might serve as a therapeutic target for the treatment of cancer. The use of anti-hB7-H3 antibodies and other molecules that modulate B7-H3 expression to treat tumors and/or up-modulate an immune response has been reported (see, *e.g.*, U.S. Patent No. 8,802,091).

SUMMARY

[0005] In one example, the present disclosure provides pharmaceutical compositions for patients whose tumors express B7-H3, including those whose tumors express low levels of B7-H3 or who have failed on other therapies. The present disclosure further provides pharmaceutical compositions comprising enoblituzumab. The disclosure further provides the use of such pharmaceutical compositions and pharmaceutical kits that that contain such pharmaceutical compositions for the treatment of cancer, and in certain examples, treatment of a cancer expressing B7-H3, for example with a therapeutically effective amount or prophylactically effective amount of enoblituzumab.

[0005a] In one aspect, the present disclosure refers to a pharmaceutical composition comprising: a) about 5 mg/mL to about 200 mg/mL enoblituzumab; b) acetate; c) sucrose; d) polysorbate 80 ("PS80"); and e) water.

[0006] In one example, the disclosure provides pharmaceutical compositions that maintain the stability of enoblituzumab across a broad concentration range,about 5 mg/mL to about 200 mg/mL, including lower concentrations (*e.g.*, about 5 mg/mL to about 60 mg/mL) and higher concentrations (*e.g.*, about 60 mg/mL to about 200 mg/mL). The disclosure further provides pharmaceutical compositions comprising enoblituzumab, acetate, sucrose, polysorbate 80 ("PS80"), and water.

[0007] The disclosure provides an example of such pharmaceutical compositions, wherein the acetate has 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. The disclosure provides an example of such pharmaceutical compositions, wherein the acetate comprises glacial acetic acid and sodium acetate.

[0008] The disclosure 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 0.05 mg/mL to about 0.6 mg/mL of PS80, and water, wherein the composition has a pH of about 4.0 to about 6.0; or

b) about 8 mM to about 24 mM acetate, about 72 mg/mL to about 108 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 4.4 to about 5.6; or

c) about 16 mM to about 24 mM acetate, about 72 mg/mL to about 108 mg/mL of sucrose, about 0.05 mg/mL to about 0.2 mg/mL of PS80, and water, wherein the composition has a pH of about 4.3 to about 5.3; or

d) about 8 mM to about 12 mM acetate, about 72 mg/mL to about 108 mg/mL of sucrose, about 0.05 mg/mL to about 0.2 mg/mL of PS80, and water, wherein the composition has a pH of about 4.5 to about 5.5; or

e) about 10 mM acetate, about 90 mg/mL of sucrose, about 0.1 mg/mL of PS80, and water, wherein the composition has a pH of about 4.6 to about 5.5; or

f) about 20 mM acetate, about 90 mg/mL of sucrose, about 0.1 mg/mL of PS80, and water, wherein the composition has a pH of about 4.4 to about 5.2.

[0009] The disclosure provides an example of such pharmaceutical compositions, wherein the acetate comprises glacial acetic acid at a concentration of about 0.1 mg/mL to about 0.65 mg/mL and sodium acetate trihydrate at a concentration of about 0.6 mg/mL to about 1.8 mg/mL.

[0010] The disclosure provides an example of such pharmaceutical compositions, wherein the enoblituzumab has a concentration of about 5 mg/mL to about 60 mg/mL. The disclosure further provides an example of such pharmaceutical compositions, wherein the enoblituzumab has a concentration of about 20 mg/mL to about 30 mg/mL. The disclosure further provides an example of such pharmaceutical compositions, wherein the enoblituzumab has a concentration of about 25 mg/mL.

[0011] The disclosure provides an example of such pharmaceutical compositions, wherein the acetate comprises glacial acetic acid at a concentration of about 0.1 mg/mL to about 0.35 mg/mL and sodium acetate trihydrate at a concentration of about 0.60 mg/mL to about 1.2 mg/mL. The disclosure further provides an example of such 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. The disclosure further provides an example of such pharmaceutical compositions, wherein the acetate

comprises glacial acetic acid at a concentration of about 0.27 mg/mL and sodium acetate trihydrate at a concentration of about 0.74 mg/mL.

[0012] The disclosure provides an example of such pharmaceutical compositions, wherein the enoblituzumab has a concentration of about 90 mg/mL to about 200 mg/mL. The disclosure further provides an example of such pharmaceutical compositions, wherein the enoblituzumab has a concentration of about 120 mg/mL.

[0013] The disclosure provides an example of such pharmaceutical compositions, wherein the acetate comprises glacial acetic acid at a concentration of about 0.4 mg/mL to about 0.65 mg/mL and sodium acetate trihydrate at a concentration of about 1.2 mg/mL to about 1.8 mg/mL. The disclosure further provides an example of such pharmaceutical compositions, wherein the acetate comprises glacial acetic acid at a concentration of about 0.52 mg/mL and sodium acetate trihydrate at a concentration of about 1.5 mg/mL.

[0014] The disclosure provides an example of such pharmaceutical compositions, wherein the concentration of sucrose is present at a concentration of about 50 mg/mL to about 130 mg/mL. The disclosure further provides an example of such pharmaceutical compositions, wherein the concentration of sucrose is present at a concentration of about 72 mg/mL to about 108 mg/mL. The disclosure further provides an example of such pharmaceutical compositions, wherein the concentration of sucrose is about 90 mg/mL.

[0015] The disclosure provides an example of such pharmaceutical compositions, wherein the PS80 is present at a concentration of about 0.05 mg/mL to about 0.6 mg/mL. The disclosure further 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.

[0016] The disclosure provides an example of such pharmaceutical compositions, wherein the composition has a pH of about 4.6 to about 5.5. The disclosure further provides an example of such pharmaceutical compositions, wherein the composition has a pH of about 4.4 to about 5.2.

[0017] The disclosure provides an example of such pharmaceutical compositions, wherein the composition comprises about 25 mg/mL of enoblituzumab, 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 4.7 to about 5.5.

[0018] The disclosure provides an example of such pharmaceutical compositions, wherein the composition comprises about 25 mg/mL of enoblituzumab, about 0.27 mg/mL of glacial acetic acid, about 0.74 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 4.6 to about 5.4.

[0019] The disclosure provides an example of such pharmaceutical compositions, wherein the composition comprises about 120 mg/mL of enoblituzumab, about 0.52 mg/mL of glacial acetic acid, about 1.5 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 4.4 to about 5.2.

[0020] The disclosure provides an example of such pharmaceutical compositions, wherein the composition does not comprise an antioxidant.

[0021] 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 at least 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 at least 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 at least about 48 months at about 2°C to about 8°C.

[0022] 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 260 to about 360 mOsm/kg H_2O.

[0023] The disclosure provides an example of such pharmaceutical compositions, wherein the composition maintains monomeric purity of the enoblituzumab 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 enoblituzumab for at least about 18 months at about 2ºC to about 8ºC.

[0024] The disclosure provides an example of such pharmaceutical compositions, wherein the composition maintains the heterogeneity profile of the enoblituzumab for about for at least about 3 months at 25ºC. The disclosure further provides an example of such pharmaceutical compositions, wherein the composition maintains the heterogeneity profile of the enoblituzumab for about for at least about 18 months at about 2ºC to about 8ºC.

[0025] The disclosure provides an example of such pharmaceutical compositions, wherein the water is sterile, nonpyrogenic, distilled water.

[0026] The disclosure provides an example of such pharmaceutical compositions, wherein the composition is sterile.

[0027] The disclosure provides a container comprising any of the pharmaceutical compositions disclosed herein. The disclosure further provides an example of such container, wherein such container comprises about 5 mL volume, about 10 mL volume, about 15 mL volume, about 17 mL volume, or about 20 mL volume of such pharmaceutical compositions.

[0027a] In one aspect, the present disclosure refers to a container comprising the pharmaceutical composition disclosed herein.

[0028] The disclosure provides an example of such containers, wherein the container comprises about 10 mL volume of the pharmaceutical composition, wherein volume comprises: (a) about 250 mg enoblituzumab; (b) about 10 mM sodium acetate; (c) about 900 mg sucrose; (d) about 1 mg PS80; and (f) water; and wherein the composition has a pH of about 4.6 to about 5.5.

[0029] The disclosure provides an example of such containers, wherein the container comprises about 10 mL volume of the pharmaceutical composition, wherein the volume comprises: (a) about 250 mg enoblituzumab; (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 the composition has a pH of about 4.7 to about 5.5.

[0030] The disclosure provides an example of such containers, wherein the container comprises about 10 mL volume of the pharmaceutical composition, wherein the volume comprises: (a) about 250 mg enoblituzumab; (b) about 2.7 mg glacial acetic acid; (c) about 7.4

mg sodium acetate trihydrate; (d) about 900 mg sucrose; (e) about 1 mg PS80; and (f) water; and wherein the composition has a pH of about 4.6 to about 5.4.

[0031] The disclosure provides an example of such containers, wherein the container comprises about 10 mL volume of the pharmaceutical composition, wherein the volume comprises: (a) about 1,200 mg enoblituzumab; (b) about 20 mM sodium acetate; (c) about 900 mg sucrose; (d) about 1 mg PS80; and (e) water; and wherein the composition has a pH of about 4.4 to about 5.2.

[0032] The disclosure provides an example of such containers, wherein the container comprises about 10 mL volume of the pharmaceutical composition, wherein the volume comprises: (a) about 1,200 mg enoblituzumab; (b) about 5.2 mg glacial acetic acid (c) about 15 mg sodium acetate trihydrate; (d) about 900 mg sucrose; (e) about 1 mg PS80; and (f) water; and wherein the composition has a pH of about 4.4 to about 5.2.

[0033] The disclosure provides an example of such containers, wherein the container comprises about 17 mL volume of the pharmaceutical composition, wherein the volume comprises: (a) about 425 mg enoblituzumab; (b) about 10 mM; (c) about 1530 mg sucrose; (d) about 1.7 mg PS80; and (e) water; and wherein the composition has a pH of about 4.6 to about 5.4.

[0034] The disclosure provides an example of such containers, wherein the container comprises about 17 mL volume of the pharmaceutical composition, wherein the volume comprises: (a) about 425 mg enoblituzumab; (b) about 3.06 mg glacial acetic acid (c) about 16.15 mg sodium acetate trihydrate; (d) about 1530 mg sucrose; (e) about 1.7 mg PS80; and (f) water; and wherein the composition has a pH of about 4.7 to about 5.5.

[0035] The disclosure provides an example of such containers, wherein the container comprises about 17 mL volume of the pharmaceutical composition, wherein the volume comprises: (a) about 425 mg enoblituzumab; (b) about 4.59 mg glacial acetic acid; (c) about 12.58 mg sodium acetate trihydrate; (d) about 1530 mg sucrose; (e) about 1.7 mg PS80; and (f) water; and wherein the composition has a pH of about 4.6 to about 5.4.

[0036] The disclosure additionally provides a sealed package comprising any of the pharmaceutical compositions disclosed herein, or any of the containers disclosed herein.

[0037] The disclosure additional provides a kit comprising any of the pharmaceutical compositions disclosed herein, any of the containers disclosed herein, or any of the sealed packages disclosed herein, and optionally further comprising instructions for administration of the pharmaceutical composition to a subject in need thereof.

[0037a] In one aspect, the present disclosure refers to a kit comprising the pharmaceutical composition disclosed herein, or the container disclosed herein, and optionally further comprising instructions for administration of the pharmaceutical composition to a subject in need thereof.

[0038] The disclosure additionally provides a sealed package comprising any of the pharmaceutical compositions disclosed herein, or 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.

[0039] The disclosure additionally provides a method of treating cancer, comprising administering enoblituzumab to a subject in need thereof using any of the pharmaceutical compositions disclosed herein, or any of the containers disclosed herein, or any of the sealed packages disclosed herein, or any of the kits disclosed herein.

[0039a] In one aspect, the present disclosure refers to use of the pharmaceutical composition disclosed herein, the container disclosed herein, or the kit disclosed herein in the manufacture of a medicament for the treatment of cancer in a subject in need thereof.

[0040] 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 the method comprises:

a) diluting the pharmaceutical composition in a container comprising 0.9% sodium chloride or 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.

[0041] The disclosure provides an example of such methods, wherein the container is an IV bag or a syringe containing 0.9% sodium chloride.

[0042] The disclosure provides an example of such methods, wherein the container is an IV bag or a syringe containing D5W.

[0043] The disclosure additionally provides the use of any of the pharmaceutical compositions disclosed herein, for the production of a medicament for the treatment of cancer in a subject in need thereof.

[0044] The disclosure additionally provides the use of any of the pharmaceutical compositions disclosed herein, or any of the containers disclosed herein, or 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.

[0045] 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 comprising 0.9% sodium chloride or 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.

[0046] The disclosure provides an example of such uses, wherein the container is an IV bag or a syringe containing 0.9% sodium chloride.

[0047] The disclosure provides an example of such uses, wherein the container is an IV bag or a syringe containing D5W.

[0048] The disclosure provides an example of the methods, or uses of the present disclosure, wherein the dosing solution maintains monomeric purity of the enoblituzumab for about 6 hours at about 25ºC or for about 24 hours at about 2ºC to about 8ºC.

[0049] The disclosure provides an example of the methods or uses of the present disclosure, wherein the administration is by IV infusion for at least about 30 minutes. The disclosure further provides an example of the methods, or uses of the present disclosure, wherein the administration is by continuous infusion for at least about 60 minutes. The disclosure further provides an example of the methods, or uses of the present disclosure, wherein the administration is by IV infusion for at least about 120 minutes.

[0050] The disclosure provides an example of the methods or uses of the present disclosure, wherein the pharmaceutical composition is diluted to obtain a weight-based treatment dose of about 6 mg/kg to about 15 mg/kg.

[0051] The disclosure provides an example of the methods or uses of the present disclosure, wherein the pharmaceutical composition is diluted to obtain a weight-based treatment dose of about 15 mg/kg

[0052] The disclosure provides an example of the methods or uses of the present disclosure, wherein administration of the dosing solution is once every 3 weeks.

[0053] The disclosure provides an example of the methods or uses of the present disclosure, wherein the cancer expresses B7-H3.

[0054] The disclosure provides an example of the methods or uses of the present disclosure, 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, 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, POLE exonuclease domain mutation positive endometrial cancer, Ewing's sarcoma, extraskeletal myxoid chondrosarcoma, gallbladder cancer, bile duct cancer, cholangiocarcinoma bile duct cancer, gastric cancer, gastroesophageal junction (GEJ) cancer, gestational trophoblastic disease, germ cell tumor, 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, 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, Merkel cell carcinoma, 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, 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.

[0055] The disclosure provides an example of the methods or uses of the present disclosure, wherein the cancer is anal cancer, bladder cancer, breast cancer, bile duct cancer, cervical cancer, colorectal cancer, endometrial cancer, gastric cancer, GEJ cancer, head and neck cancer, liver cancer, lung cancer, lymphoma, ovarian cancer, prostate cancer, skin cancer, and urothelial cancer.

[0056] The disclosure provides an example of the methods or uses of the present disclosure, wherein the anal cancer is SCAC, the lung cancer is NSCLC, the breast cancer is TNBC, the skin cancer is melanoma or Merkel cell carcinoma, the head and neck cancer is SCCHN, the prostate cancer is mCRPC. The disclosure provides an example of the methods, or uses of the present disclosure, wherein the subject is a human subject.

DETAILED DESCRIPTION OF THE INVENTION

[0057] The present invention provides pharmaceutical compositions, for storage and administration, comprising an anti-human B7-H3 ("hB7-H3") antibody ("enoblituzumab") and buffering agents. The invention further provides containers and kits comprising such pharmaceutical compositions. The invention further provides the use of such pharmaceutical compositions, containers, and kits containing enoblituzumab for the treatment of a cancer, and in certain aspects, treatment of a cancer expressing B7-H3, for example with a therapeutically effective amount or prophylactically effective amount of enoblituzumab.

I. Enoblituzumab

[0058] Enoblituzumab (also known as enoblituzumab; CAS Reg No. 1353485-38-7, see *e.g.*, US Patent No. 8,802,093) is an Fc-optimized monoclonal antibody that binds to B7-H3 and mediates enhanced ADCC activity. Enoblituzumab contains a human IgG1 Fc region containing L235V, F243L, R292P, Y300L, and P396L substitutions to enhance ADCC activity, wherein the numbering of the residues in an IgG heavy chain is that of the EU index as in Kabat *et al.,* SEQUENCES OF PROTEINS OF IMMUNOLOGICAL INTEREST, 5th Ed. Public Health Service, NH1, MD (1991), and refers to the numbering of the human IgG1 EU antibody. The amino