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A Phase 1 Study of Fosbretabulin in Combination with Everolimus in Neuroendocrine Tumors (Grades 1-3) That Have Progressed After at Least One Prior Regimen for Metastatic Disease

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BACKGROUND: We present safety data on combination of fosbretabulin with everolimus in metastatic GEPNET patients. Fosbretabulin is a synthetic, water-soluble, phosphorylated prodrug of the natural product Combretastatin A4 (CA4P). Fosbretabulin is a vascular disrupting agent(VDA).

METHODS: This is a single center, open label, phase I study involving gastroenteropancreatic neuroendocrine tumors, consisting of a dose escalation Part A followed by an expansion cohort Part B. Primary Objective is to establish the maximum tolerated dose of the combination of everolimus and fosbretabulin in neuroendocrine tumors that have progressed after at least one prior regimen for metastatic disease. Secondary Objectives include evaluation of safety profile of the combination and to observe and record anti-tumor activity. Patients were treated with daily oral everolimus (2.5 mg, 5 mg 7.5 mg). Fosbretabulin was administered IV 60mg/m2 either q3 weekly or q weekly based on partial order continuous reassessment model (PO CRM). Patients were treated for 12 weeks.

RESULTS: No maximum tolerated dose (MTD) achieved at dose of 7.5 mg daily oral everolimus in combination with weekly 60mg/m2 IV fosbretabulin.

Ten patients were on the trial at the time of abstract submission, with one unevaluable. We are currently treating last dose cohort (10 mg daily everolimus + 60 mg/m2 weekly fosbretabulin). No patient reported grade 4 toxicity. Grade 3 toxicities were each seen in 1 patient: anemia, pain, fatigue, hyperglycemia, and abdominal pain. Only one patient had a delay in treatment (three days) due to grade 3 diarrhea. No patient had radiological progression at the first q 3 monthly CT scan of chest, abdomen and pelvis.

CONCLUSION: Trial is currently accruing final 4 patients on last dose cohort and is anticipated to complete by the time of presentation. ClinicalTrials.gov Identifier: NCT03014297