Initial Results from Dose Escalation Portion from the Phase 1 Trial of SIM0505, an Antibody Drug Conjugate (ADC) Cadherin-6 (CDH6)

June 2, 2026

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Today's Speakers

Michael Richman

Chief Executive Officer, NextCure

Udayan Guha MD, PhD

Chief Medical Officer, NextCure

Rakesh Dixit, PhD, DBAT

Scientific Advisory Board, NextCure

Ursula Matulonis, MD

Chief, Gynecologic Oncology, Dana Farber Cancer Institute, and NextCure Scientific Advisory Board

Beryl Manning-Geist, MD,

Assistant Professor, Gynecology and Obstetrics, Emory University

Today's Agenda

Post-ASCO Investor Event

Welcome	Michael Richman, CEO
SIM0505 Overview	Rakesh Dixit, PhD, DBAT
ASCO 2026 Data	Ursula Matulonis, MD
Unmet Need and Clinical Perspective	Udayan Guha, MD, PhD, CMO, NextCure, Ursula Matulonis, MD, and Beryl Manning-Geist, MD
Q&A	NextCure Management and Key Opinion Leaders
Closing Comments	Michael Richman, CEO

SIM0505 Demonstrated Best-in-Class Potential in Gynecologic Cancers

- Positive SIM0505 Phase 1 dose escalation data at ASCO 2026
- 55% ORR response in gynecologic cancers at therapeutic doses*
- 52.9% ORR in ovarian cancer, 66.7% ORR in uterine serous carcinoma (USC)
- Favorable safety and tolerability in heavily treated patients
- Phase 1 dose optimization underway, with an emphasis on patients with platinum resistant ovarian cancer (PROC) and USC
- PROC and USC represent two of the most challenging gynecologic malignancies with significant unmet need

*Based on therapeutic doses (4.8, 5.6, 6.4, 7.2, and 8.0 mg/kg) at 12 weeks and best response

SIM0505 Differentiation

Rakesh Dixit, PhD, DBAT

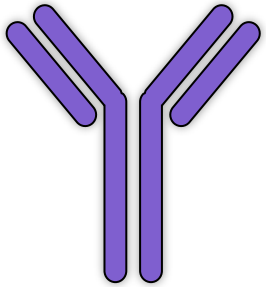
ADC Specialist,

NextCure Scientific Advisory Board

SIM0505 is a Differentiated CDH6 TOPOi ADC

VALIDATED TARGET WITH PROPRIETARY TOPOi PAYLOAD

CDH6 mAb

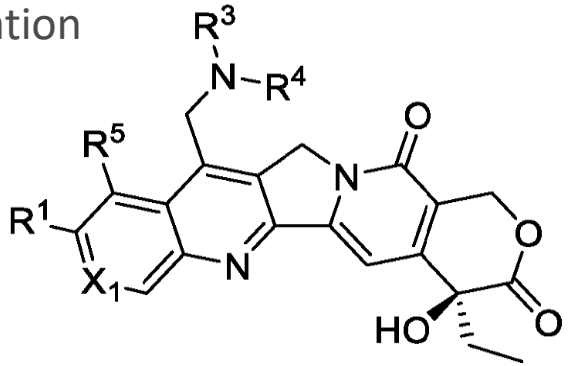


Unique Binding Epitope with Increased Affinity

Linker

GGFG Linker

Cysteine conjugation

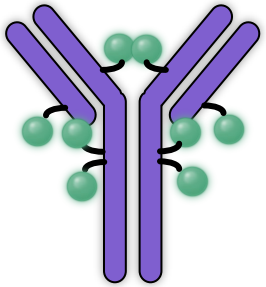


Gly-Gly-Phe-Gly Provides Tumor-Specific Cleavage

Payload CPT116 (TOPO)

High Systemic Clearance for Reduced Toxicity

DAR 8.0

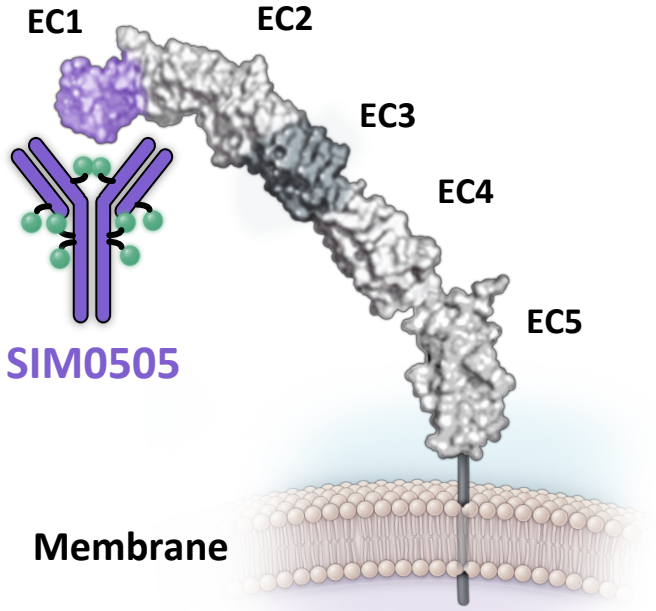


Potent Cytotoxicity with Anticipated Safety Improvement

SIM0505 Structural and Functional Differentiation by Design

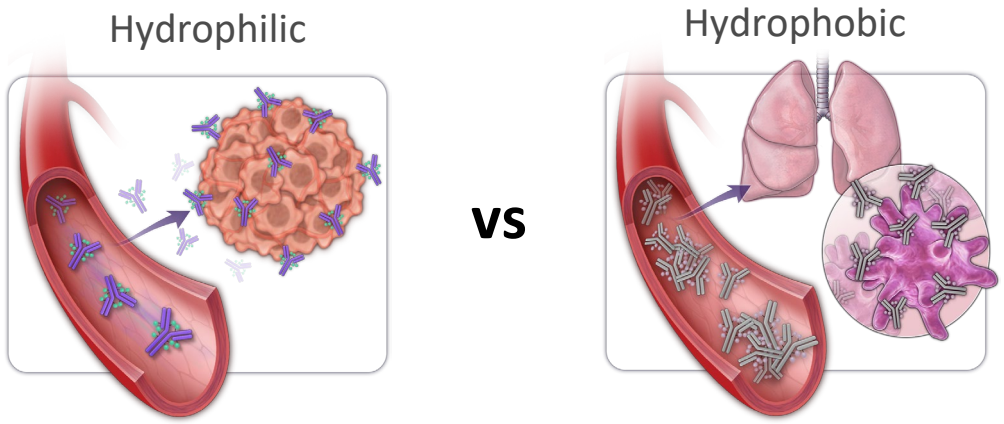
SIM0505

- Unique distal EC1 epitope on CDH6
- Ovarian, uterine, RCC, NSCLC
- High affinity & internalization
- PK proportionality



CPT116 (PAYLOAD)

- Designed for better tolerability & safety
- Hydrophilic & high systemic clearance
- Good permeability & bystander effect
- Less aggregation than hydrophobic



SIM0505 Phase 1 Dose Escalation Data

Ursula Matulonis, MD

Chief, Division of Gynecologic Oncology,

Dana Faber Cancer Institute, and NextCure

Scientific Advisory Board

SIM0505 Development Plan

COMPLETED
DOSE ESCALATION
2Q 2026

Ovarian, USC, RCC, EC

Q3W

Dose Escalation + Intermediate Doses

- 9.6 mg/kg (n = 4)
- 8.0 mg/kg (n = 10)
- 7.2 mg/kg (n = 10)
- 6.4 mg/kg (n = 13)
- 5.6 mg/kg (n = 6)
- 4.8 mg/kg (n = 6)
- 3.2 mg/kg (n = 7)
- 1.6 mg/kg (n = 3)

n = 59
(US = 25 & China = 34)

INITIATED
DOSE OPTIMIZATION
2Q 2026

PROC & USC

Q3W

- 7.2 mg/kg (n = 20-40)
- 6.4 mg/kg (n = 20-40)
- 5.6 mg/kg (n = 20-40)

- Generating recommended pivotal trial dose

Up to n = 120

PLANNING
PIVOTAL TRIAL

PROC

Q3W

R 1:1
- SIM0505 (n = 215)
- TPC* (n = 215)

- ORR (RECIST 1.1)
- PFS

Up to n = 430

*TPC: treatment of physician's choice

SIM0505 Patient Demographics

Baseline Characteristic	US Patients (n = 25)	China Patients (n = 34)	All Patients (n = 59)
Age, years			
Median (range)	63 (49-78)	56 (42-72)	58 (42-78)
Sex, n (%)			
Male	0 (0.0)	2 (5.9)	2 (3.4)
Female	25 (100)	32 (94.1)	57 (96.6)
Tumor Type, n (%)			
Ovarian	19 (76.0)	27 (79.4)	46 (78.0)
USC/other endometrial	6 (24.0)	4 (11.8)	10 (16.9)
RCC	0 (0.0)	3 (8.8)	3 (5.1)
ECOG performance status, n (%)			
0	8 (32.0)	8 (23.5)	16 (27.1)
1	17 (68.0)	26 (76.5)	43 (72.9)
Prior systemic anti-cancer regimens			
Median (range)	3 (1-9)	5 (1-12)	5 (1-12)

Data cut 07Apr26

Patient Population

- Poor performance status
  - ~73% ECOG 1
- Heavily pretreated
- ~75% of ovarian / USC patients had FIGO Stage IV metastatic tumor burden

FIGO: International Federation of Gynecology and Obstetrics

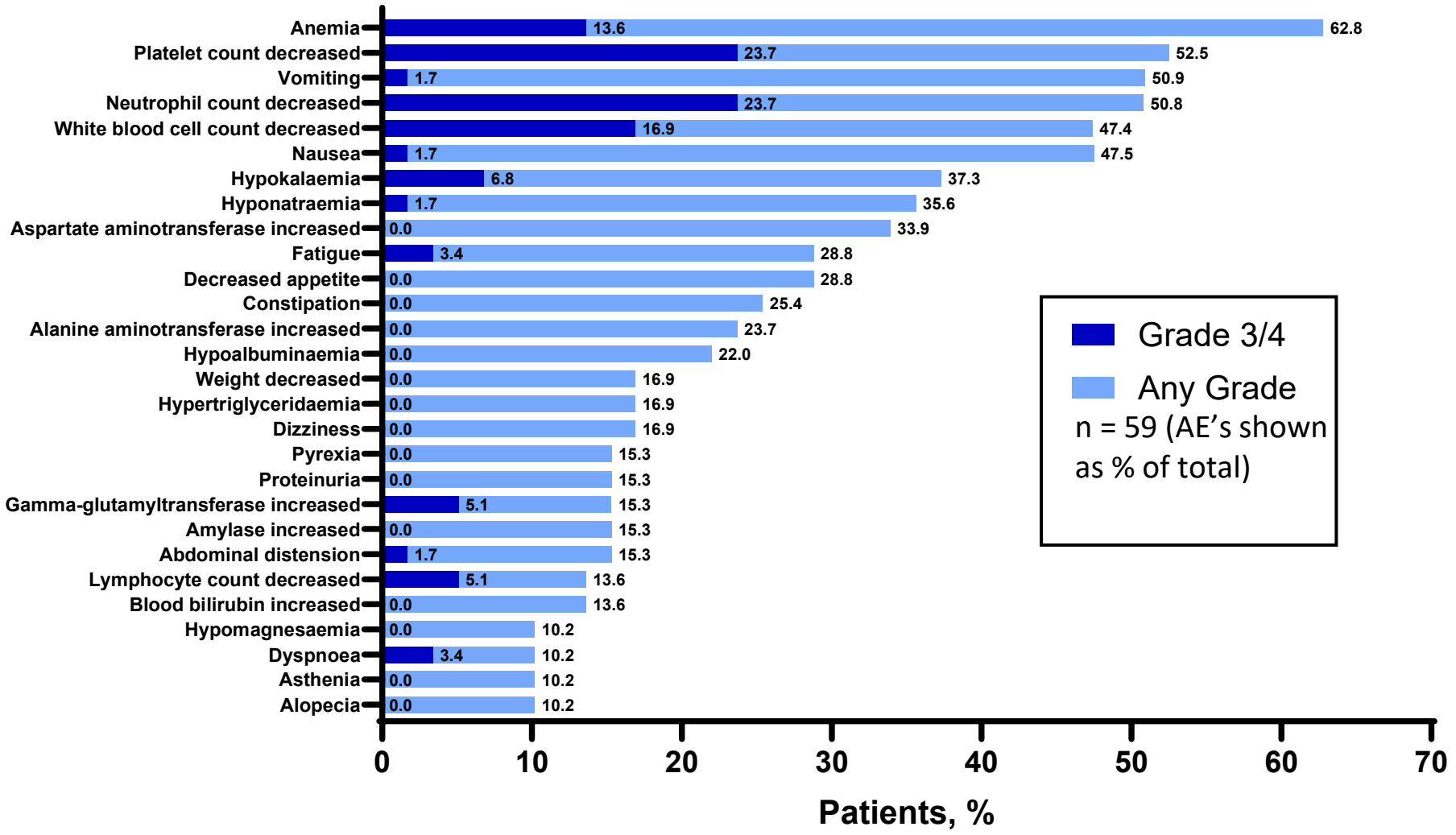
SIM0505 Has Shown a Well Manageable Safety Profile

Overview of Adverse Events	1.6 – 9.6 mg/kg (n = 59) n (%)
Treatment-emergent adverse events (TEAEs) (%)	59 (100)
Grade ≥3	32 (54.2)
Grade 5 [a]	2 (3.4)
TEAEs related to study drug (TRAEs) (%)	57 (96.6)
Grade ≥3	28 (47.5)
Grade 5	0
Any Serious adverse events (SAEs) (%)	16 (27.1)
Treatment related SAE, n (%)	10 (16.9)
TRAE Dose modifications, n (%)	
Dose interruption	14 (23.7)
Dose reduced	11 (18.6)
Dose discontinued	3 (5.1)
Interstitial Lung Disease (ILD) / Pneumonitis [b]	2 (3.3)
Grade ≥3	0 (0)

Data cut 07Apr26

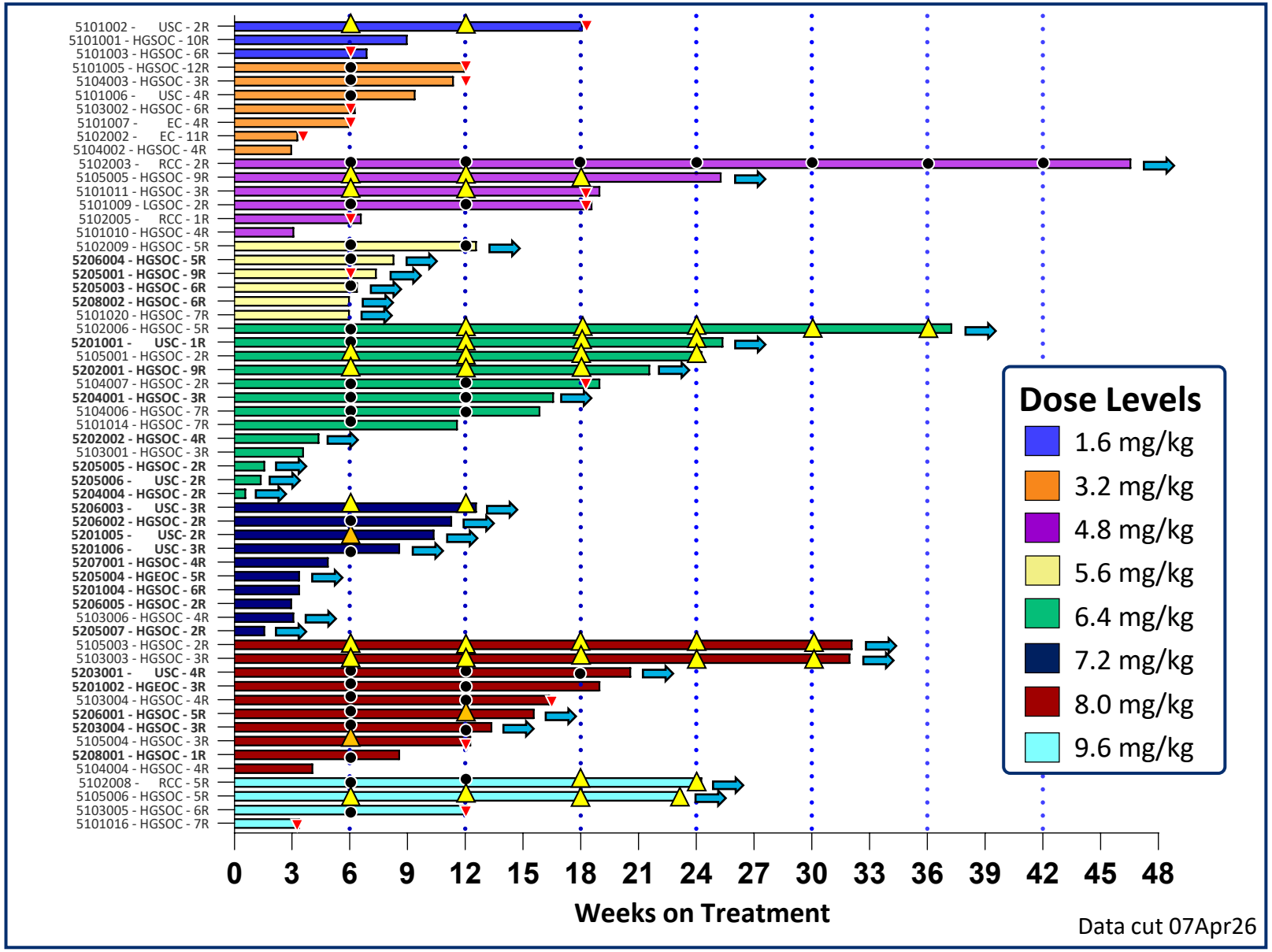
a. 1 Gr5 at 7.2 mg/kg related to disease progression, 1 Gr5 at 8.0 mg/kg complicated UTI (not related)
b. 1 Gr1 ILD at 5.6mg/kg and 1 Gr2 ILD at 6.4mg/kg

Most Common TEAEs (≥10%)



- MTD not reached
- No primary prophylaxis *required* for neutropenia & thrombocytopenia
- Grades 1 & 2 TEAEs were predominantly hematological, nausea & vomiting
- Grades 3 & 4 TEAEs were hematological and manageable

Swimmer Plot All Patients at All Doses



- 6 dose cohorts + 2 intermediate dose cohorts

PATIENTS ENROLLED	Total
TOTAL	**59**
Ovarian Cancer	46
Uterine Serous Carcinoma (USC)	8
Renal Cell Carcinoma (RCC)	3
Other Endometrial Cancer	2

- Prior systemic anti-cancer regimens: Median 5 (1-12)

Bold – US patients

On treatment

cPR

uPR

SD

RECIST PD

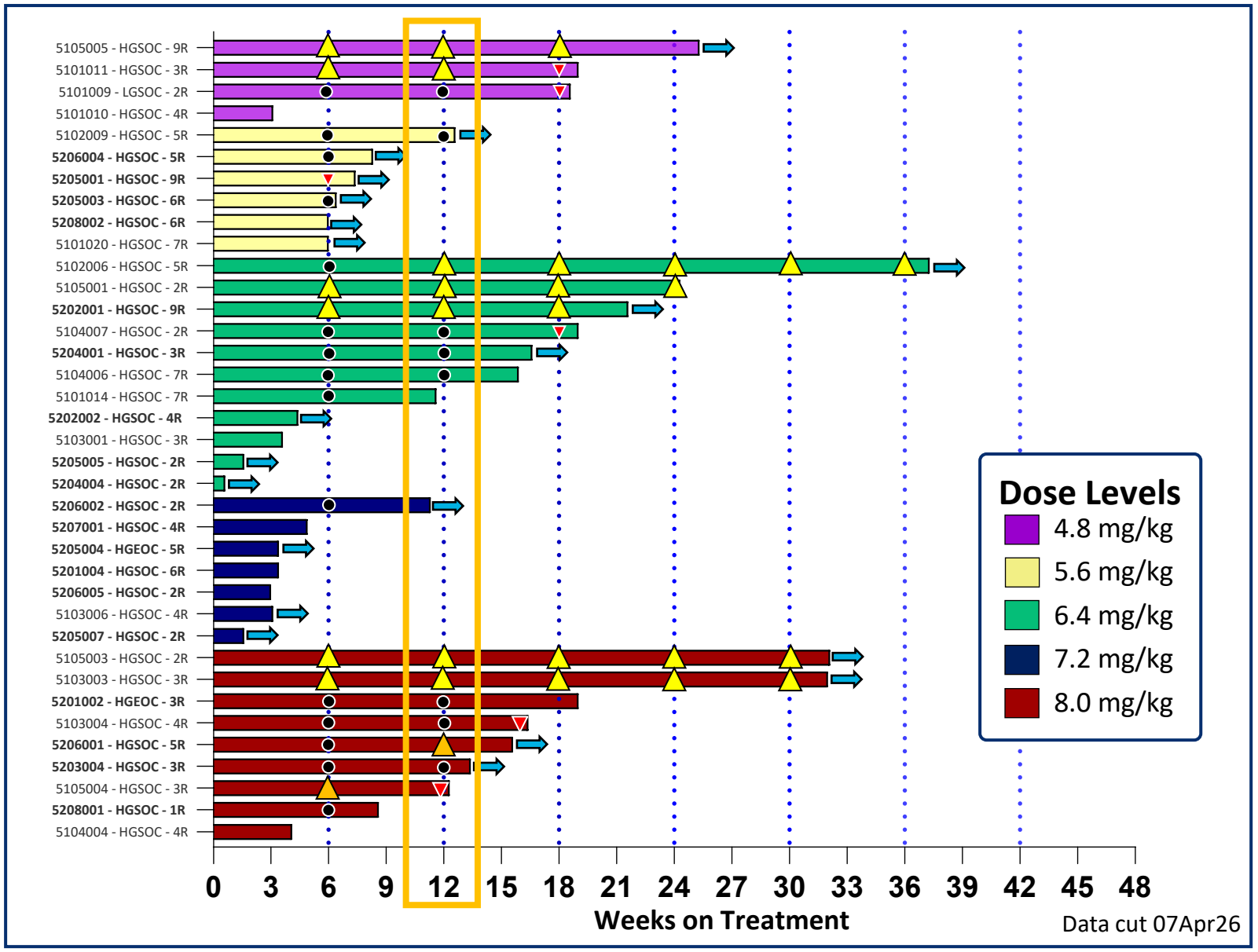
EC: endometrial cancer; HGSOC: high-grade serous ovarian cancer; HGEOC: high-grade endometroid cancer; LGSOC: low-grade serous ovarian cancer; RCC: renal cell carcinoma; USC: uterine serous carcinoma

cPR: confirmed partial response; uPR: unconfirmed partial response

ORR at 4.8 – 8.0 mg/kg: ≥12 Weeks and Best Response

Tumor type	Evaluable (n)	PRs (n)	ORR
Gynecologic Cancers (OC + USC)	20	11	55.0% (11/20)
Ovarian Cancer (OC)	17	9	52.9% (9/17)
Uterine Serous Carcinoma (USC)	3	2	66.7% (2/3)

Ovarian Cancer at Therapeutics Doses (4.8 – 8.0 mg/kg)



- n = 37 ovarian cancer patients
- Patients with at least ≥12 weeks follow-up

Evaluable	PR	ORR
n = 17	**9**	**52.9%**

- Other: 1 PR 9.6 mg/kg

On treatment

cPR
uPR
SD
RECIST PD

HGSOC: high-grade serous ovarian cancer; HGEOC: high-grade endometroid cancer; LGSOC: low-grade serous ovarian cancer
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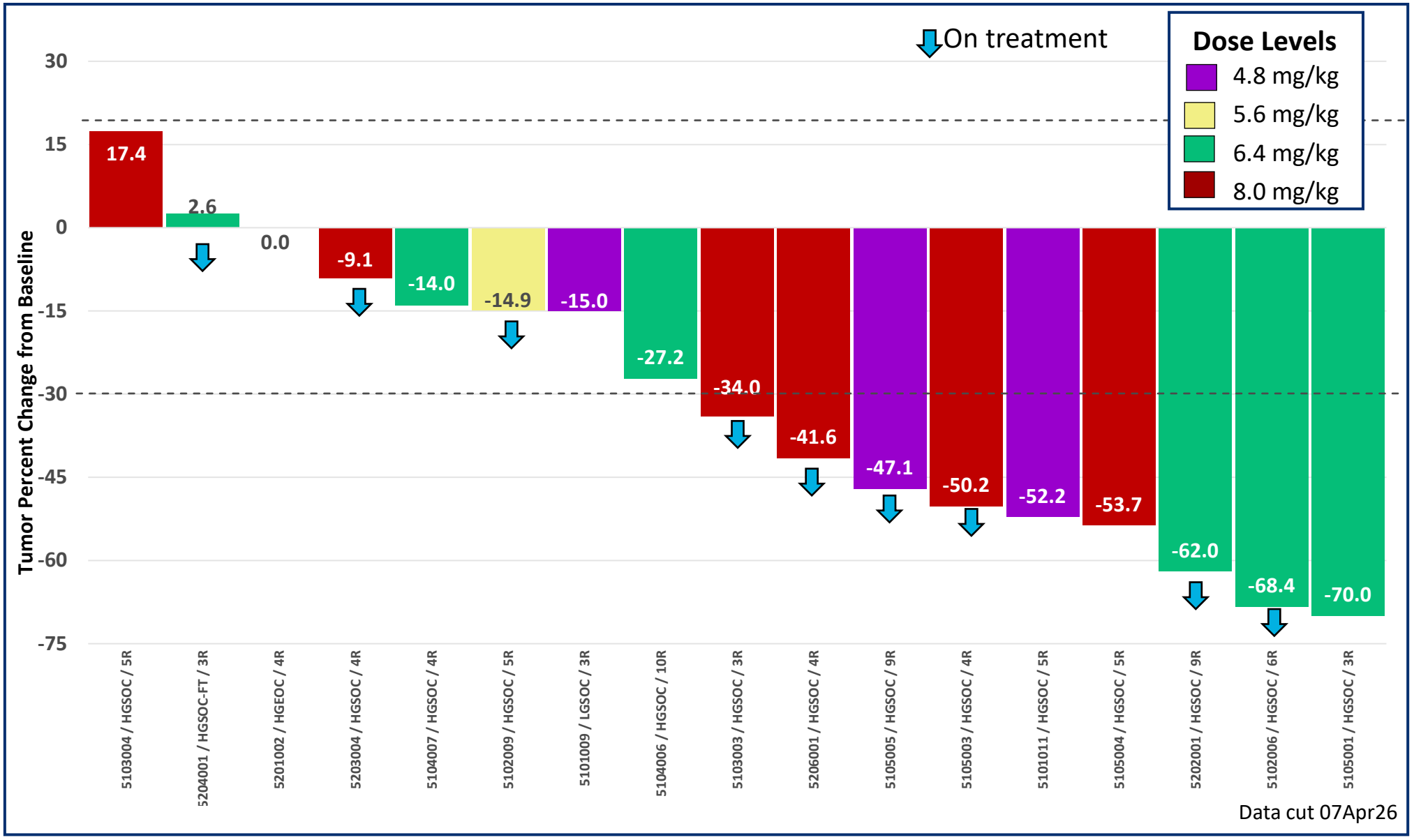
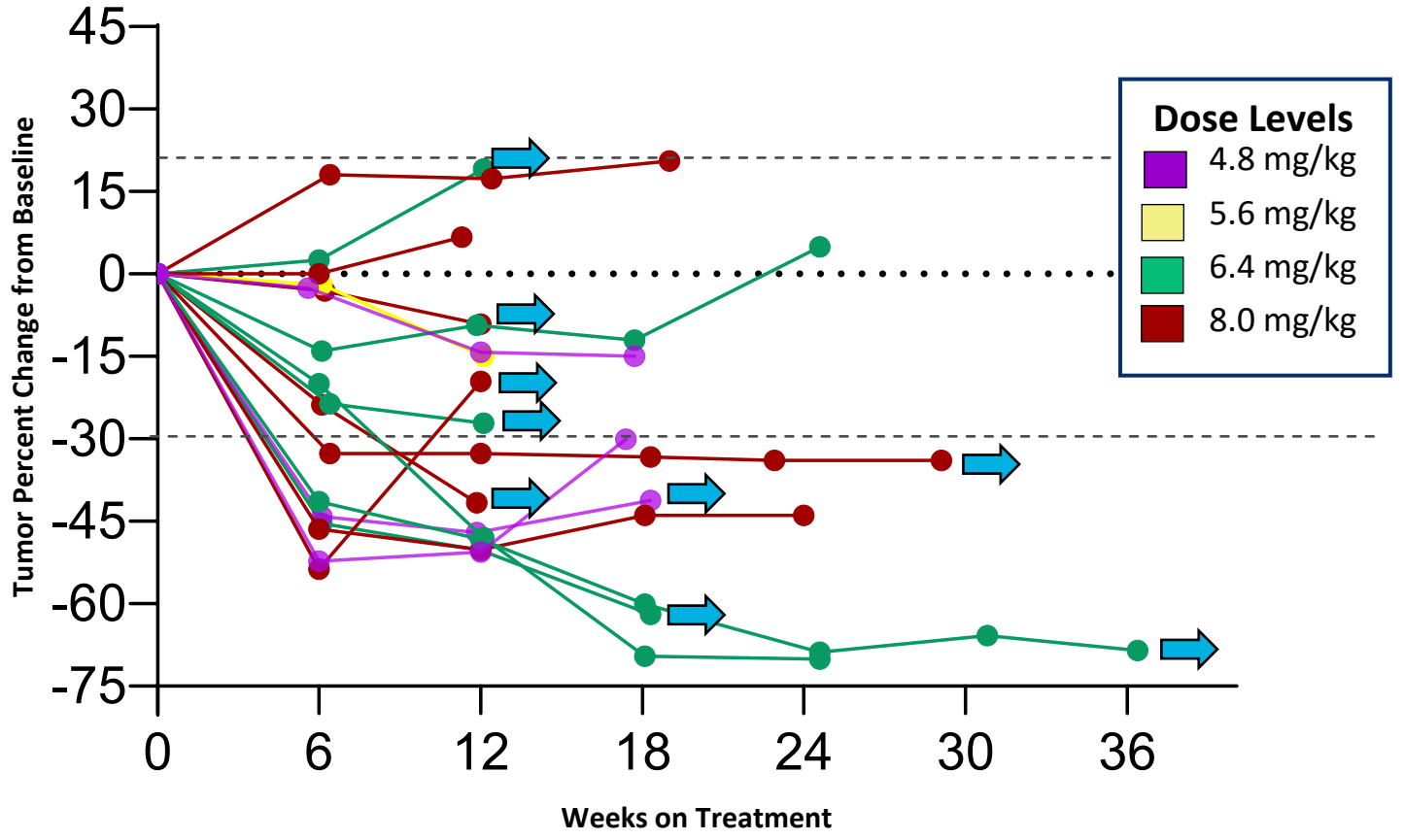
Ovarian Cancer (4.8 – 8.0 mg/kg)



- Defined therapeutic range
- Greatest tumor shrinkage at 6.4 & 8.0 mg/kg
- Up to 70% tumor shrinkage

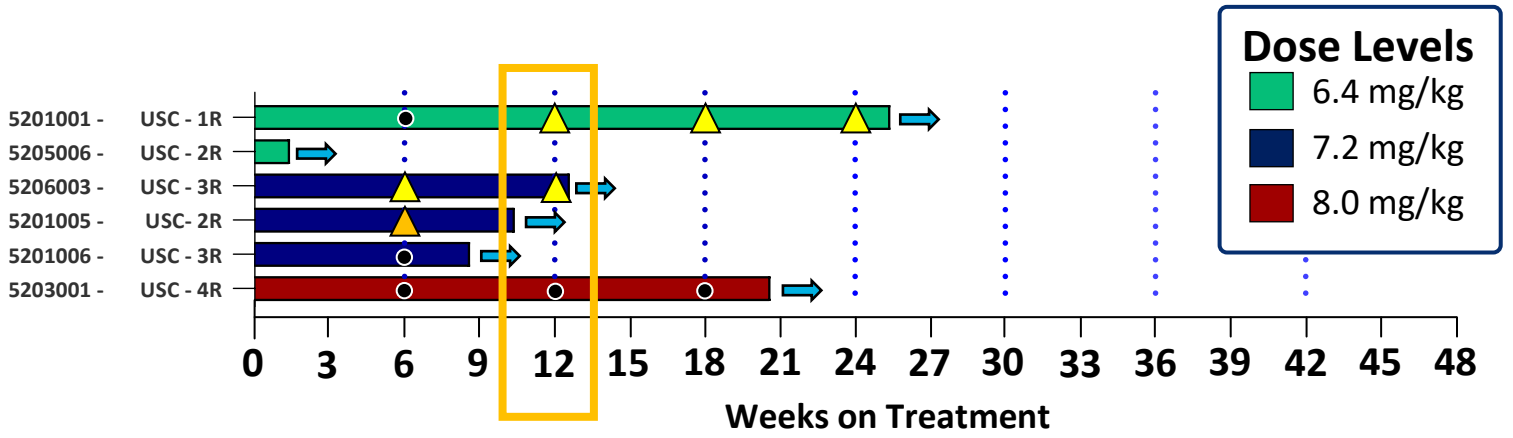
Ovarian Cancer (4.8 – 8.0 mg/kg)



Data cut 07Apr26

- Most patients (15/17) had tumor shrinkage
- Increasing tumor shrinkage with continued treatment
- The greatest tumor shrinkage and durability occurred at 6.4mg/kg

Uterine Serous Carcinoma (4.8 – 8.0 mg/kg)



Data cut 07Apr26

- Rare and highly aggressive form of endometrial cancer
- Accounts for ~10% of uterine cancer, but causes ~40% of uterine cancer deaths
- Rapid progression and poor clinical outcomes
- Treated with platinum-based chemotherapy

Data cut 07Apr26

- n = 6 USC patients enrolled
- Patients with at least ≥12 weeks follow-up

Evaluable	PR	ORR
n = 3	**2**	**66.7%**

- Other:
  - 1 PR 1.6 mg/kg
  - 1 PR 7.2 mg/kg (has not reached 12 weeks)

cPR
uPR
SD
RECIST PD
On treatment

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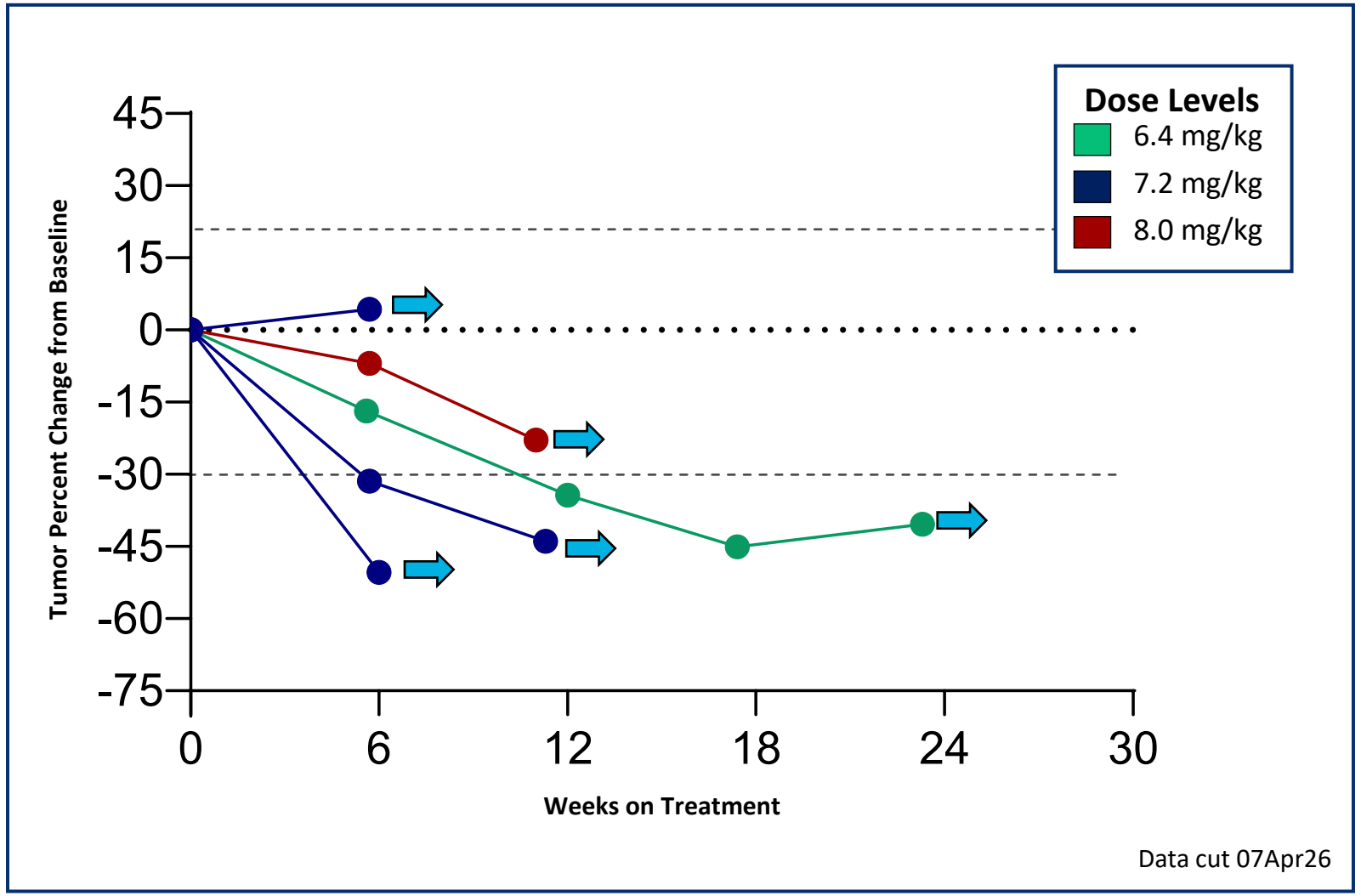
Uterine Serous Carcinoma 4.8 – 8.0 mg/kg



Clinical Perspective

Udayan Guha MD, PhD

Chief Medical Officer,
NextCure

Beryl Manning-Geist, MD,

Assistant Professor, Gynecology
and Obstetrics, Emory University

Next Steps

Michael Richman

Chief Executive Officer

NextCure

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Q&A

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Thank You!

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