M032 is a second-generation oncolytic herpes simplex virus (oHSV) that selectively replicates in tumor cells. M032 kills tumor cells directly through oncolytic replication and then proceeds to infect tumor cells in proximity, continuing the process of tumor destruction. In addition to this direct oncolytic activity, the virus carries a therapeutic payload-thus acting as a gene therapy vector-and causes the tumor cell to synthesize and secrete the immunity-stimulating protein interleukin 12 (IL-12) before cell death.

Human IL-12 is expressed and promotes an immune response against surviving tumor cells, increasing the antitumor effect of the therapy. IL-12 also produces an antiangiogenic effect, by interfering with the production of new tumor blood vessels necessary for tumor growth. Thus, M032 oHSV exerts antitumor effects through three distinct potential mechanisms. The virus has also been genetically engineered to minimize toxic effects for the patient. Preclinical animal models support the safety of intracranial inoculation with M032 in two relevant species (mouse and nonhuman primate). This clinical protocol outlines the dose-escalating phase I study for evaluation of M032 in patients with recurrent or progressive malignant glioma [1].

1)
Patel DM, Foreman PM, Nabors LB, Riley KO, Gillespie GY, Markert JM. Design of a Phase I Clinical Trial to Evaluate M032, a Genetically Engineered HSV-1 Expressing IL-12, in Patients with Recurrent/Progressive Glioblastoma Multiforme, Anaplastic Astrocytoma, or Gliosarcoma. Hum Gene Ther Clin Dev. 2016 Jun;27(2):69-78. doi: 10.1089/humc.2016.031. PubMed PMID: 27314913; PubMed Central PMCID: PMC4932657.