AbstractID: 8531 Title: Physics Support for Intraprostatic Treatment of Patients with Locally Recurrent Prostate Cancer with the PSA-Activated Protoxin PRX302

Purpose: PRX302 is a protoxin in which the native furin-cleaved pro-domain has been modified to be proteolytically cleaved by PSA. PSA releases a C-terminal inhibitory peptide to generate the active toxin, that inserts into the cell membrane to form 1.5 nm pores inducing ion leakage, loss of membrane integrity and cell death. We report on the physics support of a Phase I clinical trial of administration of PRX302 in patients with locally recurrent prostate cancer after radiation therapy. **Method and Materials:** 24 patients were enrolled. Dose-escalation consisted of seven cohorts of 3 to 6 patients, each receiving a dose between 0.03 and 3 μg of PRX302/g of prostate. PRX302 was delivered as a multi-deposit, trans-rectal ultrasound-guided, transperineal injection using a modified brachytherapy technique. Images were acquired with a Hawk Type 2102 EXL (B&K Medical, Herlev, Denmark) ultrasonic unit using a rectal probe. The ultrasound display was calibrated against the needle template before each procedure. Commercial treatment planning software (Variseed. Varian Medical Systems) was adopted to select the location and concentration of the injections. **Results:** The maximal tolerated dose was not reached despite a 100-fold dose increase. No drug-related SAEs were observed. Preliminary data suggested biological activity of PRX302. PSA levels decreased in 63% of patients. The percentage of positive prostate biopsy cores post-therapy decreased in 75% of patients with 3 patients having no positive cores at 30 days following PRX302 therapy. **Conclusions:** Active medical physics participation in these clinical trials contributed to the preliminary findings that transperineal administration of PRX302 is safe and well tolerated in patients with localized recurrent prostate cancer. MTD was not reached and PRX302 showed convincing signs of biological activity that will be further evaluated in future efficacy studies planned with medical physics input.

Conflict of Interest: This Trial was sponsored by Protox Therapeutics, Inc.