

## Section 1. Scientific Abstract

Malignant melanoma has one of the most rapidly increasing incidence rates in the U.S. Early detection and surgical excision can be curative, but once the tumor spreads beyond the skin it is one of the most deadly forms of cancer. There are currently no completely effective therapies for advanced (metastatic) disease and 10 year survival rates for these patients are very low. The objectives of the clinical program are to conduct Phase I trials of a new approach to gene therapy for the treatment of metastatic melanoma, to monitor for tumor responses attributable to treatment, and develop and characterize *in vitro* assays which can be used to identify those patients most likely to respond to this form of immuno-gene therapy. The genes selected for use in the trial are the gene for human interleukin-2 (hIL-2) and the gene for the superantigen staphylococcus enterotoxin B (SEB). In on-going preclinical trials conducted by the investigators of our laboratory program, this combination of therapeutic genes is more effective at inducing clinically significant tumor immunity than either gene used alone. The method used for gene transfection, polycationic lipid mediated DNA transfection, has been tested in animals and found to be without toxicity and effective.

The proposed phase I trial is a dose escalation study designed to determine the safety and identify toxicities associated with the direct injection of plasmid DNA coding for hIL-2 and SEB into cutaneous melanoma metastases. In addition to assessing safety and toxicity, clinical analysis of treated and untreated tumors will allow the determination of whether the proposed treatments have an effect on local or distant metastases. An understanding of how expressing this gene locally leads to the elimination of tumor tolerance and the development of cytotoxic immunity may enable the design of more effective strategies for the use of these treatments in the clinical setting.