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Dose Optimization, Efficacy, and Safety of CUSP06, a Cadherin-6 Directed Antibody-Drug Conjugate, in Platinum-Resistant Ovarian Cancer

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Disclosure

	No, nothing to disclose
x	Yes, please specify:

<i>Company Name</i>	<i>Honoraria/ Expenses</i>	<i>Consulting/ Advisory Board</i>	<i>Funded Research</i>	<i>Royalties/ Patent</i>	<i>Stock Options</i>	<i>Ownership/ Equity Position</i>	<i>Employee</i>	<i>Other (please specify)</i>
Arsenal-Bio			x					
AstraZeneca		x	x					
Atara Biotherapeutics			x					
Alkermes			x					
Corcept		x						
Context Therapeutics			x					
Genentech			x					
Genmab/Seagen Therapeutics/Pfizer		x	x					
Gilead		x						
GSK		x	x					
Immunogen	x							
Iovance			x					
Lyell Therapeutics			x					
Loxo		x	x					
Regeneron		x	x					
OnCusp		x	x					
Recursion			x					
Solve Therapeutics			x					
Takeda		x						
Tubulis		x						

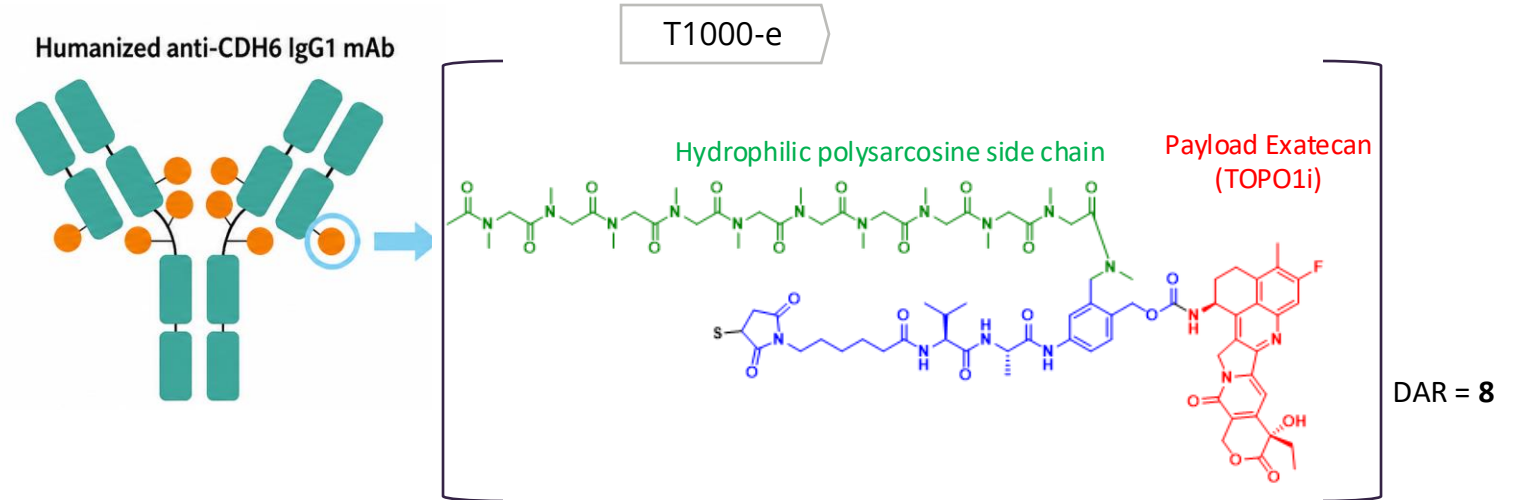
CUSP06 Overview

Cadherin-6 / K-cadherin (CDH6)

- CDH6 is a type II classic cadherin and plays a key role in embryonic kidney development.¹
- CDH6 has limited known roles in adults and expression is restricted to low/medium levels in the kidney, mammary gland and thymus¹.

CDH6 is highly expressed across multiple mid-to-large cancer indications.¹

Thoughtfully designed for improved efficacy



- CUSP06 is a novel anti-CDH6 antibody-drug conjugate with a topoisomerase I inhibitor payload (exatecan) and DAR of 8.
- Exatecan has demonstrated stronger bystander effect vs deruxtecan and is significantly less susceptible to BCRP/P-gp efflux^{2,3}.

Source: 1. Lu et al., *Pharmaceutics*, 2025; 2. Weng et al., *Cancer Discovery* 2023; 3. Lu et al., *AACR* 2023.

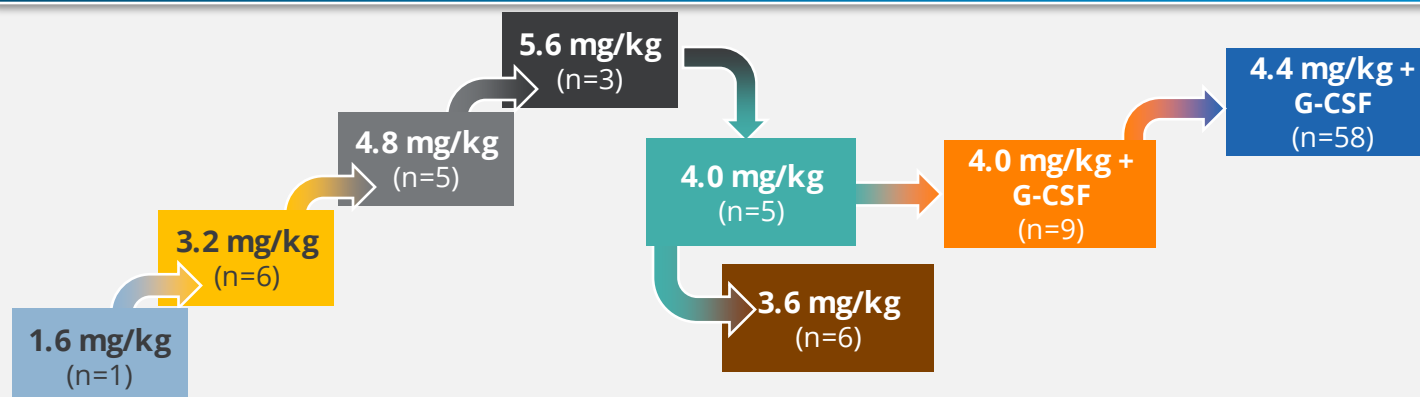
OC: Ovarian Cancer, CCA: Cholangiocarcinoma; BTC: Biliary Tract Cancer; GBM: Glioblastoma Multiforme; PDAC: Pancreatic Ductal Adenocarcinoma; GC: Gastric Cancer; EC: Endometrial Cancer; NSCLC: Non-Small Cell Lung Cancer;

CUSP06-1001 Study Design

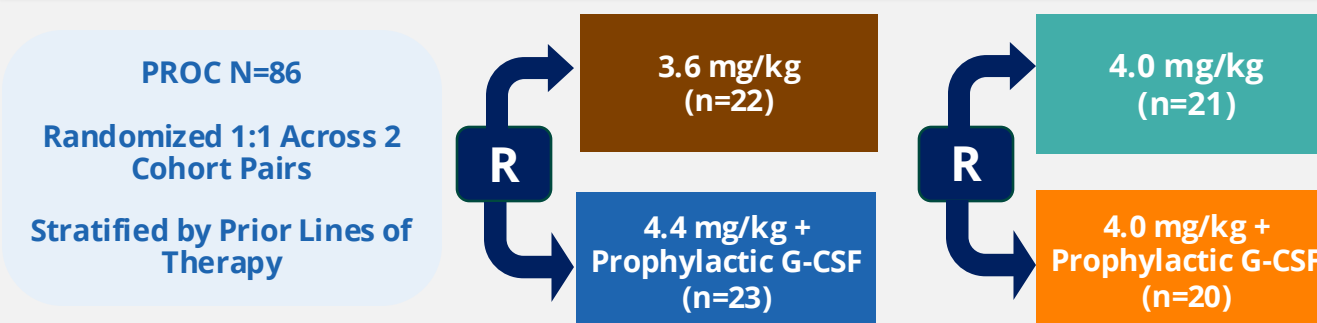
FIH study CUSP06-1001: Phase 1a/1b, open-label, multi-center dose escalation and expansion in platinum-refractory/resistant ovarian cancer (PROC), advanced RCC and other CDH6-positive solid tumors

191 patients dosed Q3W
across Phase 1a + Phase 1b as of 17JUL26

Phase 1a Dose Escalation* N=93 Total, N=32 PROC



Phase 1b Dose Optimization and Expansion N=98 Total, N=86 PROC



Phase 1b Eligibility and Endpoints

Phase 1b Key Eligibility:

- High-grade serous or endometrioid ovarian, primary peritoneal, or fallopian tube cancer which is platinum-resistant
- 1-4 prior lines of therapy, including mirvetuximab if FRα-high and a PARPi if known BRCA+
- Measurable disease per RECIST v1.1
- ECOG 0 or 1
- Prior tx with a TOP1-ADC is excluded

Phase 1b Endpoints:

- **Primary:** ORR (RECIST v1.1), safety parameters (incidence/severity of AEs and SAEs, frequency and duration of dose modifications)
- **Secondary:** CBR, DCR, DOR, TTP, PFS (RECIST v1.1), OS, PK parameters

Baseline Characteristics are Balanced Between Dosing Cohorts Across Ph1a and Ph1b

		Ph1a (n=93)	Ph1b (n=98)	Ph1b PROC (n=86)	Ph1a & Ph1b (n=191)
Age (yrs), Median (range)		62.0 (18-79)	63.0 (29-83)	63.5 (29-83)	63.0 (18-83)
Sex, Male / Female, n (%)		24 (25.8) / 69 (74.2)	7 (7.2) / 91 (92.9)	0 / 86 (100)	31 (16.2) / 160 (83.8)
Race, n (%)	White	74 (79.6)	77 (78.6)	67 (77.9)	151 (79.1)
	Black/African American	8 (8.6)	4 (4.1)	4 (4.7)	12 (6.3)
	Asian	5 (5.4)	7 (7.2)	6 (7.0)	12 (6.3)
	Other	6 (6.5)	10 (10.3)	9 (10.5)	16 (8.4)
ECOG PS, 0 / 1, n (%)		27 (29.0) / 65 (69.9)*	46 (47.4) / 52 (53.1)	42 (48.8) / 44 (51.2)	73 (38.2) / 117 (61.3)*
Prior Lines of Therapy, Median (range)		3.0 (1-9)	3.0 (1-5)	3.0 (1-5)	3.0 (1-9)
Tumor Type, n (%)	Ovarian Prior Lines	3.0 (1-9)	3.0 (1-5)	3.0 (1-5)	3.0 (1-9)
	Ovarian	38 (40.9)	88 (89.8)	86 (100)	126 (66.0)
	Prior platinum	38 (100)	88 (100)	86 (100)	126 (100)
	Prior taxane	38 (100)	88 (100)	86 (100)	126 (100)
	Prior bevacizumab	31 (81.6)	73 (83.0)	72 (83.7)	104 (82.5)
	Prior PARPi	19 (50.0)	40 (45.5)	40 (46.5)	59 (46.8)
	Prior mirvetuximab	9 (23.7)	26 (29.5)	26 (30.2)	35 (27.8)
Other Tumor Types		55 (59.1)	10 (10.2)	0	65 (34.0)

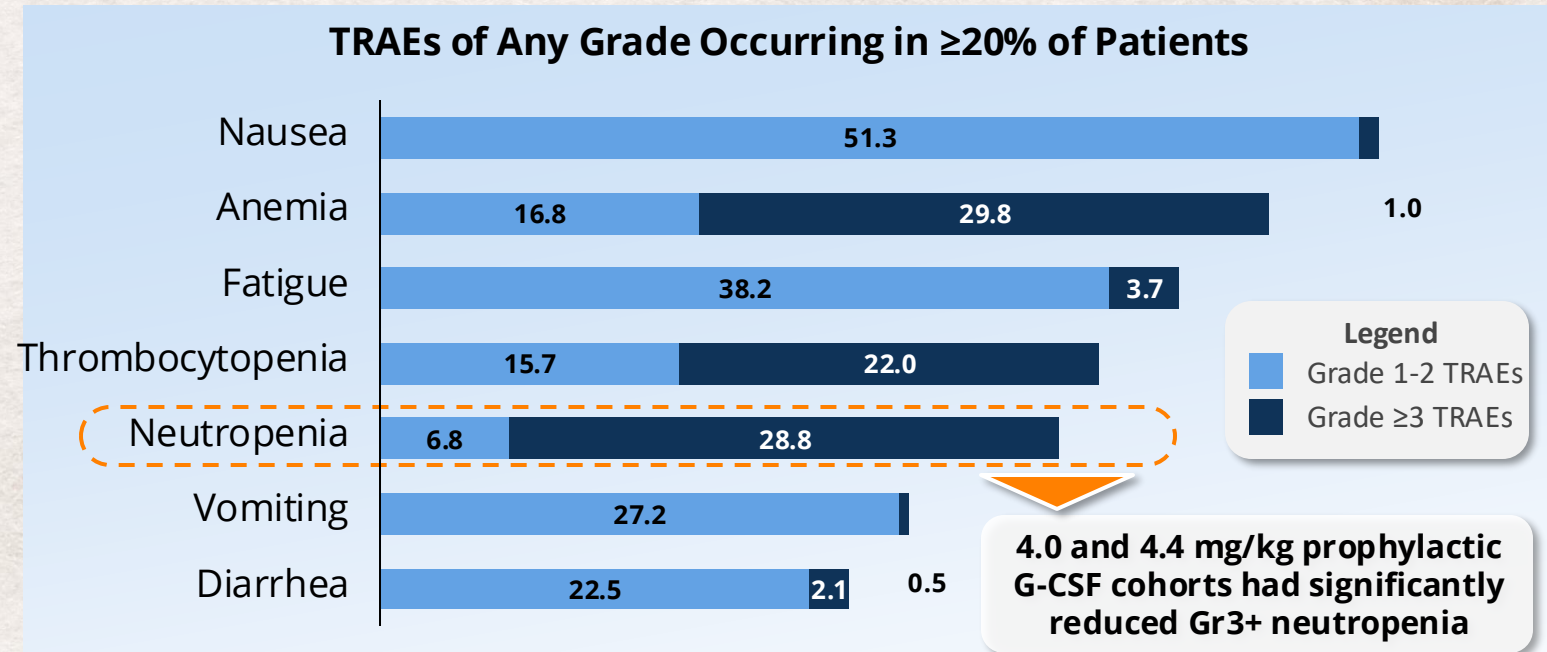
PROC: Platinum Resistant Ovarian Cancer; * Includes 1 patient with missing ECOG.

Data cut-off: 17JUL2026

Overall Safety Profile is Consistent with Other TOP1-Inhibitor ADCs: Manageable GI and Hematologic Toxicities as the Most Common TRAEs

Safety Summary	
n (%)	Total (n = 191)
Any TEAE	187 (97.9)
Grade ≥3	125 (65.5)
Grade 5	1 (0.5)
Treatment-related TEAE	165 (86.4)
Grade ≥3	99 (51.8)
Grade 5	1 (0.5)
Any SAE	71 (37.2)
Grade ≥3	65 (34.0)
Grade 5	1 (0.5)
Treatment-related SAE	25 (13.1)
Grade ≥3	24 (12.6)
Grade 5	1 (0.5)

Data cut-off: 17JUL2026; TRAEs: Treatment-Related Adverse Events



- Most common TRAEs were **hematologic** (anemia, neutropenia, thrombocytopenia), **GI** (nausea, vomiting, diarrhea), and **fatigue**, consistent with TOP-1 inhibitor ADC class effects
- One Grade 5 febrile neutropenia occurred at 5.6 mg/kg
- Dose modifications were primarily driven by hematologic AEs, consistent with mechanism, and were manageable
- **No ocular toxicity reported**
- **Pneumonitis remains rare and low-grade: 4 events in 191 pts (2.1%) - 2 Gr 1, 2 Gr 2**

Safety Profile in Ph1b PROC: Consistent with Overall Study Population

Most common TRAEs (≥ 20%) and/or Adverse Event of Special Interest - Ph1b PROC patients

	Cohort Pair 1				Cohort Pair 2					
TRAE n (%)	3.6 mg/kg (n=22)		4.4 mg/kg + G (n=23)		4.0 mg/kg (n=21)		4.0 mg/kg + G (n=20)		Total (n=86)	
	All Grade	Grade ≥3	All Grade	Grade ≥3	All Grade	Grade ≥3	All Grade	Grade ≥3	All Grade	Grade ≥3
Any TRAE	21 (95.5)	15 (68.2)	22 (95.7)	13 (56.5)	20 (95.2)	10 (47.6)	19 (95.0)	9 (45.0)	82 (95.4)	47 (54.7)
Nausea	17 (77.3)	0	17 (73.9)	0	7 (33.3)	0	12 (60.0)	1 (5.0)	53 (61.6)	1 (1.2)
Fatigue	14 (63.6)	1 (4.5)	11 (47.8)	0	5 (23.8)	1 (4.8)	10 (50.0)	2 (10.0)	40 (46.5)	4 (4.7)
Anemia	13 (59.1)	10 (45.5)	13 (56.5)	10 (43.5)	3 (14.3)	1 (4.8)	8 (40.0)	2 (10.0)	37 (43.0)	23 (26.7)
Vomiting	13 (59.1)	0	8 (34.9)	0	5 (23.8)	0	7 (35.0)	0	33 (38.4)	0
Diarrhea	8 (36.4)	0	7 (30.4)	1 (4.4)	6 (28.6)	0	8 (40.0)	2 (10.0)	29 (33.7)	3 (3.5)
Thrombocytopenia	8 (36.4)	4 (18.2)	11 (47.8)	6 (26.1)	5 (23.8)	2 (9.5)	5 (25.0)	3 (15.0)	29 (33.7)	15 (17.4)
Neutropenia	13 (59.1)	12 (54.6)	6 (26.1)	4 (17.4)	8 (38.1)	7 (33.3)	1 (5.0)	1 (5.0)	28 (32.6)	24 (27.9)
Alopecia	9 (40.9)	0	8 (34.8)	0	1 (4.8)	0	3 (15.0)	0	21 (24.4)	0
Febrile Neutropenia	1 (4.6)	1 (4.6)	1 (4.4)	1 (4.4)	0	0	2 (10.0)	2 (10.0)	4 (4.7)	4 (4.7)

Only 1 Pneumonitis event (Gr2) out of 86 pts was observed in the Ph1B PROC cohorts (1.1%)

Data cut-off: 17JUL2026

Note: Based on sequential enrollment of cohort pairs, the median duration of exposure in Cohort Pair 2 is shorter than Cohort Pair 1

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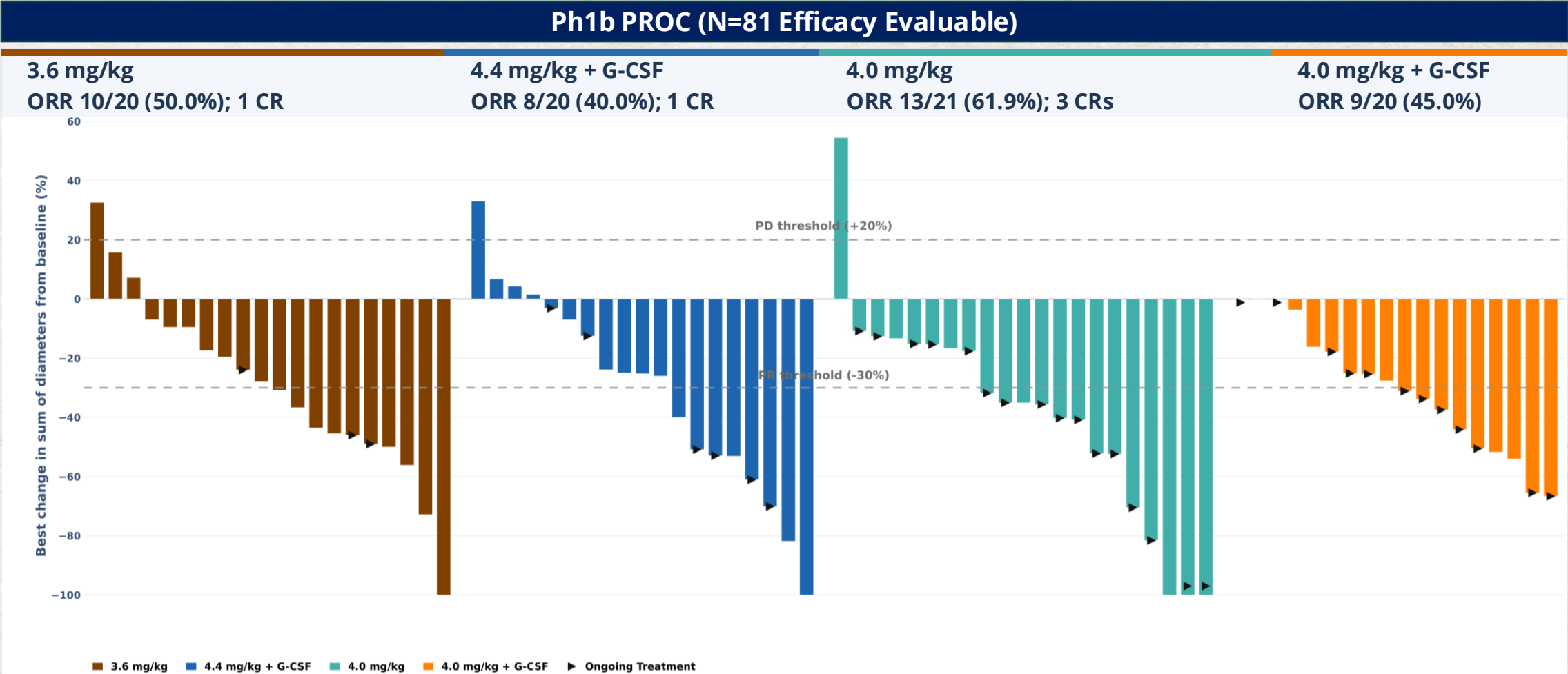
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More Reactive G-CSF Use Observed in Non-G-CSF Cohorts; Dose Modification Rate is Low and Manageable

G-CSF Use n (%)	3.6 mg/kg (n=22)	4.4 mg/kg + G (n=23)	4.0 mg/kg (n=21)	4.0 mg/kg + G (N=20)	Total (n=86)
Any G-CSF Use	14 (63.6)	23 (100)	8 (38.1)	20 (100)	65 (75.6)
Primary Prophylaxis	0	23 (100)	1 (4.8)	20 (100)	44 (51.2)
Secondary Prophylaxis	11 (50.0)	0	4 (19.1)	0	15 (17.4)
Tx for Neutropenia AE	10 (45.5)	1 (4.4)	3 (14.3)	2 (10.0)	16 (18.6)

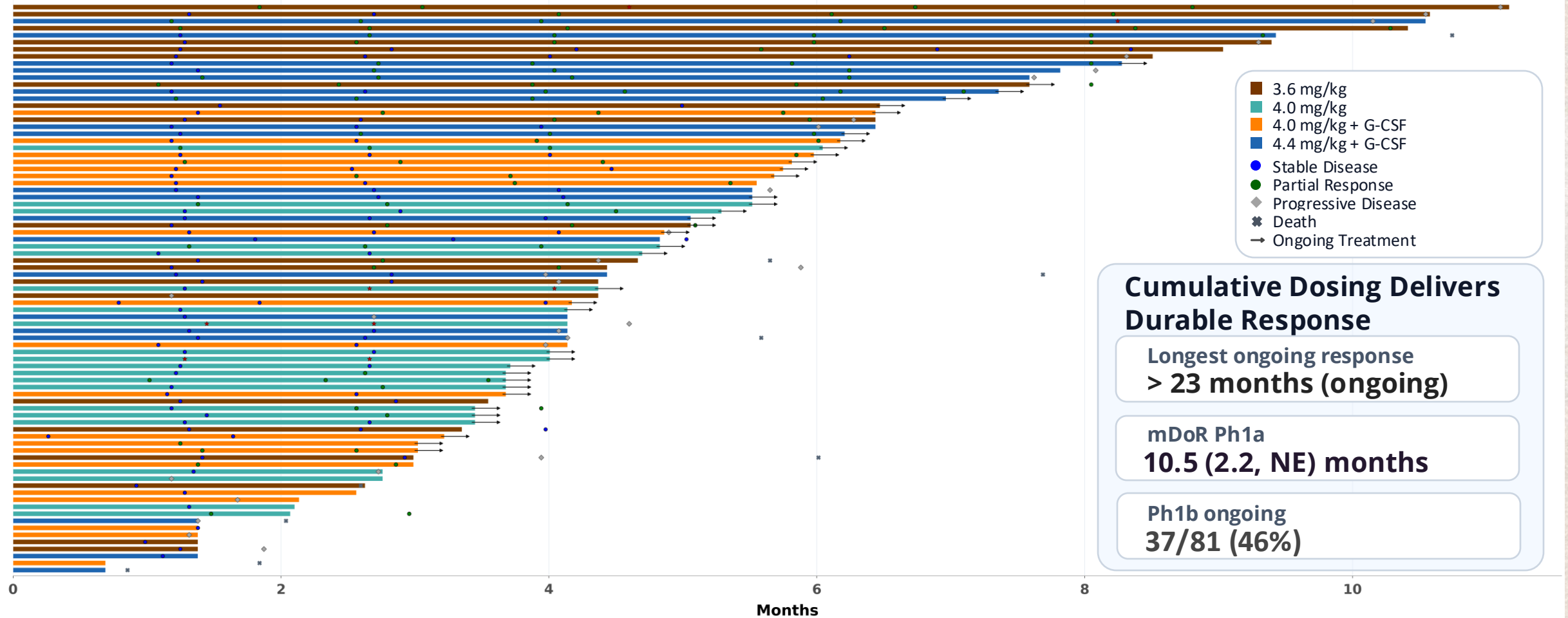
Dose Mod due to TEAE n (%)	3.6 mg/kg (n=22)	4.4 mg/kg + G (n=23)	4.0 mg/kg (n=21)	4.0 mg/kg + G (n=20)	Total (n=86)
Any Dose Mod	12 (54.6)	8 (34.8)	4 (19.1)	3 (15.0)	27 (31.4)
Delay	12 (54.6)	7 (30.4)	4 (19.1)	3 (15.0)	26 (30.2)
Reduction	6 (27.3)	3 (13.0)	3 (14.3)	2 (10.0)	14 (16.3)
Interruption	0	0	0	1 (4.4)	1 (1.2)
Withdrawal	4 (18.2)	0	0	1 (4.4)	5 (5.8)

CUSP06 Demonstrates Meaningful Responses Across Dose Levels in Ph1b PROC, Including Complete Responses



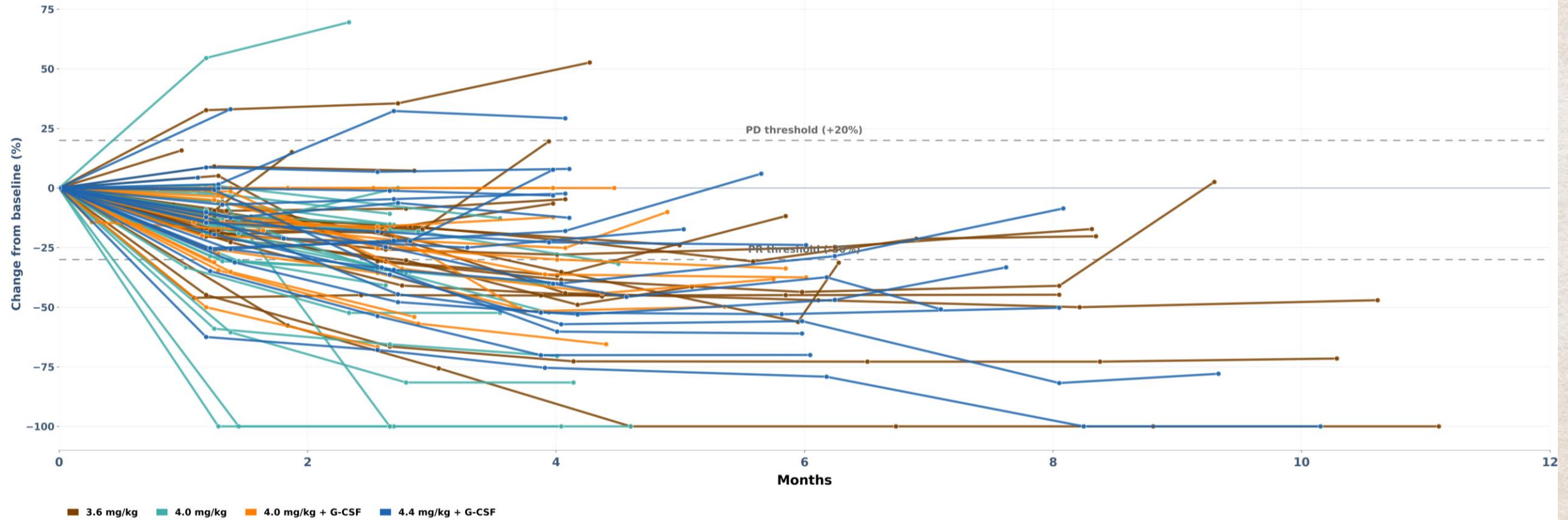
Durable Benefit Observed with Meaningful Time on Treatment with Multiple Long-duration Responders

Phase 1b PROC (N=81 Efficacy Evaluable)



Rapid, Deep, and Durable Tumor Regression in Ph1b PROC

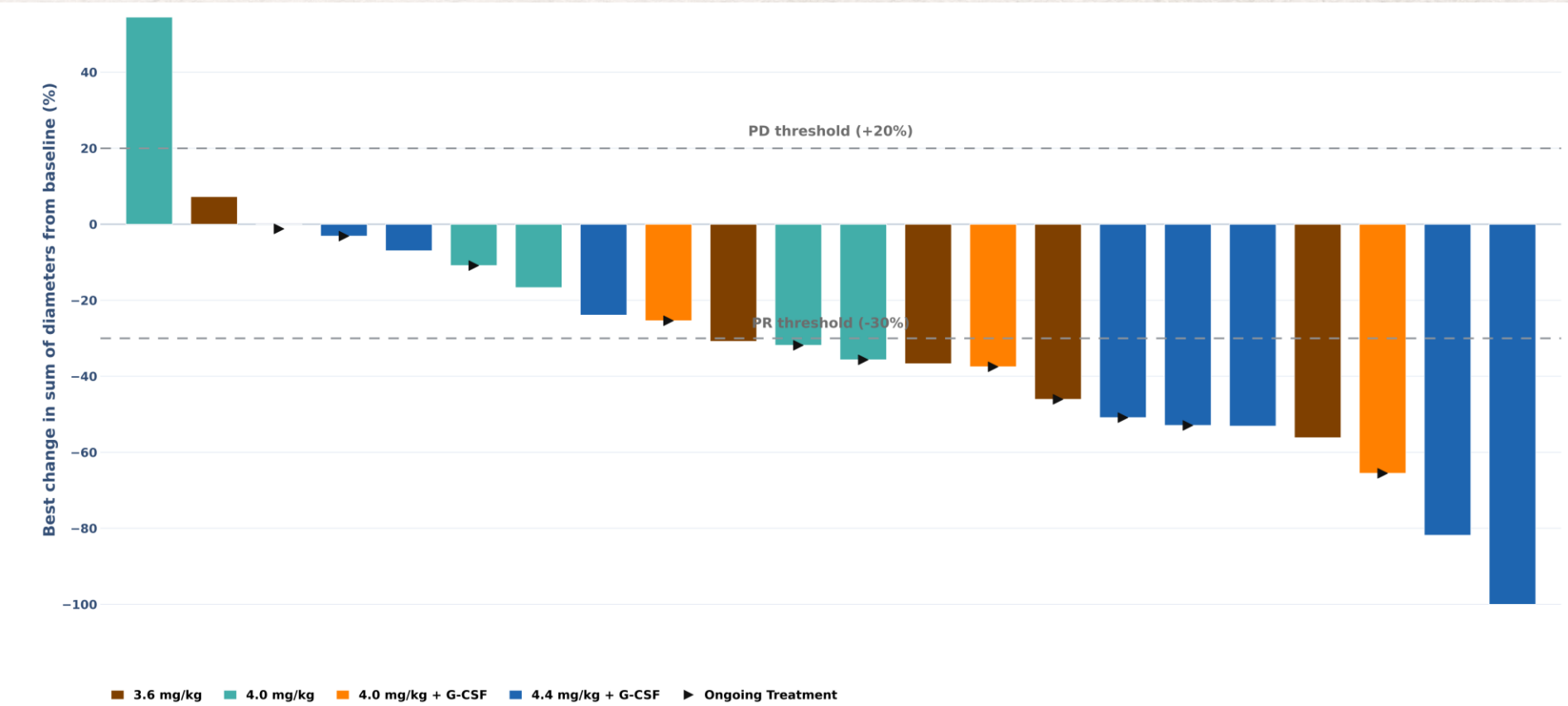
Ph1b PROC (N=81 Efficacy Evaluable)



Data cut-off: 23Sep2026

CUSP06 Demonstrates Robust Activity in Patients Previously Treated with Mirvetuximab Soravtansine

Ph1a and Ph1b Post-MIRV Patients (N=30 Efficacy Evaluable)



n (%)	Total (N = 30)
BoR	
CR	1 (3.33)
PR	15 (50.0)
SD	10 (33.3)
PD	3 (10.0)
ORR	16/30 (53.2)
CBR (CR+PR+SD)	26/30 (86.7)

Data cut-off: 23Sep2026

Summary and Conclusion

- CUSP06 is a CDH6-directed ADC delivering an exatecan (TOP1 inhibitor) payload, currently being evaluated in the Phase 1 CUSP06-1001 study in PROC.
- The safety profile was consistent with other TOP1-inhibitor ADCs, with manageable GI and hematologic toxicities as the most common TRAEs.
 - Primary prophylactic G-CSF reduced high-grade neutropenia.
 - Dose modifications were infrequent and manageable.
 - Pneumonitis was rare and low-grade.
- CUSP06 demonstrated promising clinical activity in PROC, including complete responses.
 - Encouraging activity was observed in patients previously treated with mirvetuximab.
- These data support continued development of CUSP06 in PROC.

Acknowledgements

- The patients, families and caregivers who participated in this study
- The CUSP06-1001 investigators and site teams
- IGCS for the opportunity to share these findings with the global gynecologic oncology community



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CUSP06 presentation