

# Interim results of a phase I clinical trial administering Zyflamend® to subjects with high-grade prostatic intraepithelial neoplasia

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**Background:** Subjects diagnosed with prostatic intraepithelial neoplasia (PIN) at prostate biopsy are at increased risk of developing prostate cancer on later biopsies. We initiated a phase I clinical trial to assess the safety and efficacy of the novel herbal agent, Zyflamend®, as a potential prostate cancer chemopreventive in high-risk subjects with PIN.

**Methods:** Men ages 40-75 diagnosed with high-grade PIN (without prostate cancer) on biopsy within the last six months were eligible for the study. Enrolled patients were assigned to one of eight treatment groups, with successive dose-escalation occurring in each group. Patients were evaluated every three months for eighteen months. At each three month evaluation, subjects received a physical exam including blood draws in order to monitor safety and toxicity, measure fluctuations in prostate specific antigen (PSA) and testosterone, and monitor a variety of inflammatory markers including NF- $\kappa$ B, COX-2, IL-6, and thromboxanes. At the 6, 12 and 18 month evaluations, a 12-core transrectal ultrasound guided biopsy of the prostate was performed. Biopsy tissue was evaluated for the presence of PIN and/or adenocarcinoma of the prostate and then stained for the presence of the abovementioned inflammatory biomarkers. A NCI common terminology criteria for adverse events (v3.0) based questionnaire was used to monitor side effects. Endpoints are completion of the 18 month protocol without adenocarcinoma or diagnosis of adenocarcinoma prior to 18 months.

**Results:** To date, July 2006, all 29 patients have been enrolled. The median patient age is 65.1 years with a median PSA level of 6.8. There have been no adverse events reported or toxicities apparent. None of the patients have experienced any change in serum chemistries, and there have been no EKG changes. Five patients (20%) have complained of grade I dyspepsia resolving spontaneously without intervention. Preliminary results include a total of 34 biopsies performed in 20 patients. Of 34 biopsies completed, 30 revealed no evidence of cancer (88% negative biopsy rate). Of the 4 cancers detected, all were Gleason 6 in less than 5% of the cores 21 of the 34(62%) biopsies revealed no cancer and no PIN. Overall, 50% of the patients on trial have had a decrease in serum PSA values.

**Conclusions:** The novel herbal anti-inflammatory, Zyflamend®, appears to be associated with minimal toxicity and no serious adverse events when administered orally. Initial biopsy results indicate one of the lowest progression rates in the literature. Immunohistochemical staining of the 18-month biopsies will be presented.