CLAIMS

1. A virus particle comprising a lymphocytic choriomeningitis virus (LCMV) S segment and an LCMV L segment, wherein the S segment comprises an open reading frame encoding a glycoprotein having at least 97% sequence identity to SEQ ID NO: 4, and wherein the L segment comprises an open reading frame encoding an L protein having at least 90% sequence identity to SEQ ID NO: 40, wherein the glycoprotein comprises at least one mutated amino acid residue in comparison with the glycoprotein sequence set forth in SEQ ID NO: 4.

2. The virus particle of claim 1, wherein the glycoprotein comprises at least one mutated amino acid residue at position 181 and/or 185 in comparison with the glycoprotein sequence set forth in SEQ ID NO: 4, or wherein the glycoprotein ~~preferably~~ comprises at least one mutation selected from Arg 185 → Trp and Ile 181 → Met in comparison with the glycoprotein sequence set forth in SEQ ID NO: 4.

~~3. The virus particle of claim 1 or 2, wherein the L protein comprises at position 1079 corresponding to the linear polypeptide sequence of SEQ ID NO: 40 an amino acid residue other than Lys, preferably a non basic amino acid residue, preferably a neutral hydrophilic amino acid residue, preferably an Asn or Gln, preferably a Gln.~~

~~4.~~3. A virus particle comprising a lymphocytic choriomeningitis virus (LCMV) S segment and an LCMV L segment, wherein the S segment comprises an open reading frame encoding a glycoprotein having at least 97% sequence identity to SEQ ID NO: 4, and wherein the L segment comprises an open reading frame encoding an L protein having at least 90% sequence identity to SEQ ID NO: 40, wherein the L protein comprises at position 1079 corresponding to the linear polypeptide sequence of SEQ ID NO: 40 an amino acid residue other than Lys.

~~5.~~4. The virus particle of claim ~~4~~3, wherein the L protein comprises at position 1079 corresponding to the linear polypeptide sequence of SEQ ID NO: 40 a non-basic amino acid residue, preferably a neutral hydrophilic amino acid residue, preferably an Asn or Gln, preferably a Gln.

~~6. The virus particle of claim 4 or 5, wherein the glycoprotein comprises at least one mutated amino acid residue in comparison with the glycoprotein sequence set forth in SEQ ID NO: 4, wherein the glycoprotein preferably comprises at least one mutated amino acid residue at position 181 and/or 185 in comparison with the glycoprotein sequence set forth in SEQ ID NO: 4, wherein the glycoprotein preferably comprises at least one mutation selected from Arg 185 → Trp and Ile 181 → Met in comparison with the glycoprotein sequence set forth in SEQ ID NO: 4.~~

~~7.~~5. The virus particle of any one of the preceding claims, wherein the S segment is derived from LCMV strain WE or a variant thereof and wherein the L segment is derived from LCMV strain Clone13 or a variant thereof.

~~8.~~6. The virus particle of any one of the preceding claims, wherein the S segment comprises an open reading frame encoding a nucleoprotein having at least 97% sequence identity to SEQ ID NO: 6.

~~9.~~7. The virus particle of any one of the preceding claims, wherein the L segment comprises an open reading frame encoding a Z protein having at least 90% sequence identity to SEQ ID NO: 38.

~~10.~~8. A virus particle comprising a lymphocytic choriomeningitis virus (LCMV) S segment and an LCMV L segment, wherein the S segment comprises an open reading frame encoding a glycoprotein having at least 97% sequence identity to SEQ ID NO: 4 and an open reading frame encoding a nucleoprotein having at least 97% sequence identity to SEQ ID NO: 6, and wherein the L segment comprises an open reading frame encoding an L protein having at least 90% sequence identity to SEQ ID NO: 40 and an open reading frame encoding a Z protein having at least 90% sequence identity to SEQ ID NO: 38.

~~11. The virus particle of claim 10, wherein the glycoprotein comprises at least one mutated amino acid residue in comparison with the glycoprotein sequence set forth in SEQ ID NO: 4, wherein the glycoprotein preferably comprises at least one mutated amino acid residue at position 181 and/or 185 in comparison with the glycoprotein sequence set forth in SEQ ID NO: 4, wherein the glycoprotein preferably comprises at least one mutation~~

selected from Arg 185 → Trp and Ile 181 → Met in comparison with the glycoprotein sequence set forth in SEQ ID NO: 4.

12. The virus particle of claim 10 or 11, wherein the L protein comprises at position 1079 corresponding the linear polypeptide sequence of SEQ ID NO: 40 an amino acid residue other than Lys, preferably a non basic amino acid residue, preferably a neutral hydrophilic amino acid residue, preferably an Asn or Gln, preferably a Gln.

13. The virus particle of any one of the preceding claims, wherein the virus particle is capable of promoting a stronger reduction of growth of a tumor as compared to LCMV strain WE and/or a virus particle comprising the same S segment as the virus particle and an L segment as shown in SEQ ID NO: 2.

14. The virus particle of any one of the preceding claims, wherein the virus particle is capable of promoting a stronger reduction of growth of a cold tumor as compared to LCMV strain WE and/or a virus particle comprising the same S segment as the virus particle and an L segment as shown in SEQ ID NO: 2.

15. The virus particle of any one of the preceding claims, wherein the virus particle is capable of inducing a stronger adaptive immune activation as compared to LCMV strain WE and/or a virus particle comprising the same S segment as the virus particle and an L segment as shown in SEQ ID NO: 2.

16. The virus particle of any one of the preceding claims, wherein the virus particle is capable of promoting a reduction of growth of a warm tumor that is at least as strong as compared to LCMV strain WE and/or a virus particle comprising the same S segment as the virus particle and an L segment as shown in SEQ ID NO: 2.

17. The virus particle of any one of the preceding claims, wherein the virus particle is capable of inducing decreased levels of an interferon upon systemic administration compared to LCMV strain WE, Armstrong, Clone13 and/or a virus particle comprising the same S segment as the virus particle and an L segment as shown in SEQ ID NO: 2.

~~18. The virus particle of any one of the preceding claims, wherein the virus particle is capable of inducing a lower concentration of one or more Th1- and pro-inflammatory cytokines compared to LCMV strain WE, Armstrong, Clone13 and/or a virus particle comprising the same S segment as the virus particle and an L segment as shown in SEQ ID NO: 2.~~

~~19. The virus particle of any one of the preceding claims, wherein the virus particle is capable of inducing a lower concentration of one or more Th1- and pro-inflammatory cytokines compared to LCMV strain WE, Armstrong, Clone13 and/or a virus particle comprising the same S segment as the virus particle and an L segment as shown in SEQ ID NO: 2.~~

~~20.~~9. The virus particle of any one of the preceding claims, wherein the virus particle is less pathogenic in a mouse compared to LCMV strain WE.

~~21. The virus particle of any one of the preceding claims, wherein the virus particle is capable of inducing a reduced degree of liver pathology in a mouse compared to LCMV strain WE and/or a virus particle comprising the same S segment as the virus particle and an L segment as shown in SEQ ID NO: 2.~~

~~22. The virus particle of any one of the preceding claims, wherein the virus particle shows reduced replication in neuron cells compared to LCMV strain WE and/or a virus particle comprising the same S segment as the virus particle and an L segment as shown in SEQ ID NO: 2.~~

~~23.~~10. The virus particle of any one of the preceding claims, wherein the virus particle shows increased replication in tumor cells compared to LCMV strain WE.

~~24.~~11. The virus particle of any one of the preceding claims, wherein the virus particle shows reduced replication in a healthy organ compared to LCMV strain WE and/or a virus particle comprising the same S segment as the virus particle and an L segment as shown in SEQ ID NO: 2.

~~25. The virus particle of any one of the preceding claims, wherein the S segment comprises an open reading frame encoding a glycoprotein that has at least about 98%, preferably at least about 98.5%, preferably at least about 99%, preferably at least about 99.1%,~~

preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.5%, preferably at least about 99.7% sequence identity, or is preferably identical, to a sequence set forth in SEQ ID NO: 4 or 14.

26. The virus particle of any one of the preceding claims, wherein the S segment comprises an open reading frame comprising a sequence that has at least about 87%, preferably at least about 88%, preferably at least about 89%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93%, preferably at least about 94%, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7% sequence identity, or is preferably identical, to a sequence set forth in SEQ ID NO: 3 or 13.

27. The virus particle of any one of the preceding claims, wherein the L segment comprises an open reading frame encoding an L protein having at least about 91%, preferably at least about 92%, preferably at least about 93%, preferably at least about 94%, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7% sequence identity, or is preferably identical, to a sequence set forth in SEQ ID NO: 30 or 40.

28. The virus particle of any one of the preceding claims, wherein the L segment comprises an open reading frame comprising a sequence that has at least about 83%, preferably at least about 84%, preferably at least about 85%, preferably at least about 86%, preferably at least about 87%, preferably at least about 88%, preferably at least about 89%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93%, preferably at least about 94%, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably

~~at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, preferably at least about 99.8%, preferably at least about 99.9% sequence identity, or is preferably identical, to a sequence set forth in SEQ ID NO: 29 or 39.~~

~~29. The virus particle of any one of the preceding claims, wherein the S segment comprises an open reading frame encoding a nucleoprotein, wherein said nucleoprotein has at least about 98%, preferably 98.5 %, preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is preferably identical, to a sequence set forth in any one of in SEQ ID NO: 6 or 16.~~

~~30. The virus particle of any one of the preceding claims, wherein the S segment comprises an open reading frame comprising a sequence that has at least about 86%, preferably at least about 87%, preferably at least about 88%, preferably at least about 89%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93%, preferably at least about 94%, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is preferably identical, to a sequence set forth in SEQ ID NO: 5 or 15.~~

~~31. The virus particle of any one of the preceding claims, wherein the L segment comprises an open reading frame encoding a Z protein having at least about 91%, preferably at least about 92%, preferably at least about 93%, preferably at least about 94%, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is preferably identical, to a sequence set forth in SEQ ID NO: 28 or 38.~~

~~32. The virus particle of any one of the preceding claims, wherein the L segment comprises an open reading frame comprising a sequence that has at least about 84%, preferably at least about 85%, preferably at least about 86%, preferably at least about 87%, preferably at least about 88%, preferably at least about 89%, preferably at least about 90%, preferably at least about 91%, preferably at least about 92%, preferably at least about 93%, preferably at least about 94%, preferably at least about 95%, preferably at least about 96%, preferably at least about 97%, preferably at least about 98% preferably at least about 99%, preferably at least about 99.1%, preferably at least about 99.2%, preferably at least about 99.3%, preferably at least about 99.4%, preferably at least about 99.5%, preferably at least about 99.6%, preferably at least about 99.7%, sequence identity, or that is identical, to a sequence set forth in SEQ ID NO: 27 or 37.~~

~~33.~~12. The virus particle of any one of the preceding claims, wherein the S segment comprises a sequence that has at least about 86%, ~~preferably~~ at least about 87%, ~~preferably~~ at least about 88%, ~~preferably~~ at least about 89%, ~~preferably~~ at least about 90%, ~~preferably~~ at least about 91%, ~~preferably~~ at least about 92%, ~~preferably~~ at least about 93%, ~~preferably~~ at least about 94%, ~~preferably~~ at least about 95%, ~~preferably~~ at least about 96%, ~~preferably~~ at least about 97%, ~~preferably~~ at least about 98% ~~preferably~~ at least about 99%, ~~preferably~~ at least about 99.1%, ~~preferably~~ at least about 99.2%, ~~preferably~~ at least about 99.3%, ~~preferably~~ at least about 99.4%, ~~preferably~~ at least about 99.5%, ~~preferably~~ at least about 99.6%, ~~preferably~~ at least about 99.7% sequence identity, ~~preferably~~ at least about 99.7%, ~~preferably~~ at least about 99.8%, or ~~preferably~~ at least about 99.9% sequence identity, or is ~~preferably~~ identical, to a sequence set forth in SEQ ID NO: 1 or 11.

~~34.~~13. The virus particle of any one of the preceding claims, wherein the L segment comprises a sequence that has at least about 83%, ~~preferably~~ at least about 84%, ~~preferably~~ at least about 85%, ~~preferably~~ at least about 86%, ~~preferably~~ at least about 87%, ~~preferably~~ at least about 88%, ~~preferably~~ at least about 89%, ~~preferably~~ at least about 90%, ~~preferably~~ at least about 91%, ~~preferably~~ at least about 92%, ~~preferably~~ at least about 93%, ~~preferably~~ at least about 94%, ~~preferably~~ at least about 95%, ~~preferably~~ at least about 96%, ~~preferably~~ at least about 97%, ~~preferably~~ at least about 98% ~~preferably~~ at least about 99%, ~~preferably~~ at least about 99.1%, ~~preferably~~ at least about 99.2%, ~~preferably~~ at least about 99.3%, ~~preferably~~ at least about 99.4%, ~~preferably~~ at least about 99.5%,

~~preferably~~ at least about 99.6%, ~~preferably~~ at least about 99.7% sequence identity, ~~preferably~~ at least about 99.7%, ~~preferably~~ at least about 99.8%, or ~~preferably~~ at least about 99.9% sequence identity, or is ~~preferably~~ identical, to a sequence set forth in SEQ ID NO: 21 or 31.

~~35. The virus particle of any one of the preceding claims, wherein the virus particle is infectious.~~

~~36. The virus particle of any one of the preceding claims, wherein the virus particle is replication competent.~~

~~37. The virus particle of any one of the preceding claims, wherein the virus particle is attenuated.~~

~~38. The virus particle of any one of the preceding claims, wherein the ORF encoding the glycoprotein is under control of a 5' untranslated region (UTR).~~

~~39. The virus particle of any one of the preceding claims, wherein the ORF encoding the L protein is under control of a 3' untranslated region (UTR).~~

~~40. The virus particle of any one of the preceding claims, wherein the ORF encoding the nucleoprotein is under control of a 3' untranslated region (UTR).~~

~~41. The virus particle of any one of the preceding claims, wherein the ORF encoding the Z protein is under control of a 5' untranslated region (UTR).~~

~~42.~~14. The virus particle of any one of the preceding claims, wherein the virus particle has a bi-segmented genome.

~~43.~~15. The virus particle of any one of the preceding claims, wherein the virus particle is an arenavirus particle.

~~44. The virus particle of any one of the preceding claims, wherein the virus particle is an LCMV particle.~~

~~45. The virus particle of any one of the preceding claims, wherein the virus particle does not comprise an ORF from an organism other than an LCMV.~~

~~46.~~16. A host cell comprising an LCMV S segment and an LCMV L segment as defined in any one of the preceding claims.

~~47.~~17. A host cell comprising cDNA of

(a) an ORF encoding a glycoprotein as defined in any one of claims 1-~~45~~15, an ORF encoding an L protein as defined in any one of claims 1-~~45~~15, an ORF encoding a nucleoprotein as defined in any one of claims 1-~~45~~15, and an ORF encoding a Z protein as defined in any one of claims 1-~~45~~15; and/or

(b) an LCMV S segment and an LCMV L segment as defined in any one of claims 1-~~45~~15.

~~48. The host cell of claim 46 or 47, wherein the host cell is a HEK293 cell.~~

~~49.~~18. A method of producing a virus particle of any one of claims 1-~~45~~ 15 comprising cultivating the host cell of ~~any one of~~ claim~~s~~ 16 or ~~46-48~~17 under conditions suitable for virus particle formation.

~~50. The method of claim 49 further comprising recovery and/or purification of the virus particle.~~

~~51.~~19. A pharmaceutical composition comprising a virus particle of any one of claims 1-15~~comprising an LCMV S segment and an LCMV L segment, wherein the S segment comprises an open reading frame encoding a glycoprotein having at least 97% sequence identity to SEQ ID NO: 4, and wherein the L segment comprises an open reading frame encoding an L protein having at least 90% sequence identity to SEQ ID NO: 40~~.

~~52. The pharmaceutical composition of claim 51, wherein the virus particle is a virus particle of any one of claims 1-45.~~

~~53. A virus particle comprising an LCMV S segment and an LCMV L segment, wherein the S segment comprises an open reading frame encoding a glycoprotein having at least 97% sequence identity to SEQ ID NO: 4, and wherein the L segment comprises an open~~

reading frame encoding an L protein having at least 90% sequence identity to SEQ ID NO: 40 for use in therapy.

54. The virus particle for the use of claim 53, wherein the virus particle is a virus particle of any one of claims 1-45.

55. The virus particle for the use of claim 53 or 54, wherein the use is in the treatment of cancer.

56. The virus particle for the use of any one of claims 53-55, wherein the use is in the treatment of a human subject.

57. The virus particle for the use of any one of claims 53-56, wherein the use is in the treatment of a human cancer.

58. The virus particle for the use of any one of claims 53-57, wherein the use is in the treatment of a cold tumor.

59. The virus particle for the use of any one of claims 53-58, wherein the use is in the treatment of a hot tumor.

60. The virus particle for the use of any one of claims 53-59, wherein the use is in the treatment of a tumor selected from the group consisting of anal carcinoma, bronchial carcinoma, lung carcinoma, endometrial carcinoma, gallbladder carcinoma, bladder carcinoma, hepatocellular carcinoma, testicular carcinoma, colon carcinoma, colorectal carcinoma, colorectal carcinoma, hepatocellular carcinoma, testicular carcinoma, colon carcinoma, tumor of the bladder, bladder carcinoma, tumor of the bladder, hepatocellular carcinoma, lung carcinoma, lung carcinoma, endometrial carcinoma, colorectal carcinoma, rectal carcinoma, laryngeal carcinoma, esophageal carcinoma, gastric carcinoma, breast carcinoma, renal carcinoma, ovarian carcinoma, pancreatic carcinoma, pharyngeal carcinoma, oropharyngeal carcinoma, prostate carcinoma, thyroid carcinoma, Cervical cancer, angiosarcoma, chondrosarcoma, Ewing sarcoma, fibrosarcoma, Kaposi sarcoma, liposarcoma, leiomyosarcoma, malignant fibrosis histiocytoma, lymphoma, leukemia, neurogenic sarcoma, osteosarcoma and rhabdomyosarcoma.

~~61.~~20. A use of a virus particle of any one of claims 1-15 ~~comprising an LCMV S segment and an LCMV L segment, wherein the S segment comprises an open reading frame encoding a glycoprotein having at least 97% sequence identity to SEQ ID NO: 4, and wherein the L segment comprises an open reading frame encoding an L protein having at least 90% sequence identity to SEQ ID NO: 40 for~~in the manufacture of a medicament, wherein the medicament is preferably for the treatment of cancer.

~~62. A method of treating a disease comprising administering to a subject in need thereof an effective amount of a virus particle comprising an LCMV S segment and an LCMV L segment, wherein the S segment comprises an open reading frame encoding a glycoprotein having at least 97% sequence identity to SEQ ID NO: 4, and wherein the L segment comprises an open reading frame encoding an L protein having at least 90% sequence identity to SEQ ID NO: 40, wherein the disease is preferably cancer.~~