

## **CLAIMS**

1. Use of an immunogenic composition of a DNA plasmid encoding a human telomerase reverse transcriptase (hTERT) antigen comprising a nucleic acid sequence encoding SEQ ID NO: 20, a DNA plasmid encoding a Wilms Tumor-1 (WT-1) antigen comprising a nucleic acid sequence encoding SEQ ID NO: 26, and a DNA plasmid encoding a prostate specific membrane antigen (PSMA) comprising a nucleic acid sequence encoding SEQ ID NO: 28 and a DNA plasmid comprising a nucleic acid sequence encoding the p35 subunit and the p40 subunit of interleukin-12 (IL12) in the manufacture of a medicament for the treatment of newly diagnosed glioblastoma in combination with an anti-programmed cell death receptor 1 (PD-1) antibody, wherein the anti-PD-1 antibody comprises:

three heavy chain complementarity determining regions (HCDR1, HCDR2 and HCDR3) and three light chain complementarity determining regions (LCDR1, LCDR2 and LCDR3), wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 3, HCDR2 comprises the amino acid sequence of SEQ ID NO: 4, HCDR3 comprises the amino acid sequence of SEQ ID NO: 5, LCDR1 comprises the amino acid sequence of SEQ ID NO: 6, LCDR2 comprises the amino acid sequence of SEQ ID NO: 7, and LCDR3 comprises the amino acid sequence of SEQ ID NO: 8; a heavy chain variable region (HCVR) with 90% sequence identity to SEQ ID NO: 1 and a light chain variable region (LCVR) with 90% sequence identity to SEQ ID NO: 2;

a HCVR comprising the amino acid sequence of SEQ ID NO: 1 and a LCVR comprising the amino acid sequence of SEQ ID NO: 2; or

a heavy chain comprising the amino acid sequence of SEQ ID NO: 9 and a light chain comprising the amino acid sequence of SEQ ID NO: 10.

2. Use of an anti-programmed cell death receptor 1 (PD-1) antibody and an immunogenic composition of a DNA plasmid encoding a human telomerase reverse transcriptase (hTERT) antigen comprising a nucleic acid sequence encoding SEQ ID NO: 20, a DNA plasmid encoding a Wilms Tumor-1 (WT-1) antigen comprising a nucleic acid sequence encoding SEQ ID NO: 26, a DNA plasmid encoding a prostate specific membrane antigen (PSMA) comprising a nucleic acid sequence encoding SEQ ID NO: 28, and a DNA plasmid comprising a nucleic acid sequence encoding the p35 subunit and the p40 subunit of interleukin-12 (IL-12) in the

manufacture of a medicament for combination therapy of newly diagnosed glioblastoma, wherein the anti-PD-1 antibody comprises:  
three heavy chain complementarity determining regions (HCDR1, HCDR2 and HCDR3) and three light chain complementarity determining regions (LCDR1, LCDR2 and LCDR3), wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 3, HCDR2 comprises the amino acid sequence of SEQ ID NO: 4, HCDR3 comprises the amino acid sequence of SEQ ID NO: 5, LCDR1 comprises the amino acid sequence of SEQ ID NO: 6, LCDR2 comprises the amino acid sequence of SEQ ID NO: 7, and LCDR3 comprises the amino acid sequence of SEQ ID NO: 8; a HCVR comprising the amino acid sequence of SEQ ID NO: 1 and a LCVR comprising the amino acid sequence of SEQ ID NO: 2; or  
a heavy chain comprising the amino acid sequence of SEQ ID NO: 9 and a light chain comprising the amino acid sequence of SEQ ID NO: 10.

3. The use according to claim 1 or claim 2, wherein the glioblastoma is characterized by an unmethylated O6- methylguanine methyltransferase (MGMT) gene promoter.

4. The use according to claim 1 or claim 2, wherein the glioblastoma is characterized by a methylated O6- methylguanine methyltransferase (MGMT) gene promoter.

5. The use according to any one of claims 1 to 4, wherein the anti-PD-1 antibody is prepared for intravenous or subcutaneous administration.

6. The use according to any one of claims 1 to 5, comprising 350 mg of the anti-PD-1 antibody.

7. The use according to any one of claims 1 to 6, wherein:

the IL12 p35 subunit comprises the amino acid sequence of SEQ ID NO: 23;

the IL12 p40 subunit comprises the amino acid sequence of SEQ ID NO: 25;

the IL12 p35 subunit comprises the amino acid sequence of SEQ ID NO: 23 and the IL12 p40 subunit comprises the amino acid sequence of SEQ ID NO: 25;

the nucleic acid sequence encoding the IL12 p35 subunit comprises SEQ ID NO: 22;

the nucleic acid sequence encoding the IL12 p40 subunit comprises SEQ ID NO: 24; or

the nucleic acid sequence encoding the IL12 p35 subunit comprises SEQ ID NO: 22 and the nucleic acid sequence encoding the IL12 p40 subunit comprises SEQ ID NO: 24.

8. The use according to any one of claims 1 to 7, wherein:

the nucleic acid sequence encoding the hTERT antigen comprises SEQ ID NO: 19;

the nucleic acid sequence encoding the WT-1 antigen comprises SEQ ID NO: 27; and/or

the nucleic acid sequence encoding PSMA comprises SEQ ID NO: 29.

9. The use according to claim 8, wherein the immunogenic composition comprises 3 mg of the DNA plasmid encoding hTERT, 3 mg of the DNA plasmid encoding PSMA, 3 mg of the DNA plasmid encoding WT-1, and 1 mg of the plasmid encoding IL-12.

10. The use according to any one of claims 1 to 9, wherein the immunogenic composition is to be administered by electroporation and intramuscular injection.

11. The use according to any one of claims 1 to 10, wherein the treatment further comprises radiation therapy.

12. The use according to claim 11, wherein the radiation therapy comprises 20- 50 Gy.

13. The use according to claim 12, wherein the radiation therapy is fractionated radiation therapy.

14. The use according to claim 13, wherein the fractionated radiation therapy comprises 2-20 fractions.

15. The use according to claim 14, wherein the fractionated radiation therapy comprises 40 Gy in 15 fractions.

16. The use according to any one of claims 1 to 15, wherein the treatment further comprises temozolomide.

17. The use according to claim 16, comprising 75 mg/m<sup>2</sup> temozolomide.