First-in-human study of BG-C9074, a B7-H4-targeting ADC in patients with advanced solid tumors: Preliminary results of the dose-escalation phase

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Background: B7-H4 is a transmembrane glycoprotein in the B7 superfamily with limited expression in normal tissue but is upregulated in solid tumors including cholangiocarcinoma, breast, ovarian, and endometrial cancers. BG-C9074 is an investigational topoisomerase I inhibitor antibody-drug conjugate. This abstract presents the initial results of monotherapy dose escalation from the ongoing phase 1 study.

Methods: BG-C9074-101 (NCT06233942) is a first-in-human, multicenter study designed to evaluate the safety, tolerability, pharmacokinetics, and preliminary antitumor activity (per RECIST v1.1) of BG-C9074 as monotherapy and in combination with tislelizumab in patients with advanced solid tumors. Patients with histologically or cytologically confirmed locally advanced, unresectable, or metastatic solid tumors, irrespective of B7-H4 expression, received BG-C9074 intravenously every 3 weeks in sequentially escalating dose cohorts ranging from 1 to 7 mg/kg.

Results: As of January 22, 2025, 55 patients with advanced tumors (n=25, ovarian cancer; n=16, breast cancer; n=10, cholangiocarcinoma; n=4, other tumor types) received BG-C9074 monotherapy. Three patients experienced dose-limiting toxicities including fatigue (6 mg/kg), and febrile neutropenia and thrombocytopenia (7 mg/kg). Treatment-emergent adverse events (TEAEs) were reported in 48 patients (87.3%) with grade ≥3 TEAEs occurring in 27.3% of patients. The most common TEAEs were nausea (45.5%), fatigue (38.2%), and neutropenia (32.7%), with neutropenia being the most frequent grade ≥3 TEAE (16.4%). Among 39 efficacy-evaluable patients, eight (20.5%) partial responses (n=4, confirmed; n=4, unconfirmed) were observed.

Conclusions: BG-C9074 showed a manageable safety/tolerability profile in patients with B7-H4 advanced solid tumors. Preliminary clinical responses were observed at multiple dose levels across various tumor types without selection for B7H4 expression. Dose-escalation and dose-level expansion are ongoing and updated clinical data will be presented at the conference.