

# C-12

## First in Human Phase 1/2a Study of PEN-221 Somatostatin Analog (SSA)-DM1 Conjugate for Patients (PTS) with Advanced Neuroendocrine Tumor (NET) or Small Cell Lung Cancer (SCLC): Phase 1 Results

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**BACKGROUND:** Somatostatin receptor 2 (SSTR2) is highly expressed in NET and SCLC. PEN-221, a SSA-DM1 conjugate targeting SSTR2, results in complete tumor regressions in SSTR2+ SCLC xenograft models. This study assesses safety, tolerability, pharmacokinetics (PK), and preliminary efficacy of PEN-221.

**METHODS:** Pts with progressive, advanced, radiographically SSTR2+ NET or SCLC were enrolled in escalating cohorts of 2-6 pts. The primary objective was to determine the maximum tolerated dose (MTD) of PEN-221 given every (q) 3 wks. An adaptive Bayesian logistic regression model was used to recommend doses. Intra-patient dose escalation was permitted. Preliminary efficacy was estimated using RECIST 1.1.

**RESULTS:** 23 pts with NET (n=22) or SCLC (n = 1) were treated in 7 cohorts (range 1-25 mg). As of 23 Feb 2018, the median number of cycles is 5 (range 1-19), with 5 pts ongoing. PEN-221 was well tolerated without dose limiting toxicities (DLTs) in the first 6 cohorts (1-18 mg; 20 pts). In cohort 7 (25 mg), 2 of 3 pts had DLTs that rapidly and fully resolved: Grade(G)3 ALT/AST rise (2 pts), of whom 1 had concurrent G3 total bilirubin rise and G3 mucositis. The MTD was 18 mg. The most frequent ( $\geq 20\%$  pts) related adverse events were fatigue (48%), nausea (48%), diarrhea (44%), vomiting (26%), abdominal pain (26%), and anorexia (22%). PK was dose-proportional, median  $t_{1/2}$  ~1.7 h, with plasma exposures at MTD above preclinically efficacious levels. Among 15 NET pts evaluable for response, 11 had stable disease (SD) at 9 wks, with 8 sustained for 18 – 45 wks. Target lesion shrinkage was observed in 3 pts and one pt had biomarker response.

**CONCLUSION:** PEN-221 appears well tolerated, with preliminary evidence of antitumor activity. PEN-221 (18 mg q 3 wks) is being evaluated in Phase 2a expansion cohorts enrolling midgut NET, pancreatic NET, and SCLC pts (EudraCT 2016-001468-12; NCT02936323).