

## 2.0 NON-TECHNICAL ABSTRACT

The abnormal proliferation of cells involved in the formation and growth of cancers is under the control of abnormal genes called oncogenes. A gene called E1A may be able to stop the growth of cancer cells by inducing programmed cell death or making cancer cells more sensitive to conventional chemotherapeutic drugs. The E1A gene is obtained from a small part of the DNA of a common virus and can be introduced with a gene delivery system composed of lipids (or fats) into cancer cells maintained in culture and into cancer cells in animal models. Pre-clinical toxicology studies have indicated that there were no acute toxicities associated with either E1A alone or in combination with chemotherapy. When administered in combination with standard chemotherapy agents (paclitaxel, cisplatin and/or carboplatin) to the tumor in an animal model of ovarian cancer, the E1A Lipid Complex produced tumor growth inhibition and extension of survival of treated mice compared to untreated control mice.

E1A-Lipid Complex (1:1) has been administered by direct injection into tumors in more than 35 patients with breast or head and neck cancer in a completed multi-dose phase 1 clinical trial and an ongoing multi-dose phase 2 clinical trial. These studies have demonstrated safety of the agent.

E1A-Lipid Complex (1:10) was administered by intraperitoneal infusion to 12 patients with advanced ovarian cancer and by intrapleural infusion to six patients with metastatic breast cancer in a phase 1 clinical trial. Dose limiting toxicity (acute abdominal pain, nausea, and vomiting) was observed in the ovarian cancer (intraperitoneal) patient cohort; all patients had advanced disease and significant coexisting morbidity. In an international study conducted in the United Kingdom, E1A-Lipid Complex (1:10) has been administered intraperitoneally to eight additional patients with advanced ovarian cancer. Repeat treatment of these patients was accomplished with acceptable toxicity by premedicating patients for symptoms.

The Phase I study described in this document will be conducted in epithelial ovarian cancer in patients with optimal residual disease by intraperitoneal (IP) infusion in conjunction with combination chemotherapy. The study will evaluate safety, toxicity, and establish the maximum tolerated dose (MTD) of E1A-Lipid Complex (1:3) administered by intraperitoneal infusion in a regimen with combination chemotherapy.