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The Safety and Efficacy of PEN-221 Somatostatin Analog (SSA)-DM1 Conjugate in Patients (Pts) with Advanced GI Mid-gut Neuroendocrine Tumor (NET): Phase 2 Results

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BACKGROUND: PEN-221 is a small molecule drug conjugate composed of a SSTR2 binding somatostatin analog linked to the toxin DM1. PEN-221-001 was a study which assessed the safety, tolerability, pharmacokinetics (PK), and preliminary efficacy of PEN-221 in well differentiated neuroendocrine tumors (NETs) and small cell lung cancer.

METHODS: Pts with advanced, SSTR2+ GI mid-gut NETs were enrolled in this cohort of study PEN-221-001. The primary objective was to determine the safety

and efficacy of PEN-221 given intravenously, every (q) 3 weeks. Preliminary efficacy was assessed using RECIST 1.1. A clinically meaningful efficacy result was defined as a Clinical Benefit Rate (CBR) > 75% and a median progression-free survival (mPFS) > 8 months.

RESULTS: 32 patients were enrolled between January 2018 to June 2020 and the data cut-off for this report is July 31, 2020. The mean number of cycles received was 7 (range 1-18), with 5 pts still on treatment at time of data lock. PEN-221 was well tolerated in all pts at the dose of 8.8 mg/m2. The most frequent (≥20% pts) PEN-221 related adverse events were nausea (50%), fatigue (47%), diarrhea (47%), decreased appetite (47%), peripheral neuropathy (34%), infusion reaction (31%), AST/ Alk Phos/ALT increase (28/25/22%), and anemia (25%). Only 11 (34%) of these events were ≥grade 3. Of the 26 pts who were evaluable for response, 23 (88.5%) had stable disease (SD) reported as their best response with a CBR of 88.5%. Target lesion shrinkage was observed in 10 (38%) patients. The mPFS for this cohort was 9 months (CI 5 - 16.5 months). Tumor marker data will also be presented.

CONCLUSION: PEN-221 appears well tolerated at 8.8 mg/m2 q 3 weeks and has demonstrated efficacy exceeding its clinical efficacy goals with a CBR of 88.5% and a mPFS of 9 months.

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