What is claimed is:

1. A nucleic acid comprising the nucleotide sequence of SEQ ID NOs: 1 or 2.

2. A nucleic acid comprising the nucleotide sequence of SEQ ID NOs: 3, 4, 5, 6, 7, or 8.

3. The nucleic acid of claim 1 or 2, wherein the nucleic acid is RNA.

4. A host cell comprising the nucleic acid of any one of claims 1 to 3.

5. A tri-segmented lymphocytic choriomeningitis virus (LCMV) particle comprising the nucleotide sequences of SEQ ID NOs: 3, 4, and 5.

6. A tri-segmented Pichinde virus (PICV) particle comprising the nucleotide sequences of SEQ ID NOs: 6, 7, and 8.

7. A pharmaceutical composition comprising the tri-segmented viral particle of claim 5 or 6 and a pharmaceutically acceptable carrier.

8. The tri-segmented arenavirus particle of claim 5 or 6, wherein at least one of the nucleotide sequences comprises a dinucleotide optimized HPV16 E7E6 nucleotide sequence that can:

i. have stable expression of the HPV antigen after being passaged at least 4, 5, 6, 7, 8, 9, or 10 generations;

ii. have consistent expression of the encoded HPV fusion protein; or

iii. induce strong immune responses against the encoded HPV fusion protein.

9. Use of an effective amount of an engineered replication-competent tri-segmented arenavirus particle in the manufacture of medicaments or kits for treating cancer in a patient in need thereof, wherein said tri-segmented arenavirus particle

comprises two S-segments, wherein at least one of the two S segments encodes a fusion protein of human papillomavirus strain 16 (HPV16) E7/E6, and wherein:

(1) the effective amount is about 5 x 10^5 replication-competent virus focus-forming units (RCV FFU);

(2) the effective amount is about 5 x 10^6 replication-competent virus focus-forming units (RCV FFU);

(3) the effective amount is about 5 x 10^7 replication-competent virus focus-forming units (RCV FFU);

(4) the effective amount is about 5 x 10^8 replication-competent virus focus-forming units (RCV FFU); or

(5) the effective amount is about 1 x 10^8 replication-competent virus focus-forming units (RCV FFU).

10. The use of claim 9, wherein the cancer is HPV 16^+, wherein optionally the HPV 16^+ cancer is head and neck squamous cell carcinoma, anal cancer, cervical cancer, vulvar, and/or vaginal cancer.

11. The use of claim 9, wherein (1) the patient had tumor progression or recurrence on at least one standard-of-care therapy prior to the use, wherein optionally the at least one standard-of-care therapy comprises pembrolizumab monotherapy; and/or (2) the patient has only target lesions in lymph nodes.

12. The use of any one of claims 9 to 11, wherein the medicament is to be administered by intravenous injections, wherein optionally:

(1) the intravenous injections are to be administered with a frequency of every 2 weeks, every 3 weeks, every 4 weeks, every 5 weeks, every 6 weeks, every 7 weeks, or every 8 weeks;

(2) the intravenous injections are ongoing or are to be administered for a limited number of cycles, wherein optionally:

(i) the intravenous injections are to be administered for a limited number of cycles and the limited number of cycles is two, three, four, five, or six, wherein optionally the effective amount of the engineered replication-competent tri-segmented arenavirus particle comprised in the medicament administered for a limited number of cycles is one log order

more than the effective amounts of the engineered replication-competent tri-segmented arenavirus particle comprised in the medicament administered in the ongoing intravenous injections; or

(ii) the intravenous injections are ongoing and are to be first administered with a higher frequency followed by a lower frequency, wherein optionally:

a) the intravenous injections are ongoing and are to be first administered with a frequency of every 3 weeks followed by a frequency of every 6 weeks; wherein optionally the intravenous injection are ongoing and are to be first administered with a frequency of every 3 weeks for 4 cycles followed by a frequency of every 6 weeks for subsequent cycles; or

b) the intravenous injection are ongoing and are to be first administered with a frequency of every 4 weeks followed by a frequency of every 8 weeks; wherein optionally the intravenous injection are ongoing and are to be first administered with a frequency of every 4 weeks for 4 cycles followed by a frequency of every 8 weeks for subsequent cycles; and/or

(3) the use further comprises an intratumoral injection of the medicament prior to the intravenous injections.

13. The use of any one of claims 9 to 11, wherein the medicament is to be administered by intratumoral injections.

14. The use of any one of claims 9 to 13, wherein the medicament is to be administered in combination with an effective amount of an immune checkpoint inhibitor, wherein optionally the immune checkpoint inhibitor comprises an anti-PD-1 (programmed cell death protein 1) checkpoint inhibitor, wherein optionally the anti-PD-1 checkpoint inhibitor is an antibody, and wherein optionally the antibody is nivolumab, pembrolizumab, pidilizumab or cemiplimab.

15. The use of any one of claims 9 to 14, wherein the engineered replication-competent tri-segmented arenavirus particles are derived from LCMV,

wherein optionally the LCMV is MP strain, WE strain, Armstrong strain, Armstrong Clone 13 strain, or LCMV clone 13 strain expressing the glycoprotein of LCMV strain WE instead of endogenous LCMV clone 13 glycoprotein,

wherein optionally the engineered replication-competent tri-segmented arenavirus particles comprise Construct 1,

wherein optionally the effective amount of Construct 1 is about 5 x 10^6 RCV FFU, and

wherein optionally the medicament comprising Construct 1 is to be administered with a frequency of every 3 weeks.

16. The use of any one of claims 9 to 14, wherein the engineered replication-competent tri-segmented arenavirus particles are derived from PICV,

wherein optionally the PICV is strain Munchique CoAn4763 isolate P18, or P2 strain, and

wherein optionally the engineered replication-competent tri-segmented arenavirus particles comprise Construct 2.

17. The use of any one of claims 9 to 16, wherein the treating with the medicament results in:

(1) a change in level of a cytokine or a chemokine in the serum of the patient as compared to the pre-treatment level of the patient, wherein optionally the cytokine and chemokine comprises IFN-γ, IL-12p40, IL-15, IFN-inducible protein (IP)-10, and TNFα;

(2) an increase of HPV16 E7/E6-specific T cells in the serum of the patient as compared to the pre-treatment level of the patient, wherein optionally the HPV16 E7/E6-specific T cells are positive for CD8, IFN-γ, TNFα, and/or CD107a, and wherein optionally the T cells are detected without prior *in-vitro* stimulation and/or expansion;

(3) more T cells infiltrating into tumor tissues as compared to the pre-treatment level of the patient or patients receiving placebo; and/or

(4) one or more improved efficacy endpoint using Response Evaluation Criteria in Solid Tumors (RECIST) and/or Immune Response Evaluation Criteria in Solid Tumors (iRECIST), compared to the pre-treatment level of the patient or patients receiving placebo, wherein optionally the one or more improved efficacy endpoint comprises higher percentage of objective response rate, higher percentage of disease

control rate, higher percentage of partial response, longer progression-free survival, and/or longer overall survival.

18. Use of an effective amount of a first and a second engineered replication-competent tri-segmented arenavirus particle in the manufacture of a first and a second medicament for treating cancer in a patient in need thereof,

i. wherein said first engineered replication-competent tri-segmented arenavirus particle comprises two S-segments encoding a fusion protein of human papillomavirus strain 16 (HPV16) E7/E6, wherein said first tri-segmented arenavirus particle is derived from a first arenavirus species, and wherein the effective amount of said first tri-segmented arenavirus particle is about 5×10^5, 1×10^6, 5×10^6, 1×10^7, 5×10^7, 1×10^8, 5×10^8, or 1×10^9 replication-competent virus focus-forming units (RCV FFU);

ii. wherein said second engineered replication-competent tri-segmented arenavirus particle comprises two S-segments encoding a fusion protein of HPV16 E7/E6, wherein said second tri-segmented arenavirus particle is derived from a second arenavirus species, and wherein the effective amount of said second tri-segmented arenavirus particle is about 5×10^5, 1×10^6, 5×10^6, 1×10^7, 5×10^7, 1×10^8, 5×10^8, or 1×10^9 RCV FFU; and

iii. wherein said medicaments are to be administered one or more session, wherein each session comprises (a) administering to the patient the first medicament and administering to the patient at a time point around half of the session the second medicament.

19. The use of claim 18, wherein the first arenavirus species in (i) is lymphocytic choriomeningitis virus (LCMV), and the second arenavirus species in (ii) is Pichinde virus (PICV); or wherein the first arenavirus species in (i) is PICV, and the second arenavirus species in (ii) is LCMV,

wherein optionally the LCMV is MP strain, WE strain, Armstrong strain, Armstrong Clone 13 strain, or LCMV clone 13 strain expressing the glycoprotein of LCMV strain WE instead of endogenous LCMV clone 13 glycoprotein,

wherein optionally the PICV is strain Munchique CoAn4763 isolate P18, or P2 strain,

wherein optionally the first or second engineered replication-competent tri-segmented arenavirus particles comprise Construct 1, and/or

wherein optionally the first or second engineered replication-competent tri-segmented arenavirus particles comprise Construct 2.

20. The use of claim 18, wherein the first engineered replication-competent tri-segmented arenavirus particles in (i) are Construct 2, and the second engineered replication-competent tri-segmented arenavirus particles in (ii) are Construct 1,

wherein optionally said medicaments are to be administered one or more session, wherein each session comprises:

i. administering to the patient the first medicament, wherein the first medicament comprises an effective amount of Construct 2, wherein the effective amount is about 1×10^6, 1×10^7, 1×10^8, or 1×10^9 RCV FFU; and

ii. administering to the patient at a time point around half of the session the second medicament, wherein the second medicament comprises an effective amount of Construct 1, wherein the effective amount is about 5×10^5, 5×10^6, 5×10^7, 1×10^8, or 5×10^8 RCV FFU,

wherein optionally the effective amount of Construct 2 is about 1×10^6 RCV FFU and the effective amount of Construct 1 is about 5×10^6 RCV FFU, and

wherein optionally the first and the second medicament comprising Construct 2 and Construct 1, respectively, are to be administered intravenously, and each session lasts for 6 weeks.

21. The use of any one of claims 18 to 20, wherein the cancer is HPV 16^+, wherein optionally the HPV 16^+ cancer is head and neck squamous cell carcinoma, anal cancer, cervical cancer, vulvar, and/or vaginal cancer

22. The use of any one of claims 18 to 21, wherein (1) the patient had tumor progression or recurrence on at least one standard-of-care therapy prior to the use, wherein optionally the at least one standard-of-care therapy comprises pembrolizumab monotherapy, and/or (2) the patient has only target lesions in lymph nodes.

23. The use of any one of claims 18 to 22, wherein the first and second medicament in (i) and (ii) are to be administered by intravenous injection, wherein optionally:

(1) each session lasts for 4 weeks, 6 weeks, 8 weeks, 10 weeks, 12 weeks, 14 weeks, or 16 weeks,

(2) the sessions are ongoing or are repeated for a limited number of sessions, wherein optionally:

(i) the sessions are repeated for a limited number of sessions, and the limited number of sessions is two, three, four, five, or six, wherein optionally the effective amount of the engineered replication-competent tri-segmented arenavirus particle comprised in the first medicament administered in the first session is one log order more than the effective amount of the engineered replication-competent tri-segmented arenavirus particles comprised in the first and second medicaments used in the ongoing sessions;

(ii) the sessions are ongoing and are to be first administered in shorter sessions followed by longer sessions, wherein optionally:

a) the intravenous injection are ongoing and are to be first administered with sessions each lasting 6 weeks followed by sessions each lasting 12 weeks, wherein optionally the intravenous injections are ongoing and are to be first administered with 2 sessions each lasting 6 weeks followed by sessions each lasting 12 weeks; or

b) the intravenous injections are ongoing and are to be first administered with sessions each lasting 8 weeks followed by sessions each lasting 16 weeks, wherein optionally the intravenous injections are ongoing and are to be first administered with 2 sessions each lasting 8 weeks followed by sessions each lasting 16 weeks; and/or

(3) the use further comprises an intratumoral injection of the first medicament prior to the intravenous injections of the second medicament, wherein optionally the intratumoral injection is to be administered 3 weeks prior to the intravenous injections, wherein optionally the first medicament is to be administered by intratumoral injection comprises Construct 1.

24. The use of any one of claims 18 to 22, wherein the first and/or second medicament is to be administered by intratumoral injections.

25. The use of any one of claims 18 to 24, wherein said medicaments are further to be administered with an effective amount of an immune checkpoint inhibitor, wherein optionally the immune checkpoint inhibitor comprises an anti-PD-1 (programmed cell death protein 1) checkpoint inhibitor, wherein optionally the anti-PD-1 checkpoint inhibitor is an antibody, and wherein optionally the antibody is nivolumab, pembrolizumab, pidilizumab or cemiplimab.

26. The use of any one of claims 18 to 25, wherein the treating results in:

(1) a change in level of a cytokine or a chemokine in the serum of the patient as compared to the pre-treatment level of the patient, wherein optionally the cytokine and chemokine comprises IFN-γ, IL-12p40, IL-15, IFN-inducible protein (IP)-10, and TNFα,

(2) an increase of HPV16 E7/E6-specific T cells in the serum of the patient as compared to the pre-treatment level of the patient, wherein optionally the HPV16 E7/E6-specific T cells are positive for CD8, IFN-γ, TNFα, and/or CD107, wherein optionally the T cells are detected without prior *in-vitro* stimulation and/or expansion;

(3) more T cells infiltrating into tumor tissues as compared to the pre-treatment level of the patient or patients receiving placebo, and/or

(4) one or more improved efficacy endpoint using Response Evaluation Criteria in Solid Tumors (RECIST) and/or Immune Response Evaluation Criteria in Solid Tumors (iRECIST), wherein optionally the one or more improved efficacy endpoint comprises higher percentage of objective response rate, higher percentage of disease control rate, higher percentage of partial response, longer progression-free survival, longer overall survival.

27. Use of an effective amount of Construct 1 in the manufacture of a medicament for treating cancer in a patient in need thereof, wherein the effective amount is about 5×10^5, 5×10^6, 5×10^7, 1×10^8, or 5×10^8 replication-competent virus focus-forming units (RCV FFU), and wherein the medicament is to be administered by intravenous administration with a frequency of every 3 weeks for 4 cycles followed by ongoing cycles with a frequency of every 6 weeks.

28. Use of an effective amount of Construct 1 in the manufacture of a medicament for treating cancer in a patient in need thereof, wherein the effective amount is about 5×10^5, 5×10^6, 5×10^7, 1×10^8, or 5×10^8 replication-competent virus focus-forming units (RCV FFU), and wherein the medicament is to be administered by (i) intravenous administration of the medicament with a frequency of every 3 weeks for 4 cycles followed by ongoing cycles with a frequency of every 6 weeks; and

(ii) intravenous administration to the patient of 200 mg of pembrolizumab with a frequency of every 3 weeks or 400 mg of pembrolizumab with a frequency of every 6 weeks.

29. Use of an effective amount of Construct 1 and Construct 2 in the manufacture of a first medicament comprising Construct 1 and a second medicament comprising Construct 2 for treating cancer in a patient in need thereof, wherein the effective amount of Construct 1 is about 5×10^6, 5×10^7, 1×10^8, or 5×10^8 replication-competent virus focus-forming units (RCV FFU) and the effective amount of Construct 2 is about 1×10^6, 1×10^7, or 1×10^8 RCV FFU, and wherein the medicaments are to be administered multiple sessions, wherein each session comprises:

i. intravenously administering to the patient the second medicament; and

ii. intravenously administering to the patient the first medicament at a time point around half of the session,

and wherein the first two sessions each lasts for 6 weeks, and the following ongoing sessions each lasts for 12 weeks.

30. Use of an effective amount of Construct 1 and Construct 2 in the manufacture of a first medicament comprising Construct 1 and a second medicament comprising Construct 2 for treating cancer in a patient in need thereof, wherein the effective amount of Construct 1 is about 5×10^6, 5×10^7, 1×10^8, or 5×10^8 replication-competent virus focus-forming units (RCV FFU) and the effective amount of Construct 2 is about 1×10^6, 1×10^7, or 1×10^8 RCV FFU, and wherein the administration of the medicaments comprises:

(1) multiple sessions of administering the second medicament and the first medicament, wherein each session comprises:

i. intravenously administering to the patient the second medicament; and

ii. intravenously administering to the patient the first medicament at a time point around half of the session,

and wherein the first two sessions each lasts for 6 weeks, and the following ongoing sessions each lasts for 12 weeks; and

(2) intravenously administering to the patient 200mg of pembrolizumab at a frequency of every 3 weeks or 400mg of pembrolizumab at a frequency of every 6 weeks.

31. Use of an effective amount of Construct 1 and Construct 2 in the manufacture of a first medicament comprising Construct 1 and a second medicament comprising Construct 2 for treating cancer in a patient in need thereof, wherein the effective amount of Construct 1 is about 5×10^6, 5×10^7, 1×10^8, or 5×10^8 replication-competent virus focus-forming units (RCV FFU) and the effective amount of Construct 2 is about 1×10^6, 1×10^7, or 1×10^8 RCV FFU, and wherein the administration of the medicaments comprises:

(1) administering intratumorally to the patient the first medicament; and

(2) 3 weeks later administering to the patient multiple sessions, wherein each session comprises

i. administering intravenously to the patient the second medicament; and

ii. administering intravenously to the patient the first medicament at a time point around half of the session,

and wherein the first two sessions each lasts for 6 weeks, and the following ongoing sessions each lasts for 12 weeks.

32. Use of an effective amount of Construct 1 in the manufacture of a first medicament for treating cancer in a patient in need thereof, wherein the effective amount of Construct 1 is about 5×10^6, 5×10^7, 5×10^8, 1×10^9, or 5×10^9 replication-competent virus focus-forming units (RCV FFU), and wherein the first medicament is

to be intravenously administered to the patient with a frequency of every 3 weeks for 3 cycles.

33. Use of an effective amount of Construct 1 and Construct 2 in the manufacture of a first medicament comprising Construct 1 and a second medicament comprising Construct 2 for treating cancer in a patient in need thereof, wherein the effective amount of Construct 1 is about 5×10^7, 5×10^8, 1×10^9, or 5×10^9 replication-competent virus focus-forming units (RCV FFU) and the effective amount of Construct 2 is about 1×10^7, 1×10^8, or 1×10^9 RCV FFU, and wherein said medicaments are to be administered for 3 sessions and ends after 3 sessions, wherein each session comprises

i. intravenously administering to the patient the second medicament; and

ii. intravenously administering to the patient the first medicament at a time point around half of the session,

and wherein each sessions lasts for 6 weeks.