Cell-Ig and ITIM domain) was shown to be expressed on T cells—particularly $T_{reg}$ and memory cell subsets—as well as NK cells.

**[0008]** There is a need for new therapeutics and methods that modulate cells of the immune system to mount an anti-cancer response. In particular, agents that promote an anti-cancer function of NK cells, which can eradicate cancer cells, and/or memory T cells, which can maintain a lasting anti-cancer response, are highly advantageous.

**[0009]** All references cited herein, including patent applications, patent publications, and UniProtKB/Swiss-Prot Accession numbers are herein incorporated by reference in their entirety, as if each individual reference were specifically and individually indicated to be incorporated by reference.

## SUMMARY

**[0010]** The present disclosure describes a combination treatment comprising an agent that decreases or inhibits TIGIT expression and/or activity and an anti-cancer agent and/or an anti-cancer therapy.

**[0011]** Disclosed is a method for treating or delaying progression of cancer in an individual comprising administering to the individual an effective amount of an agent that decreases or inhibits TIGIT expression and/or activity and an anti-cancer agent or an anti-cancer therapy. In one aspect, there is provided use of an agent that decreases or inhibits TIGIT expression and/or activity in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the medicament is to be administered with an anti-cancer agent or an anti-cancer therapy. Disclosed is use of an effective amount of an agent that decreases or inhibits TIGIT expression and/or activity in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the agent that decreases or inhibits TIGIT expression and/or activity is used in combination with an anti-cancer agent or an anti-cancer therapy. Disclosed is use of an effective amount of an anti-cancer agent in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the anti-cancer agent is used in combination with an agent that decreases or inhibits TIGIT expression and/or activity. Disclosed is a pharmaceutical composition comprising an agent that decreases or inhibits TIGIT expression and/or activity for use in treating or delaying progression of cancer in combination with an anti-cancer agent or an anti-cancer therapy. Disclosed is a pharmaceutical composition comprising an anti-cancer agent for use in treating or delaying progression of cancer in combination with an agent that decreases or inhibits TIGIT expression and/or activity.

**[0012]** Disclosed is a method for reducing or inhibiting cancer relapse or cancer progression in an individual comprising administering to the individual an effective amount of an agent that decreases or inhibits TIGIT expression and/or activity and an anti-cancer agent or an anti-cancer therapy. In another aspect, there is provided use of an agent that decreases or inhibits TIGIT expression and/or activity in the manufacture of a medicament for reducing or inhibiting cancer relapse or cancer progression in an individual, wherein the medicament is to be administered with an anti-cancer agent or an anti-cancer therapy. Disclosed is use of an effective amount of an agent that decreases or inhibits TIGIT expression and/or activity in the manufacture of a medicament for reducing or inhibiting cancer relapse or cancer progression in an individual, wherein the agent that decreases or inhibits TIGIT expression and/or activity is used in combination with an anti-cancer agent or an anti-cancer therapy. Disclosed is use of an effective amount of an anti-cancer agent in the manufacture of a medicament for reducing or inhibiting cancer relapse or cancer progression in an individual, wherein the anti-cancer agent is used in combination with an agent that decreases or inhibits TIGIT expression and/or activity. Disclosed is a pharmaceutical composition comprising an agent that decreases or inhibits TIGIT expression and/or activity for use in reducing or inhibiting cancer relapse or cancer progression in combination with an anti-cancer agent or an anti-cancer therapy. Disclosed is a pharmaceutical composition comprising an anti-cancer agent for use in reducing or inhibiting cancer relapse or cancer progression in combination with an agent that decreases or inhibits TIGIT expression and/or activity.

**[0013]** Disclosed is a method for treating or delaying progression of tumor immunity in an individual having cancer comprising administering to the individual an effective amount of an agent that decreases or inhibits TIGIT expression and/or activity and an anti-cancer agent or an anti-cancer therapy. In another aspect, there is provided use of an effective amount of an agent that decreases or inhibits TIGIT expression in the manufacture of a medicament for treating or delaying progression of tumor immunity in an individual having cancer, wherein the medicament is to be administered with an anti-cancer agent or an anti-cancer therapy. Disclosed is use of an effective amount of an agent that decreases or inhibits TIGIT expression and/or activity in the manufacture of a medicament for treating or delaying progression of tumor immunity in an individual having cancer, wherein the agent that decreases or inhibits TIGIT expression and/or activity is used in combination with an anti-cancer agent or an anti-cancer therapy. Disclosed is use of an effective amount of an anti-cancer agent in the manufacture of a medicament for treating or delaying progression of tumor immunity in an individual having cancer, wherein the anti-cancer agent is used in combination with an agent that decreases or inhibits TIGIT expression and/or activity. Disclosed is a pharmaceutical composition comprising an agent that decreases or inhibits TIGIT expression and/or activity for use in treating or delaying

progression of tumor immunity in combination with an anti-cancer agent or an anti-cancer therapy. Disclosed is a pharmaceutical composition comprising an anti-cancer agent for use in treating or delaying progression of tumor immunity in combination with an agent that decreases or inhibits TIGIT expression and/or activity.

**[0014]** Disclosed is a method of increasing, enhancing or stimulating an immune response or function in an individual having cancer comprising administering to the individual an effective amount of an agent that decreases or inhibits TIGIT expression and/or activity and an anti-cancer agent or an anti-cancer therapy. In another aspect, there is provided use of an agent that decreases or inhibits TIGIT expression and/or activity in the manufacture of a medicament for increasing, enhancing or stimulating an immune response or function in an individual having cancer, wherein the medicament is to be administered with an anti-cancer agent or an anti-cancer therapy. Disclosed is use of an effective amount of an agent that decreases or inhibits TIGIT expression and/or activity in the manufacture of a medicament for increasing, enhancing or stimulating an immune response or function in an individual having cancer, wherein the agent that decreases or inhibits TIGIT expression and/or activity is used in combination with an anti-cancer agent or an anti-cancer therapy. Disclosed is use of an effective amount of an anti-cancer agent in the manufacture of a medicament for increasing, enhancing or stimulating an immune response or function in an individual having cancer, wherein the anti-cancer agent is used in combination with an agent that decreases or inhibits TIGIT expression and/or activity. Disclosed is a pharmaceutical composition comprising an agent that decreases or inhibits TIGIT expression and/or activity for use in increasing, enhancing or stimulating an immune response or function in combination with an anti-cancer agent or an anti-cancer therapy. Disclosed is a pharmaceutical composition comprising an anti-cancer agent for use in increasing, enhancing or stimulating an immune response or function in combination with an agent that decreases or inhibits TIGIT expression and/or activity.

**[0015]** Disclosed is a combination comprising an effective amount of an agent that decreases or inhibits TIGIT expression and/or activity and an anti-cancer agent.

**[0016]** In certain embodiments that may be combined with any of the preceding embodiments, the individual has a T cell dysfunctional disorder. In certain embodiments that may be combined with any of the preceding embodiments, the T cell dysfunctional disorder is characterized by T cell anergy or decreased ability to secrete cytokines, proliferate or execute cytolytic activity. In certain embodiments that may be combined with any of the preceding embodiments, the T cell dysfunctional disorder is characterized by T

CLAIMS

What is claimed is:

1. Use of an agent that decreases or inhibits TIGIT expression and/or activity in the manufacture of a medicament for treating or delaying progression of cancer in an individual, wherein the medicament is to be administered with an anti-cancer agent or an anti-cancer therapy.

2. Use of an agent that decreases or inhibits TIGIT expression and/or activity in the manufacture of a medicament for reducing or inhibiting cancer relapse or cancer progression in an individual, wherein the medicament is to be administered with an anti-cancer agent or an anti-cancer therapy.

3. Use of an effective amount of an agent that decreases or inhibits TIGIT expression in the manufacture of a medicament for treating or delaying progression of tumor immunity in an individual having cancer, wherein the medicament is to be administered with an anti-cancer agent or an anti-cancer therapy.

4. Use of an agent that decreases or inhibits TIGIT expression and/or activity in the manufacture of a medicament for increasing, enhancing or stimulating an immune response or function in an individual having cancer, wherein the medicament is to be administered with an anti-cancer agent or an anti-cancer therapy.

5. The use of any one of claims 1-4, wherein the individual has a T cell dysfunctional disorder ; wherein optionally

the T cell dysfunctional disorder is characterized by T cell anergy or decreased ability to secrete cytokines, proliferate or execute cytolytic activity, or

by T cell exhaustion; and wherein optionally

the T cells are CD4+ and CD8+ T cells.

6. The use of any one of claims 1-5, wherein the agent that decreases or inhibits TIGIT expression and/or activity is selected from the group consisting of an antagonist of TIGIT expression and/or activity, an antagonist of PVR expression and/or activity, an agent that inhibits and/or blocks the interaction of TIGIT with PVR, an agent that inhibits and/or blocks the interaction of TIGIT with PVRL2, an agent that inhibits and/or blocks the interaction of TIGIT with PVRL3, an agent that inhibits and/or blocks the intracellular signaling mediated

by TIGIT binding to PVR, an agent that inhibits and/or blocks the intracellular signaling mediated by TIGIT binding to PVRL2, an agent that inhibits and/or blocks the intracellular signaling mediated by TIGIT binding to PVRL3, and combinations thereof; wherein optionally

(a) the antagonist of TIGIT expression and/or activity is selected from the group consisting of a small molecule inhibitor, an inhibitory antibody or antigen-binding fragment thereof, an aptamer, an inhibitory nucleic acid, and an inhibitory polypeptide, wherein optionally the inhibitory nucleic acid is selected from the group consisting of an antisense polynucleotide, an interfering RNA, a catalytic RNA, and an RNA-DNA chimera; or

(b) the antagonist of PVR expression and/or activity is selected from the group consisting of a small molecule inhibitor, an inhibitory antibody or antigen-binding fragment thereof, an aptamer, an inhibitory nucleic acid, and an inhibitory polypeptide; or

(c) the agent that inhibits and/or blocks the interaction of TIGIT with PVR is selected from the group consisting of a small molecule inhibitor, an inhibitory antibody or antigen-binding fragment thereof, an aptamer, an inhibitory nucleic acid, and an inhibitory polypeptide; or

(d) the agent that inhibits and/or blocks the interaction of TIGIT with PVRL2 is selected from the group consisting of a small molecule inhibitor, an inhibitory antibody or antigen-binding fragment thereof, an aptamer, an inhibitory nucleic acid, and an inhibitory polypeptide; or

(e) the agent that inhibits and/or blocks the interaction of TIGIT with PVRL3 is selected from the group consisting of a small molecule inhibitor, an inhibitory antibody or antigen-binding fragment thereof, an aptamer, an inhibitory nucleic acid, and an inhibitory polypeptide; or

(f) the agent that inhibits and/or blocks the intracellular signaling mediated by TIGIT binding to PVR is selected from the group consisting of a small molecule inhibitor, an inhibitory antibody or antigen-binding fragment thereof, an aptamer, an inhibitory nucleic acid, and an inhibitory polypeptide; or

(g) the agent that inhibits and/or blocks the intracellular signaling mediated by TIGIT binding to PVRL2 is selected from the group consisting of a small molecule inhibitor, an inhibitory antibody or antigen-binding fragment thereof, an aptamer, an inhibitory nucleic acid, and an inhibitory polypeptide; or

(h) the agent that inhibits and/or blocks the intracellular signaling mediated by TIGIT binding to PVRL3 is selected from the group consisting of a small molecule inhibitor, an inhibitory antibody or antigen-binding fragment thereof, an aptamer, an inhibitory nucleic acid, and an

inhibitory polypeptide; or

(i) the antagonist of TIGIT expression and/or activity is an anti-TIGIT antibody or antigen-binding fragment thereof, wherein optionally

(A) the anti-TIGIT antibody or antigen-binding fragment thereof is selected from the group consisting of a humanized antibody, a chimeric antibody, a bispecific antibody, a heteroconjugate antibody, and an immunotoxin, wherein optionally (B) the anti-TIGIT antibody or antigen-binding fragment thereof comprises at least one HVR comprising an amino acid sequence selected from the amino acid sequences (1) KSSQSLYYSGVKENLLA (SEQ ID NO:1), ASIRFT (SEQ ID NO:2), QQGINNPLT (SEQ ID NO:3), GFTFSSFTMH (SEQ ID NO:4), FIRSGSGIVFYADAVRG (SEQ ID NO:5), and RPLGHNTFDS (SEQ ID NO:6); or
(2) RSSQSLVNSYGNTFLS (SEQ ID NO:7), GISNRFS (SEQ ID NO:8), LQGTHQPPT (SEQ ID NO:9), GYSFTGHLMN (SEQ ID NO:10), LIIPYNGGTSYNQKFKG (SEQ ID NO:11), and GLRGFYAMDY (SEQ ID NO:12), wherein optionally

(C) the anti-TIGIT antibody or antigen-binding fragment thereof, wherein the antibody light chain comprises the amino acid sequence set forth in DIVMTQSPSSLAVSPGEKVTMTCKSSQSLYYSGVKENLLAWYQQKPGQS PKLLIYYASIRFTGVPDRFTGSGSGTDYTLTITSVQAEDMGQYFCQQGINNPLTFG DGTKLEIKR (SEQ ID NO:13) or
DVVLTQTPLSLSVSFGDQVSISCRSSQSLVNSYGNTFLSWYLHKPGQSPQLLIFGIS NRFSGVPDRFSGSGSGTDFTLKISTIKPEDLGMYYCLQGTHQPPTFGPGTKLEVK (SEQ ID NO:14), wherein optionally

(D) the antibody heavy chain comprises the amino acid sequence set forth in EVQLVESGGGLTQPGKSLKLSCEASGFTFSSFTMHWVRQSPGKGLEWVAFIRSGSGI VFYADAVRGRFTISRDNAKNLLFLQMNDLKSEDTAMYYCARRPLGHNTFDSWGQG TLVTVSS (SEQ ID NO:15) or
EVQLQQSGPELVKPGTSMKISCKASGYSFTGHLMNWVKQSHGKNLEWIGLIIPYNGG TSYNQKFKGKATLTVDKSSSTAYMELLSLTSDDSAVYFCSRGLRGFYAMDYWGQG TSVTVSS (SEQ ID NO:16), and wherein optionally (E) the antibody light chain comprises the amino acid sequence set forth in
DIVMTQSPSSLAVSPGEKVTMTCKSSQSLYYSGVKENLLAWYQQKPGQS PKLLIYYASIRFTGVPDRFTGSGSGTDYTLTITSVQAEDMGQYFCQQGINNPLTFGDG TKLEIKR (SEQ ID NO:13) or

DVVLTQTPLSLSVSFGDQVSISCRSSQSLVNSYGNTFLSWYLHKPGQSPQLLIFGISNR FSGVPDRFSGSGSGTDFTLKISTIKPEDLGMYYCLQGTHQPPTFGPGTKLEVK (SEQ ID NO:14), and the antibody heavy chain comprises the amino acid sequence set forth in EVQLVESGGGLTQPGKSLKLSCEASGFTFSSFTMHWVRQSPGKGLEWVAFIRSGSGI VFYADAVRGRFTISRDNAKNLLFLQMNDLKSEDTAMYYCARRPLGHNTFDSWGQG TLVTVSS (SEQ ID NO:15) or EVQLQQSGPELVKPGTSMKISCKASGYSFTGHLMNWVKQSHGKNLEWIGLIIPYNGG TSYNQKFKGKATLTVDKSSSTAYMELLSLTSDDSAVYFCSRGLRGFYAMDYWGQG TSVTVSS (SEQ ID NO: 16).

7. The use of claim 6(i) or 6(i)(A), wherein the anti-TIGIT antibody or antigen-binding fragment thereof comprises at least one HVR that is at least 90% identical to an HVR set forth in any one of (1) KSSQSLYYSGVKENLLA (SEQ ID NO:1), ASIRFT (SEQ ID NO:2), QQGINNPLT (SEQ ID NO:3), GFTFSSFTMH (SEQ ID NO:4), FIRSGSGIVFYADAVRG (SEQ ID NO:5), and RPLGHNTFDS (SEQ ID NO:6); or (2) RSSQSLVNSYGNTFLS (SEQ ID NO:7), GISNRFS (SEQ ID NO:8), LQGTHQPPT (SEQ ID NO:9), GYSFTGHLMN (SEQ ID NO:10), LIIPYNGGTSYNQKFKG (SEQ ID NO:11), and GLRGFYAMDY (SEQ ID NO:12); wherein optionally

the anti-TIGIT antibody or fragment thereof comprises the light chain comprising amino acid sequences at least 90% identical to the amino acid sequences set forth in DIVMTQSPSSLAVSPGEKVTMTCKSSQSLYYSGVKENLLAWYQQKPGQS PKLLIYYASIRFTGVPDRFTGSGSGTDYTLTITSVQAEDMGQYFCQQGINNPLTFGDG TKLEIKR (SEQ ID NO:13) or DVVLTQTPLSLSVSFGDQVSISCRSSQSLVNSYGNTFLSWYLHKPGQSPQLLIFGISNR FSGVPDRFSGSGSGTDFTLKISTIKPEDLGMYYCLQGTHQPPTFGPGTKLEVK (SEQ ID NO:14); and/or the heavy chain comprising amino acid sequences at least 90% identical to the amino acid sequences set forth in EVQLVESGGGLTQPGKSLKLSCEASGFTFSSFTMHWVRQSPGKGLEWVAFIRSGSGI VFYADAVRGRFTISRDNAKNLLFLQMNDLKSEDTAMYYCARRPLGHNTFDSWGQG TLVTVSS (SEQ ID NO:15) or EVQLQQSGPELVKPGTSMKISCKASGYSFTGHLMNWVKQSHGKNLEWIGLIIPYNGG TSYNQKFKGKATLTVDKSSSTAYMELLSLTSDDSAVYFCSRGLRGFYAMDYWGQG TSVTVSS (SEQ ID NO:16).

8. The use of any one of the preceding claims, wherein the medicament is to be

administered with an anti-cancer agent, and an anti-cancer therapy.

9. The use of any one of the preceding claims, wherein the anti-cancer agent is one or more anti-cancer agents; wherein optionally

the one or more anti-cancer agents are (i) two or more anti-cancer agents; or

(ii) three or more anti-cancer agents; or

(iii) four or more anti-cancer agents.

10. The use of any one of the preceding claims, wherein the anti-cancer therapy is one or more anti-cancer therapies; wherein optionally

the one or more anti-cancer therapies are (i) two or more anti-cancer therapies; or

(ii) three or more anti-cancer therapies; or

(iii) four or more anti-cancer therapies.

11. The use of any one of the preceding claims, wherein the anti-cancer therapy is selected from the group consisting of radiation therapy, surgery, chemotherapy, gene therapy, DNA therapy, viral therapy, RNA therapy, immunotherapy, bone marrow transplantation, nanotherapy, monoclonal antibody therapy, adjuvant therapy, neoadjuvant therapy, and combinations thereof.

12. The use claim 10, wherein the one or more anti-cancer therapies are selected from the group consisting of radiation therapy, surgery, chemotherapy, gene therapy, DNA therapy, viral therapy, RNA therapy, immunotherapy, bone marrow transplantation, nanotherapy, monoclonal antibody therapy, adjuvant therapy, neoadjuvant therapy, and combinations thereof.

13. The use of any one of the preceding claims, wherein the anti-cancer agent is selected from the group consisting of a chemotherapeutic or growth inhibitory agent, a targeted therapeutic agent, a T cell expressing a chimeric antigen receptor, an antibody or antigen-binding fragment thereof, an antibody-drug conjugate, an angiogenesis inhibitor, an antineoplastic agent, a cancer vaccine, an adjuvant, and combinations thereof; wherein optionally

(i) the chemotherapeutic or growth inhibitory agent is selected from the group consisting of an alkylating agent, an anthracycline, an anti-hormonal agent, an aromatase inhibitor, an anti-androgen, a protein kinase inhibitor, a lipid kinase inhibitor, an antisense oligonucleotide, a

ribozyme, an antimetabolite, a topoisomerase inhibitor, a cytotoxic agent or antitumor antibiotic, a proteasome inhibitor, an anti-microtubule agent, an EGFR antagonist, a retinoid, a tyrosine kinase inhibitor, a histone deacetylase inhibitor, and combinations thereof; or

(ii) the targeted therapeutic agent is selected from the group consisting of a B-raf inhibitor, a MEK inhibitor, a K-ras inhibitor, a c-Met inhibitor, an Alk inhibitor, a phosphatidylinositol 3-kinase inhibitor, an Akt inhibitor, an mTOR inhibitor, a dual phosphatidylinositol 3-kinase/mTOR inhibitor, and combinations thereof; or

(iii) the T cell expressing a chimeric antigen receptor comprises a dominant-negative TGF beta receptor; or

(iv) the antibody or antigen-binding fragment thereof is selected from the group consisting of alemtuzumab, bevacizumab, cetuximab, panitumumab, rituximab, pertuzumab, trastuzumab, tositumomab, apolizumab, aselizumab, atlizumab, bapineuzumab, cedelizumab, certolizumab pegol, cidfusituzumab, cidtuzumab, clivatuzumab, daclizumab, eculizumab, efalizumab, epratuzumab, erlizumab, felvizumab, fontolizumab, labetuzumab, lintuzumab, matuzumab, mepolizumab, motavizumab, motovizumab, natalizumab, nimotuzumab, nolovizumab, numavizumab, ocrelizumab, omalizumab, palivizumab, pascolizumab, pecfusituzumab, pertuzumab, pexelizumab, ralivizumab, ranibizumab, reslivizumab, reslizumab, resyvizumab, ruplizumab, sibrotuzumab, siplizumab, sontuzumab, tacatuzumab tetraxetan, tadocizumab, talizumab, tefibazumab, tocilizumab, toralizumab, tucotuzumab celmoleukin, tucusituzumab, umavizumab, urtoxazumab, ustekinumab, visilizumab, anti–IL-12, and anti-IL-17; or

(v) the antibody or antigen-binding fragment thereof specifically binds to a target selected from the group consisting of CD52, VEGF-A, EGFR, CD20, HER2, HLA-DRB, CD62L, IL-6R, amyloid beta, CD44, CanAg, CD4, TNF alpha, IL-2, CD25, complement C5, CD11a, CD22, CD18, respiratory syncytial virus F, interferon gamma, CD33, CEACAM5, IL-5, integrin alpha 4, IgE, IL-4, IL-5, CD154, FAP, CD2, MUC-1, AFP, integrin αIIbβ3, ClfA, IL6R, CD40L, EpCAM, Shiga-like toxin II, IL-12, IL-23, IL-17, and CD3; or

(vi) the antibody-drug conjugate comprises a drug selected from the group consisting of mertansine, monomethyl auristatin E, a calicheamicin, an esperamicin, and a radioisotope chelator; or

(vii) the angiogenesis inhibitor is selected from the group consisting of a VEGF antagonist and an angiopoietin 2 antagonist; or

(viii) the antineoplastic agent is selected from the group consisting of an agent targeting CSF-

1R, an interferon, GM-CSF, IL-2, IL-12, and an antibody targeting CD20; or

(ix) optionally the cancer vaccine is selected from the group consisting of a peptide cancer vaccine, a personalized peptide vaccine, a multivalent long peptide vaccine, a multi-peptide vaccine, a peptide cocktail vaccine, a hybrid peptide vaccine, and a peptide-pulsed dendritic cell vaccine.

14. The use of any one of claims 9-12, wherein the one or more anti-cancer agents are selected from the group consisting of a chemotherapeutic or growth inhibitory agent, a targeted therapeutic agent, a T cell expressing a chimeric antigen receptor, an antibody or antigen-binding fragment thereof, an antibody-drug conjugate, an angiogenesis inhibitor, an antineoplastic agent, a cancer vaccine, an adjuvant, and combinations thereof; wherein optionally

(i) the chemotherapeutic or growth inhibitory agent is selected from the group consisting of an alkylating agent, an anthracycline, an anti-hormonal agent, an aromatase inhibitor, an anti-androgen, a protein kinase inhibitor, a lipid kinase inhibitor, an antisense oligonucleotide, a ribozyme, an antimetabolite, a topoisomerase inhibitor, a cytotoxic agent or antitumor antibiotic, a proteasome inhibitor, an anti-microtubule agent, an EGFR antagonist, a retinoid, a tyrosine kinase inhibitor, a histone deacetylase inhibitor, and combinations thereof; or

(ii) the targeted therapeutic agent is selected from the group consisting of a B-raf inhibitor, a MEK inhibitor, a K-ras inhibitor, a c-Met inhibitor, an Alk inhibitor, a phosphatidylinositol 3-kinase inhibitor, an Akt inhibitor, an mTOR inhibitor, a dual phosphatidylinositol 3-kinase/mTOR inhibitor, and combinations thereof; or

(iii) the T cell expressing a chimeric antigen receptor comprises a dominant-negative TGF beta receptor; or

(iv) the antibody or antigen-binding fragment thereof is selected from the group consisting of alemtuzumab, bevacizumab, cetuximab, panitumumab, rituximab, pertuzumab, trastuzumab, tositumomab, apolizumab, aselizumab, atlizumab, bapineuzumab, cedelizumab, certolizumab pegol, cidfusituzumab, cidtuzumab, clivatuzumab, daclizumab, eculizumab, efalizumab, epratuzumab, erlizumab, felvizumab, fontolizumab, labetuzumab, lintuzumab, matuzumab, mepolizumab, motavizumab, motovizumab, natalizumab, nimotuzumab, nolovizumab, numavizumab, ocrelizumab, omalizumab, palivizumab, pascolizumab, pecfusituzumab, pertuzumab, pexelizumab, ralivizumab, ranibizumab, reslivizumab, reslizumab, resyvizumab, ruplizumab, sibrotuzumab, siplizumab, sontuzumab, tacatuzumab tetraxetan, tadocizumab,

talizumab, tefibazumab, tocilizumab, toralizumab, tucotuzumab celmoleukin, tucusituzumab, umavizumab, urtoxazumab, ustekinumab, visilizumab, anti–IL-12, and anti-IL-17; or

(v) the antibody or antigen-binding fragment thereof specifically binds to a target selected from the group consisting of CD52, VEGF-A, EGFR, CD20, HER2, HLA-DRB, CD62L, IL-6R, amyloid beta, CD44, CanAg, CD4, TNF alpha, IL-2, CD25, complement C5, CD11a, CD22, CD18, respiratory syncytial virus F, interferon gamma, CD33, CEACAM5, IL-5, integrin alpha 4, IgE, IL-4, IL-5, CD154, FAP, CD2, MUC-1, AFP, integrin αIIbβ3, ClfA, IL6R, CD40L, EpCAM, Shiga-like toxin II, IL-12, IL-23, IL-17, and CD3; or

(vi) the antibody-drug conjugate comprises a drug selected from the group consisting of mertansine, monomethyl auristatin E, a calicheamicin, an esperamicin, and a radioisotope chelator; or

(vii) the angiogenesis inhibitor is selected from the group consisting of a VEGF antagonist and an angiopoietin 2 antagonist; or

(viii) wherein optionally the antineoplastic agent is selected from the group consisting of an agent targeting CSF-1R, an interferon, GM-CSF, IL-2, IL-12, and an antibody targeting CD20; or

(ix) the cancer vaccine is selected from the group consisting of a peptide cancer vaccine, a personalized peptide vaccine, a multivalent long peptide vaccine, a multi-peptide vaccine, a peptide cocktail vaccine, a hybrid peptide vaccine, and a peptide-pulsed dendritic cell vaccine.

15. The use of any one of claims 1-12, wherein the anti-cancer agent is selected from the group consisting of a TLR agonist, tumor necrosis factor alpha, IL-1, HMGB1, an IL-10 antagonist, an IL-4 antagonist, an IL-13 antagonist, a treatment targeting CX3CL1, a treatment targeting CXCL9, a treatment targeting CXCL10, a treatment targeting CCL5, an LFA-1 agonist, an ICAM1 agonist, and a Selectin agonist.

16. The use of any one of claims 9-12, wherein the one or more anti-cancer agents are selected from the group consisting of a TLR agonist, tumor necrosis factor alpha, IL-1, HMGB1, an IL-10 antagonist, an IL-4 antagonist, an IL-13 antagonist, a treatment targeting CX3CL1, a treatment targeting CXCL9, a treatment targeting CXCL10, a treatment targeting CCL5, an LFA-1 agonist, an ICAM1 agonist, a Selectin agonist, and combinations thereof.

17. The use of any one of claims 1-16, wherein the agent that decreases or inhibits TIGIT expression and/or activity is to be administered continuously, or

intermittently.

18. The use of any one of claims 1-17, wherein the anti-cancer agent or anti-cancer therapy is to be administered continuously or .

intermittently.

19. The use of any one of the preceding claims, wherein the agent that decreases or inhibits TIGIT expression and/or activity is to be administered before the anti-cancer agent or anti-cancer therapy; or

the agent that decreases or inhibits TIGIT expression and/or activity is to be administered simultaneously with the anti-cancer agent or anti-cancer therapy; or

the agent that decreases or inhibits TIGIT expression and/or activity is to be administered after the anti-cancer agent or anti-cancer therapy.

20. The use of any one of the preceding claims, wherein the cancer is selected from the group consisting of non-small cell lung cancer, small cell lung cancer, renal cell cancer, colorectal cancer, ovarian cancer, breast cancer, pancreatic cancer, gastric carcinoma, bladder cancer, esophageal cancer, mesothelioma, melanoma, head and neck cancer, thyroid cancer, sarcoma, prostate cancer, glioblastoma, cervical cancer, thymic carcinoma, leukemia, lymphomas, myelomas, mycosis fungoides, merkel cell cancer, and other hematologic malignancies; wherein optionally

the cancer has elevated levels of T cell infiltration.

21. The use of any one of the preceding claims, wherein activated CD4 and/or CD8 T cells in the individual 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 combination; wherein optionally

the CD4 and/or CD8 T cells exhibit increased release of cytokines selected from the group consisting of IFN- γ, TNF-α and interleukins.

22. The use of claim 21, wherein the CD4 and/or CD8 T cells are effector memory T cells; optionally

characterized by having the expression of CD44$^{high}$ CD62L$^{low}$.

23. A kit comprising an anti-cancer agent and a package insert comprising instructions for using the anti-cancer agent in combination with an agent that decreases or inhibits TIGIT

expression and/or activity to treat or delay progression of cancer in an individual.

24. A kit comprising an anti-cancer agent and an agent that decreases or inhibits TIGIT expression and/or activity, and a package insert comprising instructions for using the anti-cancer agent and the agent that decreases or inhibits TIGIT expression and/or activity to treat or delay progression of cancer in an individual.

25. A kit comprising an agent that decreases or inhibits TIGIT expression and/or activity and a package insert comprising instructions for using the agent that decreases or inhibits TIGIT expression and/or activity in combination with an anti-cancer agent or an anti-cancer therapy to treat or delay progression of cancer in an individual.

26. A kit comprising an anti-cancer agent and a package insert comprising instructions for using the anti-cancer agent in combination with an agent that decreases or inhibits TIGIT expression and/or activity to reduce or inhibit cancer relapse or cancer progression in an individual having cancer.

27. A kit comprising an anti-cancer agent and an agent that decreases or inhibits TIGIT expression and/or activity, and a package insert comprising instructions for using the anti-cancer agent and the agent that decreases or inhibits TIGIT expression and/or activity to reduce or inhibit cancer relapse or cancer progression in an individual having cancer.

28. A kit comprising an agent that decreases or inhibits TIGIT expression and/or activity and a package insert comprising instructions for using the agent that decreases or inhibits TIGIT expression and/or activity in combination with an anti-cancer agent or an anti-cancer therapy to reduce or inhibit cancer relapse or cancer progression in an individual having cancer.

29. A kit comprising an anti-cancer agent and a package insert comprising instructions for using the anti-cancer agent in combination with an agent that decreases or inhibits TIGIT expression and/or activity to treat or delay progression of tumor immunity in an individual having cancer.

30. A kit comprising an anti-cancer agent and an agent that decreases or inhibits TIGIT expression and/or activity, and a package insert comprising instructions for using the anti-cancer agent and the agent that decreases or inhibits TIGIT expression and/or activity to treat or delay progression of tumor immunity in an individual having cancer.

31. A kit comprising an agent that decreases or inhibits TIGIT expression and/or activity and a package insert comprising instructions for using the agent that decreases or inhibits

TIGIT expression and/or activity in combination with an anti-cancer agent or an anti-cancer therapy to treat or delay progression of tumor immunity in an individual having cancer.

32. A kit comprising an anti-cancer agent and a package insert comprising instructions for using the anti-cancer agent in combination with an agent that decreases or inhibits TIGIT expression and/or activity to increase, enhance, or stimulate an immune response or function in an individual having cancer.

33. A kit comprising an anti-cancer agent and an agent that decreases or inhibits TIGIT expression and/or activity, and a package insert comprising instructions for using the anti-cancer agent and the agent that decreases or inhibits TIGIT expression and/or activity to increase, enhance, or stimulate an immune response or function in an individual having cancer.

34. A kit comprising an agent that decreases or inhibits TIGIT expression and/or activity and a package insert comprising instructions for using the agent that decreases or inhibits TIGIT expression and/or activity in combination with an anti-cancer agent or an anti-cancer therapy to increase, enhance, or stimulate an immune response or function in an individual having cancer.

35. The kit of any one of claims 23-34, wherein the anti-cancer agent is one or more anti-cancer agents; wherein optionally

the one or more anti-cancer agents are (i) two or more anti-cancer agents;

(ii) three or more anti-cancer agents; or

(iii) four or more anti-cancer agents.

36. The kit of any one of claims 25, 28, 31, or 34, wherein the anti-cancer therapy is one or more anti-cancer therapies; wherein optionally

the one or more anti-cancer therapies are (i) two or more anti-cancer therapies; or

(ii) three or more anti-cancer therapies; or

(iii) four or more anti-cancer therapies.

37. The kit of claim 25, 28, 31, or 34, wherein the anti-cancer therapy is selected from the group consisting of radiation therapy, surgery, chemotherapy, gene therapy, DNA therapy, viral therapy, RNA therapy, immunotherapy, bone marrow transplantation, nanotherapy, monoclonal antibody therapy, adjuvant therapy, neoadjuvant therapy, and combinations

thereof.

38. The kit of claim 25, 28, 31, 34, or 36 wherein the one or more anti-cancer therapies are selected from the group consisting of radiation therapy, surgery, chemotherapy, gene therapy, DNA therapy, viral therapy, RNA therapy, immunotherapy, bone marrow transplantation, nanotherapy, monoclonal antibody therapy, adjuvant therapy, neoadjuvant therapy, and combinations thereof.

39. The kit of any one of claims 23-38, wherein the agent that decreases or inhibits TIGIT expression and/or activity is selected from the group consisting of an antagonist of TIGIT expression and/or activity, an antagonist of PVR expression and/or activity, an agent that inhibits and/or blocks the interaction of TIGIT with PVR, an agent that inhibits and/or blocks the interaction of TIGIT with PVRL2, an agent that inhibits and/or blocks the interaction of TIGIT with PVRL3, an agent that inhibits and/or blocks the intracellular signaling mediated by TIGIT binding to PVR, an agent that inhibits and/or blocks the intracellular signaling mediated by TIGIT binding to PVRL2, and an agent that inhibits and/or blocks the intracellular signaling mediated by TIGIT binding to PVRL3; wherein optionally

(i) the antagonist of TIGIT expression and/or activity is an anti-TIGIT antibody or antigen-binding fragment thereof; and wherein optionally

(ii) the anti-TIGIT antibody or antigen-binding fragment thereof comprises at least one HVR comprising an amino acid sequence selected from the amino acid sequences (1) KSSQSLYYSGVKENLLA (SEQ ID NO:1), ASIRFT (SEQ ID NO:2), QQGINNPLT (SEQ ID NO:3), GFTFSSFTMH (SEQ ID NO:4), FIRSGSGIVFYADAVRG (SEQ ID NO:5), and RPLGHNTFDS (SEQ ID NO:6); or (2) RSSQSLVNSYGNTFLS (SEQ ID NO:7), GISNRFS (SEQ ID NO:8), LQGTHQPPT (SEQ ID NO:9), GYSFTGHLMN (SEQ ID NO:10), LIIPYNGGTSYNQKFKG (SEQ ID NO:11), and GLRGFYAMDY (SEQ ID NO:12).

40. The kit of claim 39(i) or 39(ii), wherein the anti-TIGIT antibody or antigen-binding fragment thereof, wherein the antibody light chain comprises the amino acid sequence set forth in DIVMTQSPSSLAVSPGEKVTMTCKSSQSLYYSGVKENLLAWYQQKPGQS PKLLIYYASIRFTGVPDRFTGSGSGTDYTLTITSVQAEDMGQYFCQQGINNPLTFGDG TKLEIKR (SEQ ID NO:13) or DVVLTQTPLSLSVSFGDQVSISCRSSQSLVNSYGNTFLSWYLHKPGQSPQLLIFGISNR FSGVPDRFSGSGSGTDFTLKISTIKPEDLGMYYCLQGTHQPPTFGPGTKLEVK (SEQ

ID NO:14); wherein optionally

(i) the antibody heavy chain comprises the amino acid sequence set forth in EVQLVESGGGLTQPGKSLKLSCEASGFTFSSFTMHWVRQSPGKGLEWVAFIRSGSGI VFYADAVRGRFTISRDNAKNLLFLQMNDLKSEDTAMYYCARRPLGHNTFDSWGQG TLVTVSS (SEQ ID NO:15) or EVQLQQSGPELVKPGTSMKISCKASGYSFTGHLMNWVKQSHGKNLEWIGLIIPYNGG TSYNQKFKGKATLTVDKSSSTAYMELLSLTSDDSAVYFCSRGLRGFYAMDYWGQG TSVTVSS (SEQ ID NO:16); or

(ii) the antibody light chain comprises the amino acid sequence set forth in DIVMTQSPSSLAVSPGEKVTMTCKSSQSLYYSGVKENLLAWYQQKPGQS PKLLIYYASIRFTGVPDRFTGSGSGTDYTLTITSVQAEDMGQYFCQQGINNPLTFGDG TKLEIKR (SEQ ID NO:13) or DVVLTQTPLSLSVSFGDQVSISCRSSQSLVNSYGNTFLSWYLHKPGQSPQLLIFGISNR FSGVPDRFSGSGSGTDFTLKISTIKPEDLGMYYCLQGTHQPPTFGPGTKLEVK (SEQ ID NO:14), and the antibody heavy chain comprises the amino acid sequence set forth in EVQLVESGGGLTQPGKSLKLSCEASGFTFSSFTMHWVRQSPGKGLEWVAFIRSGSGI VFYADAVRGRFTISRDNAKNLLFLQMNDLKSEDTAMYYCARRPLGHNTFDSWGQG TLVTVSS (SEQ ID NO:15) or EVQLQQSGPELVKPGTSMKISCKASGYSFTGHLMNWVKQSHGKNLEWIGLIIPYNGG TSYNQKFKGKATLTVDKSSSTAYMELLSLTSDDSAVYFCSRGLRGFYAMDYWGQG TSVTVSS (SEQ ID NO: 16).

41. The kit of claim 39(i), wherein the anti-TIGIT antibody or antigen-binding fragment thereof comprises at least one HVR that is at least 90% identical to an HVR set forth in any one of (1) KSSQSLYYSGVKENLLA (SEQ ID NO:1), ASIRFT (SEQ ID NO:2), QQGINNPLT (SEQ ID NO:3), GFTFSSFTMH (SEQ ID NO:4), FIRSGSGIVFYADAVRG (SEQ ID NO:5), and RPLGHNTFDS (SEQ ID NO:6); or (2) RSSQSLVNSYGNTFLS (SEQ ID NO:7), GISNRFS (SEQ ID NO:8), LQGTHQPPT (SEQ ID NO:9), GYSFTGHLMN (SEQ ID NO:10), LIIPYNGGTSYNQKFKG (SEQ ID NO:11), and GLRGFYAMDY (SEQ ID NO:12); wherein optionally

the light chain comprising amino acid sequences at least 90% identical to the amino acid sequences set forth in DIVMTQSPSSLAVSPGEKVTMTCKSSQSLYYSGVKENLLAWYQQKPGQS

PKLLIYYASIRFTGVPDRFTGSGSGTDYTLTITSVQAEDMGQYFCQQGINNPLTFGDG TKLEIKR (SEQ ID NO:13) or DVVLTQTPLSLSVSFGDQVSISCRSSQSLVNSYGNTFLSWYLHKPGQSPQLLIFGISNR FSGVPDRFSGSGSGTDFTLKISTIKPEDLGMYYCLQGTHQPPTFGPGTKLEVK (SEQ ID NO:14); and/or the heavy chain comprising amino acid sequences at least 90% identical to the amino acid sequences set forth in EVQLVESGGGLTQPGKSLKLSCEASGFTFSSFTMHWVRQSPGKGLEWVAFIRSGSGI VFYADAVRGRFTISRDNAKNLLFLQMNDLKSEDTAMYYCARRPLGHNTFDSWGQG TLVTVSS (SEQ ID NO:15) or EVQLQQSGPELVKPGTSMKISCKASGYSFTGHLMNWVKQSHGKNLEWIGLIIPYNGG TSYNQKFKGKATLTVDKSSSTAYMELLSLTSDDSAVYFCSRGLRGFYAMDYWGQG TSVTVSS (SEQ ID NO:16).

42. The kit of any one of claims 23-41, wherein the anti-cancer agent is selected from the group consisting of a chemotherapeutic or growth inhibitory agent, a targeted therapeutic agent, a T cell expressing a chimeric antigen receptor, an antibody or antigen-binding fragment thereof, an antibody-drug conjugate, an angiogenesis inhibitor, an antineoplastic agent, a cancer vaccine, an adjuvant, and combinations thereof ; wherein optionally

(i) the chemotherapeutic or growth inhibitory agent is selected from the group consisting of an alkylating agent, an anthracycline, an anti-hormonal agent, an aromatase inhibitor, an anti-androgen, a protein kinase inhibitor, a lipid kinase inhibitor, an antisense oligonucleotide, a ribozyme, an antimetabolite, a topoisomerase inhibitor, a cytotoxic agent or antitumor antibiotic, a proteasome inhibitor, an anti-microtubule agent, an EGFR antagonist, a retinoid, a tyrosine kinase inhibitor, a histone deacetylase inhibitor, and combinations thereof; or

(ii) the targeted therapeutic agent is selected from the group consisting of a B-raf inhibitor, a MEK inhibitor, a K-ras inhibitor, a c-Met inhibitor, an Alk inhibitor, a phosphatidylinositol 3-kinase inhibitor, an Akt inhibitor, an mTOR inhibitor, a dual phosphatidylinositol 3-kinase/mTOR inhibitor, and combinations thereof; or

(iii) the targeted therapeutic agent is selected from the group consisting of a B-raf inhibitor, a MEK inhibitor, a K-ras inhibitor, a c-Met inhibitor, an Alk inhibitor, a phosphatidylinositol 3-kinase inhibitor, an Akt inhibitor, an mTOR inhibitor, a dual phosphatidylinositol 3-kinase/mTOR inhibitor, and combinations thereof; or

(iv) the antibody or antigen-binding fragment thereof is selected from the group consisting of alemtuzumab, bevacizumab, cetuximab, panitumumab, rituximab, pertuzumab, trastuzumab, tositumomab, apolizumab, aselizumab, atlizumab, bapineuzumab, cedelizumab, certolizumab pegol, cidfusituzumab, cidtuzumab, clivatuzumab, daclizumab, eculizumab, efalizumab, epratuzumab, erlizumab, felvizumab, fontolizumab, labetuzumab, lintuzumab, matuzumab, mepolizumab, motavizumab, motovizumab, natalizumab, nimotuzumab, nolovizumab, numavizumab, ocrelizumab, omalizumab, palivizumab, pascolizumab, pecfusituzumab, pertuzumab, pexelizumab, ralivizumab, ranibizumab, reslivizumab, reslizumab, resyvizumab, ruplizumab, sibrotuzumab, siplizumab, sontuzumab, tacatuzumab tetraxetan, tadocizumab, talizumab, tefibazumab, tocilizumab, toralizumab, tucotuzumab celmoleukin, tucusituzumab, umavizumab, urtoxazumab, ustekinumab, visilizumab, anti–IL-12, and anti-IL-17; or

(v) the antibody or antigen-binding fragment thereof specifically binds to a target selected from the group consisting of CD52, VEGF-A, EGFR, CD20, HER2, HLA-DRB, CD62L, IL-6R, amyloid beta, CD44, CanAg, CD4, TNF alpha, IL-2, CD25, complement C5, CD11a, CD22, CD18, respiratory syncytial virus F, interferon gamma, CD33, CEACAM5, IL-5, integrin alpha 4, IgE, IL-4, IL-5, CD154, FAP, CD2, MUC-1, AFP, integrin αIIbβ3, ClfA, IL6R, CD40L, EpCAM, Shiga-like toxin II, IL-12, IL-23, IL-17, and CD3; or

(vi) the antibody-drug conjugate comprises a drug selected from the group consisting of mertansine, monomethyl auristatin E, calicheamicin, esperamicin, and a radioisotope chelator; or

(vii) the angiogenesis inhibitor is selected from the group consisting of a VEGF antagonist and an angiopoietin 2 antagonist; or

(viii) the antineoplastic agent is selected from the group consisting of an agent targeting CSF-1R, an interferon, GM-CSF, IL-2, IL-12, and an antibody targeting CD20; or

(ix) the cancer vaccine is selected from the group consisting of a peptide cancer vaccine, a personalized peptide vaccine, a multivalent long peptide vaccine, a multi-peptide vaccine, a peptide cocktail vaccine, a hybrid peptide vaccine, and a peptide-pulsed dendritic cell vaccine.

43. The kit of any one of claims 35-41, wherein the one or more anti-cancer agents are selected from the group consisting of a chemotherapeutic or growth inhibitory agent, a

targeted therapeutic agent, a T cell expressing a chimeric antigen receptor, an antibody or antigen-binding fragment thereof, an antibody-drug conjugate, an angiogenesis inhibitor, an antineoplastic agent, a cancer vaccine, an adjuvant, and combinations thereof; wherein optionally

(i) the chemotherapeutic or growth inhibitory agent is selected from the group consisting of an alkylating agent, an anthracycline, an anti-hormonal agent, an aromatase inhibitor, an anti-androgen, a protein kinase inhibitor, a lipid kinase inhibitor, an antisense oligonucleotide, a ribozyme, an antimetabolite, a topoisomerase inhibitor, a cytotoxic agent or antitumor antibiotic, a proteasome inhibitor, an anti-microtubule agent, an EGFR antagonist, a retinoid, a tyrosine kinase inhibitor, a histone deacetylase inhibitor, and combinations thereof; or

(ii) the targeted therapeutic agent is selected from the group consisting of a B-raf inhibitor, a MEK inhibitor, a K-ras inhibitor, a c-Met inhibitor, an Alk inhibitor, a phosphatidylinositol 3-kinase inhibitor, an Akt inhibitor, an mTOR inhibitor, a dual phosphatidylinositol 3-kinase/mTOR inhibitor, and combinations thereof; or

(iii) the targeted therapeutic agent is selected from the group consisting of a B-raf inhibitor, a MEK inhibitor, a K-ras inhibitor, a c-Met inhibitor, an Alk inhibitor, a phosphatidylinositol 3-kinase inhibitor, an Akt inhibitor, an mTOR inhibitor, a dual phosphatidylinositol 3-kinase/mTOR inhibitor, and combinations thereof; or

(iv) the antibody or antigen-binding fragment thereof is selected from the group consisting of alemtuzumab, bevacizumab, cetuximab, panitumumab, rituximab, pertuzumab, trastuzumab, tositumomab, apolizumab, aselizumab, atlizumab, bapineuzumab, cedelizumab, certolizumab pegol, cidfusituzumab, cidtuzumab, clivatuzumab, daclizumab, eculizumab, efalizumab, epratuzumab, erlizumab, felvizumab, fontolizumab, labetuzumab, lintuzumab, matuzumab, mepolizumab, motavizumab, motovizumab, natalizumab, nimotuzumab, nolovizumab, numavizumab, ocrelizumab, omalizumab, palivizumab, pascolizumab, pecfusituzumab, pertuzumab, pexelizumab, ralivizumab, ranibizumab, reslivizumab, reslizumab, resyvizumab, ruplizumab, sibrotuzumab, siplizumab, sontuzumab, tacatuzumab tetraxetan, tadocizumab, talizumab, tefibazumab, tocilizumab, toralizumab, tucotuzumab celmoleukin, tucusituzumab, umavizumab, urtoxazumab, ustekinumab, visilizumab, anti–IL-12, and anti-IL-17; or

(v) the antibody or antigen-binding fragment thereof specifically binds to a target selected from the group consisting of CD52, VEGF-A, EGFR, CD20, HER2, HLA-DRB, CD62L, IL-6R, amyloid beta, CD44, CanAg, CD4, TNF alpha, IL-2, CD25, complement C5, CD11a, CD22, CD18, respiratory syncytial virus F, interferon gamma, CD33, CEACAM5, IL-5, integrin alpha 4, IgE, IL-4, IL-5, CD154, FAP, CD2, MUC-1, AFP, integrin αIIbβ3, ClfA, IL6R, CD40L, EpCAM, Shiga-like toxin II, IL-12, IL-23, IL-17, and CD3; or

(vi) the antibody-drug conjugate comprises a drug selected from the group consisting of mertansine, monomethyl auristatin E, calicheamicin, esperamicin, and a radioisotope chelator; or

(vii) the angiogenesis inhibitor is selected from the group consisting of a VEGF antagonist and an angiopoietin 2 antagonist; or

(viii) the antineoplastic agent is selected from the group consisting of an agent targeting CSF-1R, an interferon, GM-CSF, IL-2, IL-12, and an antibody targeting CD20; or

(ix) the cancer vaccine is selected from the group consisting of a peptide cancer vaccine, a personalized peptide vaccine, a multivalent long peptide vaccine, a multi-peptide vaccine, a peptide cocktail vaccine, a hybrid peptide vaccine, and a peptide-pulsed dendritic cell vaccine.

44. The kit of any one of claims 23-41, wherein the anti-cancer agent is selected from the group consisting of a TLR agonist, tumor necrosis factor alpha, IL-1, HMGB1, an IL-10 antagonist, an IL-4 antagonist, an IL-13 antagonist, a treatment targeting CX3CL1, a treatment targeting CXCL9, a treatment targeting CXCL10, a treatment targeting CCL5, an LFA-1 agonist, an ICAM1 agonist, and a Selectin agonist.

45. The kit of any one of claims 35-41, wherein the one or more anti-cancer agents are selected from the group consisting of a TLR agonist, tumor necrosis factor alpha, IL-1, HMGB1, an IL-10 antagonist, an IL-4 antagonist, an IL-13 antagonist, a treatment targeting CX3CL1, a treatment targeting CXCL9, a treatment targeting CXCL10, a treatment targeting CCL5, an LFA-1 agonist, an ICAM1 agonist, a Selectin agonist, and combinations thereof.