**Title:** First-in-human study of BG-C9074 (B7-H4–targeting ADC) in advanced solid tumors: dose escalation and safety expansion

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**Background**:

B7-H4, a transmembrane glycoprotein, has limited expression in normal tissue, but is upregulated in a variety of solid tumors. BG-C9074 is an investigational topoisomerase I inhibitor antibody-drug conjugate (ADC) that targets B7-H4. We present results of monotherapy dose escalation and safety expansion from the ongoing phase 1 study.

**Methods**:

BG-C9074-101 (NCT06233942) is a first-in-human, multicenter study of BG-C9074 as monotherapy and in combination with other anticancer therapies in patients (pts) with advanced solid tumors. Pts with advanced solid tumors, irrespective of B7-H4 expression, received BG-C9074 IV every 3 weeks in escalating doses from 1 to 9 mg/kg. Endpoints included safety, preliminary antitumor activity (per RECIST v1.1) and pharmacokinetics.

**Results**:

As of Dec 29, 2025, 123 pts with advanced solid tumors received BG-C9074 monotherapy in phase 1a (ovarian [OC], n=62; HR+/HER2- breast cancer, n=28; triple negative breast cancer [TNBC], n=18; cholangiocarcinoma, n=11; endometrial,

n=3; squamous non-small cell lung cancer, n=1). Median (range) prior lines were 4 (0-13).

8 pts experienced DLTs (thrombocytopenia [n=2, 6.5 mg/kg; n=1, 7 mg/kg], febrile neutropenia [n=1, 6.5 mg/kg; n=1, 7 mg/kg], neutropenic infection [n=1, 7 mg/kg], fatigue [n=1, 6 mg/kg], nausea [n=1, 9 mg/kg], and unexplained death [n=1, 9 mg/kg]). Treatment-related adverse events (TRAEs) occurred in 113 pts (91.9%); grade (gr) ≥3 in 30.1%. The most common TRAEs were nausea (53.7%; gr ≥3, 4.1%), neutrophil count decreased/neutropenia (44.7%; gr ≥3, 18.7%), and fatigue (37.4%; gr ≥3, 2.4%). Hematologic and gastrointestinal toxicities were manageable with dose modifications and/or supportive care.

Among 114 efficacy-evaluable pts, confirmed ORR (cORR) was 28.1% (95% CI 20.1-37.3), including 2 CRs (1 OC, 6.5 mg/kg, 1 TNBC, 5 mg/kg) and 30 PRs (**Table**); unconfirmed ORR was 33.3% (24.8-42.8; 3 CRs, 35 PRs). Responses were observed across doses and levels of B7-H4 expression, without consistent association of response with B7-H4 expression across tumor types. Median (range) study follow-up was 6.0 (0.3-17.7) months.

ADC and free payload concentrations decreased in a biexponential manner with a half-life of ~7 days for ADC. Exposure for ADC and free payload increased approximately dose proportionally.

**Conclusions**:

BG-C9074 demonstrates a tolerable safety profile in pts with advanced solid tumors. Encouraging antitumor activity was observed in OC and TNBC. Dose expansion and optimization are ongoing.

| | OC (n=55) | TNBC (n=16) | HR+/HER2- BC (n=28) | Total (N=114) |
|---|---|---|---|---|
| cORR, % (95% CI) | 34.5 (22.2-48.6) | 31.3 (11.0-58.7) | 17.9 (6.1-36.9) | 28.1 (20.1-37.3) |
| CR, n (%) | 1 (1.8) | 1 (6.3) | 0 (0.0) | 2 (1.8) |
| PR, n (%) | 18 (32.7) | 4 (25.0) | 5 (17.9) | 30 (26.3) |
| SD, n (%) | 32 (58.2) | 5 (31.3) | 16 (57.1) | 60 (52.6) |
| PD, n (%) | 4 (7.3) | 5 (31.3) | 7 (25.0) | 17 (14.9) |
| Not evaluable, n (%) | 0 (0.0) | 1 (6.3) | 0 (0.0) | 5 (4.4) |