TPS3166 **Poster Session**

A dose escalation and cohort expansion phase I/IIa study of ACR246, an innovative 5T4- antibody drug conjugate (ADC), in patients (pts) with advanced solid tumors.

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Background: The oncofetal antigen 5T4 is overexpressed in many solid tumors with limited expression in normal adult tissues. Overexpression of 5T4 is associated with poor prognosis. 5T4 on tumor cell surface is rapidly internalized when bound to antibody and is thus an ideal target for the development of ADC drugs. ACR246 is the first next- generation 5T4-ADC consisting of a fully human monoclonal antibody that is site-specifically conjugated to a novel DNA topoisomerase I inhibitor D2102, via a stable and cleavable linker, with a drug-to-antibody ratio (DAR) of 8. ACR246 was carefully designed to improve the safety and efficacy in treating 5T4 positive solid tumors. In preclinical studies, ACR246 demonstrated robust anti-tumor activity, superior to a Dxd-5T4 ADC (as a reference) both in CDX and PDX models, including but limited to NSCLC, gastric cancer, pancreatic cancer and Esophageal cancer, and excellent tolerability, supporting further development for clinical use. **Methods:** This is an ongoing, phase I/IIa, open-label, multicenter, dose escalation and cohort expansion study of ACR246 to be injected intravenously to adult pts with advanced solid tumors. For phase I study, a Bayesian optimal interval design is adopted to assess dose levels of ACR246, 0.6, 1.2, 2.4, 3.6 and 4.5 mg/kg, administered every 3 weeks on a 21-day cycle，and intermediate dose levels of 3.0, 4.0 and 5.0 mg/kg may be evaluated based on emergent safety or pharmacologic data. The primary objectives are to evaluate safety and tolerability and determine the maximum tolerated dose (MTD) and the recommended phase 2 dose (RP2D); the second objectives include PK, immunogenicity and preliminary clinical efficacy. Dose limiting toxicity (DLT) will be assessed at each dose level. The DLT evaluation period will be 21 days. Once the RP2D is determined, phase IIa study will be conducted to further evaluate the safety, tolerability, efficacy, PK and immunogenicity of ACR246 in 5T4-positive advanced solid tumor pts (esophageal cancer, NSCLC, ovarian cancer, prostate cancer and other types of tumors) under RP2D. Approximately 77 pts ≥ 18 years of age with advanced solid tumors that have histologically or cytologically been diagnosed recurrent or metastatic unresectable advanced disease and have failed or are intolerant of systemic standard therapy or standard therapy is not available, and having adequate ECOG performance status (0-1), hematologic function, and end organ function are planned to be enrolled, with 37 pts in phase I study and approximately 40 pts in phase IIa study. 5T4 expression is not required for enrollment for phase I, but will be assessed retrospectively. The toxicity will be assessed by Common Terminology Criteria for Adverse Events v5.0 and the tumor response will be determined per RECIST v1.1. Dose levels of 0.6 mg/kg and 1.2mg/kg has completed enrollment with no DLT. Clinical trial information: NCT06238401. Research Sponsor: Hangzhou Adcoris Biopharma Co., Ltd.