

## SECTION 2 NON-TECHNICAL ABSTRACT

Prostate cancer is the most commonly diagnosed malignancy in men. Although conventional therapies (surgery and radiation therapy) produce high cure rates of early stage prostate cancer, many tumors recur. Unfortunately, patients with locally recurrent prostate cancer have no therapeutic options that have a high likelihood of eliminating the cancer with a reasonable degree of safety.

In light of this, we have developed a novel, multi-faceted gene therapy approach for the treatment of prostate cancer. Our approach utilizes a modified cold virus, called an adenovirus, to deliver a pair of therapeutic genes to prostate tumors. The adenovirus itself generates a potent anti-tumor effect by preferentially replicating in and destroying prostate tumor cells. The tumor-specific killing effect of the virus can be enhanced by combining it with a form of tumor-targeted chemotherapy called suicide gene therapy. Activation of the suicide genes renders malignant cells sensitive to specific chemical agents (prodrugs) and sensitizes them to the therapeutic effects of radiation. We have conducted two prostate cancer clinical trials to evaluate the safety of this gene therapy approach without and with radiation therapy. The treatment was well tolerated and showed signs of anti-tumor activity.

The study described here is a logical follow-up of our two previous clinical trials. Using a new and improved adenovirus, we will first determine whether combining the gene therapy with radiation therapy is safe to use in men with locally recurrent prostate cancer. If it is, we will conduct a small trial to assess how effective this therapy is at eliminating the cancer. Our hope is that the gene therapy when combined with radiation therapy will eliminate the cancer in  $\geq 20\%$  of patients. If it does, we believe this combined approach will provide a new therapeutic option for patients with locally recurrent prostate cancer.