

What is claimed is:

1. ~~A method of~~ Use of a programmed death 1 (PD-1) inhibitor in the manufacture of a medicament for treating or inhibiting cancer pain, ~~comprising:~~
  - (a) ~~selecting in~~ a patient with cancer; ~~and~~
  - (b) ~~administering to the patient a therapeutically effective amount of a programmed death 1 (PD-1) inhibitor.~~
2. The ~~method of~~ use according to claim 1, wherein the cancer is selected from anal cancer, bladder cancer, bone cancer, breast cancer, brain cancer, cervical cancer, colon cancer, colorectal cancer, endometrial cancer, esophageal cancer, head and neck cancer, kidney cancer, liver cancer, lung cancer, myeloma, ovarian cancer, pancreatic cancer, prostate cancer, salivary gland cancer, skin cancer, stomach cancer, testicular cancer, and uterine cancer.
3. The ~~method of~~ use according to claim 1 or 2, wherein the cancer is skin cancer.
4. The ~~method of~~ use according to claim 3 ~~any one of claims 1-3~~, wherein the skin cancer is a non-melanoma skin cancer.
5. The ~~method of~~ use according to claim 3 ~~any one of claims 1-4~~, wherein the skin cancer is cutaneous squamous cell carcinoma (CSCC) or basal cell carcinoma (BCC).
6. The ~~method of~~ use according to claim 5, wherein the CSCC is metastatic CSCC or unresectable locally advanced CSCC.
7. The ~~method of~~ use according to claim 5, wherein the BCC is locally advanced BCC (laBCC) or metastatic BCC.
8. The ~~method of~~ use according to claim 7, wherein the BCC has progressed on or the BCC patient was intolerant to hedgehog inhibitor (HHI) therapy.
9. The ~~method of~~ use according to any one of claims 1-8, wherein functioning and quality of life of the patient is improved or maintained from baseline, as measured by EORTC QLQ-C30 and SKINDEX-16.
10. The ~~method of~~ use according to any one of claims 1-9, wherein the patient receives analgesic therapy prior to administration of the PD-1 inhibitor.

11. The ~~method of~~use according to any one of claims 1-10, wherein the patient is to be administered analgesic therapy in combination with the PD-1 inhibitor.
12. The ~~method of~~use according to claim 10 or 11, wherein the analgesic therapy is selected from an opioid, a non-steroid anti-inflammatory drug (NSAID), a steroid, acetaminophen, and combinations thereof.
13. The ~~method of~~use according to any one of claims 10-12, wherein the analgesic therapy comprises an opioid.
14. The ~~method of~~use according to any one of claims 10-13, wherein ~~the~~ administration of the PD-1 inhibitor leads to reduced use of analgesic therapy by the patient.
15. The ~~method of~~use according to any one of claims 10-13, further comprising reducing the amount of the analgesic therapy received by the patient by 20% or more within 1 year after administration of the PD-1 inhibitor.
16. The ~~method of~~use according to any one of claims 1-15, wherein the pain is reduced by about 20% or more within 1 year after administration of the PD-1 inhibitor.
17. The ~~method of~~use according to any one of claims 1-16, wherein ~~the~~ administration of the PD-1 inhibitor concurrently leads to reduced cancer pain and at least 30% decrease in tumor cells or tumor size.
18. The ~~method of~~use according to any one of claims 1-17, wherein ~~the~~ administration of the PD-1 inhibitor concurrently leads to reduced analgesic use and at least 30% decrease in tumor cells or tumor size.
19. The ~~method of~~use according to any one of claims 1-18, wherein ~~the~~ administration of the PD-1 inhibitor concurrently leads to reduced opioid use and at least 30% decrease in tumor cells or tumor size.
20. The ~~method of~~use according to any one of claims 1-19, wherein ~~the~~ administration of the PD-1 inhibitor reduces pain, reduces the need for analgesic therapy, promotes tumor regression, reduces tumor cell load, reduces tumor burden, prevents tumor recurrence in the patient, and/or increases patient survival.

21. The ~~method of~~use according to any one of claims 1-20, wherein the PD-1 inhibitor is to be administered in combination with an additional therapeutic agent or therapy selected from an analgesic, a non-steroid anti-inflammatory drug (NSAID), radiation, surgery, a cancer vaccine, imiquimod, an anti-viral agent, photodynamic therapy, HHI therapy, a PD-L1 inhibitor, a LAG3 inhibitor, a CTLA-4 inhibitor, a GITR agonist, a TIM3 inhibitor, a BTLA inhibitor, a TIGIT inhibitor, a CD38 inhibitor, a CD47 inhibitor, an IDO inhibitor, a CD28 activator, a VEGF antagonist, an Ang2 inhibitor, a TGF $\beta$  inhibitor, an EGFR inhibitor, an antibody to a tumor-specific antigen, a cancer vaccine, a GM-CSF, an oncolytic virus, a cytotoxin, a chemotherapeutic agent, an IL-6R inhibitor, an IL-4R inhibitor, an IL-10 inhibitor, a cytokine, an antibody drug conjugate, an anti-inflammatory drug, and a dietary supplement.

22. The ~~method of~~use according to any one of claims 1-21, wherein the PD-1 inhibitor is selected from an anti-PD-1 antibody or antigen-binding fragment thereof, an anti-PD-L1 antibody or antigen-binding fragment thereof, and an anti-PD-L2 antibody or antigen-binding fragment thereof.

23. The ~~method of~~use according to any one of claims 1-22, wherein the PD-1 inhibitor is an anti-PD-1 antibody or antigen-binding fragment thereof.

24. The ~~method of~~use according to any one of claims 1-23, wherein the PD-1 inhibitor is an anti-PD-1 antibody or antigen-binding fragment thereof that comprises a heavy chain variable region (HCVR) comprising three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) and a light chain variable region (LCVR) comprising three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein: HCDR1 has an amino acid sequence of SEQ ID NO: 3; HCDR2 has an amino acid sequence of SEQ ID NO: 4; HCDR3 has an amino acid sequence of SEQ ID NO: 5; LCDR1 has an amino acid sequence of SEQ ID NO: 6; LCDR2 has an amino acid sequence of SEQ ID NO: 7; and LCDR3 has an amino acid sequence of SEQ ID NO: 8.

25. The ~~method of~~use according to claim 24, wherein the HCVR comprises an amino acid sequence of SEQ ID NO: 1.

26. The ~~method of~~use according to claim 24, wherein the LCVR comprises an amino acid sequence of SEQ ID NO: 2.

27. The ~~method of~~[use according to](#) claim 24, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises an HCVR/LCVR amino acid sequence pair of SEQ ID NOs: 1/2.
28. The ~~method of~~[use according to](#) any one of claims 23-27, wherein the anti-PD-1 antibody comprises a heavy chain and a light chain, wherein the heavy chain has an amino acid sequence of SEQ ID NO: 9.
29. The ~~method of~~[use according to](#) any one of claims 23-27, wherein the anti-PD-1 antibody comprises a heavy chain and a light chain, wherein the light chain has an amino acid sequence of SEQ ID NO: 10.
30. The ~~method of~~[use according to](#) any one of claims 23-27, wherein the anti-PD-1 antibody comprises a heavy chain and a light chain, wherein the heavy chain has an amino acid sequence of SEQ ID NO: 9 and the light chain has an amino acid sequence of SEQ ID NO: 10.
31. The ~~method of~~[use according to](#) any one of claims 1-23, wherein the PD-1 inhibitor is an anti-PD-1 antibody or antigen-binding fragment thereof comprising a HCVR with 90%, 95%, 97% or 98% sequence identity to SEQ ID NO: 1.
32. The ~~method of~~[use according to](#) any one of claims 1-23, wherein the PD-1 inhibitor is an anti-PD-1 antibody or antigen-binding fragment thereof comprising a LCVR with 90%, 95%, 97% or 98% sequence identity to SEQ ID NO: 2.
33. The ~~method of~~[use according to](#) any one of claims 1-23, wherein the PD-1 inhibitor is an anti-PD-1 antibody or antigen-binding fragment thereof comprising a HCVR with 90%, 95%, 97% or 98% sequence identity to SEQ ID NO: 1, and a LCVR with 90%, 95%, 97% or 98% sequence identity to SEQ ID NO: 2.
34. The ~~method of~~[use according to](#) any one of claims 1-27, wherein the PD-1 inhibitor is cemiplimab or a bioequivalent thereof.
35. The ~~method of~~[use according to](#) any one of claims 1-23, wherein the PD-1 inhibitor is an anti-PD-1 antibody selected from the group consisting of cemiplimab, nivolumab, pembrolizumab, pidilizumab, MEDI0608, BI 754091, PF-06801591, spartalizumab, camrelizumab, JNJ-63723283, and MCLA-134.

36. The ~~method of use according to~~ any one of claims 1-22, wherein the PD-1 inhibitor is an anti-PD-L1 antibody selected from the group consisting of REGN3504, avelumab, atezolizumab, durvalumab, MDX-1105, LY3300054, FAZ053, STI-1014, CX-072, KN035, and CK-301.
37. The ~~method of use according to~~ any one of claims 1-36, wherein the PD-1 inhibitor is to be administered at a dose of 5mg to 1500mg.
38. The ~~method of use according to~~ any one of claims 1-37, wherein the PD-1 inhibitor is to be administered at a dose of 200mg, 250mg, or 350mg.
39. The ~~method of use according to~~ any one of claims 1-36, wherein the PD-1 inhibitor is to be administered at a dose of 1 mg/kg to 20 mg/kg of the patient's body weight.
40. The ~~method of use according to~~ any one of claims 1-36, wherein the PD-1 inhibitor is to be administered at a dose of 1 mg/kg, 3 mg/kg or 10 mg/kg of the patient's body weight.
41. The ~~method of use according to~~ any one of claims 1-40, wherein the PD-1 inhibitor is to be administered as one or more doses, wherein each dose is to be administered every two weeks, three weeks, four weeks, five weeks or six weeks.
42. The ~~method of use according to~~ any one of claims 1-41, wherein the PD-1 inhibitor is to be administered intravenously or subcutaneously.
43. A kit comprising a therapeutically effective amount of a programmed death 1 (PD-1) inhibitor in combination with written instructions for use ~~in of a therapeutically effective amount of the PD-1 inhibitor for~~ treating or inhibiting cancer pain in a patient with cancer.
44. The kit of claim 43, further including instructions for use of a therapeutically effective amount of the PD-1 inhibitor for treating or inhibiting the growth of a tumor.
45. The kit of claim 43 or 44, wherein the cancer is selected from anal cancer, bladder cancer, bone cancer, breast cancer, brain cancer, cervical cancer, colon cancer, colorectal cancer, endometrial cancer, esophageal cancer, head and neck cancer, kidney cancer, liver cancer, lung cancer, myeloma, ovarian cancer, pancreatic cancer, prostate cancer, salivary gland cancer, skin cancer, stomach cancer, testicular cancer, and uterine cancer.
46. ~~A method of~~ Use of a programmed death 1 (PD-1) inhibitor in the manufacture of a medicament for reducing use of analgesic therapy by a cancer patient, ~~comprising:~~

(a) ~~selecting in~~ a patient with cancer wherein the patient is receiving analgesic therapy as a background medication prior to ~~the~~ administration of ~~a programmed death 1 (PD-1)~~ the PD-1 inhibitor to the patient; and

(b) ~~administering to the patient a therapeutically effective amount of a PD-1 inhibitor.~~

47. The ~~method of use according to~~ claim 46, wherein the cancer is selected from anal cancer, bladder cancer, bone cancer, breast cancer, brain cancer, cervical cancer, colon cancer, colorectal cancer, endometrial cancer, esophageal cancer, head and neck cancer, kidney cancer, liver cancer, lung cancer, myeloma, ovarian cancer, pancreatic cancer, prostate cancer, salivary gland cancer, skin cancer, stomach cancer, testicular cancer, and uterine cancer.

48. The ~~method of use according to~~ claim 46 or 47, wherein the cancer is skin cancer.

49. The ~~method of use according to claim 48 any one of claims 46-48,~~ wherein the skin cancer is metastatic cutaneous squamous cell carcinoma (CSCC) or unresectable locally advanced CSCC.

50. The ~~method of use according to~~ any one of claims 46-49, wherein the analgesic therapy is selected from an opioid, a non-steroid anti-inflammatory drug (NSAID), a steroid, acetaminophen, and combinations thereof.

51. The ~~method of use according to~~ any one of claims 46-50, wherein the analgesic therapy comprises an opioid.

52. The ~~method of use according to~~ any one of claims 46-51, wherein the amount of analgesic therapy received by the patient is reduced by at least 20% within 1 year after administration of the PD-1 inhibitor as compared to the amount of analgesic therapy received by the patient before administration of the PD-1 inhibitor.

53. The ~~method of use according to~~ any one of claims 46-52, wherein the administration of the PD-1 inhibitor concurrently leads to reduced analgesic use and at least 30% decrease in tumor cells or tumor size.

54. The ~~method of use according to~~ any one of claims 46-53, wherein the administration of the PD-1 inhibitor concurrently leads to reduced opioid use and at least 30% decrease in tumor cells or tumor size.

55. The ~~method of~~use according to any one of claims 46-54, wherein the administration of the PD-1 inhibitor concurrently leads to reduced cancer pain and at least 30% decrease in tumor cells or tumor size.

56. The ~~method of~~use according to any one of claims 46-55, wherein the administration of the PD-1 inhibitor concurrently leads to reduced cancer pain, reduced opioid use, and a tumor response selected from the group consisting of stable disease (SD), partial response (PR) and complete response (CR), as determined using RECIST criteria.

57. The ~~method of~~use according to any one of claims 46-56, wherein the PD-1 inhibitor is to be administered in combination with an additional therapeutic agent or therapy selected from an analgesic, a non-steroid anti-inflammatory drug (NSAID), radiation, surgery, a cancer vaccine, imiquimod, an anti-viral agent, photodynamic therapy, HHI therapy, a PD-L1 inhibitor, a LAG3 inhibitor, a CTLA-4 inhibitor, a GITR agonist, a TIM3 inhibitor, a BTLA inhibitor, a TIGIT inhibitor, a CD40 inhibitor, a CD47 inhibitor, an IDO inhibitor, a CD28 activator, a VEGF antagonist, an Ang2 inhibitor, a TGF $\beta$  inhibitor, an EGFR inhibitor, an antibody to a tumor-specific antigen, a cancer vaccine, a GM-CSF, an oncolytic virus, a cytotoxin, a chemotherapeutic agent, an IL-6R inhibitor, an IL-4R inhibitor, an IL-10 inhibitor, a cytokine, an antibody drug conjugate, an anti-inflammatory drug, and a dietary supplement.

58. The ~~method of~~use according to any one of claims 46-57, wherein the PD-1 inhibitor is selected from an anti-PD-1 antibody or antigen-binding fragment thereof, an anti-PD-L1 antibody or antigen-binding fragment thereof, and an anti-PD-L2 antibody or antigen-binding fragment thereof.

59. The ~~method of~~use according to any one of claims 46-58, wherein the PD-1 inhibitor is an anti-PD-1 antibody or antigen-binding fragment thereof.

60. The ~~method of~~use according to any one of claims 46-59, wherein the PD-1 inhibitor is an anti-PD-1 antibody or antigen-binding fragment thereof that comprises a heavy chain variable region (HCVR) comprising three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) and a light chain variable region (LCVR) comprising three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein: HCDR1 has an amino acid sequence of SEQ ID NO: 3; HCDR2 has an amino acid sequence of SEQ ID NO: 4; HCDR3 has an amino acid sequence of SEQ ID NO: 5; LCDR1 has an amino acid sequence of SEQ ID NO: 6; LCDR2

has an amino acid sequence of SEQ ID NO: 7; and LCDR3 has an amino acid sequence of SEQ ID NO: 8.

61. The ~~method of~~use according to any one of claims 46-60, wherein the PD-1 inhibitor is to be administered at a dose of 5mg to 1500mg.
62. The ~~method of~~use according to any one of claims 46-61, wherein the PD-1 inhibitor is to be administered at a dose of 200mg, 250mg, or 350mg.
63. The ~~method of~~use according to any one of claims 46-60, wherein the PD-1 inhibitor is to be administered at a dose of 1 mg/kg to 20 mg/kg of the patient's body weight.
64. The ~~method of~~use according to any one of claims 46-60, wherein the PD-1 inhibitor is to be administered at a dose of 1 mg/kg, 3 mg/kg or 10 mg/kg of the patient's body weight.
65. The ~~method of~~use according to any one of claims 46-64, wherein the PD-1 inhibitor is to be administered as one or more doses, wherein each dose is to be administered every two weeks, three weeks, four weeks, five weeks or six weeks.
66. The ~~method of~~use according to any one of claims 46-65, wherein the PD-1 inhibitor is to be administered intravenously or subcutaneously.