## BRIEF SUMMARY

**[0008]** Provided herein are methods for treating or delaying progression of cancer in an individual comprising administering to the individual an effective amount of a PD-1 axis binding antagonist and a MEK inhibitor, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist. In some embodiments, the method further comprises diagnosing the individual as having a cancer that is resistant to a B-raf antagonist, wherein the diagnosing occurs prior to administering the effective amount of the PD-1 axis binding antagonist and the MEK inhibitor. In some embodiments, the method further comprises selecting an individual for treatment based on the individual having cancer that is resistant to a B-raf antagonist or assessing that the individual is at risk of developing cancer that is resistant to a B-raf antagonist, wherein the selecting occurs prior to administering the effective amount of the PD-1 axis binding antagonist and the MEK inhibitor. In some embodiments, the individual has not been previously treated with a B-raf antagonist. In some embodiments, the individual has been previously treated with a B-raf antagonist.

**[0008a]** In one aspect, provided herein is use of an effective amount of a PD-1 axis binding antagonist and a MEK inhibitor for the manufacture of a first medicament comprising the PD-1 axis binding antagonist and a second medicament comprising the MEK inhibitor for treating or delaying progression of cancer in an individual, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

**[0008b]** In one aspect, provided herein is use of an effective amount of a PD-1 axis binding antagonist in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the PD-1 axis binding agent is used in combination with a MEK inhibitor, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

**[0008c]** In one aspect, provided herein is use of an effective amount of a MEK inhibitor in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the MEK inhibitor is used in combination with a PD-1 axis binding antagonist, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

**[0008d]** In one aspect, provided herein is a pharmaceutical composition comprising a PD-1 axis binding antagonist in combination with a MEK inhibitor for use in treating or delaying progression of cancer in an individual, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

**[0008e]** In one aspect, provided herein is a pharmaceutical composition comprising a PD-1 axis binding antagonist for use in treating or delaying progression of cancer in an individual in combination with a MEK inhibitor, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

**[0008f]** In one aspect, provided herein is a pharmaceutical composition comprising a MEK inhibitor for use in treating or delaying progression of cancer in an individual in combination with a PD-1 axis binding antagonist wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

**[0009]** Provided herein are methods for treating or delaying progression of cancer in an individual comprising (a) diagnoising the individual as having a cancer that is resistant to a B-raf antagonist; and (b) administering to the individual an effective amount of a PD-1 axis binding antagonist and a MEK inhibitor, wherein the administering occurs after diagnosing the individual. In some embodiments, the individual has not been previously treated with a B-raf antagonist. In some embodiments, the individual has been previously treated with a B-raf antagonist.

**[0010]** Provided herein are methods for treating or delaying progression of cancer in an individual comprising (a) selecting an individual for treatment based on the individual having cancer that is resistant to a B-raf antagonist or assessing that the individual is at risk of developing cancer that is resistant to a B-raf antagonist; and (b) administering to the individual an effective amount of a PD-1 axis binding antagonist and a MEK inhibitor, wherein the administering occurs after selecting the individual. In some embodiments, the individual has not been previously treated with a B-raf antagonist. In some embodiments, the individual has been previously treated with a B-raf antagonist.

**[0011]** Provided herein are methods for treating or delaying progression of cancer in an individual comprising administering to the individual an effective amount of a PD-1

axis binding antagonist and a MEK inhibitor, wherein the individual has been previously treated with a B-raf antagonist for cancer.

**[0011a]** In one aspect, provided herein is use of an effective amount of a PD-1 axis binding antagonist and a MEK inhibitor for the manufacture of a first medicament comprising the PD-1 axis binding antagonist and a second medicament comprising the MEK inhibitor for treating or delaying progression of cancer in an individual, wherein the individual has been previously treated with a B-raf antagonist for cancer.

**[0011b]** In one aspect, provided herein is use of an effective amount of a PD-1 axis binding antagonist in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the PD-1 axis binding agent is used in combination with a MEK inhibitor, wherein the individual has been previously treated with a B-raf antagonist for cancer.

**[0011c]** In one aspect, provided herein is use of an effective amount of a MEK inhibitor in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the MEK inhibitor is used in combination with a PD-1 axis binding antagonist, wherein the individual has been previously treated with a B-raf antagonist for cancer.

**[0011d]** In one aspect, provided herein is a pharmaceutical composition comprising a PD-1 axis binding antagonist in combination with a MEK inhibitor for use in treating or delaying progression of cancer in an individual, wherein the individual has been previously treated with a B-raf antagonist for cancer.

**[0011e]** In one aspect, provided herein is a pharmaceutical composition comprising a PD-1 axis binding antagonist for use in treating or delaying progression of cancer in an individual in combination with a MEK inhibitor, wherein the individual has been previously treated with a B-raf antagonist for cancer.

**[0011f]** In one aspect, provided herein is a pharmaceutical composition comprising a MEK inhibitor for use in treating or delaying progression of cancer in an individual in combination with a PD-1 axis binding antagonist wherein the individual has been previously treated with a B-raf antagonist for cancer.

**[0012]** In some embodiments, the cancer in the individual has progressed within 1 month, 6 months, 1 year, or 5 years after completing a B-raf antagonist-based therapy regimen. In some embodiments, the B-raf antagonist is a small molecule inhibitor, an antibody, a peptide, a peptidomimetic, an aptamer or a polynucleotide. In some embodiments, the B-raf antagonist is dabrafenib, vemurafenib, GSK 2118436, RAF265, XL281, ARQ736, BAY73-4506, sorafenib, PLX4720, PLX-3603, GSK2118436, GDC-0879, or N-(3-(5-(4-chlorophenyl)-1H-pyrrolo[2,3-b]pyridine-3-carbonyl)-2,4-difluorophenyl)propane-1-sulfonamide. In some embodiments, the B-raf antagonist is a selective B-raf antagonist of B-raf V600. In some embodiments, the selective B-raf antagonist of B-raf V600 is a selective antagonist of B-raf V600E. In some embodiments, the selective B-raf antagonist of B-raf V600 is a selective antagonist of B-raf V600E, B-raf V600K, and/or V600D. In some embodiments, the selective B-raf antagonist of B-raf V600 is a selective antagonist of B-raf V600R.

**[0013]** In some embodiments, the cancer contains a BRAF V600E mutation, a BRAF wildtype, a KRAS wildtype, or an activating KRAS mutation. In some embodiments, the treatment results in a sustained response in the individual after cessation of the treatment. In some embodiments, the individual has colorectal cancer, melanoma, lung cancer, ovarian cancer, breast cancer, pancreatic cancer, hematological malignancy, bladder cancer, and/or renal cell carcinoma. In some embodiments, the cancer is metastatic.

**[0014]** In some embodiments, the PD-1 axis binding antagonist is selected from the group consisting of a PD-1 binding antagonist, a PD-L1 binding antagonist and a PD-L2 binding antagonist. In some embodiments, the PD-1 axis binding antagonist is a PD-1 binding antagonist. In some embodiments, the PD-1 binding antagonist inhibits the binding of PD-1 to its ligand binding partners. In some embodiments, the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L1, PD-1 to PD-L2, or PD-1 to both PD-L1 and PD-L2. In some embodiments, the PD-1 binding antagonist is an antibody. In some embodiments, the PD-1 binding antagonist is MDX-1106, Merck 3745, CT- 011, MEDI-0680, PDR001, REGN2810, BGB-108, BGB-A317, or AMP-224. In some embodiments, the PD-1 binding antagonist is nivolumab, pembrolizumab, pidilizumab, MEDI-0680, PDR001, REGN2810, BGB-108, BGB-A317, or AMP-224. In some embodiments, the PD-1 axis binding antagonist is a PD-L1 binding antagonist. In some embodiments, the PD-L1 binding antagonist inhibits the binding of

some embodiments, the PD-1 axis binding antagonist and/or the MEK inhibitor is administered intravenously, intramuscularly, subcutaneously, topically, orally, transdermally, intraperitoneally, intraorbitally, by implantation, by inhalation, intrathecally, intraventricularly, or intranasally.

**[0016]** In another aspect, provided herein are kits comprising a PD-1 axis binding antagonist and a package insert comprising instructions for using the PD-1 axis binding antagonist in combination with a MEK inhibitor to treat or delay progression of cancer in an individual, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist. In another aspect, provided herein are kits comprising a PD-1 axis binding antagonist and a MEK inhibitor, and a package insert comprising instructions for using the PD-1 axis binding antagonist and the MEK inhibitor to treat or delay progression of cancer in an individual, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist. In another aspect, provided herein are kits comprising a MEK inhibitor and a package insert comprising instructions for using the MEK inhibitor in combination with a PD-1 axis binding antagonist to treat or delay progression of cancer in an individual, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist. In another aspect, provided herein are kits comprising a PD-1 axis binding antagonist and a package insert comprising instructions for using the PD-1 axis binding antagonist in combination with a MEK inhibitor to treat or delay progression of cancer in an individual, wherein the individual has been previously treated with a B-raf antagonist for cancer. In another aspect, provided herein are kits comprising a PD-1 axis binding antagonist and a MEK inhibitor, and a package insert comprising instructions for using the PD-1 axis binding antagonist and the MEK inhibitor to treat or delay progression of cancer in an individual, wherein the individual has been previously treated with a B-raf antagonist for cancer. In another aspect, provided herein are kits comprising a MEK inhibitor and a package insert comprising instructions for using the MEK inhibitor in combination with a PD-1 axis binding antagonist to treat or delay progression of cancer in an individual, wherein the individual has been previously treated with a B-raf antagonist for cancer.

**[0017]** In some embodiments, the individual is a human.

**[0018]** It is to be understood that one, some, or all of the properties of the various embodiments described herein may be combined to form other embodiments of the present disclosure. These and other aspects of the invention will become apparent to one of skill in the

art. These and other embodiments of the disclosure are further described by the detailed description that follows.

## BRIEF DESCRIPTION OF THE DRAWINGS

**[0019]** **FIG. 1** shows tumor re-growth upon treatment with anti-PDL1, a MEK inhibitor, or both. The graph shows the percent tumor volume change over time during treatment with the indicated agent(s).

**[0020]** **FIG. 2** shows individual animal responses to treatment with Vemurafenib followed by anti-PDL1, a MEK inhibitor, or both. Each bar depicts the percent change in tumor growth upon crossover from Vemurafenib to the indicated treatment in an individual animal.

## DETAILED DESCRIPTION

### I. General techniques

**[0021]** The techniques and procedures described or referenced herein are generally well understood and commonly employed using conventional methodology by those skilled in the art, such as, for example, the widely utilized methodologies described in Sambrook et al., *Molecular Cloning: A Laboratory Manual* 3d edition (2001) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.; *Current Protocols in Molecular Biology* (F.M. Ausubel, et al. eds., (2003)); the series *Methods in Enzymology* (Academic Press, Inc.): *PCR 2: A Practical Approach* (M.J. MacPherson, B.D. Hames and G.R. Taylor eds. (1995)), Harlow and Lane, eds. (1988) *Antibodies, A Laboratory Manual*, and *Animal Cell Culture* (R.I. Freshney, ed. (1987)); *Oligonucleotide Synthesis* (M.J. Gait, ed., 1984); *Methods in Molecular Biology*, Humana Press; *Cell Biology: A Laboratory Notebook* (J.E. Cellis, ed., 1998) Academic Press; *Animal Cell Culture* (R.I. Freshney), ed., 1987); *Introduction to Cell and Tissue Culture* (J.P. Mather and P.E. Roberts, 1998) Plenum Press; *Cell and Tissue Culture: Laboratory Procedures* (A. Doyle, J.B. Griffiths, and D.G. Newell, eds., 1993-8) J. Wiley and Sons; *Handbook of Experimental Immunology* (D.M. Weir and C.C. Blackwell, eds.); *Gene Transfer Vectors for Mammalian Cells* (J.M. Miller and M.P. Calos, eds., 1987); *PCR: The Polymerase Chain Reaction*, (Mullis et al., eds., 1994); *Current Protocols in Immunology* (J.E. Coligan et al., eds., 1991); *Short Protocols in Molecular Biology* (Wiley and Sons, 1999); *Immunobiology* (C.A. Janeway and P. Travers, 1997); *Antibodies* (P. Finch, 1997); *Antibodies: A Practical Approach* (D. Catty., ed., IRL Press, 1988-1989); *Monoclonal Antibodies: A Practical Approach* (P. Shepherd and C.

# CLAIMS

What is claimed is:

1. Use of an effective amount of a PD-1 axis binding antagonist and a MEK inhibitor for the manufacture of a first medicament comprising the PD-1 axis binding antagonist and a second medicament comprising the MEK inhibitor for treating or delaying progression of cancer in an individual, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

2. Use of an effective amount of a PD-1 axis binding antagonist in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the PD-1 axis binding agent is used in combination with a MEK inhibitor, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

3. Use of an effective amount of a MEK inhibitor in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the MEK inhibitor is used in combination with a PD-1 axis binding antagonist, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

4. A pharmaceutical composition comprising a PD-1 axis binding antagonist in combination with a MEK inhibitor for use in treating or delaying progression of cancer in an individual, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

5. A pharmaceutical composition comprising a PD-1 axis binding antagonist for use in treating or delaying progression of cancer in an individual in combination with a MEK inhibitor, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

6. A pharmaceutical composition comprising a MEK inhibitor for use in treating or delaying progression of cancer in an individual in combination with a PD-1 axis binding antagonist wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

7. The use or pharmaceutical composition of any one of claims 1-6, further comprising diagnosing the individual as having a cancer that is resistant to a B-raf antagonist, wherein the diagnosing occurs prior to administering the effective amount of the PD-1 axis binding antagonist and the MEK inhibitor.

8. The use or pharmaceutical composition of any one of claims 1-7, wherein the individual has not been previously treated with a B-raf antagonist.

9. The use or pharmaceutical composition of any one of claims 1-7, wherein the individual has been previously treated with a B-raf antagonist.

10. Use of an effective amount of a PD-1 axis binding antagonist and a MEK inhibitor for the manufacture of a first medicament comprising the PD-1 axis binding antagonist and a second medicament comprising the MEK inhibitor for treating or delaying progression of cancer in an individual, wherein the individual has been previously treated with a B-raf antagonist for cancer.

11. Use of an effective amount of a PD-1 axis binding antagonist in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the PD-1 axis binding agent is used in combination with a MEK inhibitor, wherein the individual has been previously treated with a B-raf antagonist for cancer.

12. Use of an effective amount of a MEK inhibitor in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the MEK inhibitor is used in combination with a PD-1 axis binding antagonist, wherein the individual has been previously treated with a B-raf antagonist for cancer.

13. A pharmaceutical composition comprising a PD-1 axis binding antagonist in combination with a MEK inhibitor for use in treating or delaying progression of cancer in an individual, wherein the individual has been previously treated with a B-raf antagonist for cancer.

14. A pharmaceutical composition comprising a PD-1 axis binding antagonist for use in treating or delaying progression of cancer in an individual in combination with a MEK inhibitor, wherein the individual has been previously treated with a B-raf antagonist for cancer.

15. A pharmaceutical composition comprising a MEK inhibitor for use in treating or delaying progression of cancer in an individual in combination with a PD-1 axis binding antagonist wherein the individual has been previously treated with a B-raf antagonist for cancer.

16. The use or pharmaceutical composition of any one of claims 9-15, wherein the cancer in the individual has progressed within 1 month, 6 months, 1 year, or 5 years after completing a B-raf antagonist-based therapy regimen.

17. The use or pharmaceutical composition of any one of claims 1-16, wherein the B-raf antagonist is a small molecule inhibitor, an antibody, a peptide, a peptidomimetic, an aptamer or a polynucleotide.

18. The use or pharmaceutical composition of claim 17, wherein the B-raf antagonist is dabrafenib, vemurafenib, GSK 2118436, RAF265, XL281, ARQ736, BAY73-4506, sorafenib, PLX4720, PLX-3603, GSK2118436, GDC-0879, or N-(3-(5-(4-chlorophenyl)-1H-pyrrolo[2,3-b]pyridine-3-carbonyl)-2,4-difluorophenyl)propane-1-sulfonamide.

19. The use or pharmaceutical composition of claim 17, wherein the B-raf antagonist is a selective B-raf antagonist of B-raf V600.

20. The use or pharmaceutical composition of claim 17, wherein the selective B-raf antagonist of B-raf V600 is a selective antagonist of B-raf V600E.

21. The use or pharmaceutical composition of claim 17, wherein the selective B-raf antagonist of B-raf V600 is a selective antagonist of B-raf V600E, B-raf V600K, and/or V600D.

22. The use or pharmaceutical composition of claim 17, wherein the selective B-raf antagonist of B-raf V600 is a selective antagonist of B-raf V600R.
23. The use or pharmaceutical composition of any one of claims 1-22, wherein the cancer contains a BRAF V600E mutation, a BRAF wildtype, a KRAS wildtype, or an activating KRAS mutation.
24. The use or pharmaceutical composition of any one of claims 1-23, wherein the treatment results in a sustained response in the individual after cessation of the treatment.
25. The use or pharmaceutical composition of any one of claims 1-24, wherein the individual has colorectal cancer, melanoma, lung cancer, ovarian cancer, breast cancer, pancreatic cancer, hematological malignancy, bladder cancer, and/or renal cell carcinoma.
26. The use or pharmaceutical composition of claim 25, wherein the cancer is metastatic.
27. The use or pharmaceutical composition of any one of the preceding claims, wherein the PD-1 axis binding antagonist is selected from the group consisting of a PD-1 binding antagonist, a PD-L1 binding antagonist and a PD-L2 binding antagonist.
28. The use or pharmaceutical composition of claim 27, wherein the PD-1 axis binding antagonist is a PD-1 binding antagonist.
29. The use or pharmaceutical composition of claim 28, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to its ligand binding partners.
30. The use or pharmaceutical composition of claim 29, wherein the PD-1 binding antagonist inhibits the binding of PD-1 to PD-L1, PD-1 to PD-L2, or PD-1 to both PD-L1 and PD-L2.
31. The use or pharmaceutical composition of any one of claims 28-30, wherein the PD-1 binding antagonist is an antibody.
32. The use or pharmaceutical composition of any one of claims 28-30, wherein the PD-1 binding antagonist is
nivolumab, pembrolizumab, pidilizumab, MEDI-0680, PDR001, REGN2810, BGB-108, BGB-A317, or AMP-224.
33. The use or pharmaceutical composition of claim 27, wherein the PD-1 axis binding antagonist is a PD-L1 binding antagonist.
34. The use or pharmaceutical composition of claim 33, wherein the PD-L1 binding antagonist inhibits the binding of PD-L1 to PD-1, PD-L1 to B7-1, or PD-L1 to both PD-1 and B7-1.
35. The use or pharmaceutical composition of claim 33 or claim 34, wherein the PD-L1 binding antagonist is an anti-PD-L1 antibody.
36. The use or pharmaceutical composition of claim 35, wherein the anti-PD-L1 antibody is a monoclonal antibody.
37. The use or pharmaceutical composition of claim 35, wherein the anti-PD-L1 antibody is an antibody fragment

selected from the group consisting of Fab, Fab'-SH, Fv, scFv, and $(Fab')_2$ fragments.

38. The use or pharmaceutical composition of any one of claims 35-37, wherein the anti-PD-L1 antibody is a humanized antibody or a human antibody.

39. The use or pharmaceutical composition of any one of claim 35, wherein the PD-L1 binding antagonist is selected from the group consisting of: YW243.55.S70, atezolizumab, durvalumab, MDX-1105, and avelumab.

40. The use or pharmaceutical composition of any one of claims 35-38, wherein the antibody comprises a heavy chain comprising HVR-H1 sequence of SEQ ID NO:15, HVR-H2 sequence of SEQ ID NO:16, and HVR-H3 sequence of SEQ ID NO:3; and a light chain comprising HVR-L1 sequence of SEQ ID NO:17, HVR-L2 sequence of SEQ ID NO:18, and HVR-L3 sequence of SEQ ID NO:19.

41. The use or pharmaceutical composition of any one of claims 35-38, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:24 or SEQ ID NO:28 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:21.

42. The use or pharmaceutical composition of claim 27, wherein the PD-1 axis binding antagonist is a PD-L2 binding antagonist.

43. The use or pharmaceutical composition of claim 42, wherein the PD-L2 binding antagonist is an antibody.

44. The use or pharmaceutical composition of claim 42, wherein the PD-L2 binding antagonist is an immunoadhesin.

45. The use or pharmaceutical composition of any one of claims 1-44, wherein the MEK inhibitor is a competitive inhibitor of MEK.

46. The use or pharmaceutical composition of any one of claims 1-44, wherein the MEK inhibitor is more selective against an activating KRAS mutation.

47. The use or pharmaceutical composition of any one of claims 1-44, wherein the MEK inhibitor is an allosteric inhibitor of MEK.

48. The use or pharmaceutical composition of any one of claims 1-44, wherein the MEK inhibitor is more selective against an activating BRAF mutation.

49. The use or pharmaceutical composition of any one of claims 1-44, wherein the MEK inhibitor is a compound of the formula (I), (II), (III), (IV), (V), (VI) or (VII), or a pharmaceutically acceptable salt or solvate thereof.

50. The use or pharmaceutical composition of any one of claims 1-44, wherein the MEK inhibitor is selected from the group consisting of G02442104, G-38963, G02443714, G00039805 and GDC-0973, or a pharmaceutically acceptable salt or solvate thereof.

51. The use or pharmaceutical composition of claim 50, wherein the MEK inhibitor is G02443714, G02442104 or

G00039805.

52. The use or pharmaceutical composition of any one of claims 1-51, wherein the MEK inhibitor is administered continuously.

53. The use or pharmaceutical composition of any one of claims 1-51, wherein the MEK inhibitor is administered intermittently.

54. The use or pharmaceutical composition of any one of claims 1-51, wherein the MEK inhibitor is administered before the PD-1 axis binding antagonist.

55. The use or pharmaceutical composition of any one of claims 1-51, wherein the MEK inhibitor is administered simultaneous with the PD-1 axis binding antagonist.

56. The use or pharmaceutical composition of any one of claims 1-51, wherein the MEK inhibitor is administered after the PD-1 axis binding antagonist.

57. The use or pharmaceutical composition of any one of claims 1-56, wherein the PD-1 axis binding antagonist and/or the MEK inhibitor is administered intravenously, intramuscularly, subcutaneously, topically, orally, transdermally, intraperitoneally, intraorbitally, by implantation, by inhalation, intrathecally, intraventricularly, or intranasally.

58. A kit comprising a PD-1 axis binding antagonist and a package insert comprising instructions for using the PD-1 axis binding antagonist in combination with a MEK inhibitor to treat or delay progression of cancer in an individual, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

59. A kit comprising a PD-1 axis binding antagonist and a MEK inhibitor, and a package insert comprising instructions for using the PD-1 axis binding antagonist and the MEK inhibitor to treat or delay progression of cancer in an individual, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

60. A kit comprising a MEK inhibitor and a package insert comprising instructions for using the MEK inhibitor in combination with a PD-1 axis binding antagonist to treat or delay progression of cancer in an individual, wherein the individual has cancer or is at risk of developing cancer that is resistant to a B-raf antagonist.

61. A kit comprising a PD-1 axis binding antagonist and a package insert comprising instructions for using the PD-1 axis binding antagonist in combination with a MEK inhibitor to treat or delay progression of cancer in an individual, wherein the individual has been previously treated with a B-raf antagonist for cancer.

62. A kit comprising a PD-1 axis binding antagonist and a MEK inhibitor, and a package

insert comprising instructions for using the PD-1 axis binding antagonist and the MEK inhibitor to treat or delay progression of cancer in an individual, wherein the individual has been previously treated with a B-raf antagonist for cancer.

63. A kit comprising a MEK inhibitor and a package insert comprising instructions for using the MEK inhibitor in combination with a PD-1 axis binding antagonist to treat or delay progression of cancer in an individual, wherein the individual has been previously treated with a B-raf antagonist for cancer.

64. The kit of any one of claims 58-63, wherein the PD-1 axis binding antagonist is an anti-PD-L1 antibody.

65. The kit of any one of claims 58-63, wherein the PD-1 axis binding antagonist is an anti-PD-1 antibody.

66. The kit of any one of claims 58-63, wherein the PD-1 axis binding antagonist is an anti-PD-1 immunoadhesin.