

## M-I

### 1. Scientific Abstract

Lung cancer is the most lethal malignancy in the United States, claiming over 150,000 lives each year and with an overall 5-year survival of 12 – 14%. Novel therapeutic approaches for this disease are needed. One possible approach is the use of antigen-specific cancer vaccines. Of several categories of tumor antigens, cancer-testis (CT) antigens, normally expressed only in germ cells in the testis and in various types of cancers, are highly attractive vaccine targets. NY-ESO-1 is the most immunogenic CT antigen known to date, eliciting spontaneous humoral and cellular immune responses in cancer patients with NY-ESO-1 positive tumors. NY-ESO-1 vaccine trials carried out using peptides, protein and DNA in viral vectors have shown NY-ESO-1 specific immune responses following vaccination. In this proposed phase I trial, we plan to immunize eligible lung cancer patients with NY-ESO-1 plasmid DNA (pPJV7611) cancer vaccine, delivered by PowderJect® device. PowderJect is a particle-mediated epidermal delivery (PMED) system in which protein or DNA vaccines are delivered intraepidermally using a helium-powered delivery system. This delivery method has been shown to successfully induce antibody and T cell responses against hepatitis B antigen in humans. We hypothesize that NY-ESO-1 plasmid DNA (pPJV7611) cancer vaccine, consisting of plasmid (pPJV7611) containing NY-ESO-1 cDNA coated onto microscopic gold particles will be able to deliver NY-ESO-1 plasmid cDNA to Langerhans cells and keratinocytes in the epidermal layer of the skin, and these professional and non-professional antigen-presenting cells will process the NY-ESO-1 protein and present the NY-ESO-1 peptide/HLA complexes to CD4+ and CD8+ T cells leading to humoral and cell-mediated immune responses that are potentially stronger than those induced with other antigen forms and delivery methods.

The primary objective of the study is to evaluate the safety of the NY-ESO-1 plasmid DNA (pPJV7611) cancer vaccine. The study will also monitor the immune response to NY-ESO-1 when administered as PMED. Assessments will be: humoral responses by ELISA to detect NY-ESO-1 serum antibody; and cellular immune response, *in vitro*, by the generation of NY-ESO-1 specific CD8+ T-cells and CD4+ T-cells. Although tumor response to vaccination is not a specific aim of this trial, responses in patients with measurable disease will be recorded. Subsequent Phase II trials in lung cancer and other tumor types with appropriate dose will be planned.