TPS3163 **Poster Session**

A phase 1 study to evaluate the safety and tolerability of the antibody–drug conjugate (ADC) MesoC2 (PF-08052666) in patients with advanced solid tumors.

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Background: MesoC2 (PF-08052666) is an ADC that targets mesothelin (MSLN), a cell-surface glycoprotein overexpressed in solid tumors including mesothelioma, ovarian cancer, pancreatic cancer, non-small cell lung cancer (NSCLC), endometrial cancer (EC), and colorectal cancer (CRC), but with limited expression in normal tissues. MesoC2 is constructed from a recombinant human IgG1 anti-MSLN monoclonal antibody conjugated to a cleavable tripeptide linker that carries a topoisomerase 1 inhibitor (TOP1) payload. The average number of TOP1 molecules per antibody is 8. Following high-affinity binding to MSLN on the cell surface, MesoC2 is internalized, the linker is cleaved, and the released payload inhibits DNA religation during amplification, leading to cell cycle arrest and cell death. MesoC2 has shown potent antitumor efficacy in in vitro assays and xenograft models and an acceptable safety profile in cynomolgus monkeys. The aim of this first-in-human study is to explore the safety, tolerability, and preliminary efficacy of MesoC2 in patients with certain advanced solid tumors. **Methods:** In this phase 1, open-label study, up to 365 patients with mesothelioma, platinum-resistant ovarian cancer (PROC), pancreatic ductal adenocarcinoma (PDAC), NSCLC, EC, or CRC will receive intravenous infusion of MesoC2 in dose escalation (n=45), dose and schedule optimization (n=40), and disease-specific dose expansion cohorts (n=280; includes a biology cohort to evaluate exploratory biomarkers). Key inclusion criteria are histologically or cytologically confirmed metastatic or locally advanced mesothelioma, PROC, PDAC, NSCLC, EC, or CRC who have relapsed or progressed following standard therapies; aged ≥18 years; ECOG performance status score of 0 or 1; and available archival tumor tissue (a fresh biopsy is required if unavailable). Key exclusion criteria include prior or current treatment with systemic anticancer therapy or focal radiotherapy within 4 weeks prior to first dose of MesoC2, prior anti-MSLN therapies, and any unresolved toxicities from prior therapy greater than G1 at the time of starting study treatment, except alopecia. Primary endpoints include type, incidence, and severity of adverse events (AEs), frequency of dose modifications due to AEs, incidence of dose-limiting toxicities, cumulative safety, pharmacokinetics, pharmacodynamics, and preliminary antitumor activity. Key additional endpoints include objective and best response rates per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1), duration of response, progression-free survival, overall survival, MSLN expression in blood and tissue, and changes in tumor-specific biomarkers. Enrollment is ongoing; clinical trial information: NCT06466187. A genAI tool (01/06/25; Pfizer; GPT-4o) developed the 1st draft; authors assume content responsibility. Clinical trial information: NCT06466187. Research Sponsor: Pfizer Inc.