Protocol Title: Zonisamide as a New Treatment for Co-occurring Post-Traumatic Stress-Disorder (PTSD) and Alcohol Use Disorder (AUD)

Objective: To determine if zonisamide is a safe and efficacious treatment for PTSD and AUD.

Hypothesis: We hypothesize that treatment with zonisamide will decrease both PTSD symptoms and the proportion of heavy drinking days, compared to treatment with placebo.

Primary Inclusion Criteria: Veterans with co-occurring PTSD and AUD.

Subject Completion Target: n = 60 subjects (30 study drug, 30 placebo)

Study Protocol:

Screening: Subjects are pre-screened by phone and at a first study visit. Prior to initiation of the in-person screen, subjects provide written informed consent. Subjects complete an alcohol breathalyzer test to determine breath alcohol concentration (BAC), and must have a BAC of < 0.02% before screening assessments can begin. Eligible subjects complete a packet of self-assessments, report personal and family medical history, receive a physical/neurologic exam, and provide blood/urine samples. Ineligible or uninterested subjects are referred to clinical care.
Total estimated time per subject for screening: 6-12 hours

Testing: Subjects are randomized 1:1 to receive either study drug or placebo daily for 35±4days, followed by a 14-day down-titration period with follow-up (FU). Subjects complete the Clinician-Administered PTSD Scale 5 (CAPS-5) and self-report percent of heavy drinking days (%HDD) to provide measurements of the study drug's effect on PTSD and AUD symptoms, respectively. Subjects provide Fear-Potentiated Startled (FPS) responses and blood samples for phosphatidylethanol analysis as surrogate measures of study drug efficacy. Safety endpoints, adverse events (AEs), vital signs, and laboratory measures are tracked for each subject to assess study drug safety.
Total estimated time for testing: 49±4 days

Study Drug: Up to 400 mg of Zonisamide (ZNS) will be administered once daily, per os (PO, by mouth). ZNS is a medication approved by the FDA as an adjunct treatment for partial seizures. ZNS enhances GABA function, blocks voltage-sensitive sodium channels and T-type calcium channels, and inhibits carbonic anhydrase. This protocol has been granted IND Exemption Status.

Projected Study Timeline:

Meeting & setup discussion: *May 2016 – August 2016*
Begin contract & IRB process: *April 2017 – March 2018*
Subject enrollment period: *June 2018 –*