## CLAIMS

WHAT IS CLAIMED IS:

1. A composition comprising a replication-defective vector, wherein the replication-defective vector comprises:

a nucleic acid sequence encoding for a tumor neo-antigen; and
a nucleic acid sequence encoding for ALT-803.

2. The composition of claim 1, wherein the replication-defective vector is an adenovirus vector.

3. The composition of any one of claims 1 or 2, wherein the replication defective vector comprises a deletion in an E2b region, an E1 region, an E3 region, an E4 region, or any combination thereof.

4. The composition of any one of claims 1-3, wherein the replication-defective vector is not a gutted vector.

5. The composition of any one of claims 1-4, wherein the ALT-803 is at least 80%, at least 85%, at least 90%, at least 95%, or at least 99% identical to a sequence of any one of SEQ ID NO: 88 – SEQ ID NO: 89.

6. The composition of any one of claims 1-5, wherein the replication-defective vector further comprises a nucleic acid sequence encoding for a linker.

7. The composition of claim 6, wherein the linker is a polyalanine linker, or a polyglycine linker.

8. The composition of claim 6 or claim 7, wherein the linker comprises a mixture of alanines and glycines.

9. The composition of any one of claims 6-8, wherein the linker is any one of SEQ ID NO: 91 – SEQ ID NO: 105.

10. The composition of any one of claims 1-9, wherein the composition comprises at least ten adenovirus vectors.

11. The composition of any one of claims 1-10, wherein the tumor neo-antigen comprises a tumor neo-epitope derived from WT1, HPV-E6, HPV-E7, p53, MAGE-A1, MAGE-A2, MAGE-A3, MAGE-A4, MAGE-A6, MAGE-A10, MAGE-A12, BAGE, DAM-6, DAM-10, Folate receptor alpha, GAGE-

1, GAGE-2, GAGE-8, GAGE-3, GAGE-4, GAGE-5, GAGE-6, GAGE-7B, NA88-A, NY-ESO-1, MART-1, MC1R, Gp100, PSA, PSM, Tyrosinase, TRP-1, TRP-2, ART-4, CAMEL, CEA, Cyp-B, Her1, Her2/neu, Her3, Her 4, BRCA1, Brachyury, Brachyury (TIVS7-2, polymorphism), Brachyury (IVS7 T/C polymorphism), T Brachyury, T, hTERT, hTRT, iCE, MUC1, MUC1 (VNTR polymorphism), MUC1c, MUC1n, MUC2, PRAME, P15, PSCA, PSMA, RU1, RU2, SART-1, SART-3, AFP, β-catenin/m, Caspase-8/m, CDK-4/m, ELF2M, GnT-V, G250, HSP70-2M, HST-2, KIAA0205, MUM-1, MUM-2, MUM-3, Myosin/m, RAGE, SART-2, TRP-2/INT2, 707-AP, Annexin II, CDC27/m, TPl/mbcr-abl, ETV6/AML, LDLR/FUT, Pml/RARα, TEL/AML1, or any combination thereof.

12. The composition of any one of claims 1-11, wherein the tumor neo-antigen is a tumor neo-epitope with an amino acid sequence of any one of SEQ ID NO: 1 – SEQ ID NO: 22, a nucleotide sequence of any one of SEQ ID NO: 23 – SEQ ID NO: 30, or has one of the following mutation: Q678P mutation of gene SLC4A11, D1143N mutation of gene SIGLEC1, A292T mutation of gene SIGLEC14, T2356M mutation of PIEZO2, S1613L mutation of gene FAT4, R268C mutation of gene FCRL1, or V73M mutation of gene VIPR2, or R346W mutation of gene FLRT2.

13. The composition of any one of claims 1-12, wherein the replication-defective vector further comprises a nucleic acid sequence encoding a costimulatory molecule.

14. The composition of any one of claims 1-13, wherein the composition additionally comprises an engineered natural killer (NK) cell.

15. The composition of any one of claims 1-14, wherein the composition additionally comprises an immunostimulant.

16. The composition of any one of claims 1-15, wherein the composition additionally comprises a therapeutically effective amount of an immune pathway checkpoint inhibitor.

17. The composition of any one of claims 1-16, wherein the replication-defective vector further comprises a nucleic acid sequence encoding a reporter.

18. A composition comprising a cell comprising the composition of any one of claims 1-17.

19. The composition of any one of claims 1-18 for use in therapy.

20. The composition of any one of claims 1-18 for use in treating a cancer.

21. Use of the composition of any one of claims 1-18 in the manufacture of a pharmaceutical composition for treating a cancer.

22. A pharmaceutical composition for use in treating a cancer, the pharmaceutical composition comprising a replication-defective vector, wherein the replication-defective vector comprises

a nucleic acid sequence encoding for a tumor neo-antigen; and
a nucleic acid sequence encoding for ALT-803.

23. Use of a pharmaceutical composition in the manufacture of a medicament for the treatment of a cancer, the pharmaceutical composition comprising a replication-defective vector, wherein the replication-defective vector comprises

a nucleic acid sequence encoding for a tumor neo-antigen; and

a nucleic acid sequence encoding for ALT-803.

24. The pharmaceutical composition for use of claim 22, or the use of claim 23, wherein the replication-defective vector is an adenovirus vector.

25. The pharmaceutical composition for use of claim 22 or 24, or the use of claim 23 or 24, wherein the replication defective vector comprises a deletion in an E2b region, an E1 region, an E3 region, an E4 region, or any combination thereof.

26. The pharmaceutical composition for use of any one of claims 22, 24 or 25, or the use of any one of claims 23-25, wherein the replication-defective vector is not a gutted vector.

27. The pharmceutical composition for use of any one of claims 22 or 24-26, or the use of any one of claims 23-26, wherein the ALT-803 is at least 80%, at least 85%, at least 90%, at least 95%, or at least 99% identical to a sequence of any one of SEQ ID NO: 88 – SEQ ID NO: 89.

28. The pharmaceutical composition for use of any one of claims 22 or 24-27, or the use of any one of claims 23-27, wherein the replication-defective vector further comprises a nucleic acid sequence encoding for a linker.

29. The pharmaceutical composition for use of claim 28, or the use ofclaim 28, wherein the linker is a polyalanine linker, or a polyglycine linker.

30. The pharmaceutical composition for use of claim 28 or claim 29, or the use of claim 28 or claim 29, wherein the linker comprises a mixture of alanines and glycines.

31. The pharmaceutical composition for use of any one of claims 28-30, or the use of any one of claims 28-30, wherein the linker is any one of SEQ ID NO: 91 – SEQ ID NO: 105.

32. The pharmaceutical composition for use of any one of claims 22 or 24-31, or the use of any one of claims 23-31, wherein the tumor neo-antigen comprises a tumor neo-epitope derived from WT1, HPV-E6, HPV-E7, p53, MAGE-A1, MAGE-A2, MAGE-A3, MAGE-A4, MAGE-A6, MAGE-A10, MAGE-A12, BAGE, DAM-6, DAM-10, Folate receptor alpha, GAGE-1, GAGE-2, GAGE-8, GAGE-3, GAGE-4, GAGE-5, GAGE-6, GAGE-7B, NA88-A, NY-ESO-1, MART-1, MC1R, Gp100, PSA, PSM, Tyrosinase, TRP-1, TRP-2, ART-4, CAMEL, CEA, Cyp-B, Her1, Her2/neu, Her3, Her 4, BRCA1, Brachyury, Brachyury (TIVS7-2, polymorphism), Brachyury (IVS7 T/C polymorphism), T Brachyury, T, hTERT, hTRT, iCE, MUC1, MUC1 (VNTR polymorphism), MUC1c, MUC1n, MUC2, PRAME, P15, PSCA, PSMA, RU1, RU2, SART-1, SART-3, AFP, β-catenin/m, Caspase-8/m, CDK-4/m, ELF2M, GnT-V, G250, HSP70-2M, HST-2, KIAA0205, MUM-1, MUM-2, MUM-3, Myosin/m, RAGE, SART-2, TRP-2/INT2, 707-AP, Annexin II, CDC27/m, TPl/mbcr-abl, ETV6/AML, LDLR/FUT, Pml/RARα, TEL/AML1, or any combination thereof.

33. The pharmaceutical composition for use of any one of claims 22 or 24-32, or the use of any one of claims 23-32, wherein the tumor neo-antigen is a tumor neo-epitope with an amino acid sequence of any one of SEQ ID NO: 1 – SEQ ID NO: 22, a nucleotide sequence of any one of SEQ ID NO: 23 – SEQ ID NO: 30, or has one of the following mutation: Q678P mutation of gene SLC4A11, D1143N mutation of gene SIGLEC1, A292T mutation of gene SIGLEC14, T2356M mutation of PIEZO2, S1613L mutation of gene FAT4, R268C mutation of gene FCRL1, or V73M mutation of gene VIPR2, or R346W mutation of gene FLRT2.