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.

~~1~~9. Use of an effective amount of engineered replication-competent tri-segmented arenavirus particle in the manufacture of medicaments or kits~~A method~~ for treating cancer in a patient in need thereof, wherein said tri-segmented arenavirus particle comprises ~~comprising administering to the patient an effective amount of engineered replication-competent tri-segmented arenavirus particles comprising~~ two S-segments, wherein at least one of the two S

segments ~~encoding~~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. A method for treating cancer in a patient in need thereof comprising administering to the patient an effective amount of engineered replication-competent tri-segmented arenavirus particles comprising two S-segments encoding a fusion protein of human papillomavirus strain 16 (HPV16) E7/E6, wherein~~

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

~~3. A method for treating cancer in a patient in need thereof comprising administering to the patient an effective amount of engineered replication-competent tri-segmented arenavirus particles comprising two S-segments encoding a fusion protein of human papillomavirus strain 16 (HPV16) E7/E6, wherein~~

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

~~4. A method for treating cancer in a patient in need thereof comprising administering to the patient an effective amount of engineered replication-competent tri-segmented arenavirus particles comprising two S-segments encoding a fusion protein of human papillomavirus strain 16 (HPV16) E7/E6, wherein~~

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

~~5. A method for treating cancer in a patient in need thereof comprising administering to the patient an effective amount of engineered replication-competent tri-segmented arenavirus particles comprising two S-segments encoding a fusion protein of human papillomavirus strain 16 (HPV16) E7/E6, wherein~~

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

~~6~~10. The ~~method of any one of claims 1 to 5~~use of claim 9, wherein the cancer is HPV 16^+~~.~~,

~~7. The method of claim 6,~~ wherein optionally the HPV 16^+ cancer is head and neck squamous cell carcinoma~~.~~,

~~8. The method of claim 6, wherein the HPV 16^+ cancer is~~ anal cancer, cervical cancer, vulvar, and/or vaginal cancer.

~~9~~11. The ~~method of any one of claims 1 to 8~~ use of claim 9, wherein (1) the patient had tumor progression or recurrence on at least one standard-of-care therapy prior to the ~~method~~use~~.~~,

~~10. The method of claim 9,~~ wherein optionally the at least one standard-of-care therapy comprises pembrolizumab monotherapy~~.~~; and/or

~~11. The method of any one of claims 1 to 10, wherein~~ (2) the patient has only target lesions in lymph nodes.

12. The ~~method of any one of claims 1 to 11~~use of any one of claims 9 to 11, wherein the medicament is to be administered by ~~administration of the engineered replication-competent tri-segmented arenavirus particle comprises~~ intravenous injections, wherein optionally~~.~~;

~~13. The method of claim 12,~~ (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~~.~~;

~~14. The method of claim 12 or 13, wherein~~ (2) the intravenous injections are ongoing or are to be administered for a limited number of cycles~~.~~, wherein optionally:

~~15. The method of claim 14, wherein~~ (i) the intravenous injections are to be administered for ~~the~~a limited number of cycles and the limited number of cycles is two, three, four, five, or six~~.~~, wherein optionally

~~16. The method of claim 15, wherein~~ 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 ~~used~~ in the ongoing intravenous injections~~.~~; or

~~17. The method of claim 14, wherein~~ (ii) the intravenous injections are ongoing and are to be first administered with a higher frequency followed by a lower frequency~~.~~, wherein optionally:

~~18. The method of claim 17, wherein~~ 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~~.~~;

~~19. The method of claim 18,~~ 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

~~20. The method of claim 17, wherein~~ 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

~~21. The method of claim 20, wherein~~ 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

~~22. The method of any one of claims 12 to 21, wherein the~~ (3) the use ~~method~~ further comprises an intratumoral injection prior to the intravenous injections.

~~23~~13. The ~~method of any one of claims 1 to 11~~ use of any one of claims 9 to 11, wherein the ~~administration of the engineered replication-competent tri-segmented arenavirus particle~~ medicament is to be administered ~~comprises~~by intratumoral injections.

~~24~~14. The ~~method of any one of claims 1 to 23~~ use of any one of claims 9 to 13, wherein ~~the method further comprises~~ the medicament is to be administered ~~administering~~in combination with an effective amount of an immune checkpoint inhibitor~~.~~,

~~25. The method of claim 24,~~ wherein optionally the immune checkpoint inhibitor comprises an anti-PD-1 (programmed cell death protein 1) checkpoint inhibitor~~.~~, wherein optionally

~~26. The method of claim 25, wherein~~ the anti-PD-1 checkpoint inhibitor is an antibody~~.~~, and

~~27. The method of claim 26,~~ wherein optionally the antibody is nivolumab, pembrolizumab, pidilizumab or cemiplimab.

~~28~~15. The ~~method~~use of any one of claims ~~1 to 27~~ 9 to 14, wherein the engineered replication-competent tri-segmented arenavirus particles are derived from ~~lymphocytic choriomeningitis virus (~~LCMV~~).~~,

~~29. The method of claim 28,~~ 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~~.~~,

~~30. The method of claim 29,~~ wherein optionally the engineered replication-competent tri-segmented arenavirus particles comprise Construct 1~~.~~,

~~31. The method of claim 30,~~ 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.

~~32~~16. The ~~method~~ use of any one of claims ~~1 to 27~~ 9 to 14, wherein the engineered replication-competent tri-segmented arenavirus particles are derived from ~~Pichinde virus (~~PICV~~).~~,

~~33. The method of claim 32,~~ wherein optionally the PICV is strain Munchique CoAn4763 isolate P18, or P2 strain~~.~~, and

~~34. The method of claim 33,~~ wherein optionally the engineered replication-competent tri-segmented arenavirus particles comprise Construct 2.

~~35~~17. The ~~method~~use of any one of claims ~~1 to 34~~9 to 16, wherein the treating with the medicament results in:

~~the method 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~~.~~,

~~36. The method of claim 35,~~ wherein optionally the cytokine and chemokine comprises IFN-γ, IL-12p40, IL-15, IFN-inducible protein (IP)-10, and TNFα~~.~~;

~~37. The method of any one of claims 1 to 36, wherein the method results in~~

(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~~.~~,

~~38. The method of claim 37,~~ wherein optionally the HPV16 E7/E6-specific T cells are positive for CD8, IFN-γ, TNFα, and/or CD107a~~.~~, and wherein

~~39. The method of claim 37 or 38, wherein~~ optionally the T cells are detected without prior *in-vitro* stimulation and/or expansion~~.~~;

~~40. The method of any one of claims 1 to 39, wherein the method results in~~ (3) more T cells infiltrating into tumor tissues as compared to the pre-treatment level of the patient or patients receiving placebo~~.~~; and/or

~~41. The method of any one of claims 1 to 40, wherein the method results in~~ (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~~.~~,

~~42. The method of claim 41,~~ 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.

~~43~~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, ~~A method for treating cancer in a patient in need thereof comprising one or more session, wherein each session comprises~~

i. wherein said ~~administering to the patient an effective amount of~~ first engineered replication-competent tri-segmented arenavirus particles ~~comprising~~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, wherein the effective amount of said first tri-segmented arenavirus particle is about 5 x 10^5, 1 x 10^6, 5 x 10^6, 1 x 10^7, 5 x 10^7, 1 x 10^8, 5 x 10^8, or 1 x 10^9 replication-competent virus focus-forming units (RCV FFU); and

ii. wherein said second engineered replication-competent tri-segmented arenavirus particle comprises ~~administering to the patient an effective amount of engineered replication-competent tri-segmented arenavirus particles comprising~~ 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 ~~at a time point around half of the session,~~ wherein the effective amount of said second tri-segmented arenavirus particle is about 5 x 10^5, 1 x 10^6, 5 x 10^6, 1 x 10^7, 5 x 10^7, 1 x 10^8, 5 x 10^8, or 1 x 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.

~~44~~19. The ~~method~~use of claim ~~43~~ 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

~~45. The method of claim 43,~~ wherein the first arenavirus species in (i) is PICV, and the second arenavirus species in (ii) is LCMV~~.~~,

~~46. The method of claim 44 or 45~~, 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,

~~47. The method of claim 46,~~ wherein optionally the first or second~~the~~ engineered replication-competent tri-segmented arenavirus particles comprise Construct 1~~.~~, and/or

~~48. The method of claim 44 or 45, wherein the PICV is strain Munchique CoAn4763 isolate P18, or P2 strain.~~

~~49. The method of claim 48,~~ wherein optionally the first or second~~the~~ engineered replication-competent tri-segmented arenavirus particles comprise Construct 2.

~~50~~20. The ~~method~~use of claim ~~45~~ 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~~.~~,

~~51. The method of claim 50 comprising~~ 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 x 10^6, 1 x 10^7, 1 x 10^8, or 1 x 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 ~~at a time point around half of the session~~, wherein the effective amount is about 5 x 10^5, 5 x 10^6, 5 x 10^7, 1 x 10^8, or 5 x 10^8 RCV FFU~~.~~,

~~52. The method of claim 51, wherein~~ wherein optionally the effective amount of Construct 2 is about 1 x 10^6 RCV FFU and the effective amount of Construct 1 is about 5 x 10^6 RCV FFU, and wherein optionally the first and the second medicament comprising Construct 2 and Construct 1, ~~-~~are to be administered intravenously, and each session lasts for 6 weeks.

~~53~~21. The ~~method~~use of any one of claims ~~43~~18 to ~~52~~20, wherein the cancer is HPV 16^+~~.~~,

~~54. The method of claim 53,~~ wherein optionally the HPV 16^+ cancer is head and neck squamous cell carcinoma~~.~~,

~~55. The method of claim 53, wherein the HPV 16^+ cancer is~~ anal cancer, cervical cancer, vulvar, and/or vaginal cancer.

~~56~~22. The ~~method~~use of any one of claims ~~43 to 55~~18 to 21, wherein the patient had tumor progression or recurrence on at least one standard-of-care therapy prior to the ~~method~~ use.,

~~57. The method of claim 56,~~ wherein optionally the at least one standard-of-care therapy comprises pembrolizumab monotherapy~~.~~, and/or

~~58. The method of any one of claims 43 to 57, wherein~~ (2) the patient has only target lesions in lymph nodes.

~~59~~23. The ~~method~~use of any one of claims ~~43 to 58~~18 to 22, wherein the first and second medicament in (i) and (ii) are to be administered by ~~administration of the engineered replication competent tri-segmented arenavirus particles in (i) and (ii) comprises~~ intravenous injection~~.~~, wherein optionally:

~~60. The method of claim 59, wherein~~

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

~~61. The method of claim 59 or 60, wherein~~

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

~~62. The method of claim 61, wherein~~ (i) the sessions are repeated for a limited number of sessions and the limited number of sessions is two, three, four, five, or six~~.~~,

~~63. The method of claim 62,~~ wherein optionally the effective amount of the engineered replication-competent tri-segmented arenavirus particles 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~~.~~;

~~64. The method of claim 61, wherein the intravenous injections~~ (ii) the sessions are ongoing and are to be first administered in shorter sessions followed by longer sessions~~.~~, wherein optionally:

~~65. The method of claim 64, wherein~~ 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~~.~~

~~66. The method of claim 65,~~ , 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

~~67. The method of claim 64, wherein~~ (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~~.~~,

~~68. The method of claim 67,~~ wherein optionally the intravenous injection are ongoing and are to be first administered with 2 sessions each lasting 8 weeks followed by sessions each lasting 16 weeks~~.~~; and/or

~~69. The method of any one of claims 59 to 68, wherein the method~~ (3) the use further comprises an intratumoral injection of the first medicament prior to the intravenous injections of the second medicament~~.~~,

~~70. The method of claim 69, wherein~~ wherein optionally the intratumoral injection is to be administered 3 weeks prior to the intravenous injections~~.~~,

~~71. The method of claim 69 or 70,~~ wherein optionally the first medicament is to be administered by ~~the~~ intratumoral injection ~~is administered with~~ comprises Construct 1.

~~72~~24. The ~~method~~use of any one of claims ~~43 to 58~~18 to 22, wherein ~~the administration of the engineered replication-competent tri-segmented arenavirus particle comprises~~ the first and/or the second medicament is to be administered by intratumoral injections.

~~73~~25. The ~~method~~use of any one of claims ~~43 to 72~~18 to 24, wherein said medicament are further to be administered ~~the method further comprises administering~~ with an effective amount of an immune checkpoint inhibitor~~.~~,

~~74. The method of claim 73,~~ wherein optionally the immune checkpoint inhibitor comprises an anti-PD-1 (programmed cell death protein 1) checkpoint inhibitor~~.~~,

~~75. The method of claim 74,~~ wherein optionally the anti-PD-1 checkpoint inhibitor is an antibody~~.~~, and

~~76. The method of claim 75,~~ wherein optionally the antibody is nivolumab, pembrolizumab, pidilizumab or cemiplimab.

~~77~~26. The ~~method~~use of any one of claims ~~43~~18 to ~~76~~25, wherein the ~~method~~ 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.

78. The method of claim 77, wherein optionally the cytokine and chemokine comprises IFN-γ, IL-12p40, IL-15, IFN-inducible protein (IP)-10, and TNFα.,

79. The method of any one of claims 43 to 78, wherein the method results in (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.,

80. The method of claim 79, wherein optionally the HPV16 E7/E6-specific T cells are positive for CD8, IFN-γ, TNFα, and/or CD107a.,

81. The method of claim 79 or 80, wherein optionally the T cells are detected without prior *in-vitro* stimulation and/or expansion.;

82. The method of any one of claims 43 to 81, wherein the method results in (3) more T cells infiltrating into tumor tissues as compared to the pre-treatment level of the patient or patients receiving placebo., and/or

83. The method of any one of claims 43 to 82, wherein the method results in (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).,

84. The method of claim 83, 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.

~~85~~27. Use of an effective amount of Construct 1 in the manufacture of a medicament ~~A method~~ for treating cancer in a patient in need thereof, ~~comprising administering to the patient an effective amount of Construct 1,~~ wherein the effective amount is about 5 x 10^5, 5 x 10^6, 5 x 10^7, 1 x 10^8, or 5 x 10^8 replication-competent virus focus-forming units (RCV FFU), and wherein the medicament is to be ~~Construct 1 is~~ administered by intravenous administration ~~intravenously~~ with a frequency of every 3 weeks for 4 cycles followed by ongoing cycles with a frequency of every 6 weeks.

~~86~~28. Use of an effective amount of Construct 1 in the manufacture of a medicament ~~A method~~ for treating cancer in a patient in need thereof, ~~comprising~~

~~(i) administering to the patient an effective amount of Construct 1,~~ wherein the effective amount is about 5 x 10^5, 5 x 10^6, 5 x 10^7, 1 x 10^8, or 5 x 10^8 replication-competent virus focus-forming units (RCV FFU), and wherein the medicament is to be administered by (i) intravenous administration ~~Construct 1 is administered intravenously~~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 200 mg of ~~administering to the patient 200 mg of~~ pembrolizumab ~~intravenously~~ with a frequency of every 3 weeks or 400 mg of pembrolizumab ~~intravenously~~ with a frequency of every 6 weeks

~~87~~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 ~~A method for treating cancer in a patient in need thereof comprising multiple sessions, wherein each session comprises~~

~~i. administering to the patient an effective amount of Construct 2 intravenously, wherein~~ the effective amount of Construct 1 is 5 x 10^6, 5 x 10^7, 1 x 10^8, or 5 x 10^8 replication-competent virus focus-forming units (RCV FFU) and the effective amount of Construct 2 is about 1 x 10^6, 1 x 10^7, or 1 x 10^8 RCV FFU, a~~about 1 x 10^6 replication-competent virus focus-forming units (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.

~~ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 5 x 10^6 RCV FFU,~~

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

~~88. A method for treating cancer in a patient in need thereof comprising multiple sessions, wherein each session comprises~~

~~i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^7 replication-competent virus focus-forming units (RCV FFU); and~~

~~ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 5 x 10^6 RCV FFU,~~

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

~~89. A method for treating cancer in a patient in need thereof comprising multiple sessions, wherein each session comprises~~

~~i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^7 replication-competent virus focus-forming units (RCV FFU); and~~

~~ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 5 x 10^7 RCV FFU,~~

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

90. A method for treating cancer in a patient in need thereof comprising multiple sessions, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^8 replication-competent virus focus-forming units (RCV FFU); and

ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 5 x 10^7 RCV FFU,

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

91. A method for treating cancer in a patient in need thereof comprising multiple sessions, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^8 replication-competent virus focus-forming units (RCV FFU); and

ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 1 x 10^8 RCV FFU,

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

92. A method for treating cancer in a patient in need thereof comprising multiple sessions, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^8 replication-competent virus focus-forming units (RCV FFU); and

ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 5 x 10^8 RCV FFU,

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

93. A method for treating cancer in a patient in need thereof comprising

(1) multiple sessions of administering Construct 2 and Construct 1, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^6 replication-competent virus focus-forming units (RCV FFU); and

ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 5 x 10^6 RCV FFU,

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

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

94. A method for treating cancer in a patient in need thereof comprising

(1) multiple sessions of administering Construct 2 and Construct 1, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^7 replication-competent virus focus-forming units (RCV FFU); and

ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 5 x 10^6 RCV FFU,

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

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

95. A method for treating cancer in a patient in need thereof comprising

(1) multiple sessions of administering Construct 2 and Construct 1, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1×10^7 replication-competent virus focus-forming units (RCV FFU); and

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

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

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

96. A method for treating cancer in a patient in need thereof comprising

(1) multiple sessions of administering Construct 2 and Construct 1, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1×10^8 replication-competent virus focus-forming units (RCV FFU); and

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

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

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

97. A method for treating cancer in a patient in need thereof comprising

(1) multiple sessions of administering Construct 2 and Construct 1, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^8 replication-competent virus focus-forming units (RCV FFU); and

ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 1 x 10^8 RCV FFU,

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

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

98. A method for treating cancer in a patient in need thereof comprising

(1) multiple sessions of administering Construct 2 and Construct 1, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^8 replication-competent virus focus-forming units (RCV FFU); and

ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 5 x 10^8 RCV FFU,

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

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

99. A method for treating cancer in a patient in need thereof comprising

(1) administering intratumorally to the patient an effective amount of Construct 1, wherein the effective amount of Construct 1 is about 5 x 10^6 replication-competent virus focus-forming units (RCV FFU); and

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

i. administering intravenously to the patient an effective amount of Construct 2, wherein the effective amount is about 1 x 10^6 RCV FFU; and

ii. administering intravenously to the patient an effective amount of Construct 1 at a time point around half of the session, wherein the effective amount is about 5 x 10^6 RCV FFU,

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

100. A method for treating cancer in a patient in need thereof comprising

(1) administering intratumorally to the patient an effective amount of Construct 1, wherein the effective amount of Construct 1 is about 5 x 10^6 replication-competent virus focus-forming units (RCV FFU); and

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

i. administering intravenously to the patient an effective amount of Construct 2, wherein the effective amount is about 1 x 10^7 RCV FFU; and

ii. administering intravenously to the patient an effective amount of Construct 1 at a time point around half of the session, wherein the effective amount is about 5 x 10^6 RCV FFU,

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

101. A method for treating cancer in a patient in need thereof comprising

(1) administering intratumorally to the patient an effective amount of Construct 1, wherein the effective amount of Construct 1 is about 5 x 10^7 replication-competent virus focus-forming units (RCV FFU); and

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

i. administering intravenously to the patient an effective amount of Construct 2, wherein the effective amount is about 1 x 10^7 RCV FFU; and

ii. administering intravenously to the patient an effective amount of Construct 1 at a time point around half of the session, wherein the effective amount is about 5 x 10^7 RCV FFU,

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

102. A method for treating cancer in a patient in need thereof comprising

(1) administering intratumorally to the patient an effective amount of Construct 1, wherein the effective amount of Construct 1 is about 5 x 10^7 replication-competent virus focus-forming units (RCV FFU); and

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

i. administering intravenously to the patient an effective amount of Construct 2, wherein the effective amount is about 1 x 10^8 RCV FFU; and

ii. administering intravenously to the patient an effective amount of Construct 1 at a time point around half of the session, wherein the effective amount is about 5 x 10^7 RCV FFU,

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

103. A method for treating cancer in a patient in need thereof comprising

(1) administering intratumorally to the patient an effective amount of Construct 1, wherein the effective amount of Construct 1 is about 1 x 10^8 replication-competent virus focus-forming units (RCV FFU); and

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

i. administering intravenously to the patient an effective amount of Construct 2, wherein the effective amount is about 1 x 10^8 RCV FFU; and

ii. administering intravenously to the patient an effective amount of Construct 1 at a time point around half of the session, wherein the effective amount is about 1 x 10^8 RCV FFU,

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

104. A method for treating cancer in a patient in need thereof comprising

(1) administering intratumorally to the patient an effective amount of Construct 1, wherein the effective amount of Construct 1 is about 5 x 10^8 replication-competent virus focus-forming units (RCV FFU); and

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

i. administering intravenously to the patient an effective amount of Construct 2, wherein the effective amount is about 1 x 10^8 RCV FFU; and

ii. administering intravenously to the patient an effective amount of Construct 1 at a time point around half of the session, wherein the effective amount is about 5 x 10^8 RCV FFU,

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

105. A method for treating cancer in a patient in need thereof comprising administering to the patient an effective amount of Construct 1, wherein the effective amount is about 5 x 10^6, 5 x 10^7, 5 x 10^8, 1 x 10^9, or 5 x 10^9 replication-competent virus-focus-forming units (RCV FFU), and wherein Construct 1 is administered intravenously with a frequency of every 3 weeks for 3 cycles and the method ends after 3 cycles.

106. A method for treating cancer in a patient in need thereof comprising 3 sessions, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^7 replication-competent virus-focus-forming units (RCV FFU); and

ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 5 x 10^7 RCV FFU,

and wherein each sessions lasts for 6 weeks, and the method ends after 3 sessions.

107. A method for treating cancer in a patient in need thereof comprising 3 sessions, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^8 replication-competent virus-focus-forming units (RCV FFU); and

ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 5 x 10^7 RCV FFU,

and wherein each sessions lasts for 6 weeks, and the method ends after 3 sessions.

108. A method for treating cancer in a patient in need thereof comprising 3 sessions, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^8 replication-competent virus focus-forming units (RCV FFU); and

ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 5 x 10^8 RCV FFU,

and wherein each sessions lasts for 6 weeks, and the method ends after 3 sessions.

109. A method for treating cancer in a patient in need thereof comprising 3 sessions, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^9 replication-competent virus focus-forming units (RCV FFU); and

ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 5 x 10^8 RCV FFU,

and wherein each sessions lasts for 6 weeks, and the method ends after 3 sessions.

110. A method for treating cancer in a patient in need thereof comprising 3 sessions, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^9 replication-competent virus focus-forming units (RCV FFU); and

ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 1 x 10^9 RCV FFU,

and wherein each sessions lasts for 6 weeks, and the method ends after 3 sessions.

111. A method for treating cancer in a patient in need thereof comprising 3 sessions, wherein each session comprises

i. administering to the patient an effective amount of Construct 2 intravenously, wherein the effective amount is about 1 x 10^9 replication-competent virus focus-forming units (RCV FFU); and

ii. administering to the patient an effective amount of Construct 1 intravenously at a time point around half of the session, wherein the effective amount is about 5 x 10^9 RCV FFU,

and wherein each sessions lasts for 6 weeks, and the method ends after 3 sessions.

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

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

114. The nucleotide sequence of claim 112 or 113, wherein the nucleotide sequence is RNA.

115. A host cell comprising the nucleotide sequence of any one of claims 112 to 114.

116. A tri-segmented LCMV particle comprising the nucleotide sequences of SEQ ID NOs: 3, 4, and 5.

~~117. A tri-segmented PICV particle comprising the nucleotide sequences of SEQ ID NOs: 6, 7, and 8.~~

~~118. A pharmaceutical composition comprising the tri-segmented viral particle of claim 116 or 117 and a pharmaceutically acceptable carrier.~~

~~119. The tri-segmented arenavirus particle of claim 116 or 117, wherein the dinucleotide optimized HPV16 E7E6 nucleotide sequence 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~~

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

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 x 10^6, 5 x 10^7, 1 x 10^8, or 5 x 10^8 replication-competent virus focus-forming units (RCV FFU) and the effective amount of Construct 2 is about 1 x 10^6, 1 x 10^7, or 1 x 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 x 10^6, 5 x 10^7, 5 x 10^8, 1 x 10^9, or 5 x 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 x 10^7, 5 x 10^8, 1 x 10^9, or 5 x 10^9 replication-competent virus focus-forming units (RCV FFU) and the effective amount of Construct 2 is about 1 x 10^7, 1 x 10^8, or 1 x 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 a the first medicament at a time point around half of the session,

and wherein each sessions lasts for 6 weeks.