TPS8128 **Poster Session**

An open-label, multicenter, phase 1/2 study of peluntamig (PT217), an anti-DLL3/anti-CD47 bispecific antibody, in patients with DLL3-expressing cancers such as SCLC, LCNEC and EP-NEC (SKYBRIDGE study).

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Background: Neuroendocrine carcinomas (NECs) are aggressive cancers with limited median survival. Over 90% of the NEC cases originate from the lung, including small cell lung cancer (SCLC) and large cell neuroendocrine carcinoma (LCNEC) of the lung. The rest of the cases are extra-pulmonary NECs (EP-NECs), including gastroenteropancreatic neuroendocrine carcinoma (GEP-NEC) and neuroendocrine prostate cancer (NEPC). Despite the initial impressive responses to platinum-based chemotherapy with or without an immune checkpoint inhibitor (ICI), at progression, resistance and clinical deterioration are common. High mortality rates and limited treatment options with durability highlight a significant unmet medical need. NECs are known to be heterogeneous. One unifying feature is the consistent surface expression of DLL3, making targeting DLL3 an attractive treatment approach. Peluntamig (PT217) is an IgG1 based anti-DLL3/anti-CD47 bispecific antibody that activates both innate and adaptive immunity to target cells that express DLL3 and/or overexpress CD47. **Methods:** The study consists of 4 parts: Monotherapy Dose Escalation (Part A), Dose Expansion (Part B), Chemotherapy Combination Therapy (Part C), and ICI Combination Therapy (Part D). Each part includes multiple cohorts. The study is designed to evaluate the safety, tolerability, pharmacokinetic (PK), pharmacodynamic (PD), and preliminary efficacy of peluntamig. Parts A, C and D are ongoing. Cohort C1 will enroll patients with first-line (1L) LCNEC of the lung and EP-NEC and patients with second-line (2L) SCLC who have (defined as progression $\geq$ 90 days after last dose of platinum therapy). Patients will receive peluntamig and SOC CE. Cohort C2 will enroll SCLC, LCNEC of the lung and EP-NEC patients eligible for 2L paclitaxel therapy. Patients will receive peluntamig and SOC paclitaxel. Cohort D1 will enroll 2L LCNEC of the lung, EP-NEC and ES-SCLC patients who have progressed/relapsed from their 1L treatment that may have included an ICI. Patients will receive peluntamig + atezolizumab. Cohort D2 will enroll 1L patients with ES-SCLC who have completed their induction therapy with CE plus atezolizumab and are eligible to continue with atezolizumab treatment. Patients will receive peluntamig + atezolizumab as maintenance therapy. Cohort D3 will enroll 1L patients with ES-SCLC who are treatment-naïve. Patients will receive peluntamig + CE + atezolizumab. Dose escalation, guided by a 3+3 design, will be conducted independently for each cohort. Patients will be backfilled to DLT-cleared dose levels to further evaluate safety, tolerability, PK and efficacy. Potentially active cohorts will be further investigated in dose randomization studies in Part B. Clinical trial information: NCT05652686. Research Sponsor: None.