

Section 2. Non-Technical Abstract

Malignant melanoma has been increasing rapidly in the U.S. Early detection and surgical excision of the tumor 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 patients are very low. The objectives of the clinical program are to conduct safety studies (Phase I) in human patients of a new gene therapy for the treatment of metastatic melanoma. Additionally, data will be collected to monitor tumor responses attributable to treatment, and information will be collected on assays which can later be used to identify patients most likely to respond to this form of treatment. The genes selected for use in the trial encode for the human interleukin-2 (hIL-2) protein and the superantigen staphylococcus enterotoxin B (SEB) protein. After the genes are injected into the tumors, these proteins will be produced by the tumor cells. These proteins will then circulate through the body and should lead to stimulation of an immune response toward the tumor cells themselves, "tumor immunity". In on-going animal studies conducted by our laboratory, this combination of hIL-2 and SEB proteins is more effective at inducing clinically significant tumor immunity than either gene used alone.

The proposed Phase I trial is designed to determine the safety and identify toxicities associated with the direct injection of increasing doses of hIL-2 and SEB genes into melanoma tumors found in the skin. In addition to assessing safety and toxicity, clinical analysis of treated and untreated tumors will provide information on the local or distant growth (metastases) affected by the treatments. An understanding of how expressing this gene locally leads to the body's attack on the tumor may enable us to design other effective treatment strategies.