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Preliminary Safety and Efficacy of Rovalpituzumab Tesirine in Patients with Delta-Like Protein 3-Expressing Advanced Solid Tumors

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BACKGROUND: Rovalpituzumab tesirine (Rova-T™) is an antibody-drug conjugate targeting delta-like protein 3 (DLL3), an atypical Notch receptor family ligand expressed in high-grade neuroendocrine carcinomas (NECs).

METHODS: This is a Phase 1/2, open-label, multicenter study (NCT02709889) to determine safety/tolerability of Rova-T in 8 cohorts: malignant

melanoma, medullary thyroid cancer (MTC), glioblastoma (GBM), large cell NEC (LCNEC), neuroendocrine prostate cancer (NEPC), high-grade gastroenteropancreatic NEC (GEP NEC), other NEC, and other solid tumors. Eligible adults have a histologically confirmed, DLL3-expressing, advanced solid tumor relapsed/refractory to standard therapy, and no prior exposure to a pyrrolobenzodiazepine-based drug. A 3+3 dose escalation is used in each cohort, at doses 0.2-0.4 mg/kg of Rova-T administered intravenously on Day 1 of each 42-day cycle, and proceeding until a maximum tolerated dose (MTD) is determined. A 2-stage design will be used for disease-specific expansion cohorts.

RESULTS: As of 3 April 2017, 31 pts (2 melanoma, 2 MTC, 3 GBM, 3 LCNEC, 3 NEPC, 3 GEP NEC, 10 other NEC, 5 other solid tumor) have been treated (26 pts at 0.2 mg/kg, 5 pts at 0.3 mg/kg Rova-T). MTD has not been reached. Twenty-six pts (84%) had an adverse event (AE), and only 3/31 pts (10%) had a Grade 3+ AE deemed to be related to Rova-T. Common AEs were fatigue (32%), nausea (29%), and constipation (23%). Four pts had serosal effusions, 2 (6%) of which were assessed to be drug-related, and 3 pts (10%) had adverse skin reactions. Ten pts (32%) discontinued treatment, 5 for progressive disease and 4 due to AEs. Eleven pts have had post-baseline tumor assessments, and anti-tumor activity has been observed in multiple disease cohorts.

CONCLUSION: Preliminary safety and efficacy data of Rova-T warrant continued study in these disease populations, and will be updated at time of presentation.