Protocol Title: An Open-label Phase 1/2A Study to Evaluate the Safety, Pharmacokinetics, Pharmacodynamics, and Preliminary Efficacy of TRC253, an Androgen Receptor Antagonist, in Patients with Metastatic Castration-Resistant Prostate Cancer

Target Population: Metastatic Castrate-Resistant Prostate Cancer (mCRPC)

Summary: This is a multi-center, first-in-human, open-label, Phase 1/2A dose-escalation study in which eligible patients with mCRPC will receive oral doses of TRC253. The objective of Part 2 is to gather additional information on the safety, pharmacokinetics and pharmacodynamic characteristics, and the clinical efficacy of TRC253 in a pre-defined population of patients with mCRPC. Patients enrolled into Part 2 will have received prior treatment with Enzalutamide or Apalutamide and showed characteristics of acquired resistance based on changes in PSA serum levels.

Key Inclusion Criteria:
- Must have received Enzalutamide or Apalutamide. (Part 2 only)
- Must have shown clinical characteristics of acquired resistance to Enzalutamide or Apalutamide. (Part 2 only)
- Histologically confirmed adenocarcinoma of the prostate with metastatic disease.
- ECOG Performance Status of 0 or 1.
- Prior orchiectomy or serum testosterone levels < 50 ng/dL within 4 weeks prior to start of study drug.
- Adequate baseline organ function.
- Ongoing androgen depletion therapy with a GnRH analog or inhibitor, or orchiectomy.
- For patients previously treated with 1st generation anti-androgens (i.e., Flutamide, Nilutamide, or Bicalutamide), discontinuation of Flutamide or Nilutamide therapy must occur > 4 weeks (> 6 weeks for Bicalutamide) prior to start of study drug with no evidence of an anti-androgen withdrawal response (i.e., no decline in serum PSA).
- For patients previously treated with chemotherapy, targeted therapy, immunotherapy, or treatment with an investigational anticancer agent, discontinuation must have occurred ≥ 2 weeks, or after at least 4 half-lives, whichever is longer, prior to study drug administration.
  - For Enzalutamide and Apalutamide, the washout period will be at least 3 weeks prior to start of study drug with no evidence of an anti-androgen withdrawal response (i.e., no decline in serum PSA).
- For patients previously treated with other agents approved for the treatment of prostate cancer (5-α reductase inhibitors, estrogens, others), discontinuation of therapy must be ≥ 4 weeks prior to start of study drug.
- Palliative radiotherapy (to bone or soft tissue lesions) must be completed > 2 weeks prior to start of study drug.
- For patients receiving bone-loss prevention treatment (e.g., bisphosphonates or denosumab), the patient must be on stable dose ≥ 4 weeks prior to start of study drug.

Key Exclusion Criteria:
- History of seizures.
- Previously documented or current brain metastases.
- Untreated spinal cord compression.
- History of clinically significant cardiovascular disease.
- Second primary malignancy that has not been in remission for greater than 3 years. Exceptions that do not require a 3-year remission include: related non-melanoma skin cancer or resected melanoma in situ.
- Known allergies, hypersensitivity, or intolerance to TRC253 or its excipients.

Contacts:
- Principal Investigator: Marc Matrana, MD
- Research Nurses (RN): Jessica Rentfrow (jessica.rentfrow@ochsner.org, ext. 32652)  
  Amanda Woolery (amanda.woolery@ochsner.org, ext. 20275)

For additional information: https://clinicaltrials.gov/ct2/show/NCT02987829