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Declarations under Rule 4.17:

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- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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(54) **Title:** COMBINATION THERAPY TO TREAT BRAIN CANCER

(57) **Abstract:** Provided herein are methods of treating brain cancer in a subject, comprising evaluating one or more biological samples from a subject who has brain cancer for the presence of a miRNAs and administering 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 to said subject if the subject has an increased expression level of the miR-331-3p miRNA or isomiRs thereof and the miR-1537-3p miRNA or isomiRs thereof relative to a control population of subjects. Also provided herein are methods of treating brain cancer in a subject, comprising measuring an expression level of at least one mRNA biomarker selected from SYNGR3, OTX1, GABBR2, LHX1, CADM3, MLLT11, MNX1, GRB14, SLC34A2, PHYHIP, WNT10B, SLC17A6, CRLF1, HOXD13, TGFβR3, UBA7, SFRP4, or any combination thereof, in a tumor sample from a subject and administering IL-12; an immunogenic composition hTERT, WT-1, and PSMA; and an anti-PD-1 antibody to said subject if the expression level of SYNGR3, OTX1, GABBR2, LHX1, CADM3, MLLT11, MNX1, GRB14, SLC34A2, PHYHIP, WNT10B, SLC17A6, CRLF1 and HOXD13 is decreased or if the expression level of TGFβR3, UBA7, SFRP4 is increased.



WO 2023/019240 A2