Title: Consideration of Adjusted Ideal Body Weight Dosing in BG-C9074 (B7-H4 – targeting ADC) from pharmacokinetics, efficacy and safety perspectives

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Background:

B7-H4 is a transmembrane glycoprotein that 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 the pharmacokinetic (PK) and exposure-response (ER) analyses supporting the implementation of adjusted ideal body weight (AiBW)-based dosing in the ongoing phase 1 study.

Methods:

BG-C9074-101 (NCT06233942) is a first-in-human, multicenter study designed to assess BG-C9074 as monotherapy and in combination with other anticancer therapies in patients (pts) with advanced solid tumors. Total body weight (TBW) and AiBW-based dosing were evaluated at 1–7 mg/kg and 6.5–9 mg/kg, respectively, administered intravenously every 3 weeks. PK samples were collected to measure serum ADC and plasma free P1021 payload analytes at Cycle 1 and steady state (Cycle 5). A population PK model, incorporating both ADC and payload, was developed and used to evaluate safety and efficacy ER relationships.

Results:

As of October 30, 2025, PK, safety, and efficacy data were available for 107 pts with advanced solid tumors. TBW dosing of BG-C9074 led to a maximum tolerated dose < 7 mg/kg. The ADC and free payload exposures increased with BW for TBW dosing, while ADC clearance moderately increased with BW leading to higher exposure in high BW patients (**Table 1**). Higher ADC exposure was associated with an increased incidence of Grade ≥3 treatment-related adverse events (TRAEs), predominantly neutropenia. Early dose modifications and use of granulocyte colony-

stimulating factor were more frequent at higher doses and exposures. Increased and sustained tumor shrinkage observed in pts with ovarian cancer (OC) with higher ADC exposure. AiBW enabled a higher tolerable dose at 8 mg/kg, by normalizing ADC and payload exposure across all bodyweight ranges.

Conclusions:

AiBW dosing effectively reduced PK variability compared with TBW dosing, providing more consistent exposure across BW. Higher ADC exposure was associated with increased efficacy, but also with a higher incidence of manageable TRAEs. AiBW optimizes the risk-benefit profiles across BW.

Table 1.

	Underweight (< 18.5 kg/m^2)	**Normal (18.5 – 24.9 kg/m^2)**	**Overweight (25 – 29.9 kg/m^2)**	**Obese (⩾30 kg/m^2)**
Simulated Cycle1 Median ADC exposure at 7 mg/kg TBW (ng/mL)	352	464	533	626
Simulated Cycle 1 Median ADC exposure at 7 mg/kg AiBW (ng/mL)	411	448	464	481
ADC Exposure Tertile	**1**	**2**	**3**	
Grade ≥3 TRAE	16.2% (6/37)	27.8% (10/36)	37.8% (14/37)	
Grade ≥3 Neutropenia	10.8% (4/37)	19.4% (7/36)	27% (10/37)	
Dose modifications	16.2% (6/37)	19.4% (7/36)	27% (10/37)	
Median tumor shrinkage in	-28.9%	-33.3%	-48%	

OC at Week 24 Tumor Assessment (N=25)				