TPS3161 **Poster Session**

A phase 1, first-in-human study of AMT-676, an anti-CDH17 antibody-drug conjugate, in patients with advanced gastrointestinal tumors.

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Background: Cadherin-17 (CDH17), also known as liver-intestine-cadherin, is a transmembrane protein that is highly expressed in a variety of gastrointestinal cancers, including colorectal, gastric, esophageal adenocarcinoma, cholangiocarcinoma, pancreatic ductal, and gastrointestinal neuroendocrine tumors. The overexpression of CDH17 is associated with tumor metastasis and progression to advanced tumor stages. AMT-676 is a novel antibody-drug conjugate (ADC) that targets CDH17. It is comprised of a humanized IgG1 monoclonal antibody specific to CDH17, conjugated to the potent topoisomerase I inhibitor exatecan, with a drug-to-antibody ratio of 4, linked through a proprietary T-moiety technology. Preclinical studies have demonstrated significant anti-tumor activity of AMT-676 across multiple gastrointestinal cancer models and great tolerability in safety studies, highlighting its potential as a therapeutic agent for CDH17-expressing malignancies. **Methods:** This phase 1, open-label, multicenter study aims to determine the Maximum Tolerated Dose (MTD) and the Recommended Phase 2 Dose (RP2D) of AMT-676, as well as to assess its safety, tolerability, anti-drug activity, pharmacokinetics, pharmacodynamics, immunogenicity and preliminary efficacy in patients with advanced solid tumors. Tumor types that express CDH17 including gastrointestinal cancers, treated with or with no standard therapeutic options are to be enrolled. AMT-676 will be administered intravenously on a 21-day cycle. The dose escalation will be guided by the Bayesian Optimal Interval (BOIN) design, incorporating an accelerated titration approach to evaluate 6 cohorts: 1.6, 3.2, 4.8, 6.4, 8, and 10 mg/kg. Three backfilling cohorts at doses that have demonstrated safety will also be included, each enrolling up to 18 patients, to gather additional data on safety, pharmacokinetics, pharmacodynamics, and preliminary efficacy, thereby supporting the selection of an optimized dose for expansion. Mandatory pre-study biopsy sample collection for retrospective immunohistochemistry (IHC) analysis will facilitate a comprehensive exploratory biomarker plan, potentially correlating CDH17 levels with treatment responses. The study is actively enrolling participants for the dose escalation phase. Cohorts 1-4 have been completed DLT evaluation and enrollment of cohort 5 began in December 2024. Clinical trial information: NCT06400485. Research Sponsor: Multitude therapeutics Inc.