

WHAT IS CLAIMED:

1. A method of treatment for cancer comprising administering nivolumab and an anti-PVRIG antibody, wherein said anti-PVRIG antibody is administered as a stable liquid pharmaceutical formulation and, wherein the stable liquid pharmaceutical formulation of the anti-PVRIG antibody comprises:

- (a) an anti-PVRIG antibody, wherein said anti-PVRIG antibody comprises:
 - i) a heavy chain variable domain comprising the vhCDR1, vhCDR2, and vhCDR3 from the heavy chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:4), and
 - ii) a light chain variable domain comprising the vlCDR1, vlCDR2, and vlCDR3 from the light chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:9);
 - (b) from 10 mM to 100 mM histidine;
 - (c) from 30 mM to 100 mM NaCl;
 - (d) from 20 mM to 150 mM L-Arginine; and
 - (e) from 0.005% to 0.1% w/v polysorbate 80,
- wherein the composition has a pH from 5.5 to 7.0.

2. The method of treatment according to any one of claim 1, wherein said anti-PVRIG antibody comprises a CH1-hinge-CH2-CH3 sequence of IgG4 (SEQ ID NO:17 or SEQ ID NO:50), wherein said hinge region optionally comprises mutations.

3. The method of treatment according to any one of claims 1 or 2, wherein said anti-PVRIG antibody comprises the CH1-hinge-CH2-CH3 region from IgG1, IgG2, IgG3, or IgG4, wherein said hinge region optionally comprises mutations.

4. The method of treatment according to any one of claims 1-3, wherein said heavy chain variable domain is from the heavy chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:4) and said light chain variable domain is from the light chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:9).

5. The method of treatment according to any one of claims 1-4, wherein said anti-PVRIG antibody comprises a CL region of human kappa 2 light chain.

6. The method of treatment according to any one of claims 1-5, wherein said pharmaceutical formulation comprises from 10 mM to 80 mM histidine, from 15 mM to 70 mM histidine, from 20 mM to 60 mM histidine, from 20 mM to 50 mM histidine, or from 20 mM to 30 mM histidine.
7. The method of treatment according to any one of claims 1-6, wherein said pharmaceutical formulation comprises about 25 mM histidine.
8. The method of treatment according to any one of claims 1-7, wherein said pharmaceutical formulation comprises from 30 mM to 100 mM NaCl, from 30 mM to 90 mM NaCl, from 40 mM to 80 mM NaCl, from 30 mM to 70 mM histidine, or from 45 mM to 70 mM NaCl.
9. The method of treatment according to any one of claims 1-8, wherein said pharmaceutical formulation comprises about 60 mM NaCl.
10. The method of treatment according to any one of claims 1-9, wherein said pharmaceutical formulation comprises from 20 mM to 140 mM L-arginine, from 30 mM to 140 mM L-arginine, from 40 mM to 130 mM L-arginine, from 50 mM to 120 mM L-arginine, from 60 mM to 110 mM L-arginine, from 70 mM to 110 mM L-arginine, from 80 mM to 110 mM L-arginine, or from 90 mM to 110 mM L-arginine.
11. The method of treatment according to any one of claims 1-10, wherein said pharmaceutical formulation comprises about 100 mM L-arginine.
12. The method of treatment according to any one of claims 1-11, wherein said pharmaceutical formulation comprises from 0.006% to 0.1% w/v polysorbate 80, from 0.007% to 0.09% w/v polysorbate 80, from 0.008% to 0.08% w/v polysorbate 80, from 0.009% to 0.09% w/v polysorbate 80, from 0.01% to 0.08% w/v polysorbate 80, from 0.01% to 0.07% w/v polysorbate 80, from 0.01% to 0.07% w/v polysorbate 80, or from 0.01% to 0.06% w/v polysorbate 80, or from 0.009% to 0.05% w/v polysorbate 80.
13. The method of treatment according to any one of claims 1-12, wherein said pharmaceutical formulation comprises about 0.01% polysorbate 80.
14. The method of treatment according to any one of claims 1-13, wherein said pH is from 6 to 7.0.

15. The method of treatment according to any one of claims 1-14, wherein said pH is from 6.3 to 6.8.
16. The method of treatment according to any one of claims 1-15, wherein said pH is 6.5 +/- 0.2.
17. The method of treatment according to any one of claims 1-16, wherein said anti-PVRIG antibody is at a concentration of from 10 mg/mL to 40 mg/mL, 15 mg/mL to 40 mg/mL, 15 mg/mL to 30 mg/mL, 10 mg/mL to 25 mg/mL, or 15 mg/mL to 25 mg/mL.
18. The method of treatment according to any one of claims 1-17, wherein said formulation is stable at 2°C to 8°C for at least 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, 9 weeks, or 10 weeks.
19. The method of treatment according to any one of claims 1-18, wherein said formulation is stable at about 20°C to 25 °C for at least 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, or 6 weeks.
20. The method of treatment according to any one of claims 1-19, wherein said formulation is stable at 35°C to 40°C for at least 1 week, 2 weeks, 3 weeks, 4 weeks, or 5 weeks.
21. The method of treatment according to any one of claims 1-20, wherein said anti-PVRIG antibody is at a concentration of about 20 mg/mL.
22. The method of treatment according to any one of claims 1-21, wherein said anti-PVRIG antibody formulation comprises:
 - a) a heavy chain comprising:
 - i) a VH-CH1-hinge-CH2-CH3, wherein the VH is from CHA.7.518.1.H4(S241P) (SEQ ID NO:4) and wherein the CH1-hinge-CH2-CH3 region is from IgG4; and
 - b) a light chain comprising:
 - i) a VL-CL, wherein the VL from CHA.7.518.1.H4(S241P) (SEQ ID NO:9) and wherein the CL region is from human kappa 2 light chain.

23. The method of treatment according to claim 24, wherein said hinge region optionally comprises mutations.
24. The method of treatment of claim 23, wherein said hinge region optionally comprises mutations.
25. The method of treatment according to any one of claims 1-24, wherein said anti-PVRIG antibody formulation comprises:
- i) a heavy chain comprising the heavy chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:8); and
 - ii) a light chain comprising the light chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:13).
26. The method of treatment according to any one of claims 1-25, said anti-PVRIG antibody formulation comprising:
- (a) an anti-PVRIG antibody, wherein said anti-PVRIG antibody comprises:
 - i) a heavy chain variable domain comprising the vhCDR1, vhCDR2, and vhCDR3 from the heavy chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:4), and
 - ii) a light chain variable domain comprising the vlCDR1, vlCDR2, and vlCDR3 from the light chain of CHA.7.518.1.H4(S241P) (SEQ ID NO:9);
 - (b) about 25 mM histidine;
 - (c) about 60 mM NaCl;
 - (d) about 100 mM L-Arginine; and
 - (e) about 0.01% w/v polysorbate 80,
- wherein the composition has a pH from 6.5 +/- 0.2.
27. The method of treatment according to any one of claims 1-26, said anti-PVRIG antibody formulation comprising:
- (a) an anti-PVRIG antibody, wherein said anti-PVRIG antibody comprises:

i) a heavy chain comprising the heavy chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:8); and

ii) a light chain comprising the light chain from CHA.7.518.1.H4(S241P) (SEQ ID NO:13);

(b) about 25 mM histidine;

(c) about 60 mM NaCl;

(d) about 100 mM L-Arginine; and

(e) about 0.01% w/v polysorbate 80,

wherein the composition has a pH from 6.5 +/- 0.2.

28. The method of treatment according to any one of claims 1-27, wherein said anti-PVRIG antibody is administered at a dosage of about 0.01 mg/kg to about 20 mg/kg of the anti-PVRIG antibody or about 0.01 mg/kg to about 10 mg/kg of the anti-PVRIG antibody.

29. The method of treatment according to any one of claims 1-27, wherein said anti-PVRIG antibody is administered at a dosage of about 0.01 mg/kg, 0.03 mg/kg, 0.1 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg, 10 mg/kg, or 20 mg/kg of the anti-PVRIG antibody.

30. The method of treatment according to any one of claims 1-29, wherein said nivolumab is administered at a dosage of about 360 mg of nivolumab or 480 mg of nivolumab.

31. The method of treatment according to any one of claims 1-30, wherein said anti-PVRIG antibody is administered 20 mg/kg every 4 weeks.

32. The method of treatment according to any one of claims 1-31, wherein said cancer wherein said cancer selected from the group consisting of prostate cancer, liver cancer (HCC), colorectal cancer (CRC), colorectal cancer MSS (MSS-CRC; including refractory MSS colorectal), CRC (MSS unknown), ovarian cancer (including ovarian carcinoma), endometrial cancer (including endometrial carcinoma), breast cancer, pancreatic cancer, stomach cancer, cervical cancer, head and neck cancer, thyroid cancer, testis cancer, urothelial cancer, lung cancer, melanoma, non-melanoma skin cancer (squamous and basal cell carcinoma), glioma, renal cell cancer (RCC), renal cell carcinoma (RCC), lymphoma

(non-Hodgkins' lymphoma (NHL) and Hodgkin's lymphoma (HD)), Acute myeloid leukemia (AML), T cell Acute Lymphoblastic Leukemia (T-ALL), Diffuse Large B cell lymphoma, testicular germ cell tumors, mesothelioma, esophageal cancer, triple negative breast cancer, Merkel Cells cancer, MSI-high cancer, KRAS mutant tumors, adult T-cell leukemia/lymphoma, pleural mesothelioma, anal SCC, neuroendocrine lung cancer (including neuroendocrine lung carcinoma), NSCLC, NSCL (large cell), NSCLC large cell, NSCLC squamous cell, cervical SCC, malignant melanoma, pancreatic cancer, pancreatic adenocarcinoma, NSCLC, adenoid cystic cancer (including adenoid cystic carcinoma), primary peritoneal cancer, microsatellite stable primary peritoneal cancer, platinum resistant microsatellite stable primary peritoneal cancer, and/or Myelodysplastic syndromes (MDS).

33. The nivolumab and an anti-PVRIG antibody combination treatment according to any one of the method of treatment claims 1-32, for use in a method of treating cancer.

34. The use according to claim 33, wherein said cancer wherein said cancer selected from the group consisting of prostate cancer, liver cancer (HCC), colorectal cancer (CRC), colorectal cancer MSS (MSS-CRC; including refractory MSS colorectal), CRC (MSS unknown), ovarian cancer (including ovarian carcinoma), endometrial cancer (including endometrial carcinoma), breast cancer, pancreatic cancer, stomach cancer, cervical cancer, head and neck cancer, thyroid cancer, testis cancer, urothelial cancer, lung cancer, melanoma, non-melanoma skin cancer (squamous and basal cell carcinoma), glioma, renal cell cancer (RCC), renal cell carcinoma (RCC), lymphoma (non-Hodgkins' lymphoma (NHL) and Hodgkin's lymphoma (HD)), Acute myeloid leukemia (AML), T cell Acute Lymphoblastic Leukemia (T-ALL), Diffuse Large B cell lymphoma, testicular germ cell tumors, mesothelioma, esophageal cancer, triple negative breast cancer, Merkel Cells cancer, MSI-high cancer, KRAS mutant tumors, adult T-cell leukemia/lymphoma, pleural mesothelioma, anal SCC, neuroendocrine lung cancer (including neuroendocrine lung carcinoma), NSCLC, NSCL (large cell), NSCLC large cell, NSCLC squamous cell, cervical SCC, malignant melanoma, pancreatic cancer, pancreatic adenocarcinoma, NSCLC, adenoid cystic cancer (including adenoid cystic carcinoma), primary peritoneal cancer, microsatellite stable primary peritoneal cancer, platinum resistant microsatellite stable primary peritoneal cancer, and/or Myelodysplastic syndromes (MDS).