A Phase I Trial of AEZS-108 (AN-152) in Castration- and Taxane-Resistant Prostate Cancer

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ABSTRACT

Background: Options for patients with castration-resistant prostate cancer (CRPC) are limited and targeted therapies that directly target the LHRH receptor (LHRH-R) are currently not available. The objective of this study was to evaluate the safety and efficacy of AEZS-108 in men with castration-resistant prostate cancer (CRPC). Preliminary studies will identify predictive markers, including LHRH-R expression, in human castration-resistant prostate cancer (CRPC) cells. In addition, an LHRH-R inhibitor is being tested in male athymic mice with human prostate cancer (HT149 and PC3) and human breast cancer (MCF-7) xenografts.

Methods: This is a single-arm study with a phase I/II in leading (testing dose levels) to phase II clinical trial. The study began in November 2015 and is ongoing. Eligible criteria include adequate organ function and progression of disease despite prior therapy with an LHRH agonist and at least one taxane-based regimen. Patients will be required to discontinue LHRH agonist use except for nonselective receptor downregulation. The primary endpoint is to determine the phase I recommended dose in male patients who meet all eligibility criteria.

RESULTS: In total, 13 patients have been enrolled. The first two planned dose levels had no limiting toxicities observed. Two patients on the third dose level experienced a dose-limiting toxicity (DLT) at that dose level. Treatment with AEZS-108 was well tolerated overall. AEZS-108-related adverse events were generally well managed with dose adjustments or dose interruptions. The DLT observed was fatigue, which occurred at the 48-hour postinfusion timepoint. AEZS-108 administration was well tolerated overall. AEZS-108-related adverse events were generally well managed with dose adjustments or dose interruptions. The DLT observed was fatigue, which occurred at the 48-hour postinfusion timepoint.

CONCLUSIONS: AEZS-108 has demonstrated acceptable safety in patients with castration-resistant prostate cancer. AEZS-108 administration was well tolerated overall. AEZS-108-related adverse events were generally well managed with dose adjustments or dose interruptions. The DLT observed was fatigue, which occurred at the 48-hour postinfusion timepoint. AEZS-108 administration was well tolerated overall. AEZS-108-related adverse events were generally well managed with dose adjustments or dose interruptions. The DLT observed was fatigue, which occurred at the 48-hour postinfusion timepoint.