

Phase 2 Study of Fosbretabulin Tromethamine (CA4P) for the Treatment of Well-Differentiated, Low-to-Intermediate-Grade Unresectable, Recurrent or Metastatic Pancreatic or Gastrointestinal Neuroendocrine Tumors/Carcinoid with Elevated Biomarkers

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Background: Fosbretabulin is a reversible tubulin depolymerizing agent that targets tumor vascular endothelial cells leading to selective tumor vascular shutdown. As highly vascular tumors, GI-NETs are rational clinical targets for VDAs such as fosbretabulin. Based on the propensity for GI-NETs to produce bioactive compounds that mediate systemic symptoms, fosbretabulin induced tumor vascular shutdown may result in a reduction in the production of these biologically active compounds, and potentially lead to improved patient symptoms, quality of life, and long term outcomes.

Methods: This Phase 2 open label, multi-center trial, will include 20 patients with well-differentiated, low-to-intermediate-grade, advanced PNET or GI-NET who have

relapsed after receiving prior treatment, including octreotide, chemotherapy or targeted therapy. Treatment will consist of weekly fosbretabulin for 9 weeks at which point subjects, if benefiting from therapy based on biomarker reduction or symptom control, may continue fosbretabulin in a separate study.

The primary objective is biochemical response as determined by tumor marker change from baseline. Secondary objectives include safety and symptom control (using QLQ-C30 and QLQ-GINET21). ORR and evaluation of pretreatment serum VEGF-A as a potential predictive biomarker are exploratory endpoints. Main inclusion criteria: biopsy-proven well-differentiated, low-to-intermediate-grade PNET or GI-NET with elevated biomarkers; if symptomatic, prior or ongoing SSA or serotonin synthesis inhibitor treatment; ECOG PS 0-2; adequate hematologic and organ function; radiographically evaluable disease. Key exclusion criteria: inadequately controlled hypertension; significant cardiac or vascular disease; active CNS metastasis; acquired or congenital QTc prolongation or treatment with agents definitely associated with QTc prolongation or torsades de pointes. Statistical analysis of the primary and other study endpoints will chiefly be descriptive.

Results: This trial is currently ongoing with results expected in 2016.

Conclusion: Fosbretabulin represents a promising agent for PNET and GI-NET based on preclinical data. Results of this early phase study are eagerly awaited.