

## 2.0 NON-TECHNICAL ABSTRACT

Ovarian cancer is the fourth most common cause of cancer death among women in the United States. Approximately one in seventy women will develop ovarian cancer in her lifetime. If diagnosed early and treated before the cancer has spread, 90% of women will live for more than five years. However, most women are diagnosed with advanced stages of disease. Overall, only 42% of women diagnosed with ovarian cancer will live for more than five years. Clearly, new therapies are needed.

A gene called E1A may be able to stop the growth of cancer by making the tumor cells die or making them more sensitive to other cancer treatments like chemotherapy or radiation therapy. The E1A gene is obtained from a small part of the DNA of a common cold virus. It can be introduced into tumor cells by combining it with some lipid or fat, and then injecting it directly into tumors or into body cavities where tumors might be present. In this case, the combination is called tgDCC-E1A. tgDCC-E1A has been given to mice in experimental models of ovarian cancer with and without chemotherapy. It has been shown to be safe, to make the tumors smaller, and to help the mice with cancer live longer.

tgDCC-E1A has been given via infusion into the abdomen to over 40 women with ovarian cancer. The first studies were conducted using tgDCC-E1A alone. Side effects consisting of nausea, vomiting, abdominal pain, and fever developed in patients treated at the highest doses. A more recent study has been conducted using tgDCC-E1A in combination with a certain chemotherapy regimen which combined paclitaxel delivered intravenously and cisplatin delivered by infusion into the abdomen. In that study, subjects tolerated higher doses of tgDCC-E1A. Some symptoms of nausea, vomiting and abdominal pain were seen, but have not been as severe.

Since the most recent study of tgDCC-E1A with chemotherapy was designed, the standard treatment of ovarian cancer has evolved. Women who develop recurrent ovarian cancer more than six months after their last treatment are now treated with a related intravenous chemotherapy drug called carboplatin.

Because the standard of care for ovarian cancer has evolved, Targeted Genetics Corporation would like to study tgDCC-E1A in combination with carboplatin. In this study, up to 18 women with recurrent ovarian cancer will receive an infusion of tgDCC-E1A into the abdomen and an infusion of carboplatin into the vein once every 28 days for up to

five cycles. Subjects will be carefully monitored for safety. Groups of three study subjects each will be administered tgDCC-E1A at one of three doses until the highest safe dose can be determined. Determination of the highest safe dose will allow larger studies to be conducted to determine if tgDCC-E1A plus carboplatin is effective in treating women with ovarian cancer.