SUMMARY

In a first aspect, the present disclosure describes vaccine conjugates comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2) conjugated to at least one target protein or fragment thereof, wherein the at least one target protein is overexpressed in a cancer.

In some examples, the mutant SMEZ-2 comprises mutations W75L and K182Q. In certain examples, the mutant SMEZ-2 comprises mutations W75L, K182Q, and/or D42C. In particular examples, the mutant SMEZ-2 comprises mutations W75L, K182Q, and D42C.

In some examples, the conjugate comprises a linker, such as between SMEZ-2 and the at least one target protein. In certain examples, the linker is a peptide linker, such as a glycine-serine linker. For example, the linker is AIA or GGGGS.

In certain examples, the at least one target protein is a neoantigen or tumor-associated antigen (TAA). In specific examples, the target protein is anterior gradient 2 (AGR2), such as AGR2 is human AGR2. In some examples, the at least one target protein is human epidermal growth factor receptor 2 (HER2), prostate-specific membrane antigen (PSMA), melanoma-associated antigen 3 (MAGE-A3), NY-ESO-1, IL-8, or GDF-15. In some examples, the at least one target protein is CD33 or a fragment thereof, mesothelin (MSLN), B-cell maturation antigen (BCMA), GPRC5D, CD123, CLL-1 (CD371), CD19, CD30, or CD20. In some examples, the CD33 or fragment thereof comprises one or more amino acid substitutions. In some examples, full length CD33 has an amino acid substitution at Asparagine 98. In some examples, CD33 comprises a truncated version of CD33 consisting of the CD33-IgC domain, such as CD33-IgC comprising an amino acid substitution at Aspartic acid 231 or Cysteine 154. In some examples, the one or more amino acid substitutions are at D231, D246, C154 and/or C169. In some examples, the one or more amino acid substitutions are D231E, D246E, C154S and/or C169S.

In certain examples, the vaccine conjugate comprises at least a second target protein or fragment thereof. In some examples, the at least one target protein is CD38.

In some examples, the at least one target protein is an immune checkpoint protein. In particular examples, the immune checkpoint protein is CTLA-4, PD-1, PD-L1, PD-L2, LAG-3, BTLA, B7H3, B7H4, TIM3, KIR, or A2aR.

In a further aspect, there is described a pharmaceutical composition comprising a vaccine conjugate of the present disclosure (*e.g.*, vaccine conjugates comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2) conjugated to at least one target protein or fragment thereof,

wherein the at least one target protein is overexpressed in a cancer) and an adjuvant. In some examples, the adjuvant is Incomplete Freund's Adjuvant. In certain examples, the conjugate is formulated as a 1:1 emulsification with Incomplete Freund's Adjuvant (IFA). In some examples, the conjugate is formulated for intravenous infusion, subcutaneous injection, or intramuscular injection.

In another aspect, there is described an expression vector comprising a sequence encoding mutant SMEZ-2 fused to a sequence encoding a target protein or fragment thereof, wherein the vector encodes a vaccine conjugate described herein. In some examples, the target protein is a neoantigen or TAA. In certain examples, the vector encodes a vaccine conjugate of the present disclosure (*e.g.*, vaccine conjugates comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2) conjugated to at least one target protein or fragment thereof). Also described herein in another aspect is a host cell comprising an expression vector of the present disclosure. In some examples, the host cell is *E. coli*, human embryonic kidney cell (HEK293), or Chinese hamster ovary (CHO) cell.

In yet another example, there is described a method for stimulating an immune response in a subject, comprising administering to the subject an effective amount of a vaccine conjugate of the present disclosure (*e.g.*, vaccine conjugates comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2) conjugated to at least one target protein or fragment thereof, wherein the at least one target protein is overexpressed in a cancer) or a pharmaceutical composition of the present disclosure. In one aspect, there is described a use of a vaccine conjugate as described herein in the manufacture of a medicament for stimulating an immune response in a subject.

In some examples, the immune response is an anti-cancer immune response. In certain examples, the subject has a cancer. In specific examples, the cancer is oral cancer, oropharyngeal cancer, nasopharyngeal cancer, respiratory cancer, urogenital cancer, gastrointestinal cancer, central or peripheral nervous system tissue cancer, an endocrine or neuroendocrine cancer or hematopoietic cancer, glioma, sarcoma, carcinoma, lymphoma, melanoma, fibroma, meningioma, brain cancer, oropharyngeal cancer, nasopharyngeal cancer, renal cancer, biliary cancer, pheochromocytoma, pancreatic islet cell cancer, Li-Fraumeni tumors, thyroid cancer, parathyroid cancer, pituitary tumors, adrenal gland tumors, osteogenic sarcoma tumors, multiple neuroendocrine type I and type II tumors, breast cancer, lung cancer, head and neck cancer, prostate cancer, esophageal cancer, tracheal cancer, liver cancer, bladder cancer, stomach cancer, pancreatic cancer, ovarian cancer, uterine cancer, cervical cancer, testicular cancer, colon cancer, rectal cancer or skin cancer. In particular examples, the cancer is pancreatic cancer, such

pancreatic ductal adenocarcinoma (PDAC). In certain examples, the cancer is breast cancer. In some examples, the cancer is multiple myeloma or lymphoma, such as T cell non-Hodgkin's lymphoma.

In certain examples, the immune response is an anti-AGR2 specific immune response. In some examples, the anti-AGR2 specific immune response is detected by measuring an increased titer of AGR2 specific immunoglobulins in a sample of said subject's blood. In other examples, the immune response is an anti-CD38, anti-PD1, anti-CTLA4, or anti-PDL1 response and is measured by measuring an increased titer of CD38, PD1, CTLA4, or PDL1 specific immunoglobulins in a sample of said subject's blood.

In some examples, the conjugate is administered by injection, such as intravenous infusion.

In additional examples, the method further comprises administering a second anti-cancer therapy to said subject. In some examples, the second anti-cancer therapy is immunotherapy, chemotherapy, radiotherapy, gene therapy, surgery, hormonal therapy, anti-angiogenic therapy or cytokine therapy. In some examples, the second anti-cancer therapy is immunotherapy, such as an immune checkpoint inhibitor. For example, the immune checkpoint inhibitor is selected from an inhibitor of CTLA-4, PD-1, PD-L1, PD-L2, LAG-3, BTLA, B7H3, B7H4, TIM3, KIR, or A2aR. In specific examples, the immune checkpoint inhibitor comprises an anti-PD1 agent, such as an anti-PD1 antibody, anti-PDL1 antibody, or an anti-PDL2 antibody. In certain examples, the anti-PD1 agent is nivolumab, pembrolizumab, pidilizumab, KEYTRUDA®, AMP-514, REGN2810, CT-011, BMS 936559, MPDL328OA or AMP-224. In some examples, the immune checkpoint inhibitor is an anti-CTLA-4 antibody. For example, the anti-CTLA-4 antibody is tremelimumab, YERVOY®, or ipilimumab. In some examples, the further anti-cancer therapy comprises a TLR9 agonist, such as CpG ODN1826, and/or CD40 agonist, such as CD40 agonistic antibody. In certain examples, the subject is administered an immune checkpoint inhibitor and TLR9 agonist.

A further example refers to a method of treating a subject having a cancer comprising administering a vaccine conjugate of the present disclosure (*e.g.*, vaccine conjugates comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2) conjugated to at least one target protein or fragment thereof, wherein the at least one target protein is overexpressed in a cancer) or a pharmaceutical composition of the present

disclosure to the subject. In one aspect, there is described a use of a vaccine conjugate as described herein or a pharmaceutical composition as described herein in the manufacture of a medicament for treating a subject having a cancer.

In some examples, the cancer is oral cancer, oropharyngeal cancer, nasopharyngeal cancer, respiratory cancer, urogenital cancer, gastrointestinal cancer, central or peripheral nervous system tissue cancer, an endocrine or neuroendocrine cancer or hematopoietic cancer, glioma, sarcoma,

carcinoma, lymphoma, melanoma, fibroma, meningioma, brain cancer, oropharyngeal cancer, nasopharyngeal cancer, renal cancer, biliary cancer, pheochromocytoma, pancreatic islet cell cancer, Li-Fraumeni tumors, thyroid cancer, parathyroid cancer, pituitary tumors, adrenal gland tumors, osteogenic sarcoma tumors, multiple neuroendocrine type I and type II tumors, breast cancer, lung cancer, head and neck cancer, prostate cancer, esophageal cancer, tracheal cancer, liver cancer, bladder cancer, stomach cancer, pancreatic cancer, ovarian cancer, uterine cancer, cervical cancer, testicular cancer, colon cancer, rectal cancer or skin cancer. In specific examples, the cancer is pancreatic cancer, such as pancreatic ductal adenocarcinoma (PDAC). In particular examples, the cancer is breast cancer. In some examples, the cancer is multiple myeloma or lymphoma, such as T cell non-Hodgkin's lymphoma.

In further examples, the method further comprises administering at least one immune checkpoint inhibitor to the subject. In some examples, administering at least one immune checkpoint inhibitor to the subject comprises administering at least one immune checkpoint inhibitor before the vaccine conjugate. In other examples, administering at least one immune checkpoint inhibitor to the subject comprises administering at least one immune checkpoint inhibitor after or concomitantly with the vaccine conjugate. For example, the immune checkpoint inhibitor is selected from an inhibitor of CTLA-4, PD-1, PD-L1, PD-L2, LAG-3, BTLA, B7H3, B7H4, TIM3, KIR, or A2aR. In specific examples, the immune checkpoint inhibitor comprises an anti-PD1 agent, such as an anti-PD1 antibody, anti-PDL1 antibody, or an anti-PDL2 antibody. In certain examples, the anti-PD1/PDL agent is nivolumab, pembrolizumab, pidilizumab, KEYTRUDA®, AMP-514, REGN2810, CT-011, BMS 936559, MPDL328OA or AMP-224. In some examples, the immune checkpoint inhibitor is an anti-CTLA-4 antibody. For example, the anti-CTLA-4 antibody is tremelimumab, YERVOY®, or ipilimumab. In some examples, the subject is administered two immune checkpoint inhibitors. In particular examples, the two immune checkpoint inhibitors are an anti-PD1 antibody and an anti-CTL4 antibody. In some examples, the vaccine conjugate is administered two or more times. In some examples, the further anti-cancer therapy comprises a TLR9 agonist, such as CpG ODN1826, and/or CD40 agonist, such as CD40 agonistic antibody. In certain examples, the subject is administered an immune checkpoint inhibitor and TLR9 agonist.

In additional examples, the method further comprises administering a further anti-cancer therapy to the subject. In some examples, the further anti-cancer therapy is chemotherapy,

radiotherapy, gene therapy, surgery, hormonal therapy, anti-angiogenic therapy or cytokine therapy.

Another example refers to a kit comprising a vaccine conjugate of the present disclosure (*e.g.*, vaccine conjugates comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2) or a pharmaceutical composition of the present disclosure. In some examples, the kit further comprises an immune checkpoint inhibitor. For example, the immune checkpoint inhibitor is an anti-PD1 antibody or CTLA-4 antibody.

A further example refers to a composition comprising a vaccine conjugate of the present disclosure (*e.g.*, vaccine conjugates comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2) or a pharmaceutical composition of the present disclosure for use in treating a cancer. In some examples, the composition further comprises an immune checkpoint inhibitor.

In another example, the present disclosure describes vaccine conjugates comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2) conjugated to CD33 or fragment thereof.

In some examples, the mutant SMEZ-2 comprises mutations W75L and K182Q. In certain examples, the mutant SMEZ-2 comprises mutations W75L, K182Q, and/or D42C. In particular examples, the mutant SMEZ-2 comprises mutations W75L, K182Q, and D42C. In certain examples, the vaccine conjugate comprises at least a second target protein or fragment thereof.

In some examples, the CD33 or fragment thereof comprises one or more amino acid substitutions. In some examples, full length CD33 has an amino acid substitution at Asparagine 98. In some examples, CD33 comprises a truncated version of CD33 consisting of the CD33-IgC domain, such as CD33-IgC comprising an amino acid substitution at Aspartic acid 231 or Cysteine 154. In some examples, the one or more amino acid substitutions are at D231, D246, C154 and/or C169. In certain examples, the one or more amino acid substitutions are D231E, D246E, C154S and/or C169S.

In certain examples, the linker is a peptide linker, such as a glycine serine linker, particularly a GGGGS linker.

A further example refers to a pharmaceutical composition comprising a vaccine conjugate of the present disclosure (*e.g.*, vaccine conjugates comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2) conjugated to CD33) and an adjuvant. In some examples, the adjuvant is Incomplete Freund's Adjuvant. In certain examples, the conjugate is formulated as a 1:1

emulsification with Incomplete Freund's Adjuvant (IFA). In some examples, the conjugate is formulated for intravenous infusion, subcutaneous, or intramuscular injection.

Another example refers to an expression vector comprising a sequence encoding mutant SMEZ-2 fused to a sequence encoding CD33 or fragment thereof. Also described herein is a host cell comprising an expression vector of the present disclosure, such as *E. coli*, human embryonic kidney cell (HEK293), or Chinese hamster ovary (CHO) cell.

In yet another example, there is described a method for stimulating an immune response in a subject, comprising administering to the subject an effective amount of a vaccine conjugate of the present disclosure (*e.g.*, vaccine conjugates comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2) conjugated to CD33 or fragment thereof) or a pharmaceutical composition of the present disclosure.

In some examples, the immune response is an anti-cancer immune response. In certain examples, the subject has a cancer. In specific examples, the cancer is oral cancer, oropharyngeal cancer, nasopharyngeal cancer, respiratory cancer, urogenital cancer, gastrointestinal cancer, central or peripheral nervous system tissue cancer, an endocrine or neuroendocrine cancer or hematopoietic cancer, glioma, sarcoma, carcinoma, lymphoma, melanoma, fibroma, meningioma, brain cancer, oropharyngeal cancer, nasopharyngeal cancer, renal cancer, biliary cancer, pheochromocytoma, pancreatic islet cell cancer, Li-Fraumeni tumors, thyroid cancer, parathyroid cancer, pituitary tumors, adrenal gland tumors, osteogenic sarcoma tumors, multiple neuroendocrine type I and type II tumors, breast cancer, lung cancer, head and neck cancer, prostate cancer, esophageal cancer, tracheal cancer, liver cancer, bladder cancer, stomach cancer, pancreatic cancer, ovarian cancer, uterine cancer, cervical cancer, testicular cancer, colon cancer, rectal cancer or skin cancer. In particular examples, the cancer is acute myelogenous leukemia.

In certain examples, the immune response is an anti-CD33 specific immune response. In some examples, the anti-CD33 specific immune response is detected by measuring an increased titer of CD33 specific immunoglobulins in a sample of said subject's blood.

In some examples, the conjugate is administered by injection, such as intravenous infusion.

In additional examples, the method further comprises administering a second anti-cancer therapy to said subject. In some examples, the second anti-cancer therapy is immunotherapy, chemotherapy, radiotherapy, gene therapy, surgery, hormonal therapy, anti-angiogenic therapy or cytokine therapy. In some examples, the second anti-cancer therapy is immunotherapy, such as an

immune checkpoint inhibitor. For example, the immune checkpoint inhibitor is selected from an inhibitor of CTLA-4, PD-1, PD-L1, PD-L2, LAG-3, BTLA, B7H3, B7H4, TIM3, KIR, or A2aR. In specific examples, the immune checkpoint inhibitor comprises an anti-PD1 agent, such as an anti-PD1 antibody, anti-PDL1 antibody, or an anti-PDL2 antibody. In certain examples, the anti-PD1 agent is nivolumab, pembrolizumab, pidilizumab, KEYTRUDA®, AMP-514, REGN2810, CT-011, BMS 936559, MPDL328OA or AMP-224. In some examples, the immune checkpoint inhibitor is an anti-CTLA-4 antibody. For example, the anti-CTLA-4 antibody is tremelimumab, YERVOY®, or ipilimumab.

A further example refers to a method of treating a subject having a cancer comprising administering a vaccine conjugate of the present disclosure (*e.g.*, vaccine conjugates comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2) conjugated to CD33 or fragment thereof) or a pharmaceutical composition of the present disclosure to the subject.

In some examples, the cancer is oral cancer, oropharyngeal cancer, nasopharyngeal cancer, respiratory cancer, urogenital cancer, gastrointestinal cancer, central or peripheral nervous system tissue cancer, an endocrine or neuroendocrine cancer or hematopoietic cancer, glioma, sarcoma, carcinoma, lymphoma, melanoma, fibroma, meningioma, brain cancer, oropharyngeal cancer, nasopharyngeal cancer, renal cancer, biliary cancer, pheochromocytoma, pancreatic islet cell cancer, Li-Fraumeni tumors, thyroid cancer, parathyroid cancer, pituitary tumors, adrenal gland tumors, osteogenic sarcoma tumors, multiple neuroendocrine type I and type II tumors, breast cancer, lung cancer, head and neck cancer, prostate cancer, esophageal cancer, tracheal cancer, liver cancer, bladder cancer, stomach cancer, pancreatic cancer, ovarian cancer, uterine cancer, cervical cancer, testicular cancer, colon cancer, rectal cancer or skin cancer. In specific examples, the cancer is acute myelogenous leukemia.

In further examples, the method further comprises administering at least one immune checkpoint inhibitor to the subject. In some examples, administering at least one immune checkpoint inhibitor to the subject comprises administering at least one immune checkpoint inhibitor before the vaccine conjugate. In other examples, administering at least one immune checkpoint inhibitor to the subject comprises administering at least one immune checkpoint inhibitor after or concomitantly with the vaccine conjugate. For example, the immune checkpoint inhibitor is selected from an inhibitor of CTLA-4, PD-1, PD-L1, PD-L2, LAG-3, BTLA, B7H3, B7H4, TIM3, KIR, or A2aR. In specific examples, the immune checkpoint inhibitor comprises an anti-PD1/PDL

agent, such as an anti-PD1 antibody, anti-PDL1 antibody, or an anti-PDL2 antibody. In certain examples, the anti-PD1 agent is nivolumab, pembrolizumab, pidilizumab, KEYTRUDA®, AMP-514, REGN2810, CT-011, BMS 936559, MPDL328OA or AMP-224. In some examples, the immune checkpoint inhibitor is an anti-CTLA-4 antibody. For example, the anti-CTLA-4 antibody is tremelimumab, YERVOY®, or ipilimumab. In some examples, the subject is administered two immune checkpoint inhibitors. In particular examples, the two immune checkpoint inhibitors are an anti-PD1 antibody and an anti-CTL4 antibody. In some examples, the vaccine conjugate is administered two or more times.

In additional examples, the method further comprises administering a further anti-cancer therapy to the subject. In some examples, the further anti-cancer therapy is chemotherapy, radiotherapy, gene therapy, surgery, hormonal therapy, anti-angiogenic therapy or cytokine therapy.

Another example refers to a kit comprising a vaccine conjugate of the present disclosure (*e.g.*, vaccine conjugates comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2)) or a pharmaceutical composition of the present disclosure. In some examples, the kit further comprises an immune checkpoint inhibitor. For example, the immune checkpoint inhibitor is an anti-PD1 antibody or CTLA-4 antibody.

In another aspect, there is described a composition comprising a vaccine conjugate of the present disclosure (*e.g.*, vaccine conjugates comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2) or a pharmaceutical composition of the present disclosure for use in therapy. In some examples, the composition further comprises an immune checkpoint inhibitor.

It is contemplated that any method or composition described herein can be implemented with respect to any other method or composition described herein. For example, a compound synthesized by one method may be used in the preparation of a final compound according to a different method.

The use of the word “a” or “an” when used in conjunction with the term “comprising” in the claims and/or the specification may mean “one,” but it is also consistent with the meaning of

WHAT IS CLAIMED IS:

1. A vaccine conjugate comprising mutant Streptococcal Mitogenic Exotoxin Z-2 (SMEZ-2) conjugated to at least one target protein or fragment thereof, wherein the at least one target protein is overexpressed in a cancer.

2. The conjugate of claim 1, wherein the mutant SMEZ-2 comprises mutations W75L, K182Q, and/or D42C.

3. The conjugate of claim 1 or 2, further comprising a peptide linker, optionally a glycine-serine linker comprising the sequence AIA or GGGGS.

4. The conjugate of any of claims 1-3, wherein the at least one target protein is a neoantigen or tumor-associated antigen (TAA).

5. The conjugate of any of claims 1-4, wherein the at least one target protein is CD33 or fragment thereof, anterior gradient 2 (AGR2), CD38, PD-1, PD-L1, CTLA-4, human epidermal growth factor receptor 2 (HER2), prostate-specific membrane antigen (PSMA), melanoma-associated antigen 3 (MAGE-A3), NY-ESO-1, IL-8, Growth/differentiation factor-15 (GDF-1), mesothelin (MSLN), B-cell maturation antigen (BCMA), GPRC5D, CD123, CLL-1 (CD371), CD19, CD30, CD20, or PSCA.

6. The conjugate of claim 1, wherein (a) the at least one target protein is CD33 or fragment thereof, (b) the CD33 or fragment thereof comprises one or more amino acid substitutions and/or (c) the CD33 consists of the CD33-IgC domain, optionally wherein the one or more amino acid substitutions are at D231, D246, C154 and/or C169, optionally D231E, D246E, C154S and/or C169S.

7. A pharmaceutical composition comprising a vaccine conjugate of any of claims 1-6 and an adjuvant.

8. The composition of claim 7, wherein (a) the adjuvant is Incomplete Freund's Adjuvant, (b) the conjugate is formulated as a 1:1 emulsification with Incomplete Freund's Adjuvant (IFA), or (c) the conjugate is formulated for intravenous infusion.

9. An expression vector comprising a sequence encoding mutant SMEZ-2 fused to a sequence encoding a target protein or fragment thereof, wherein the vector encodes a vaccine conjugate of any of claims 1-6.

10. A host cell comprising an expression vector of claim 9.

11. Use of a vaccine conjugate of any of claims 1-6 or a pharmaceutical composition of claim 7 or 8 in the manufacture of a medicament for stimulating an immune response in a subject.

12. The use of claim 11, wherein the immune response is an anti-cancer immune response, wherein the subject has a cancer.

13. The use of claim 11, wherein the cancer is pancreatic cancer, optionally pancreatic ductal adenocarcinoma (PDAC), breast cancer, multiple myeloma, lymphoma, optionally T cell non-Hodgkin's lymphoma, or leukemia, optionally acute myelogenous leukemia (AML).

14. The use of any of claims 11-13, wherein the immune response is an anti-AGR2 specific immune response detected by measuring an increased titer of AGR2 specific immunoglobulins in a sample of said subject's blood.

15. The use of any of claims 11-14, further comprising a second anti-cancer therapy to be administered to said subject selected from the group consisting of immunotherapy, chemotherapy, radiotherapy, gene therapy, surgery, hormonal therapy, anti-angiogenic therapy and cytokine therapy.

16. Use of a vaccine conjugate of any of claims 1-6 or a pharmaceutical composition of claim 7 or 8 in the manufacture of a medicament for treating a subject having a cancer.

17. The use of claim 16, wherein the cancer is (a) oral cancer, oropharyngeal cancer, nasopharyngeal cancer, respiratory cancer, urogenital cancer, gastrointestinal cancer, central or peripheral nervous system tissue cancer, an endocrine or neuroendocrine cancer or hematopoietic cancer, glioma, sarcoma, carcinoma, lymphoma, melanoma, fibroma, meningioma, brain cancer, oropharyngeal cancer, nasopharyngeal cancer, renal cancer, biliary cancer, pheochromocytoma, pancreatic islet cell cancer, Li-Fraumeni tumors, thyroid cancer, parathyroid cancer, pituitary tumors, adrenal gland tumors, osteogenic sarcoma tumors, multiple neuroendocrine type I and type II tumors, breast cancer, lung cancer, head and neck cancer, prostate cancer, esophageal cancer, tracheal cancer, liver cancer, bladder cancer, stomach cancer, pancreatic cancer, ovarian cancer, uterine cancer, cervical cancer, testicular cancer, colon cancer, rectal cancer or skin cancer, or (b) pancreatic cancer, optionally pancreatic ductal adenocarcinoma (PDAC), breast cancer, multiple myeloma, lymphoma, optionally T cell non-Hodgkin's lymphoma, or leukemia, optionally acute myelogenous leukemia (AML).

18. The use of claim 16 or 17, further comprising at least one immune checkpoint inhibitor to be administered to the subject or a further anti-cancer therapy to be administered to the subject, optionally wherein the further anti-cancer therapy is chemotherapy, radiotherapy, gene therapy, surgery, hormonal therapy, anti-angiogenic therapy or cytokine therapy.

19. The use of any of claims 16-18, wherein the vaccine conjugate is to be administered two or more times.

20. The use of claim 18, wherein the further anti-cancer therapy comprises a TLR9 agonist, optionally CpG ODN1826 and/or CD40 agonist, optionally a CD40 agonistic antibody.

21. A composition comprising a vaccine conjugate of any of claims 1-6 or a pharmaceutical composition of claim 7 or 8 for use in therapy.