

What is claimed:

1. An immunogenic composition comprising human telomerase reverse transcriptase (hTERT), Wilms Tumor-1 (WT-1), and prostate specific membrane antigen (PSMA).
2. The immunogenic composition of claim 1 wherein hTERT is encoded by a DNA plasmid, WT-1 is encoded by a DNA plasmid, and/or PSMA is encoded by a DNA plasmid.
3. The immunogenic composition of claim 2, wherein hTERT, WT-1, and PSMA are encoded by the same DNA plasmid; wherein two of hTERT, WT-1, and PSMA are encoded by the same DNA plasmid; or wherein hTERT, WT-1, and PSMA are encoded by different DNA plasmids.

4. The immunogenic composition of any preceding claim wherein:

the hTERT comprises the amino acid sequence of SEQ ID NO: 20 or is encoded by the nucleic acid sequence of SEQ ID NO: 19;

the WT-1 comprises the amino acid sequence of SEQ ID NO: 26 or is encoded by the nucleic acid sequence of SEQ ID NO: 27; and/or

the PSMA comprises the amino acid sequence of SEQ ID NO: 28 or is encoded by the nucleic acid sequence of SEQ ID NO: 29.

5. A vaccine comprising:

the immunogenic composition of any preceding claim;

IL12; and

an anti-programmed cell death receptor 1 (PD-1) antibody.

6. The vaccine of claim 5, wherein the anti-PD-1 antibody:

comprises the heavy chain complementarity determining regions (HCDR1, HCDR2 and HCDR3) of a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 1 and three light chain complementarity determining regions (LCDR1, LCDR2 and LCDR3) of a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 2;

comprises three HCDRs (HCDR1, HCDR2 and HCDR3) and three LCDRs (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;
comprises a HCVR with 90% sequence identity to SEQ ID NO: 1;
comprises a LCVR with 90% sequence identity to SEQ ID NO: 2;
comprises a HCVR with 90% sequence identity to SEQ ID NO: 1 and a LCVR with 90% sequence identity to SEQ ID NO: 2;
comprises 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;
comprises 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;
is an IgG4 antibody; or
is REGN2810 or a biosimilar or bioequivalent thereof.
7. The vaccine of claim 5 or claim 6, wherein the IL-12 is encoded by a DNA plasmid.
8. The vaccine of claim 5, claim 6, or claim 7, 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 IL12 p35 subunit is encoded by the nucleic acid sequence of SEQ ID NO: 22;
the IL12 p40 subunit is encoded by the nucleic acid sequence of SEQ ID NO: 24; or
the IL12 p35 subunit is encoded by the nucleic acid sequence of SEQ ID NO: 22 and the IL12 p40 subunit is encoded by the nucleic acid sequence of SEQ ID NO: 24.
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, or both.
9. A method of treating brain cancer in a subject, comprising administering to the subject:
interleukin-12 (IL-12);
an immunogenic composition of human telomerase reverse transcriptase (hTERT), Wilms Tumor-1 (WT-1), and prostate specific membrane antigen (PSMA); and
an anti-programmed cell death receptor 1 (PD-1) antibody.
10. A vaccine for use in treating brain cancer in a subject, wherein the vaccine comprises:
an immunogenic composition of human telomerase reverse transcriptase (hTERT), Wilms Tumor-1 (WT-1), and prostate specific membrane antigen (PSMA); and
an anti-programmed cell death receptor 1 (PD-1) antibody.

11. The method of claim 9 or vaccine for use of claim 10 wherein the subject has an unmethylated O6-methylguanine methyltransferase (MGMT) gene promoter.
12. The method of claim 9 or vaccine for use of claim 10 wherein the subject has a methylated O6-methylguanine methyltransferase (MGMT) gene promoter.
13. The method or vaccine for use of any one of claims 9 to 12, wherein IL-12 is encoded by a DNA plasmid.
14. The method or vaccine for use of any one of claims 9 to 13, wherein hTERT is encoded by a DNA plasmid, WT-1 is encoded by a DNA plasmid, and/or PSMA is encoded by a DNA plasmid.
15. The method or vaccine for use of claim 14, wherein hTERT, WT-1, and PSMA are encoded by the same DNA plasmid; two of hTERT, WT-1, and PSMA are encoded by the same DNA plasmid; or wherein hTERT, WT-1, and PSMA are each encoded by a different DNA plasmid.
16. The method or vaccine for use of any one of claims 9 to 15, wherein the anti-PD-1 antibody:
 - comprises the heavy chain complementarity determining regions (HCDR1, HCDR2 and HCDR3) of a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 1 and three light chain complementarity determining regions (LCDR1, LCDR2 and LCDR3) of a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 2;
 - comprises three HCDRs (HCDR1, HCDR2 and HCDR3) and three LCDRs (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;
 - comprises a HCVR with 90% sequence identity to SEQ ID NO: 1;
 - comprises a LCVR with 90% sequence identity to SEQ ID NO: 2;
 - comprises a HCVR with 90% sequence identity to SEQ ID NO: 1 and a LCVR with 90% sequence identity to SEQ ID NO: 2;
 - comprises 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;
 - comprises 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;

is an IgG4 antibody; or
is REGN2810 or a biosimilar or bioequivalent thereof.

17. The method or vaccine for use of any one of claims 9 to 16 wherein the anti-PD-1 antibody is administered intravenously or subcutaneously.
18. The method or vaccine for use of any one of claims 9 to 17 wherein 350 mg of the anti-PD-1 antibody is administered every three weeks.
19. The method or vaccine for use of any one of claims 9 to 18, 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 IL12 p35 subunit is encoded by the nucleic acid sequence of SEQ ID NO: 22;
 - the IL12 p40 subunit is encoded by the nucleic acid sequence of SEQ ID NO: 24; or
 - the IL12 p35 subunit is encoded by the nucleic acid sequence of SEQ ID NO: 22 and the IL12 p40 subunit is encoded by the nucleic acid sequence of SEQ ID NO: 24.
20. The method or vaccine for use of any one of claims 9 to 19 wherein
 - the hTERT comprises the amino acid sequence of SEQ ID NO: 20 or is encoded by the nucleic acid sequence of SEQ ID NO: 19;
 - the WT-1 comprises the amino acid sequence of SEQ ID NO: 26 or is encoded by the nucleic acid sequence of SEQ ID NO: 27; and/or
 - the PSMA comprises the amino acid sequence of SEQ ID NO: 28 or is encoded by the nucleic acid sequence of SEQ ID NO: 29.
21. The method or vaccine for use of claim 20, comprising the method comprises administering to the subject, or wherein the vaccine 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.
22. The method or vaccine for use of any one of claims 9 to 21, wherein the IL-12 and the immunogenic composition are co-administered by intramuscular injection every three weeks for four doses and then every nine weeks.

23. The method or vaccine for use of claim 22 further comprising electroporation following each intramuscular injection.
24. The method or vaccine for use of any one of claims 9 to 23, further comprising administering to the subject one or more doses of radiation therapy.
25. The method or vaccine for use of claim 24, wherein each dose of radiation therapy comprises 20-50 Gy.
26. The method or vaccine for use of claim 25, wherein the radiation therapy is fractionated radiation therapy.
27. The method or vaccine for use of claim 26, wherein the fractionated radiation therapy comprises 2-20 fractions.
28. The method or vaccine for use of claim 27, wherein the fractionated radiation therapy comprises 40 Gy in 15 fractions.
29. The method or vaccine for use of claim 28, wherein the fractionated radiotherapy is given over 21 consecutive days.
30. The method or vaccine for use of any one of claims 9 to 29, further comprising administering to the subject one or more doses of a chemotherapeutic agent; optionally wherein the chemotherapeutic agent is temozolomide.
31. The method or vaccine for use of claim 30 comprising administering 75 mg/m² temozolomide to the subject daily for 21 consecutive days with the fractionated radiotherapy.
32. The method or vaccine for use of claim 30 or claim 31, further comprising administering temozolomide maintenance therapy to the subject if the subject has a tumor having a methylated MGMT promoter.
33. The method or vaccine for use of any one of claims 9 to 32, wherein the brain cancer is glioblastoma.
34. The method or vaccine for use according to claim 33, wherein the brain cancer is MGMT-methylated glioblastoma.

35. The method or vaccine for use according to claim 33, wherein the brain cancer is MGMT-unmethylated glioblastoma.
36. The method or vaccine for use of any one of claims 9 to 35, wherein the method is clinically proven safe, clinically proven effective, or both.
37. The immunologic composition according to any one of claims 1 to 4 for use in the manufacture of a medicament for treating a brain cancer.
38. The immunologic composition for use according to claim 37, wherein the brain cancer is glioblastoma.
39. The immunologic composition for use according to claim 38, wherein the brain cancer is MGMT-methylated glioblastoma.
40. The immunologic composition for use according to claim 38, wherein the brain cancer is MGMT-unmethylated glioblastoma.