

**Project Title:** Gene Therapy for the Treatment of Malignant Brain Tumors with In Vivo Tumor Transduction with the Herpes Thymidine Kinase Gene/Ganciclovir System.

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### **Non-technical Abstract**

We have investigated the possibility of transferring a “sensitivity” gene into a growing brain tumor. The purpose is to make the tumor sensitive to a type of chemotherapy that is relatively non-toxic to the rest of the body. The gene we have selected is the Herpes Simplex-thymidine kinase (HS-tk) gene. Herpes Simplex is a virus that can be killed by a drug called ganciclovir (GCV). By transferring the HS-tk gene into the tumor, using a disabled mouse virus called a “vector”, we then essentially convert the tumor to be like a herpes virus and now the tumor can be killed with GCV.

Experiments in rats have shown that the direct injection of mouse cells producing a HS-tk vector into a growing brain tumor can result in complete destruction of the tumor with GCV therapy. We found no evidence of spread of the virus to the normal brain tissue or to other parts of the body. Based upon these findings, an initial trial is underway at the National Institutes of Health (NIH). To date, one person has been treated without evidence of toxicity. We now proposed a second human clinical trial for patients who are currently ineligible for treatment in the NIH trial due to the large size of their tumor. In this study, patients will undergo surgery to remove as much of the tumor as possible followed by repeated treatments of HS-tk vector-producer cells (VPC) into growing their human brain tumors in an attempt to induce regression of the tumor with GCV therapy. The patient population consists of individuals who have failed standard therapy and have recurrent primary or metastatic brain tumors with an expected survival of weeks to a few months.