity of the retifanlimab for about for at least about 3 months at about 25°C. The disclosure further provides an example of such pharmaceutical compositions, wherein the composition maintains monomeric purity of the retifanlimab for about for at least about 18 months at about 2°C to about 8°C.

[0018] The disclosure provides an example of such pharmaceutical compositions, wherein the composition maintains the heterogeneity profile of the retifanlimab for about for at least about 3 months at 25°C. The disclosure further provides an example of such pharmaceutical compositions, wherein the composition maintains the heterogeneity profile of the retifanlimab for about for at least about 18 months at about 2°C to about 8°C.

[0019] The disclosure further provides an example of any of the pharmaceutical compositions disclosed herein, wherein the water is sterile, nonpyrogenic, distilled water.

[0020] The disclosure further provides an example of the pharmaceutical compositions disclosed herein, wherein the pharmaceutical composition is sterile.
[0021] The disclosure additionally provides a container comprising any of the pharmaceutical compositions disclosed herein, wherein such container comprises about 10 mL volume, about 15 mL volume, or about 20 mL of such pharmaceutical compositions.
[0022] The disclosure further provides an example of such pharmaceutical compositions, wherein the pharmaceutical compositions do not comprise an antioxidant.
[0023] The disclosure provides an example of such a container, wherein the about 10 mL volume of such a pharmaceutical composition comprises: (a) about 250 mg retifanlimab; (b) about 1.8 mg glacial acetic acid; (c) about 9.5 mg sodium acetate trihydrate; (d) about 900 mg sucrose; (e) about 1 mg PS80; and (f) water; and wherein such composition has a pH of about 4.8 to about 5.4.
[0024] The disclosure further provides an example of such a container, wherein the about 15 mL volume of such a pharmaceutical composition comprises: (a) about 375 mg retifanlimab; (b) about 2.7 mg glacial acetic acid; (c) about 14.25 mg sodium acetate trihydrate; (d) about 1350 mg sucrose; (e) about 1.5 mg PS80; and (f) water; and wherein the composition has a pH of about 4.8 to about 5.4.
[0025] The disclosure further provides an example of such a container, wherein the about 20 mL volume of such a pharmaceutical composition comprises: (a) about 500 mg retifanlimab; (b) about 3.6 mg glacial acetic acid; (c) about 19 mg sodium acetate trihydrate; (d) about 1800 mg sucrose; (e) about 2 mg PS80; and (f) water; and wherein the composition has a pH of about 4.8 to about 5.4.
[0025a] In one aspect, the present disclosure refers to a container comprising the pharmaceutical composition as disclosed herein, wherein the container comprises: (a) about 10 mL volume of the pharmaceutical composition, wherein the about 10 mL volume of the pharmaceutical composition comprises: (i) about 250 mg retifanlimab; (ii) about 1.8 mg glacial acetic acid; (iii) about 9.5 mg sodium acetate trihydrate; (iv) about 900 mg sucrose; (v) about 1 mg PS80; and (vi) water; and wherein the composition has a pH of about 4.8 to about 5.4; (b) about 15 mL volume of the pharmaceutical composition, wherein the about 15 mL volume of the pharmaceutical composition comprises: (i) about 375 mg retifanlimab; (ii) about 2.7 mg glacial acetic acid; (iii) about 14.25 mg sodium acetate trihydrate; (iv) about 1350 mg sucrose; (v) about 1.5 mg PS80; and (vi) water; and wherein the composition has a pH of about 4.8 to about 5.4; (c) about 20 mL volume of the pharmaceutical composition, wherein the about 20 mL volume of the pharmaceutical composition comprises: (i) about 500 mg retifanlimab; (ii) about 3.6 mg glacial acetic acid; (iii) about 19 mg sodium acetate trihydrate; (iv) about 1800 mg sucrose; (v) about 2 mg PS80; and (vi) water; and wherein the composition has a pH of about 4.8 to about 5.4.
[0026] The disclosure additionally provides a kit comprising any of the pharmaceutical compositions disclosed herein, or any of the containers disclosed herein, and optionally comprising instructions for administration of the pharmaceutical composition to a subject in need thereof. In one aspect, the present disclosure refers to a kit comprising the pharmaceutical composition as disclosed herein, or the container as disclosed herein, and optionally further comprising instructions for administration of the pharmaceutical composition to a subject in need thereof.
[0027] The disclosure additionally provides a kit comprising a container comprising a pharmaceutical composition, the composition comprising:

a) about 21 mg/mL to about 29 mg/mL of retifanlimab, about 0.16 mg/mL to about 0.20 mg/mL of glacial acetic acid, about 0.86 mg/mL to about 1.1 mg/mL of sodium acetate trihydrate, about 76 mg/mL to about 104 mg/mL of sucrose, about 0.08

mg/mL to about 0.53 mg/mL of PS80, and water, wherein the composition has a pH of about 4.5 to about 5.7; or

b) about 22.5 mg/mL to about 27.5 mg/mL of retifanlimab, about 0.16 mg/mL to about 0.20 mg/mL of glacial acetic acid, about 0.86 mg/mL to about 1.1 mg/mL of sodium acetate trihydrate, about 76 mg/mL to about 104 mg/mL of sucrose, about 0.08 mg/mL to about 0.53 mg/mL of PS80, and water, wherein the composition has a pH of about 4.5 to about 5.7; or

c) about 250 mg retifanlimab, about 1.8 mg glacial acetic acid, about 9.5 mg sodium acetate trihydrate, about 900 mg sucrose, about 1 mg PS80, and wherein the composition has a pH of about 4.8 to about 5.4; or

d) about 375 mg retifanlimab, about 2.7 mg glacial acetic acid, about 14.25 mg sodium acetate trihydrate, about 1350 mg sucrose, about 1.5 mg PS80, and wherein the composition has a pH of about 4.8 to about 5.4; or

e) about 500 mg retifanlimab, about 3.6 mg glacial acetic acid, about 19 mg sodium acetate trihydrate, about 1800 mg sucrose, about 2 mg PS80, and wherein the composition has a pH of about 4.8 to about 5.4; and

optionally comprising instructions for administration of the pharmaceutical composition to a subject in need thereof.

[0027a] In one aspect, the present disclosure refers to a kit comprising a container comprising a pharmaceutical composition, the composition comprising:

(a) about 21 mg/mL to about 29 mg/mL of retifanlimab, about 0.16 mg/mL to about 0.20 mg/mL of glacial acetic acid, about 0.86 mg/mL to about 1.1 mg/mL of sodium acetate trihydrate, about 76 mg/mL to about 104 mg/mL of sucrose, about 0.08 mg/mL to about 0.53 mg/mL of PS80, and water, wherein the composition has a pH of about 4.5 to about 5.7; or

(b) about 22.5 mg/mL to about 27.5 mg/mL of retifanlimab, about 0.16 mg/mL to about 0.20 mg/mL of glacial acetic acid, about 0.86 mg/mL to about 1.1 mg/mL of sodium acetate trihydrate, about 76 mg/mL to about 104 mg/mL of sucrose, about 0.08 mg/mL to about 0.53 mg/mL of PS80, and water, wherein the composition has a pH of about 4.5 to about 5.7; or

(c) about 250 mg retifanlimab, about 1.8 mg glacial acetic acid, about 9.5 mg sodium acetate trihydrate, about 900 mg sucrose, about 1 mg PS80, and wherein said composition has a pH of about 4.8 to about 5.4; or

(d) about 375 mg retifanlimab, about 2.7 mg glacial acetic acid, about 14.25 mg sodium acetate trihydrate, about 1350 mg sucrose, about 1.5 mg PS80, and wherein said composition has a pH of about 4.8 to about 5.4; or

(e) about 500 mg retifanlimab, about 3.6 mg glacial acetic acid, about 19 mg sodium acetate trihydrate, about 1800 mg sucrose, about 2 mg PS80, and wherein said composition has a pH of about 4.8 to about 5.4; and

optionally further comprising instructions for administration of the pharmaceutical composition to a subject in need thereof.

[0028] The disclosure provides an example of such kits, wherein the composition comprises about 25 mg/mL of retifanlimab, about 0.18 mg/mL of glacial acetic acid, about 0.95 mg/mL of sodium acetate trihydrate, about 90 mg/mL of sucrose, about 0.1 mg/mL of PS80, and water, wherein the composition has a pH of about 4.8 to about 5.4.

[0029] The disclosure provides an example of such kits, wherein the composition comprises about 250 mg retifanlimab, about 1.8 mg glacial acetic acid, about 9.5 mg sodium acetate trihydrate, about 900 mg sucrose, about 1 mg PS80, and wherein the composition has a pH of 4.8 to 5.4. The disclosure further provides an example of such kits, wherein the composition comprises about 375 mg retifanlimab, about 2.7 mg glacial acetic acid, about 14.25 mg sodium acetate trihydrate, about 1350 mg sucrose, about 1.5 mg PS80, and wherein the composition has a pH of about 4.8 to about 5.4.

[0030] The disclosure provides an example of such kits, wherein the composition comprises about 500 mg retifanlimab, about 3.6 mg glacial acetic acid, about 19 mg sodium

acetate trihydrate, about 1800 mg sucrose, about 2 mg PS80, and wherein the composition has a pH of about 4.8 to about 5.4.

[0031] The disclosure additionally provides a sealed package comprising any of the pharmaceutical compositions disclosed herein, any of the containers disclosed herein, or any of the kits disclosed herein, and optionally further comprising instructions for administration of the pharmaceutical composition to a subject in need thereof.

[0032] The disclosure further provides a method of treating cancer, comprising administering retifanlimab to a subject in need thereof using any of the pharmaceutical compositions disclosed herein, any of the containers disclosed herein, and of the kits disclosed herein, or any of the sealed kits disclosed herein. In one aspect, the present disclosure refers to use of the pharmaceutical composition as disclosed herein, for the production of a medicament for the treatment of cancer in a subject in need thereof. In one aspect, the present disclosure refers to use of the pharmaceutical composition as disclosed herein, the container as disclosed herein, the kit as disclosed herein, in the manufacture of a medicament for the treatment of cancer in a subject in need thereof.

[0033] The disclosure additionally provides a method of treating cancer, comprising administering retifanlimab to a subject in need thereof using any of the pharmaceutical compositions disclosed herein, any of the containers disclosed herein, any of the sealed packages disclosed herein, or any of the kits disclosed herein, wherein such a method comprises:

a) diluting the pharmaceutical composition in a container:

   in 0.9% sodium chloride, or

   in 5% dextrose in water (D5W),

   to obtain a dosing solution;

b) inverting the container to mix the diluted solution; and

c) attaching the container containing the dosing solution to a device for administration to the subject.

[0034] The disclosure also provides the use of any of the pharmaceutical compositions disclosed herein, any of the containers disclosed herein, any of the sealed packages disclosed herein, or any of the kits disclosed herein, for the treatment of cancer in a subject in need thereof.

[0035] The disclosure additionally provides the use of any of the pharmaceutical compositions disclosed herein, any of the containers disclosed herein, any of the sealed packages disclosed herein, or any of the kits disclosed herein, for the treatment of cancer in a subject in need thereof, wherein the use comprises:

a) diluting the pharmaceutical composition in a container:

   in 0.9% sodium chloride; or

in 5% dextrose in water (D5W),

to obtain a dosing solution;

b) inverting the container to mix the diluted solution; and

c) attaching the container containing the dosing solution to a device for administration to the subject.

[0036] The disclosure further provides an example of the methods or uses of the present disclosure, wherein the container is an IV bag containing 0.9% sodium chloride. The disclosure further provides an example of such uses, wherein the container is an IV bag containing D5W.

[0037] The disclosure provides an example any of the methods disclosed herein, or any of the uses disclosed herein, wherein the dosing solution maintains monomeric purity of the retifanlimab for about 6 hours at 25^{o}C or for about 24 hours at about 2^{o}C to about 8^{o}C.

[0038] The disclosure provides an example any of the methods disclosed herein, or any of the uses disclosed herein, wherein the administration is by IV infusion for at least 30 minutes. The disclosure further provides an example any of the methods disclosed herein, or any of the uses disclosed herein, wherein the administration is by IV infusion for at least 60 minutes.

[0039] The disclosure provides an example any of the methods disclosed herein, or any of the uses disclosed herein, wherein the pharmaceutical composition is diluted to obtain a flat dose of about 375 mg. The disclosure further provides an example any of the methods disclosed herein or any of the uses disclosed herein, wherein the pharmaceutical composition is diluted to obtain a flat dose of about 500 mg.

[0040] The disclosure provides an example any of the methods disclosed herein, or any of the uses disclosed herein, wherein administration of the dosing solution is once every 2 weeks, or once every 3 weeks, or once every 4 weeks.

[0041] The disclosure provides an example any of the methods disclosed herein, or any of the uses disclosed herein, wherein the cancer expresses PD-L1.

[0042] The disclosure provides an example any of the methods disclosed herein, or any of the uses disclosed herein, wherein the cancer is selected from the group consisting of: adrenal gland cancer, AIDS-associated cancer, alveolar soft part sarcoma, anal cancer, squamous cell carcinoma of the anal canal (SCAC), bladder cancer, bone cancer, brain and

spinal cord cancer, breast cancer, HER2+ breast cancer or Triple-Negative Breast Cancer (TNBC), carotid body tumor, cervical cancer, HPV-related cervical cancer, chondrosarcoma, chordoma, chromophobe renal cell carcinoma, clear cell carcinoma, colon cancer, colorectal cancer, desmoplastic small round cell tumor, ependymoma, endometrial cancer, unselected endometrial cancer, MSI-high endometrial cancer, dMMR endometrial cancer, DNA polymerase ε (POLE) exonuclease domain mutation positive endometrial cancer, Ewing's sarcoma, extraskeletal myxoid chondrosarcoma, gallbladder or bile duct cancer, cholangiocarcinoma bile duct cancer, gastric cancer, gastroesophageal junction (GEJ) cancer, gestational trophoblastic disease, germ cell tumor, glioma, glioblastoma, head and neck cancer, squamous cell carcinoma of head and neck (SCCHN), a hematological malignancy, a hepatocellular carcinoma, islet cell tumor, Kaposi's Sarcoma, kidney cancer, renal cell carcinomas (RCC), clear cell RRC, papillary RCC and chromophobe RCC, leukemia, acute myeloid leukemia, liposarcoma/malignant lipomatous tumor, liver cancer, hepatocellular carcinoma liver cancer (HCC), lymphoma, diffuse large B-cell lymphoma (DLBCL), non-Hodgkin's lymphoma (NHL), lung cancer, small cell lung cancer (SCLC), non-small cell lung cancer (NSCLC), medulloblastoma, melanoma, uveal melanoma, meningioma, mesothelioma, mesothelial pharyngeal cancer, multiple endocrine neoplasia, multiple myeloma, myelodysplastic syndrome, neuroblastoma, neuroendocrine tumors, ovarian cancer, pancreatic cancer, papillary thyroid carcinoma, parathyroid tumor, pediatric cancer, peripheral nerve sheath tumor, pharyngeal cancer, pheochromocytoma, pituitary tumor, prostate cancer, metastatic castration resistant prostate cancer (mCRPC), posterious uveal melanoma, renal metastatic cancer, rhabdoid tumor, rhabdomyosarcoma, sarcoma, skin cancer, Merkel cell carcinoma, a small round blue cell tumor of childhood, neuroblastoma, rhabdomyosarcoma, soft-tissue sarcoma, squamous cell cancer, stomach cancer, synovial sarcoma, testicular cancer, thymic carcinoma, thymoma, thyroid cancer, urothelial cancer, and uterine cancer.

[0043] The disclosure provides an example any of the methods disclosed herein, or any of the uses disclosed herein, wherein the cancer is anal cancer, breast cancer, colorectal cancer, endometrial cancer, gastric cancer, GEJ cancer, head and neck cancer, kidney cancer, liver cancer, lung cancer, lymphoma, melanoma, multiple myeloma, ovarian cancer, pancreatic cancer, prostate cancer, and skin cancer, and urothelial cancer. The disclosure further provides an example any of the methods disclosed herein, or any of the uses disclosed herein, wherein the cancer is SCAC, NSCLC, MSI-high endometrial cancer, dMMR endometrial cancer, POLE exonuclease domain mutation positive endometrial cancer,

melanoma, Merkel cell carcinoma, SCCHN, mCRPC, RCC, clear cell RCC, or urothelial cancer.

[0044] The disclosure further provides an example of any of the methods disclosed herein, or any of the uses disclosed herein, wherein the subject is a human subject.

[0045] Both the foregoing summary and the following description of the drawings and detailed description are exemplary and explanatory. They are intended to provide further details of the disclosure, but are not to be construed as limiting. Other objects, advantages, and novel features will be readily apparent to those skilled in the art from the following detailed description of the disclosure.

BRIEF DESCRIPTION OF THE FIGURES

[0046] **Figure 1** shows the prediction profiler for the formulations stored at 5 ± 3°C for 6 months (2-8°C 6 M). High molecular weight species (HMWS), monomer, acidic variants (AV), main charge peak (MP), basic variants (BV), sub-visible particles (≥10 μm and ≥25 μm) are plotted (rows) over changes in sucrose concentration, pH, PS-80 concentration, retifanlimab concentration, and ionic strength (columns).

DETAILED DESCRIPTION

[0047] The present disclosure provides pharmaceutical compositions, for storage and administration, comprising a human PD-1 ("hPD-1") antibody ("retifanlimab") and buffering agents. The disclosure further provides containers and kits comprising such pharmaceutical compositions. The disclosure further provides the use of such pharmaceutical compositions, containers, and kits containing retifanlimab for the treatment of a cancer, and in certain embodiments treatment of a cancer expressing PD-L1, for example with a therapeutically effective amount or prophylactically effective amount of retinfanlimab.

[0048] Retifanlimab (also known as MGA012 and INCMGA00012; CAS Reg No. 2079108-44-2) is a humanized hinge-stabilized IgG4κ monoclonal antibody that recognizes and binds to human PD-1 expressed by T and B-lymphocytes. Retifanlimab contains a human IgG4 Fc region containing a serine to proline mutation in the hinge region (S228P) to reduce or eliminate hinge inter-chain disulfide instability, wherein the numbering of the residues in an IgG heavy chain is that of the EU index as in Kabat (Kabat, *Sequences Of Proteins Of Immunological Interest* (National Institutes of Health, Bethesda, Md., 1987 and 1991), and refers to the numbering of the human IgG4 EU antibody. The amino acid sequences of the