HDP-101, a BCMA-Targeting Antibody-Drug Conjugate with a Novel Amanitin Payload, Establishes the Recommended Phase 2 Dose (RP2D) in a clinical Phase 1 trial on Relapsed/Refractory Multiple Myeloma

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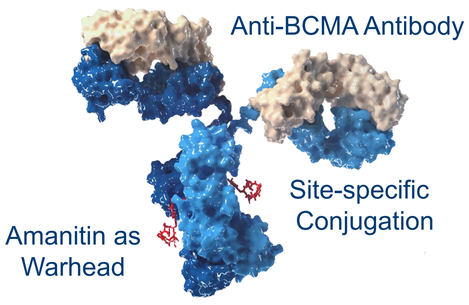
INTRODUCTION AND BACKGROUND

HDP-101 (INN: pamlectabart tismanitin) is a **novel antibody-drug conjugate (ADC)** targeting **B-cell maturation antigen (BCMA)** with a synthetic **amanitin payload**.

Based on extensive preclinical myeloma-models it showed strong anti-tumor activity, in particular also against low-BCMA expressing MM cells.



HDP-101-01: DESIGN & METHODOLOGY

- **Design**: Global, first-in-human, open-label, non-randomized, multi-center phase 1/2a clinical trial in Relapsed/Refractory Multiple Myeloma (RRMM).
- **Aim**: Determination of the recommended Phase 2 Dose (RP2D) and evaluation of the initial safety and efficacy for further evaluation of the POC.
- **Methodology**: Phase 1 study with adaptive Bayesian logistic regression model (BLRM) with overdose control for accelerated titration.

RESULTS

Demographics

- As of the 03-September-2026 data cut-off, 10 Phase 1 dose-escalation cohorts (20-218 µg/kg) had completed DLT evaluation, with 53 patients dosed and included in the Phase 1 analysis.
- Median age was 69 years (range, 43–90); 22 patients were female and 31 male.
- Patients were **heavily pretreated**, with **a median of 5 prior lines/treatments** (range, 2–15).

Demographics	Total (N=53) *	Prior Therapy	Total (N=53)
Age (years)		**Number of prior treatments**	
Median	69	Median	5
Min, Max	43-90	Range	2-15
Gender		**BCMA-ADC/TCE/CAR-T Treatment**	
Female	22	Anti-BCMA-ADC (%)	5 (9%)
Male	31	BCMA TCE/CAR-T (%)	14 (26%)

** All patients treated in the Phase 1 dose-escalation cohorts (Cohorts 1-10)*

Safety

- Results are based on the DCO of 03-September-2026, with a total of 84 patients enrolled and 53 dosed for Phase 1 study.
- HDP-101 demonstrated a **manageable safety profile**, that was further improved following the implementation of a split dose to optimize the schedule and dosing.
- **Adverse events were reversible**, and **no treatment related Grade 5 events** were observed with **the MTD not reached.**

Most Common Treatment-Emergent AEs (TEAEs)

Preferred Term	Any grade (N, %)	Grade 3-4 (N, %)
Thrombocytopenia	20(38%)	12(23%)
Anemia	13(25%)	4(8%)
Aspartate aminotransferase increased	11(21%)	2(4%)
Arthralgia	10(19%)	0(0%)
Fatigue	10(19%)	0(0%)
Proteinuria	9(17%)	4(8%)
Platelet count decreased	9(17%)	4(8%)
Neutropenia	8(15%)	3(6%)
Diarrhea	8(15%)	0(0%)
Alanine aminotransferase increased	8(15%)	1(2%)
Upper respiratory tract infection	7(13%)	1(2%)
Nausea	7(13%)	0(0%)

Safety	Cohort 8 140 µg/kg	Cohort 9 175 µg/kg	Cohort 10 218 µg/kg
Safety-evaluable patients, n	8	6	5
DLTs	1 (12.5%) Syncope	1 (16.7%) Platelet count decrease	1 (20%) Thrombocytopenia
Grade 3 TEAEs	3 (37.5%)	4 (66.7%)	5 (100%)
Grade 4 TEAEs	0	2 (33.3%)	3 (60%)

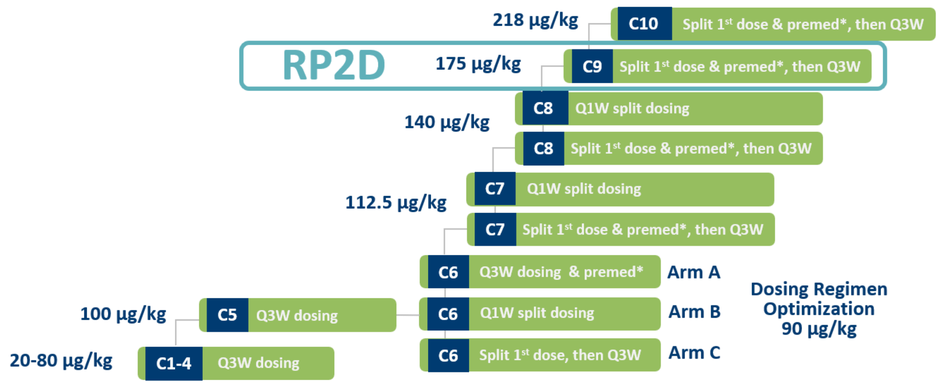
Data cutoff: 03 September 2026

PK/PD

- Dose-proportional PK (Cmax, AUC) was observed with a half-life of approx. 9 days
- Current PK/PD modeling supported that split dose reduce the impact of HDP-101 on platelets and liver function.

STUDY PROGRESS

- **Dose escalation completed, MTD not reached**. Enrollment into Phase 2a expansion has started.
- Patients were dosed every 3 weeks (Q3W) up to Cohort 5 (100 µg/kg). **From Cohort 6 (90 µg/kg)**, based on PK/PD modeling, **dosing optimization strategies** were introduced including **split dosing and/or premedication with corticosteroids and antihistamines**, to mitigate the risk of adverse events such as **thrombocytopenia** and **liver enzyme elevations**.
- Based on the totality of safety, PK/PD, and efficacy data, and considering the balance of exposure, tolerability, and response, **175 µg/kg was selected as RP2D**, with a split first dose and premedication, followed by Q3W dosing.



Efficacy

- **Clinical responses were observed from ≥90 µg/kg**, with increasing efficacy at higher doses.
- Across cohorts 5-9 (90-175 µg/kg/cycle), the **ORR was 42%** (13/31 evaluable patients), including **7x PR, 3x VGPR, and 3x sCR**. (Figure 1)
- Notably, responses were also observed in patients previously exposed to BCMA-targeted therapies.

Efficacy	Cohort 8 140 µg/kg	Cohort 9 175 µg/kg	Cohort 10 218 µg/kg
Efficacy-evaluable patients, n	7	5	5
Median follow-up, month (range)	12.8 (2.3-14.1)	5.3 (3.7-9.5)	1.5 (0.9-7.0)
ORR	4/7 (57.1%)	2/5 (40%)	2/5 (40%)
≥VGPR rate	3/7 (42.9%)	1/5 (20%)	0/5 (0%)
≥CR rate	2/7 (28.6%)	0/5 (0%)	0/5 (0%)
Individual DOR	11.1+, 11+, 9.5+, 4.6	7.6+, 2.1+	3.2+, 2.6
Median PFS, month (95% CI)	5.95 (1.48–NR)	2.83 (0.72-NR)	0.95 (0.76-NR)

Data cutoff: 03 September 2026

Treatment duration and response by patients

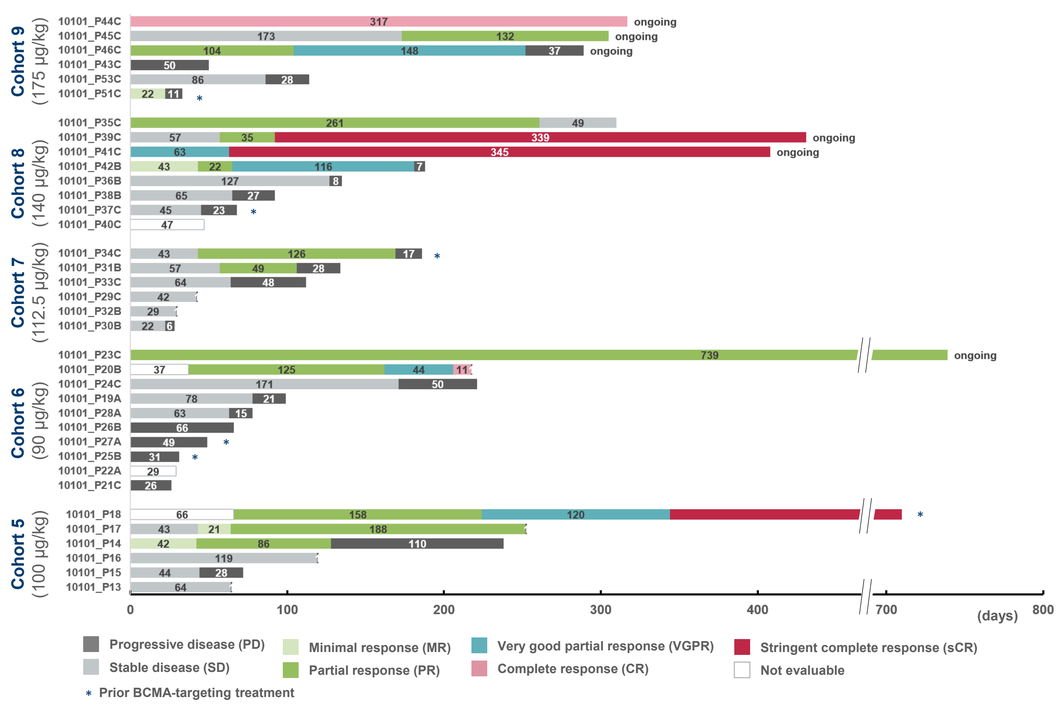


Figure 1: Swimmer plot depicting treatment response duration in Cohorts 5-9.
(data cutoff: 03 September 2026)

CONCLUSIONS

- HDP-101 demonstrates **clinical activity with a favorable safety profile** in heavily pretreated RRMM, supporting its development as a **novel BCMA-targeted ADC with an amanitin payload**.
- **An RP2D of 175 µg/kg was established**, enabling Phase 2a expansion to further characterize efficacy and safety at the selected dose.
- The **preliminary safety profile** in the ongoing Phase 2a study remains **consistent with that observed in Phase 1**.

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