CLAIMS

What is claimed is:

1. Use of an anti-PD-1 antagonist antibody that inhibits binding of PD-L1 to PD-1 in the manufacture of a medicament for:

treating or delaying progression of cancer in an individual;

reducing or inhibiting cancer relapse or cancer progression in an individual;

treating or delaying progression of a viral infection in an individual; or

reducing or inhibiting progression of a viral infection in an individual,

wherein the individual is to be administered an effective amount of an anti-TIGIT antagonist antibody that inhibits and/or blocks interaction of CD226 with TIGIT.

2. Use of an anti-PD-1 antagonist antibody that inhibits binding of PD-L1 to PD-1 and an anti-TIGIT antagonist antibody that inhibits and/or blocks interaction of CD226 with TIGIT in the manufacture of a medicament for:

treating or delaying progression of cancer in an individual;

reducing or inhibiting cancer relapse or cancer progression in an individual;

treating or delaying progression of a viral infection in an individual; or

reducing or inhibiting progression of a viral infection in an individual.

3. Use of an anti-TIGIT antagonist antibody that inhibits and/or blocks interaction of CD226 with TIGITin the manufacture of a medicament for:

treating or delaying progression of cancer in an individual;

reducing or inhibiting cancer relapse or cancer progression in an individual;

treating or delaying progression of a viral infection in an individual; or

reducing or inhibiting progression of a viral infection in an individual,

wherein the individual is to be administered an effective amount of an anti-PD-1 antagonist antibody that inhibits binding of PD-L1 to PD-1.

4. The use of any one of claims 1-3, wherein the viral infection is an unresolved acute viral infection or a chronic viral infection.

5. The use of any one of claims 1-4, wherein the medicament is to be administered with at least one chemotherapeutic agent.

6. The use of any one of claims 1-5, wherein CD4 and/or CD8 T cells in the individual have increased or enhanced priming, activation, proliferation, cytokine release, and/or cytolytic activity relative to prior to the administration of the antibody combination.

7. The use of any one of claims 1-6, wherein the number of CD4 and/or CD8 T cells is elevated relative to prior to administration of the antibody combination.

8. The use of any one of claims 1-7, wherein the number of activated CD4 and/or CD8 T cells is elevated relative to prior to administration of the antibody combination.

9. The use of any one of claims 1-8, wherein activated CD4 and/or CD8 T cells are characterized by γ-IFN^{+} producing CD4 and/or CD8 T cells and/or enhanced cytolytic activity relative to prior to the administration of the antibody combination.

10. The use of any one of claims 6-9, wherein the CD4 and/or CD8 T cells exhibit increased release of cytokines selected from the group consisting of IFN- γ, TNF-α, and interleukins.

11. The use of any one of claims 6-10, wherein the CD4 and/or CD8 T cells are effector memory T cells.

12. The use of claim 11, wherein the CD4 and/or CD8 effector memory T cells are characterized by γ-IFN^{+} producing CD4 and/or CD8 T cells and/or enhanced cytolytic activity.

13. The use of claim 11, wherein the CD4 and/or CD8 effector memory T cells are characterized by expression of CD44^{high} CD62L^{low}.

14. The use of any one of claims 1-13, wherein the cancer has elevated levels of T cell infiltration.

15. The use of any one of claims 1-14, wherein the anti-TIGIT antagonist antibody inhibits and/or blocks the interaction of TIGIT with PVR.

16. The use of any one of claims 1-15, wherein the anti-TIGIT antagonist antibody comprises six HVRs comprising the amino acid sequences: (1) an HVR-L1 sequence of KSSQSLYYSGVKENLLA (SEQ ID NO:1), an HVR-L2 sequence of ASIRFT (SEQ ID NO:2), an HVR-L3 sequence of QQGINNPLT (SEQ ID NO:3), an HVR-H1 sequence of GFTFSSFTMH (SEQ ID NO:4), an HVR-H2 sequence of FIRSGSGIVFYADAVRG (SEQ ID NO:5), and an HVR-H3 sequence of RPLGHNTFDS (SEQ ID NO:6); or
(2) an HVR-L1 sequence of RSSQSLVNSYGNTFLS (SEQ ID NO:7), an HVR-L2 sequence of GISNRFS (SEQ ID NO:8), an HVR-L3 sequence of LQGTHQPPT (SEQ ID NO:9), an HVR-H1 sequence of GYSFTGHLMN (SEQ ID NO:10), an HVR-H2 sequence of LIIPYNGGTSYNQKFKG (SEQ ID NO:11), and an HVR-H3 sequence of GLRGFYAMDY (SEQ ID NO:12).

17. The use of claim 16, wherein the anti-TIGIT antagonist antibody comprises a light chain comprising an amino acid sequence having at least 90% sequence identity to the amino

acid sequence set forth in
DIVMTQSPSSLAVSPGEKVTMTCKSSQSLYYSGVKENLLAWYQQKPGQS
PKLLIYYASIRFTGVPDRFTGSGSGTDYTLTITSVQAEDMGQYFCQQGINNPLTFGDGT
KLEIKR (SEQ ID NO:13) or
DVVLTQTPLSLSVSFGDQVSISCRSSQSLVNSYGNTFLSWYLHKPGQSPQLLIFGISNR
FSGVPDRFSGSGSGTDFTLKISTIKPEDLGMYYCLQGTHQPPTFGPGTKLEVK (SEQ ID
NO: 14).

18. The use of claim 16 or 17, wherein the anti-TIGIT antagonist antibody comprises a heavy chain comprising an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in
EVQLVESGGGLTQPGKSLKLSCEASGFTFSSFTMHWVRQSPGKGLEWVAFIRSGSGIV
FYADAVRGRFTISRDNAKNLLFLQMNDLKSEDTAMYYCARRPLGHNTFDSWGQ
GTLVTVSS (SEQ ID NO: 15) or
EVQLQQSGPELVKPGTSMKISCKASGYSFTGHLMNWVKQSHGKNLEWIGLIIPYNGG
TSYNQKFKGKATLTVDKSSSTAYMELLSLTSDDSAVYFCSRGLRGFYAMDYWG
QGTSVTVSS (SEQ ID NO: 16).

19. The use of any one of claims 16-18, wherein the anti-TIGIT antagonist antibody, comprises a light chain comprising an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in
DIVMTQSPSSLAVSPGEKVTMTCKSSQSLYYSGVKENLLAWYQQKPGQS
PKLLIYYASIRFTGVPDRFTGSGSGTDYTLTITSVQAEDMGQYFCQQGINNPLTFGDGT
KLEIKR (SEQ ID NO:13) or
DVVLTQTPLSLSVSFGDQVSISCRSSQSLVNSYGNTFLSWYLHKPGQSPQLLIFGISNR
FSGVPDRFSGSGSGTDFTLKISTIKPEDLGMYYCLQGTHQPPTFGPGTKLEVK (SEQ ID
NO: 14),
and a heavy chain comprising an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in
EVQLVESGGGLTQPGKSLKLSCEASGFTFSSFTMHWVRQSPGKGLEWVAFIRSGSGIV
FYADAVRGRFTISRDNAKNLLFLQMNDLKSEDTAMYYCARRPLGHNTFDSWGQ
GTLVTVSS (SEQ ID NO: 15) or
EVQLQQSGPELVKPGTSMKISCKASGYSFTGHLMNWVKQSHGKNLEWIGLIIPYNGG
TSYNQKFKGKATLTVDKSSSTAYMELLSLTSDDSAVYFCSRGLRGFYAMDYWG
QGTSVTVSS (SEQ ID NO: 16).

20. The use of claim 19, wherein the anti-TIGIT antagonist antibody comprises a light chain comprising an amino acid sequence set forth in DIVMTQSPSSLAVSPGEKVTMTCKSSQSLYYSGVKENLLAWYQQKPGQS PKLLIYYASIRFTGVPDRFTGSGSGTDYTLTITSVQAEDMGQYFCQQGINNPLTFGDGT KLEIKR (SEQ ID NO:13) or DVVLTQTPLSLSVSFGDQVSISCRSSQSLVNSYGNTFLSWYLHKPGQSPQLLIFGISNR FSGVPDRFSGSGSGTDFTLKISTIKPEDLGMYYCLQGTHQPPTFGPGTKLEVK (SEQ ID NO: 14),
and a heavy chain comprising an amino acid sequence set forth in EVQLVESGGGLTQPGKSLKLSCEASGFTFSSFTMHWVRQSPGKGLEWVAFIRSGSGIV FYADAVRGRFTISRDNAKNLLFLQMNDLKSEDTAMYYCARRPLGHNTFDSWGQ GTLVTVSS (SEQ ID NO: 15) or EVQLQQSGPELVKPGTSMKISCKASGYSFTGHLMNWVKQSHGKNLEWIGLIIPYNGG TSYNQKFKGKATLTVDKSSSTAYMELLSLTSDDSAVYFCSRGLRGFYAMDYWG QGTSVTVSS (SEQ ID NO: 16).

21. The use of any one of claims 1-20, wherein the anti-TIGIT antagonist antibody is selected from the group consisting of a human antibody, a humanized antibody, a chimeric antibody, a bispecific antibody, and a heteroconjugate antibody.

22. The use of claim 21, wherein the anti-TIGIT antagonist antibody is a human antibody.

23. The use of claim 21, wherein the anti-TIGIT antagonist antibody is a humanized antibody.

24. The use of any one of claims 1-23, wherein the anti-TIGIT antagonist antibody is a monoclonal antibody.

25. The use of any one of claims 1-24, wherein the anti-TIGIT antagonist antibody is a full-length antibody.

26. The use of any one of claims 1-25, wherein the anti-TIGIT antagonist antibody is an IgG antibody.

27. The use of claim 26, wherein the anti-TIGIT antagonist antibody is an IgG1 antibody.

28. The use of claim 26, wherein the anti-TIGIT antagonist antibody is an IgG4 antibody.

29. The use of any one of claims 1-24, wherein the anti-TIGIT antagonist antibody is an antigen-binding antibody fragment.

30. The use of any one of claims 1-29, wherein the anti-PD-1 antagonist antibody is selected from the group consisting of a human antibody, a humanized antibody, a chimeric

antibody, a bispecific antibody, and a heteroconjugate antibody.

31. The use of claim 30, wherein the anti-PD-1 antagonist antibody is a human antibody.

32. The use of claim 30, wherein the anti-PD-1 antagonist antibody is a humanized antibody.

33. The use of any one of claims 1-30, wherein the anti-PD-1 antagonist antibody is a monoclonal antibody.

34. The use of any one of claims 1-33, wherein the anti-PD-1 antagonist antibody is a full-length antibody.

35. The use of any one of claims 1-34, wherein the anti-PD-1 antagonist antibody is an IgG antibody.

36. The use of claim 35, wherein the anti-PD-1 antagonist antibody is an IgG1 antibody.

37. The use of claim 35, wherein the anti-PD-1 antagonist antibody is an IgG4 antibody.

38. The use of any one of claims 1-33, wherein the anti-PD-1 antagonist antibody is an antigen-binding antibody fragment.

39. The use of any one of claims 1-29, wherein the anti-PD-1 antagonist antibody is nivolumab or pembrolizumab.

40. The use of any one of claims 1-39, wherein the cancer is selected from the group consisting of a non-small cell lung cancer, a renal cell cancer, a colorectal cancer, an ovarian cancer, a breast cancer, a pancreatic cancer, a gastric carcinoma, a bladder cancer, an esophageal cancer, a mesothelioma, a melanoma, a head and neck cancer, a thyroid cancer, a sarcoma, a prostate cancer, a glioblastoma, a cervical cancer, a thymic carcinoma, a leukemia, a lymphoma, a myeloma, a mycosis fungoides, a Merkel cell cancer, and a hematologic malignancy.

41. The use of any one of claims 1-40, wherein the anti-TIGIT antagonist antibody is to be administered continuously.

42. The use of any one of claims 1-40, wherein the anti-TIGIT antagonist antibody is to be administered intermittently.

43. The use of any one of claims 1-42, wherein the anti-TIGIT antagonist antibody is to be administered before the anti-PD-1 antagonist antibody.

44. The use of any one of claims 1-42, wherein the anti-TIGIT antagonist antibody is to be administered simultaneously with the anti-PD-1 antagonist antibody.

45. The use of any one of claims 1-42, wherein the anti-TIGIT antagonist antibody is to be administered after the anti-PD-1 antagonist antibody.

46. The use of any one of claims 1-45, wherein the anti-TIGIT antagonist antibody has a modified effector function.

47. The use of claim 46, wherein the anti-TIGIT antagonist antibody has a reduced or minimal effector function.

48. The use of claim 47, wherein the anti-TIGIT antagonist antibody comprises an N297A or D265A/N297A substitution in the constant region.

49. The use of claim 46, wherein the modified effector function results in improved internalization capability, increased complement-mediated cell killing, or increased antibody-dependent cellular cytotoxicity.

50. The use of any one of claims 1-49, wherein the anti-PD-1 antagonist antibody has a modified effector function.

51. The use of claim 50, wherein the anti-PD-1 antagonist antibody has a reduced or modified effector function.

52. The use of claim 51, wherein the anti-PD-1 antagonist antibody comprises an N297A or D265A/N297A substitution in the constant region.

53. The use of claim 50, wherein the modified effector function results in improved internalization capability, increased complement-mediated cell killing, or increased antibody-dependent cellular cytotoxicity.

54. A kit comprising an anti-PD-1 antagonist antibody and an anti-TIGIT antagonist antibody as a combined preparation for simultaneous, separate, or sequential use for:

treating or delaying progression of cancer in an individual;

reducing or inhibiting cancer relapse or cancer progression in an individual;

treating or delaying progression of a viral infection in an individual; or

reducing or inhibiting progression of a viral infection in an individual,

wherein the anti-PD-1 antagonist antibody inhibits binding of PD-L1 to PD-1 and the anti-TIGIT antagonist antibody inhibits and/or blocks interaction of CD226 with TIGIT.