SKB264 ADC: A first-in-human study of SKB264 in patients with locally advanced unresectable/metastatic solid tumors who are refractory to standard therapies (Abstract ID: TPS3659)

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Background
Elevated expression of trophoblast antigen 2 (TROP2) is often associated with tumor invasion/agression, progression, and metastasis. Efficacies of anti-TROP2 antibody conjugated drugs (ADC) have been demonstrated both preclinically and in the clinic.

SKB264 is being developed as a further optimized TROP2-targeting ADC with a proprietary cytotoxic, belotecan-derivative payload and novel linker.

SKB264 is internalized and its payload is released inside the cells in a TROP2 expression dependent manner. Payload release also occurred extracellularly. Extensive preclinical evidence demonstrated SKB264 antitumor activity in vitro, in xenograft and patient-derived xenograft (PDX) models. In addition, Safety studies have demonstrated an acceptable safety profile to allow SKB264 to be used in clinical studies.

The primary study objectives

- **Phase I**: To determine the maximum tolerated dose (MTD) and/or the recommended Phase II dose (RP2D).
- **Phase II**: To evaluate the objective response rate (ORR) [Complete Response (CR) + Partial Response (PR)] of SKB264 at the RP2D.

The secondary study objectives

**Phase I**

- To determine the dose limiting toxicities (DLTs), overall safety and tolerability profile.
- To evaluate preliminary efficacy on the basis of ORR, Duration of Response (DOR), Progression free survival (PFS) and overall survival (OS).
- To characterize the pharmacokinetics (PK) of SKB264-ADC, SKB264-TAB, and free KL610023 payload.
- To assess the incidence of anti drug antibody (ADA) formation to SKB264.
- To assess levels of TROP2 expression in tumor tissue and correlation of these levels with efficacy and toxicity.

**Phase II**

- To obtain additional characterization of the safety of SKB264 at the RP2D.
- To evaluate efficacy in patients treated with SKB264 as monotherapy on the basis of DOR, PFS and OS.
- To assess the incidence of ADA formation to SKB264.
- To characterize the PK of SKB264-ADC, SKB264-TAB, and free KL610023 payload.
- To assess levels of TROP2 expression in tumor tissue and correlation of these levels with responses and toxicity.

Study Design

- Refractory patients with locally advanced or metastatic solid tumors
- Subjects will not be screened according to TROP2 expression before enrollment, but tissue specimens from archived materials in order to do the retrospective analysis.
- Dose escalation and MTD identification will be directed using a Bayesian logistic regression model (BLRM) with overdose control.
- Assess the DLT at least 28 days from the first dose.

Eligibility Criteria

**Major Inclusion**

<table>
<thead>
<tr>
<th>Phase I</th>
<th>Phase II</th>
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<tr>
<td>Male or female patient ≥ 18 years</td>
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<tr>
<td>Histologically documented, incurable, locally advanced or metastatic cancer that are refractory to standard therapies</td>
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<td>Measurable or evaluable disease by CT/MRI</td>
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**Major Exclusion**

- Severe or uncontrolled cardiac disease requiring treatment
- Symptomatic brain metastases or any radiation or surgery for brain metastases within 3 months
- Documented Grade ≥ 2 peripheral neuropathy
- Have known prior positive test results for human immunodeficiency virus

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