MB-101

MB-101 Glioblastoma multiforme (GBM) is the most common brain and central nervous system (CNS) cancer, accounting for 15.1% of all primary brain tumors, and 55.1% of all gliomas. There are an estimated 12,120 new glioblastoma cases predicted in 2016 in the U.S. Malignant brain tumors are the most common cause of cancer-related deaths in adolescents and young adults aged 15-39 and the most common cancer occurring among 15-19 year olds in the U.S. While GBM is a rare disease (2-3 cases per 100,000 person life years in U.S. and E.U.), it is quite lethal with 5-year survival rates historically less than 10%. Chemotherapy with temozolomide and radiation are shown to extend mean overall survival from 4.5 to 15 months, while surgery remains the standard of care. GBM remains difficult to treat due to the inherent resistance of the tumor to conventional therapies.

Immunotherapy approaches targeting brain tumors offer promise over conventional treatments. IL13Rα2 is an attractive target for CAR T therapy as it has limited expression in normal tissue but is over-expressed on the surface of greater than 50% of GBM's. CAR T cells are designed to express membrane-tethered IL-13 receptor ligand (IL-13) with high affinity for IL13Rα2 and reduced binding to IL13Rα1 in order to reduce healthy tissue targeting.

We are developing an optimized CAR T product incorporating enhancements in CAR design and T cell engineering to improve antitumor potency and T cell persistence. We include a second generation hinge optimized CAR containing mutations in the IgG4 linker to reduce off target Fc interactions as well as the 41BB (CD137) co-stimulatory signaling domain for improved survival and maintenance of memory T cells as well as extracellular domain of CD20 as a selection/safety marker. In order to further improve persistence, central memory T cells (TCM) are isolated and enriched. The manufacturing process limits ex vivo expansion in order to reduce T cell exhaustion and maintain a TCM phenotype.

In collaboration with the COH, we have an on-going phase I clinical study to assess the feasibility and safety of using TCM enriched IL13Rα2-specific CAR engineered T cells and are currently treating patients with recurrent/refractory GBM. We will assess the T cell persistence and determine the potential immunogenicity of the cells to determine a recommended phase II dose.