Claims

1. A vaccine comprising a first component (K) and a second component (V), wherein the first component (K) comprises a complex, said complex consisting of or comprising:
   (i) a cell penetrating peptide;
   (ii) an antigenic domain, comprising at least one antigen or antigenic epitope; and
   (iii) at least one TLR peptide agonist,

   wherein the components i) – iii) are covalently linked, and
   wherein the second component (V) comprises an oncolytic rhabdovirus.

2. The vaccine according to claim 1, wherein the complex of the first component (K) is a peptide, polypeptide, or protein.

3. The vaccine according to claim 1 or claim 2, wherein the complex of the first component (K) is a recombinant peptide, polypeptide or protein.

4. The vaccine according to any one of claims 1 to 3, wherein the cell penetrating peptide of the first component (K) comprises an amino acid sequence according to any one of SEQ ID NO: 2 (Z13), SEQ ID NO: 3 (Z14), SEQ ID NO: 4 (Z15), or SEQ ID NO: 5 (Z18).

~~5. The vaccine according to any one of claims 1 to 4, wherein the complex of the first component (K) comprises more than one TLR peptide agonist, in particular 2, 3, 4, 5, 6, 7, 8, 9, 10 or more TLR peptide agonists.~~

~~6. The vaccine according to any one of claims 1 to 5, wherein the at least one TLR peptide agonist is a TLR2, TLR4 and/or TLR5 peptide agonist.~~

~~7.~~5. The vaccine according to any one of claims 1 to ~~6~~4, wherein the at least one TLR peptide agonist is a TLR2 peptide agonist and/or a TLR4 peptide agonist.

8.6. The vaccine according to any one of claims 1 to 75, wherein the TLR peptide agonist comprises or consists of an amino acid sequence according to SEQ ID NO: 6 and/or SEQ ID NO: 7, or a functional sequence variant of SEQ ID NO: 6 and/or SEQ ID NO: 7.

9. The vaccine according to any one of claims 1 to 8, wherein the TLR2 peptide agonist is annexin II or an immunomodulatory fragment thereof.

10. The vaccine according to any one of claims 1 to 9, wherein the TLR2 agonist comprises or consists of an amino acid sequence according to the annexin II coding sequence SEQ ID NO: 4 or SEQ ID NO: 7 of WO 2012/048190 A1 or fragments or variants thereof.

11. The vaccine according to any one of claims 1 to 10, wherein the TLR4 agonist comprises or consists of an amino acid sequence according to SEQ ID NO: 8 (TLR4 peptide agonist EDA).

12. The vaccine according to any one of claims 1 to 10, wherein the TLR2 agonist comprises of an amino acid sequence according to SEQ ID NO: 9 (High mobility group box 1 protein), or at least one immunomodulatory fragment thereof.

13. The vaccine according to any one of claims 1 to 12, wherein the at least one antigen or antigenic epitope of the antigenic domain of said first component (K) is selected from the group consisting of a peptide, a polypeptide, or a protein.

14.7. The vaccine according to any one of claims 1 to 136, wherein the antigenic domain of said first component (K) comprises more than one antigen or antigenic epitope, in particular 2, 3, 4, 5, 6, 7, 8, 9, 10 or more antigens or antigenic epitopes.

15.8. The vaccine according to any one of claims 1 to 147, wherein the more than one antigen or antigenic epitope, in particular 2, 3, 4, 5, 6, 7, 8, 9, 10 or more antigens or antigenic epitopes are positioned consecutively in the antigenic domain of the first component.

16. The vaccine according to any one of claims 1 to 15, wherein the at least one antigen or antigenic epitope is at least one CD4+ epitope and/or at least one CD8+ epitope.

~~17.~~9. The vaccine according to any one of claims 1 to ~~16~~8, wherein the at least one antigen or antigenic epitope comprises or consists of at least one tumor or cancer epitope.

~~18. The vaccine according to claim 17, wherein the at least one tumor epitope of said first component (K) is selected from a tumor associated antigen, tumor-specific antigen, or tumor neoantigen.~~

~~19. The vaccine according to claim 17 or 18, wherein at least one tumor epitope of the antigenic domain of said first component (K) is selected from the group of tumors comprising endocrine tumors, gastrointestinal tumors, genitourinary and gynecologic tumors, breast cancer, head and neck tumors, hematopoietic tumors, skin tumors, thoracic and respiratory tumors.~~

~~20.~~10. ~~-~~The vaccine according to ~~any one of claims 17 to 19~~claim 9, wherein at least one tumor or cancer epitope of the antigenic domain of said first component (K) is selected from the group of tumors or cancers of: gastrointestinal tumors comprising anal cancer, appendix cancer, cholangiocarcinoma, carcinoid tumor, gastrointestinal colon cancer, extrahepatic bile duct cancer, gallbladder cancer, gastric (stomach) cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor (GIST), hepatocellular cancer, pancreatic cancer, rectal cancer, colorectal cancer, or metastatic colorectal cancer.

~~21.~~11. The vaccine according to any one of claims ~~17 to 20~~9 to 10, wherein at least one tumor or cancer epitope of the antigenic domain of said first component (K) is selected from the group of tumor associated antigens, tumor-specific antigens, or tumor neoantigens of colorectal cancer, or metastatic colorectal cancer.

~~22. The vaccine according to any one of claims 17 to 21, wherein at least one tumor or cancer epitope of the antigenic domain of said first component (K) is an epitope of an antigen selected from the group consisting of EpCAM, HER-2, MUC-1, TOMM34, RNF 43, KOC1, VEGFR, βhCG, survivin, CEA, TGFβR2, p53, KRas, OGT, CASP5, COA-1, MAGE, SART, IL13Ralpha2, ASCL2, NY-ESO-1, MAGE-A3, PRAME, WT1.~~

~~23. The vaccine according to any of claims 17 to 22, wherein at least one tumor or cancer epitope of the antigenic domain of said first component (K) is an epitope of an antigen selected from the group consisting of ASCL2, EpCAM, MUC-1, survivin, CEA, KRas,~~

~~MAGE-A3 and IL13Ralpha2, preferably the at least one tumor epitope is an epitope of an antigen selected from the group consisting of ASCL2, EpCAM, MUC-1, survivin, CEA, KRas and MAGE-A3, more preferably the at least one tumor epitope is an epitope of an antigen selected from the group consisting of ASCL2, EpCAM, MUC-1, survivin and CEA and even more preferably the at least one tumor epitope is an epitope of an antigen selected from the group consisting of ASCL2, EpCAM, survivin and CEA.~~

~~24. The vaccine according to any of claims 1 to 23, wherein the antigenic domain of said first component (K) comprises at least one epitope of survivin.~~

~~25.~~12. The vaccine according to any of claims 1 to 11~~24~~, wherein the antigenic domain of said first component (K) comprises a peptide consisting of the amino acid sequence according to SEQ ID NO: 12, or a fragment thereof having a length of at least 10 amino acids, or a functional sequence variant thereof having at least 70%, 75%, 80%, 85%, 90% or 95% sequence identity.

~~26.~~13. The vaccine according to any of claims 1 to ~~25~~12, wherein the antigenic domain of said first component (K) comprises a peptide having an amino acid sequence according to SEQ ID NO: 23 or a functional sequence variant thereof having at least 70%, 75%, 80%, 85%, 90% or 95% sequence identity.

~~27.~~14. The vaccine according to any of claims 1 to ~~26~~13, wherein the antigenic domain of said first component (K) comprises a peptide consisting of the amino acid sequence according to SEQ ID NO: 22.

~~28. The vaccine according to any of claims 1 to 27, wherein the antigenic domain of said first component (K) comprises at least one epitope of CEA.~~

~~29.~~15. The vaccine according to any of claims 1 to ~~28~~14, wherein the antigenic domain of said first component (K) comprises a peptide having an amino acid sequence according to SEQ ID NO: 24, or a fragment thereof having a length of at least 10 amino acids, or a functional sequence variant thereof having at least 70% sequence identity.

~~30.~~16. The vaccine according to any of claims 1 to ~~29~~15, wherein the antigenic domain comprises a peptide having an amino acid sequence according to SEQ ID NO:

25 or a functional sequence variant thereof having at least 70%, 75%, 80%, 85%, 90% or 95% sequence identity.

~~31.~~17. The vaccine according to any of claims 1 to ~~30~~16, wherein the antigenic domain of said first component (K) comprises a peptide having an amino acid sequence according to SEQ ID NO: 26 and/or a peptide having an amino acid sequence according to SEQ ID NO: 27.

~~32. The vaccine according to any of claims 1 to 31, wherein the antigenic domain of said first component (K) comprises at least one epitope of ASCL2.~~

~~33.~~18. The vaccine according to any of claims 1 to ~~32~~17, wherein the antigenic domain of said first component (K) comprises a peptide having an amino acid sequence according to SEQ ID NO: 15, or a fragment thereof having a length of at least 10 amino acids, or a functional sequence variant thereof having at least 70%, 75%, 80%, 85%, 90% or 95% sequence identity.

~~34.~~19. The vaccine according to any of claims 1 to ~~33~~18, wherein the antigenic domain of said first component (K) comprises a peptide consisting of an amino acid sequence according to SEQ ID NO: 18 or a functional sequence variant thereof having at least 70%, 75%, 80%, 85%, 90% or 95% sequence identity.

~~35.~~20. The vaccine according to any of claims 1 to ~~34~~19, wherein the antigenic domain comprises a peptide consisting of an amino acid sequence according to SEQ ID NO: 16 and/or a peptide having an amino acid sequence according to SEQ ID NO: 17.

~~36. The vaccine according to any of claims 1 to 35, wherein the antigenic domain comprises~~

~~a) one or more epitopes of EpCAM or functional sequence variants thereof;~~
~~b) one or more epitopes of MUC-1 or functional sequence variants thereof;~~
~~c) one or more epitopes of survivin or functional sequence variants thereof;~~
~~d) one or more epitopes of CEA or functional sequence variants thereof;~~
~~e) one or more epitopes of KRas or functional sequence variants thereof;~~
~~f) one or more epitopes of MAGE-A3 or functional sequence variants thereof, and/or~~
~~g) one or more epitopes of ASCL2 or functional sequence variants thereof.~~

~~37. The vaccine according to any of claims 1 to 36, wherein the antigenic domain of said first component (K) comprises~~

~~a) one or more epitopes of EpCAM or functional sequence variants thereof;~~

~~b) one or more epitopes of MUC-1 or functional sequence variants thereof;~~

~~d) one or more epitopes of CEA or functional sequence variants thereof; and/or~~

~~f) one or more epitopes of MAGE-A3 or functional sequence variants thereof.~~

~~38. The vaccine according to any of claims 1 to 36, wherein the antigenic domain comprises~~

~~a) one or more epitopes of EpCAM or functional sequence variants thereof;~~

~~b) one or more epitopes of MUC-1 or functional sequence variants thereof;~~

~~d) one or more epitopes of CEA or functional sequence variants thereof; and/or~~

~~e) one or more epitopes of KRas or functional sequence variants thereof.~~

~~39. The vaccine according to any of claims 1 to 36, wherein the antigenic domain comprises~~

~~a) one or more epitopes of EpCAM or functional sequence variants thereof;~~

~~c) one or more epitopes of survivin or functional sequence variants thereof;~~

~~d) one or more epitopes of CEA or functional sequence variants thereof; and/or~~

~~f) one or more epitopes of MAGE-A3 or functional sequence variants thereof.~~

~~40. The vaccine according to any of claims 1 to 36 wherein the antigenic domain of said first component (K) comprises~~

~~a) one or more epitopes of EpCAM or functional sequence variants thereof;~~

~~d) one or more epitopes of CEA or functional sequence variants thereof; and/or~~

~~f) one or more epitopes of MAGE-A3 or functional sequence variants thereof.~~

~~41. The vaccine according to any of claims 1 to 36, wherein the antigenic domain comprises~~

~~b) one or more epitopes of MUC-1 or functional sequence variants thereof;~~

~~c) one or more epitopes of survivin or functional sequence variants thereof; and/or~~

~~f) one or more epitopes of MAGE-A3 or functional sequence variants thereof.~~

~~42. The vaccine according to any of claims 1 to 36, wherein the antigenic domain of said first component (K) comprises~~

~~a) one or more epitopes of EpCAM or functional sequence variants thereof;~~

~~b) one or more epitopes of MUC-1 or functional sequence variants thereof;~~

~~c) one or more epitopes of survivin or functional sequence variants thereof; and/or~~

~~d) one or more epitopes of CEA or functional sequence variants thereof.~~

~~43. The vaccine according to claim 42, wherein the antigenic domain comprises~~

~~a) one or more epitopes of EpCAM or functional sequence variants thereof;~~

~~b) one or more epitopes of MUC-1 or functional sequence variants thereof; and/or~~

~~d) one or more epitopes of CEA or functional sequence variants thereof.~~

~~44. The vaccine according to claim 43, wherein the antigenic domain comprises~~

~~a) one or more epitopes of EpCAM or functional sequence variants thereof; and/or~~

~~d) one or more epitopes of CEA or functional sequence variants thereof.~~

~~45.~~21. The vaccine according to any of claims 1 to 37, wherein the antigenic domain comprises

a) one or more epitopes of EpCAM or functional sequence variants thereof;

c) one or more epitopes of survivin or functional sequence variants thereof;

d) one or more epitopes of CEA or functional sequence variants thereof; and/or

g) one or more epitopes of ASCL2 or functional sequence variants thereof.

~~46. The vaccine according to claim 45, wherein the antigenic domain of said first component (K) comprises~~

~~- one or more epitopes of survivin or functional sequence variants thereof; and~~

~~- one or more epitopes of CEA or functional sequence variants thereof.~~

~~47. The vaccine according to claim 45, wherein the antigenic domain of said first component (K) comprises~~

~~- one or more epitopes of survivin or functional sequence variants thereof; and~~

~~- one or more epitopes of ASCL2 or functional sequence variants thereof.~~

~~48. The vaccine according to claim 45, wherein the antigenic domain of said first component (K) comprises~~

- ~~one or more epitopes of CEA or functional sequence variants thereof; and~~
- ~~one or more epitopes of ASCL2 or functional sequence variants thereof.~~

~~49.~~22. The vaccine according to ~~any one of claims 45-48~~claim 21, wherein the antigenic domain of said first component (K) comprises

- one or more epitopes of survivin or functional sequence variants thereof;
- one or more epitopes of CEA or functional sequence variants thereof; and
- one or more epitopes of ASCL2 or functional sequence variants thereof.

~~50. The vaccine according to claim 49, wherein the antigenic domain comprises in N- to C-terminal direction:~~

- ~~one or more epitopes of CEA or functional sequence variants thereof;~~
- ~~one or more epitopes of survivin or functional sequence variants thereof; and~~
- ~~one or more epitopes of ASCL2 or functional sequence variants thereof.~~

~~51.~~23. The vaccine according to any one of claims 1 to ~~50~~22, wherein the antigenic domain comprises in N- to C-terminal direction:

- a peptide having an amino acid sequence according to SEQ ID NO: 24, or a fragment thereof having a length of at least 10 amino acids, or a functional sequence variant thereof having at least 70% sequence identity;
- a peptide having an amino acid sequence according to SEQ ID NO: 12, or a fragment thereof having a length of at least 10 amino acids, or a functional sequence variant thereof having at least 70% sequence identity; and
- a peptide having an amino acid sequence according to SEQ ID NO: 15, or a fragment thereof having a length of at least 10 amino acids, or a functional sequence variant thereof having at least 70% sequence identity.

~~52.~~24. The vaccine according to claim ~~51~~23, wherein the C-terminus of the peptide consisting of an amino acid sequence according to SEQ ID NO: 24, or the fragment or variant thereof, is directly linked to the N-terminus of the peptide consisting of an amino acid sequence according to SEQ ID NO: 12, or the fragment or variant thereof; and the C-terminus of the peptide consisting an amino acid sequence according to SEQ ID NO: 12, or the fragment or variant thereof, is directly linked to the N-terminus of the peptide having an amino acid sequence according to SEQ ID NO: 15, or the fragment or variant thereof.

~~53.~~25. The vaccine according to claim ~~52~~ 24 , wherein the antigenic domain of the complex of said first component (K) comprises a peptide consisting of an amino acid sequence according to SEQ ID NO: 25 or a functional sequence variant thereof having at least 70%, 75%, 80%, 85%, 90% or 95% sequence identity; a peptide consisting of an amino acid sequence according to SEQ ID NO: 23 or a functional sequence variant thereof having at least 70%, 75%, 80%, 85%, 90% or 95% sequence identity; and a peptide consisting of an amino acid sequence according to SEQ ID NO: 18 or a functional sequence variant thereof having at least 70%, 75%, 80%, 85%, 90% or 95% sequence identity.

~~54.~~26. The vaccine according to claim ~~53~~25, wherein the antigenic domain of the complex of said first component (K) comprises a peptide consisting of an amino acid sequence according to SEQ ID NO: 45 or a functional sequence variant thereof having at least 70%, 75%, 80%, 85%, 90%, 95% sequence identity.

~~55.~~27. The vaccine according to claim ~~54~~26, wherein the complex of the first component (K) comprises or consists of an amino acid sequence according to SEQ ID NO: 60, or a functional sequence variant thereof having at least 70%, 75%, 80%, 85%, 90% or 95% sequence identity.

~~56.~~28. The vaccine according to any one of the preceding claims, wherein the oncolytic rhabdovirus of the second component (V) is a recombinant rhabdovirus, in particular selected from the genus of vesiculovirus.

~~57. The vaccine according to claim 56, wherein the oncolytic recombinant rhabdovirus of the second component (V) is selected from the genus of vesiculovirus.~~

~~58. The vaccine according to claim 57, wherein the oncolytic recombinant vesiculovirus is selected from the group comprising: Vesicular stomatitis alagoas virus (VSAV), Carajás virus (CJSV), Chandipura virus (CHPV), Cocal virus (COCV), Vesicular stomatitis Indiana virus (VSIV), Isfahan virus (ISFV), Maraba virus (MARAV), Vesicular stomatitis New Jersey virus (VSNJV), or Piry virus (PIRYV).~~

~~59.~~29. The vaccine according to claim ~~57 or 58~~28, wherein the oncolytic recombinant vesiculovirus is a recombinant vesicular stomatitis virus, which is preferably one of Vesicular stomatitis Indiana virus (VSIV) or Vesicular stomatitis New Jersey virus (VSNJV).

~~60.~~30. The vaccine according to claim ~~59~~29, wherein the oncolytic recombinant vesicular stomatitis virus is replication-competent.

~~61. The vaccine according to claim 59 or 60, wherein the oncolytic recombinant vesicular stomatitis virus~~

~~(i) lacks a functional gene coding for glycoprotein G, and/or~~

~~(ii) lacks a functional glycoprotein G.~~

~~62. The vaccine according to any one of claims 59 to 61, wherein~~

~~(i) the gene coding for the glycoprotein G is replaced by the gene coding for the glycoprotein GP of another virus, and/or~~

~~(ii) the glycoprotein G is replaced by the glycoprotein GP of another virus.~~

~~63. The vaccine according to claim 62, wherein~~

~~(i) the gene coding for the glycoprotein G is replaced by the gene coding for the glycoprotein GP of an arenavirus, and/or~~

~~(ii) the glycoprotein G is replaced by the glycoprotein GP of an arenavirus.~~

~~64. The vaccine according to claim 62, or claim 63, wherein~~

~~(i) the gene coding for the glycoprotein G is replaced by the gene coding for the glycoprotein GP of Dandenong virus or Mopeia virus, and/or~~

~~(ii) the glycoprotein G is replaced by the glycoprotein GP of Dandenong virus or Mopeia virus.~~

~~65.~~31. The vaccine according to any one of claims ~~61 to 64~~29 to 30, wherein the oncolytic recombinant vesiculovirus

(i) lacks a functional gene for glycoprotein G and the gene coding for the glycoprotein G is replaced by the gene coding for the glycoprotein GP of Lymphocyte choriomeningitis virus (LCMV), and/or

(ii) lacks a functional glycoprotein G and the glycoprotein G is replaced by the glycoprotein GP of LCMV.

~~66.~~32. The vaccine according to claim ~~65~~31, wherein the glycoprotein GP of LCMV comprises the amino acid sequence according to SEQ ID NO: 46, or a functional sequence variant thereof which is at least 80%, 85%, 90%, 95% identical thereto.

~~67.~~33. The vaccine according to any one of claims ~~59~~ 29 to ~~66~~32, wherein the oncolytic recombinant vesicular stomatitis virus of the second component (V) encodes in its genome at least one antigen or antigenic epitope according to any one of claims 22 to 54, wherein the gene coding for the glycoprotein G of the vesicular stomatitis virus is replaced by the gene coding for the glycoprotein GP of lymphocyte choriomeningitis virus (LCMV), and/or the glycoprotein G of the vesicular stomatitis virus is replaced by the glycoprotein GP of LCMV.

~~68.~~34. The vaccine according to any one of claims ~~59~~ 29 to ~~67~~33, wherein the oncolytic recombinant vesicular stomatitis virus of the second component (V) encodes in its genome a vesicular stomatitis virus nucleoprotein (N), large protein (L), phosphoprotein (P), matrix protein (M), glycoprotein (G) and at least one antigen or antigenic epitope according to any one of claims 22 to 54, wherein the gene coding for the glycoprotein G of the vesicular stomatitis virus is replaced by the gene coding for the glycoprotein GP of lymphocyte choriomeningitis virus (LCMV), and/or the glycoprotein G is replaced by the glycoprotein GP of LCMV.

~~69.~~35. The vaccine according to any one of claims ~~59~~ 29 to ~~68~~34, wherein the oncolytic recombinant vesicular stomatitis virus of the second component (V) encodes in its genome a vesicular stomatitis virus nucleoprotein (N), large protein (L), phosphoprotein (P), matrix protein (M), glycoprotein (G) and at least one antigen or antigenic epitope according to any one of claims 22 to 54, wherein the gene coding for the glycoprotein G of the vesicular stomatitis virus is replaced by the gene coding for the glycoprotein GP of lymphocyte choriomeningitis virus (LCMV), and/or the glycoprotein G is replaced by the glycoprotein GP of LCMV, and wherein

- the nucleoprotein (N) comprises an amino acid as set forth in SEQ ID NO:49 or a functional variant at least 80%, 85%, 90%, 92%, 94%, 96%, 98% identical to SEQ ID NO: 49,
- wherein the phosphoprotein (P) comprises an amino acid as set forth in SEQ ID NO:50 or a functional variant at least 80%, 85%, 90%, 92%, 94%, 96%, 98% identical to SEQ ID NO: 50,
- wherein the large protein (L) comprises an amino acid as set forth in SEQ ID NO:51 or a functional variant at least 80%, 85%, 90%, 92%, 94%, 96%, 98% identical to SEQ ID NO: 51,
- the matrix protein (M) comprises an amino acid as set forth in SEQ ID NO:52 or a functional variant at least 80%, 85%, 90%, 92%, 94%, 96%, 98% identical to SEQ ID NO: 52.

~~70.~~36. The vaccine according to any one of claims ~~59~~ 29 to ~~69~~34, wherein the oncolytic recombinant vesicular stomatitis virus of the second component (V) encodes in its genome a second antigenic domain consisting of the amino acid sequence of the antigenic domain of the first component (K) as defined in any one of claims 22 to 54.

~~71. The vaccine according to claim 70, wherein the second antigenic domain encoded in the genome of the oncolytic recombinant vesicular stomatitis virus of the second component (V) comprises at least one antigen or antigenic epitope selected from the group comprising:~~

- ~~CEA (SEQ ID NO: 24)~~
- ~~Surivin (SEQ ID NO: 12)~~
- ~~ASCL2 (SEQ ID NO: 15)~~
- ~~MUC-1 (SEQ ID NO: 19)~~
- ~~EpCAM (SEQ ID NO: 40)~~
- ~~KRas (SEQ ID NO: 30)~~
- ~~MAGE-A3 (SEQ ID NO: 10).~~

~~72.~~37. The vaccine according to claim ~~71~~36, wherein the second antigenic domain encoded in the genome of the oncolytic recombinant vesicular stomatitis virus of the second component (V) comprises at least one antigen or antigenic epitope of CEA (SEQ ID NO: 24).

~~73.~~38. The vaccine according to claim ~~71~~ 36 or ~~72~~37, wherein the second antigenic domain encoded in the genome of the oncolytic recombinant vesicular stomatitis virus of the second component (V) comprises at least one antigen or antigenic epitope of survivin (SEQ ID NO: 12).

~~74.~~39. The vaccine according to any one of claims ~~71~~ 36 to ~~73~~38, wherein the second antigenic domain encoded in the genome of the oncolytic recombinant vesicular stomatitis virus of the second component (V) comprises at least one antigen or antigenic epitope of ASCL2 (SEQ ID NO: 15).

~~75. The vaccine according to any one of claims 71 to 74, wherein the second antigenic domain of the oncolytic recombinant vesicular stomatitis virus of the second component (V) comprises, preferably in N- to C-terminal direction:~~

- ~~a peptide having an amino acid sequence according to SEQ ID NO: 24, or a fragment thereof having a length of at least 10 amino acids, or a functional sequence variant thereof having at least 70% sequence identity;~~
- ~~a peptide having an amino acid sequence according to SEQ ID NO: 12, or a fragment thereof having a length of at least 10 amino acids, or a functional sequence variant thereof having at least 70% sequence identity; and~~
- ~~a peptide having an amino acid sequence according to SEQ ID NO: 15, or a fragment thereof having a length of at least 10 amino acids, or a functional sequence variant thereof having at least 70% sequence identity.~~

~~76. The vaccine according to claim 75, wherein the second antigenic domain of the oncolytic recombinant vesicular stomatitis virus of the second component (V) comprises a peptide consisting of an amino acid sequence according to SEQ ID NO: 25 or a functional sequence variant thereof having at least 70%, 75%, 80%, 85%, 90% or 95% sequence identity; a peptide consisting of an amino acid sequence according to SEQ ID NO: 23 or a functional sequence variant thereof having at least 70%, 75%, 80%, 85%, 90% or 95% sequence identity; and a peptide consisting of an amino acid sequence according to SEQ ID NO: 18 or a functional sequence variant thereof having at least 70%, 75%, 80%, 85%, 90% or 95% sequence identity.~~

~~77.~~40. The vaccine according to claim ~~76~~36, wherein the oncolytic recombinant vesicular stomatitis virus of the second component (V) encodes in its genome a second antigenic domain comprising the amino acid sequence consisting of SEQ ID NO: 45.

~~78.~~41. The vaccine according to claim ~~77~~40, wherein the complex of the first component (K) consists of the amino acid sequence according to SEQ ID NO: 60 and wherein the oncolytic recombinant vesicular stomatitis virus of the second component (V) encodes in its genome

- a phosphoprotein (P) comprising the amino acid consisting of SEQ ID NO: 54,
- a nucleoprotein (N) comprising the amino acid sequence consisting of SEQ ID NO: 55,
- a matrix protein (M) comprising the amino acid sequence consisting of SEQ ID NO: 56,
- a large protein (L) comprising the amino acid sequence consisting of SEQ ID NO: 57,

- a glycoprotein (GP) comprising the amino acid sequence consisting of SEQ ID NO: 58, and
- an antigenic domain which comprises the amino acid sequence consisting of SEQ ID NO: 59.

~~79.~~42. The vaccine according to any one of claims 1 to ~~78~~ 41 for use in the treatment and/or prevention of a tumor or cancer in a patient in need thereof.

~~80. The vaccine for use according to claim 79, wherein the tumor is selected from endocrine tumors, gastrointestinal tumors, genitourinary and gynecologic tumors, head and neck tumors, hematopoietic tumors, skin tumors, thoracic and respiratory tumors.~~

~~81.~~43. The vaccine for use according to claim ~~79 or 80~~42, wherein the tumor is selected from the group of gastrointestinal tumors comprising anal cancer, appendix cancer, cholangiocarcinoma, carcinoid tumor, gastrointestinal colon cancer, extrahepatic bile duct cancer, gallbladder cancer, gastric (stomach) cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor (GIST), hepatocellular cancer, pancreatic cancer, rectal cancer, colorectal cancer, or metastatic colorectal cancer.

~~82.~~44. The vaccine for use according to claim ~~81~~43, wherein the tumor is one of colorectal cancer, or metastatic colorectal cancer.

~~83.~~45. The vaccine for use according to any one of claims ~~79~~ 42 to ~~82~~44, wherein the first component (K) and the second component (V) are each to be administered at least once.

~~84.~~46. The vaccine for use according to claim ~~83~~45, wherein the first component (K) is to be administered prior to the administration of the second component (V).

~~85.~~47. The vaccine for use according to claim ~~83~~ 45 or ~~84~~46, wherein the first component (K) is to be administered at least twice, preferably prior to and subsequent to the administration of the second component (V).

~~86.~~48. The vaccine for use according to claim ~~85~~47, wherein the first component (K) and second component (V) are to be administered in the order K-V-K, K-V-K-K, K-V-V-K, preferably in the order K-V-K, or K-V-K-K.

87.49. The vaccine for use according to any one of claims 83-45 to 8648, wherein the first component (K) and second component (V) are to be administered between 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19, 20, 21 days apart, preferably between about 5, 6, 7, 8, 9, 10 days to about 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 days apart from each other, preferably between about 11, 12, 13, 14 days to about 15, 16, 17, 18, 19, 20, 21 days.

88.50. The vaccine for use according to claim 8749, wherein the first component (K) is to be administered at least once about 10, 11, 12, 13, 14 days to about 20, 22, 24, 26, 28, 30 days following the administration of the second component (V).

89. An oncolytic recombinant vesicular stomatitis virus encoding in its genome at least one antigen or antigenic epitope according to any one of claims 22 to 54, wherein the gene coding for the glycoprotein G of the vesicular stomatitis virus is replaced by the gene coding for the glycoprotein GP of lymphocyte choriomeningitis virus (LCMV), and/or the glycoprotein G is replaced by the glycoprotein GP of LCMV.

90. The oncolytic recombinant vesicular stomatitis virus according to claim 89 encoding in its genome a vesicular stomatitis virus nucleoprotein (N), large protein (L), phosphoprotein (P), matrix protein (M), glycoprotein (G) and at least one antigen or antigenic epitope according to any one of claims 22 to 54, wherein the gene coding for the glycoprotein G of the vesicular stomatitis virus is replaced by the gene coding for the glycoprotein GP of lymphocyte choriomeningitis virus (LCMV), and/or the glycoprotein G is replaced by the glycoprotein GP of LCMV.

91. An oncolytic recombinant vesicular stomatitis virus as defined in any one of claims 69 to 78.

92. The oncolytic recombinant vesicular stomatitis virus according to any one of claims 89 to 91 for use in the treatment and/or prevention of a tumor or cancer.

93. The oncolytic recombinant vesicular stomatitis virus according to any one of claims 89 to 92 for use in a vaccine according to any one of claims 1-88.

94. The complex of the first component (K) as defined according to claim 55, or as defined according to any one of claims 1-54, for use in combination with a chemotherapeutic

~~agent, immunotherapeutic agent, such as an immune checkpoint inhibitor, or targeted drug.~~

~~95. The complex of the first component (K) according to claim 55 for use in combination with the oncolytic recombinant vesicular stomatitis virus of the vaccine as defined in any one of claims 89 to 91, optionally in combination with a chemotherapeutic agent, immunotherapeutic agent, such as an immune checkpoint inhibitor, or targeted drug.~~

~~96. The oncolytic vesicular stomatitis virus according to any one of claims 89 to 91 for use in combination with the complex of the first component (K) as defined in claim 55, optionally in combination with a chemotherapeutic agent, immunotherapeutic agent, such as an immune checkpoint inhibitor, or targeted drug.~~

~~97.~~51. The vaccine according to any one of claims ~~79~~ 42 to ~~88~~ 50 for use in combination with a chemotherapeutic agent, immunotherapeutic agent, such as an immune checkpoint inhibitor, or targeted drug.

~~98.~~52. Use of an effective amount of the vaccine according to any one of claims 1-~~78~~41 in the manufacture of a medicament ~~Method of~~ for treating a patient in need thereof afflicted with a tumor, wherein ~~the method~~said medicament is to be administered to ~~comprises administering to~~ said patient~~, an effective amount of the vaccine according to any one of claims 1-78~~.

~~99.~~53. ~~Method of treating a patient in need thereof~~The use according to claim ~~98~~52, wherein the tumor is selected from endocrine tumors, gastrointestinal tumors, genitourinary and gynecologic tumors, breast cancer, head and neck tumors, hematopoietic tumors, skin tumors, thoracic and respiratory tumors, preferably colorectal cancer or metastatic colorectal cancer.

~~100.~~54. ~~Method of treating a patient in need thereof~~The use according to claim ~~98~~ 52 or claim ~~99~~53, wherein the vaccine is to be co-administered with one or more of an immunotherapeutic agent, such as an immune checkpoint inhibitor, a chemotherapeutic agent, or a targeted drug.

~~101.~~55. ~~Method of treating a patient in need thereof~~The use according to claim ~~100~~54, wherein the checkpoint modulator is to be administered concomitantly, sequentially, alternately or following the administration of the vaccine.

~~102.~~56. ~~Method of treating a human in need thereof~~ The use according to claim ~~101~~55, wherein the checkpoint modulator is to be administered from about 1 to about 14 days prior to the administration of the vaccine.

~~103.~~57. ~~Method of treating a patient in need thereof~~The use according to any one of claims ~~98 to 102~~52 to 56, wherein the first component (K) and second component (V) of the vaccine are to be administered intravenously, subcutaneously, or intramuscularly.

~~104.~~58. ~~Method of treating a patient in need thereof~~ The use according to any one of claims ~~98 to 103~~52 to 57, wherein the first component (K) and the second component (V) of the vaccine are to be administered by different routes of administration.

~~105.~~59. ~~Method of treating a patient in need thereof~~The use according to claim ~~104~~58, wherein the first component (K) of the vaccine is to be administered intramuscular and the second component (V) of the vaccine is to be administered intravenously, or intratumorally, preferably, intravenously.

~~106.~~60. ~~Method of treating a patient in need thereof~~The use according to any one of claims ~~98 to 105~~52 to 59, wherein about 0.5 nmol to about 10 nmol of the complex of the first component (K) of the vaccine are to be administered.

~~107.~~61. ~~Method of treating a human in need thereof~~The use according to any one of claims ~~98 to 106~~52 to 60, wherein the recombinant VSV of the second component (V) of the vaccine is dosed from about 10^6 $TCID_{50}$ to about 10^{11} $TCID_{50}$.

~~108.~~62. ~~Method of treating a human in need thereof~~The use according to any one of claims ~~98 to 107~~52 to 61, wherein the first component (K) and the second component (V) of the vaccine, which is preferably according to claim 77 or claim 78, are to be administered in the order first component (K), followed by the second component (V), preferably in the order K-V-K.

~~109.~~63. ~~Method of treating a human in need thereof~~The use according to any one of claims ~~98 to 108~~52 to 62, wherein the first component (K) and the second component (V) of the vaccine are to be administered sequentially, wherein the first component (K)

and the second component (V) are to be administered from about 7 days to about 30 days apart from each other.

~~110.~~64. ~~Method of treating a human in need thereof~~The use according to any one of claims ~~98 to 109~~52 to 63, wherein ~~the method comprises administering to said patient~~ the first component (K) is to be administered to said patient at least once from about 21 days to about 180 days following the last administration of the first component (K).

~~111.~~65. Kit for use in vaccination in treating and/or preventing a tumor or cancer, wherein the kit comprises the vaccine according to any one of claims ~~1-78~~41.

~~112.~~66. The kit for use according to claim ~~111~~65, wherein the kit further comprises at least one of a chemotherapeutic agent, an immune checkpoint inhibitor, targeted drug, or immunotherapeutic agent for use in combination with the vaccine.

~~113.~~67. Use of the vaccine according to any one of claims 1-~~78~~41 in the manufacture of a medicament for ~~Method of~~ increasing the infiltration of a tumor with tumor antigen-specific T-cells in a patient, ~~the method comprising administering~~wherein said medicament is to be administered to a patient afflicted with a tumor or cancer ~~the vaccine according to any one of claims 1-78~~.

~~114. A vesicular stomatitis virus, wherein the RNA genome of the vesicular stomatitis virus comprises or consists of an RNA sequence identical or at least 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 80.~~

~~115. The vesicular stomatitis virus according to claim 114, wherein the vesicular stomatitis virus encodes in its genome~~

- ~~a phosphoprotein (P) comprising the amino acid consisting of SEQ ID NO: 50,~~
- ~~a nucleoprotein (N) comprising the amino acid sequence consisting of SEQ ID NO: 49,~~
- ~~a matrix protein (M) comprising the amino acid sequence consisting of SEQ ID NO: 52,~~
- ~~a large protein (L) comprising the amino acid sequence consisting of SEQ ID NO: 51,~~
- ~~a glycoprotein (GP) comprising the amino acid sequence consisting of SEQ ID NO: 53, and~~

- ~~an antigenic domain which comprises the amino acid sequence consisting of SEQ ID NO: 45 or SEQ ID NO: 59.~~

~~116.~~68. The vaccine according to any one of claims 1 to ~~78~~41, wherein the oncolytic rhabdovirus of the second component (V) is a vesicular stomatitis virus, wherein the RNA genome of the vesicular stomatitis virus comprises or consists of an RNA sequence identical or at least 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 80.

~~117.~~69. The vaccine according to claim ~~116~~68, wherein the vesicular stomatitis virus encodes in its genome

- a phosphoprotein (P) comprising the amino acid consisting of SEQ ID NO: 50,
- a nucleoprotein (N) comprising the amino acid sequence consisting of SEQ ID NO: 49,
- a matrix protein (M) comprising the amino acid sequence consisting of SEQ ID NO: 52,
- a large protein (L) comprising the amino acid sequence consisting of SEQ ID NO: 51,
- a glycoprotein (GP) comprising the amino acid sequence consisting of SEQ ID NO: 53, and
- an antigenic domain which comprises the amino acid sequence consisting of SEQ ID NO: 45 or SEQ ID NO: 59.

~~118.~~70. A polypeptide comprising or consisting of an amino acid sequence of SEQ ID NO: 60 for use in an immunization regimen in combination with a vesicular stomatitis virus, wherein the RNA genome of the vesicular stomatitis virus comprises or consists of an RNA sequence identical or at least 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 80.

~~119.~~71. The polypeptide for use in an immunization regimen in combination with the vesicular stomatitis virus according to claim ~~118~~70, wherein the vesicular stomatitis virus encodes in its genome

- a phosphoprotein (P) comprising the amino acid consisting of SEQ ID NO: 50,

- a nucleoprotein (N) comprising the amino acid sequence consisting of SEQ ID NO: 49,
- a matrix protein (M) comprising the amino acid sequence consisting of SEQ ID NO: 52,
- a large protein (L) comprising the amino acid sequence consisting of SEQ ID NO: 51,
- a glycoprotein (GP) comprising the amino acid sequence consisting of SEQ ID NO: 53, and
- an antigenic domain which comprises the amino acid sequence consisting of SEQ ID NO: 45 or SEQ ID NO: 59.

~~120.~~72. A vesicular stomatitis virus, wherein the RNA genome of the vesicular stomatitis virus comprises or consists of an RNA sequence identical or at least 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 80 for use in an immunization regimen in combination with a polypeptide comprising or consisting of an amino acid sequence of SEQ ID NO: 60.

~~121.~~73. The vesicular stomatitis virus for use in an immunization regimen in combination with the polypeptide according to claim ~~120~~72, wherein the vesicular stomatitis virus encodes in its genome

- a phosphoprotein (P) comprising the amino acid consisting of SEQ ID NO: 50,
- a nucleoprotein (N) comprising the amino acid sequence consisting of SEQ ID NO: 49,
- a matrix protein (M) comprising the amino acid sequence consisting of SEQ ID NO: 52,
- a large protein (L) comprising the amino acid sequence consisting of SEQ ID NO: 51,
- a glycoprotein (GP) comprising the amino acid sequence consisting of SEQ ID NO: 53, and
- an antigenic domain which comprises the amino acid sequence consisting of SEQ ID NO: 45 or SEQ ID NO: 59.

~~122.~~74. A kit of parts comprising a polypeptide and a vesicular stomatitis virus, wherein the polypeptide comprises or consists of an amino acid sequence of SEQ ID NO: 60, and wherein the RNA genome of the vesicular stomatitis virus comprises or

consists of an RNA sequence identical or at least 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 80.

~~123.~~75. The kit of parts according to claim ~~122~~74, wherein the vesicular stomatitis virus encodes in its genome

- a phosphoprotein (P) comprising the amino acid consisting of SEQ ID NO: 50,
- a nucleoprotein (N) comprising the amino acid sequence consisting of SEQ ID NO: 49,
- a matrix protein (M) comprising the amino acid sequence consisting of SEQ ID NO: 52,
- a large protein (L) comprising the amino acid sequence consisting of SEQ ID NO: 51,
- a glycoprotein (GP) comprising the amino acid sequence consisting of SEQ ID NO: 53, and
- an antigenic domain which comprises the amino acid sequence consisting of SEQ ID NO: 45 or SEQ ID NO: 59.

~~124.~~76. The ~~complex of the first component (K) for use according to claim 94 or 95, the virus for use according to claim 96, the vaccine for use according to claim 97, the method~~ use according to claim ~~100~~54, or the kit according to claim ~~112~~66, wherein the immune checkpoint inhibitor is selected from the group consisting of pembrolizumab; nivolumab; pidilizumab; cemiplimab; PDR-001; atezolizumab; avelumab; durvalumab, an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:61 and a light chain comprising the amino acid sequence of SEQ ID NO:62; an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:63 and a light chain comprising the amino acid sequence of SEQ ID NO:64; an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:65 and a light chain comprising the amino acid sequence of SEQ ID NO:66; an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:67 and a light chain comprising the amino acid sequence of SEQ ID NO:68; and an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:69 and a light chain comprising the amino acid sequence of SEQ ID NO:70.

~~125.~~77. The vaccine according to claim ~~78~~ 41 or claim ~~116~~68, or the kit of parts according to claim ~~122 or 123~~74 or 75, further comprising an immune checkpoint

inhibitor of the PD-1/PD-L1 pathway, preferably selected from the group consisting of pembrolizumab; nivolumab; pidilizumab; cemiplimab; PDR-001; atezolizumab; avelumab; durvalumab, an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:61 and a light chain comprising the amino acid sequence of SEQ ID NO:62; an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:63 and a light chain comprising the amino acid sequence of SEQ ID NO:64; an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:65 and a light chain comprising the amino acid sequence of SEQ ID NO:66; an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:67 and a light chain comprising the amino acid sequence of SEQ ID NO:68; and an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:69 and a light chain comprising the amino acid sequence of SEQ ID NO:70.

~~126.~~78. The polypeptide for use according to claim ~~118 or 119~~70 or 71; or the virus for use according to claim ~~120 or 121~~72 or 73; wherein the combination further comprises an immune checkpoint inhibitor of the PD-1/PD-L1 pathway, preferably selected from the group consisting of pembrolizumab; nivolumab; pidilizumab; cemiplimab; PDR-001; atezolizumab; avelumab; durvalumab, an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:61 and a light chain comprising the amino acid sequence of SEQ ID NO:62; an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:63 and a light chain comprising the amino acid sequence of SEQ ID NO:64; an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:65 and a light chain comprising the amino acid sequence of SEQ ID NO:66; an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:67 and a light chain comprising the amino acid sequence of SEQ ID NO:68; and an antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:69 and a light chain comprising the amino acid sequence of SEQ ID NO:70.

~~127.~~79. The vaccine for use according to any one of claims ~~79~~ 42 to ~~88~~ 51~~and 97~~; the virus for use according to any one of claims ~~93, 96, 120, 121~~72, 73, ~~124~~ 76 and ~~126~~78; ~~the complex of the first component (K) for use according to any one of claims 95 and 124~~; the ~~method~~ use according to any one of claims ~~98 to 110~~52 to 64, ~~113~~ 67 and ~~124~~76; the kit for use according to any one of claims ~~111~~65, ~~112~~ 66 and ~~124~~76; or the polypeptide for use according to any one of claims ~~118~~70, ~~119~~ 71 and ~~126~~78; wherein

the first component (K) and the second component (V) are to be administered as heterologous prime-boost vaccine.