CF33-CD19T ONCOLYTIC VIRUS (ONCARLYTICS) TARGETS HEPATOCELLULAR CARCINOMA (HCC) AND IN COMBINATION WITH ARTEMIS® CD19 T CELLS RESULTS IN SIGNIFICANT TUMOR KILLING

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Background Hepatocellular carcinoma (HCC) is the second leading cause of cancer-related deaths in the world with a 5-year survival rate at less than 12%. Currently, curative treatments include ablation, surgical resection, and liver transplantation. For majority of patients with advanced-stage disease, treatment with agents such as sorafenib, lenvatinib, and atezolizumab/bevacizumab and other investigational agents yield modest success rates and justify the need for further development of new therapies. T cell therapy against HCC targeting antigens such as alpha-fetoprotein (AFP) and glypican-3 (GPC-3) have shown some efficacy in clinical trials with conventional challenges against solid tumors including antigen heterogeneity, the immunosuppressive tumor microenvironment, and off-tumor on-target activity. Therefore, novel therapies are desperately needed to improve clinical outcomes for patients with HCC.

Methods We have developed a novel chimeric vaccinia-based oncolytic virus, called onCARlytics (CF33-CD19t, Imugene Limited in collaboration with City of Hope), that delivers a non-signaling, truncated CD19t (CD19t) antigen to tumors that allows for targeting of solid tumors by CD19 T cells. Once the CD19 is expressed on solid tumor cells, to enable cell killing, we have combined onCARlytics with CD19 ARTEMIS® T cell, a CD19-targeting adoptive engineered T cell powered by the ARTEMIS® antibody-T-cell receptor (AbTCR) platform (Eureka Therapeutics, Inc). The ARTEMIS® AbTCR distinguishes itself from CAR by recruiting the endogenous CD3 complex and utilizing the same activation and regulatory signaling pathways employed by natural TCRs, which enables both potent killing activity against CD19+ tumor cells and a superior safety profile.

Results When administrated after onCARlytics, CD19 ARTEMIS® T cells were able to induce potent cytolytic activity against HCC tumor cells and demonstrated robust in vivo anti-tumor efficacy against human HCC tumor xenografts.

Conclusions In summary, ARTEMIS® CD19 T cells combined with onCARlytics is a potentially effective immunotherapy strategy for the treatment of patients with HCC and can be applied to other solid tumors.