

DESIGNED

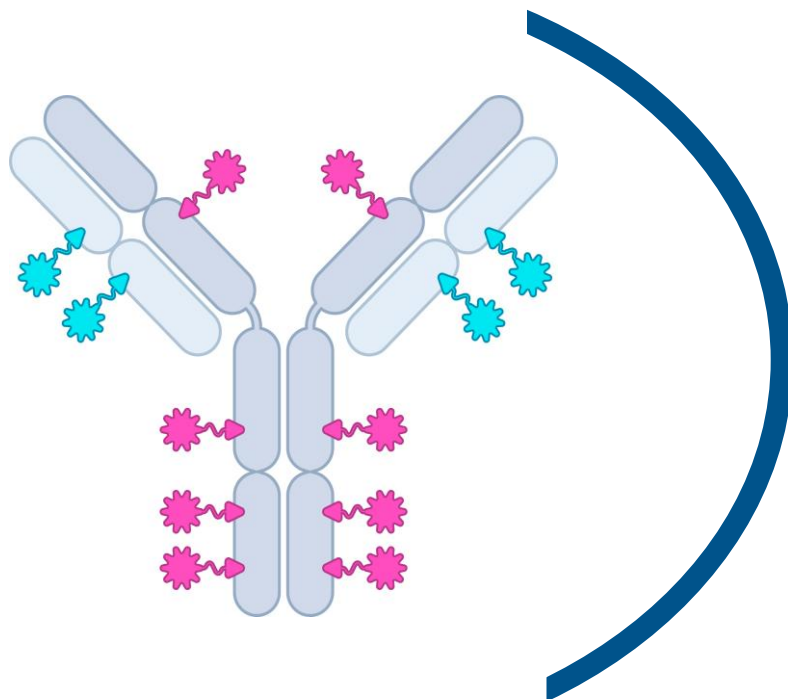
TO DELIVER

STRO-227 Preclinical Characterization

Daniel Calarese, PhD

SUTRO
BIOPHARMA

World ADC 2026, San Diego
October 14, 2026



1

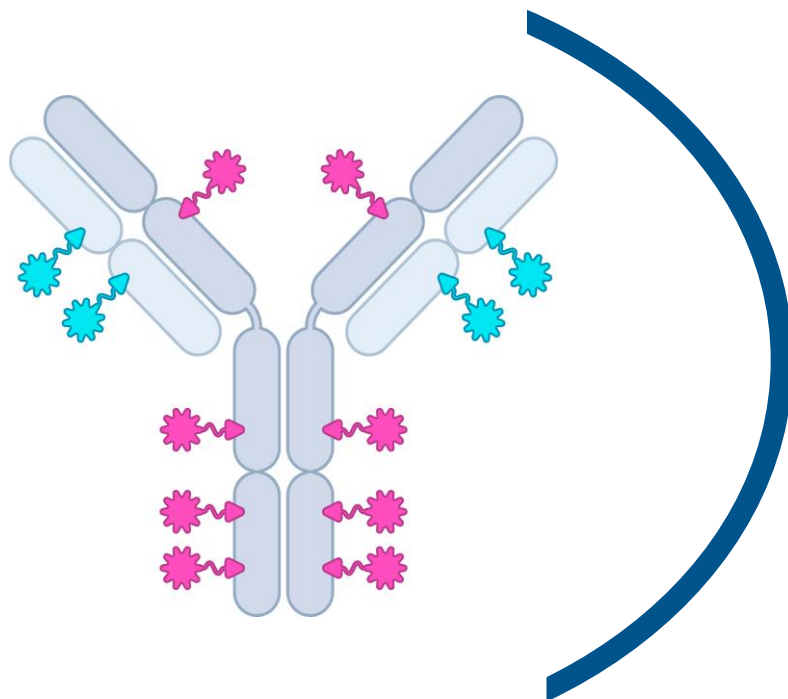
Sutro Site-Selective ADC Platform

2

Topo1i x MTI Dual-Payload Proof of Concept

3

STRO-227: PTK7-Targeted Dual-Payload ADC



1

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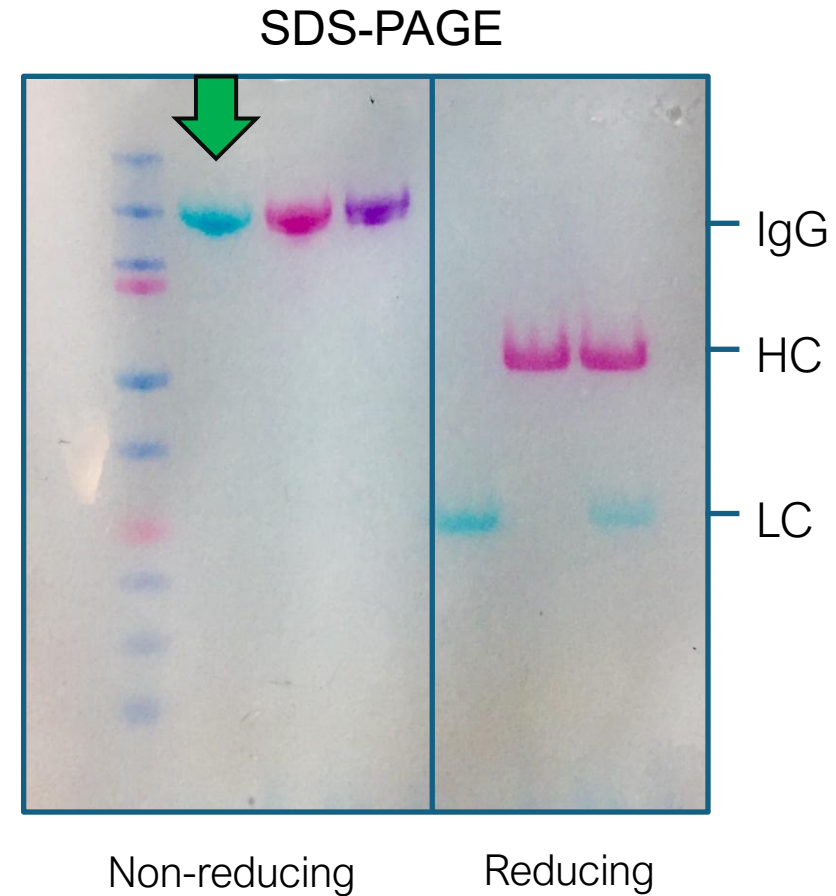
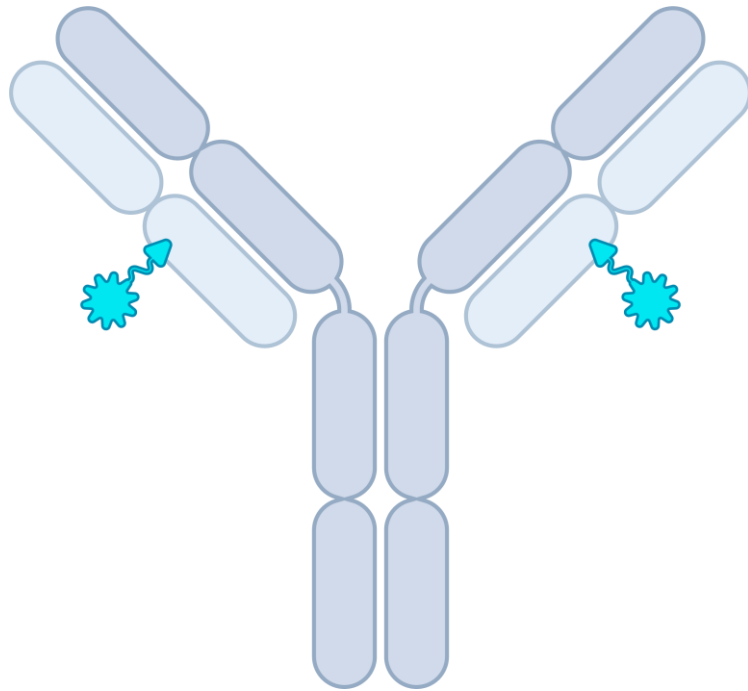
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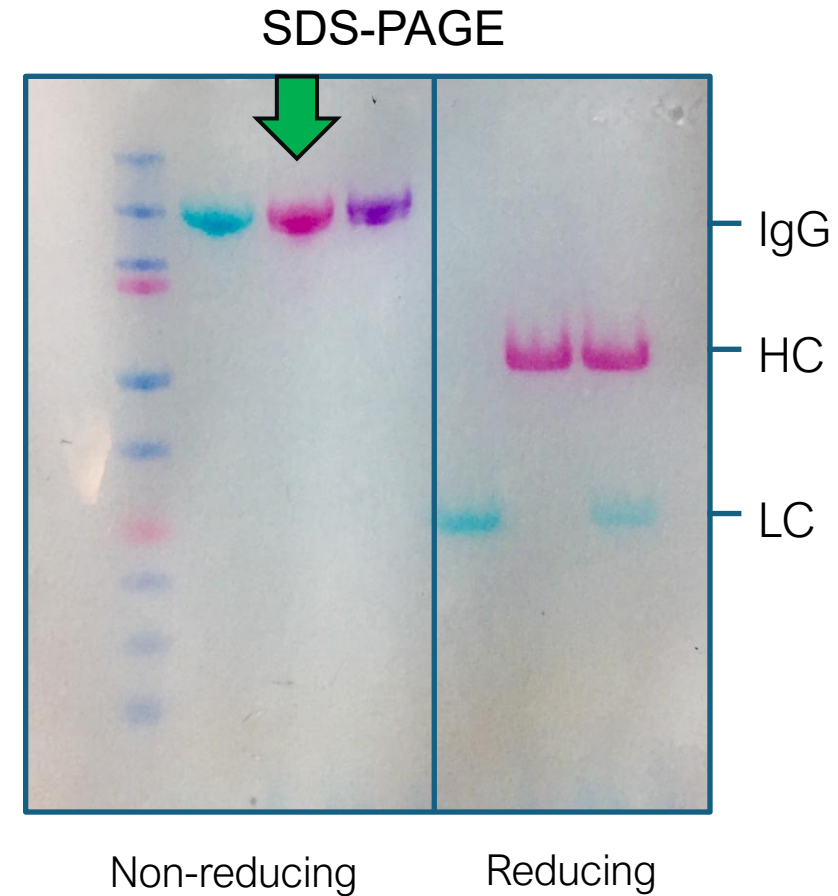
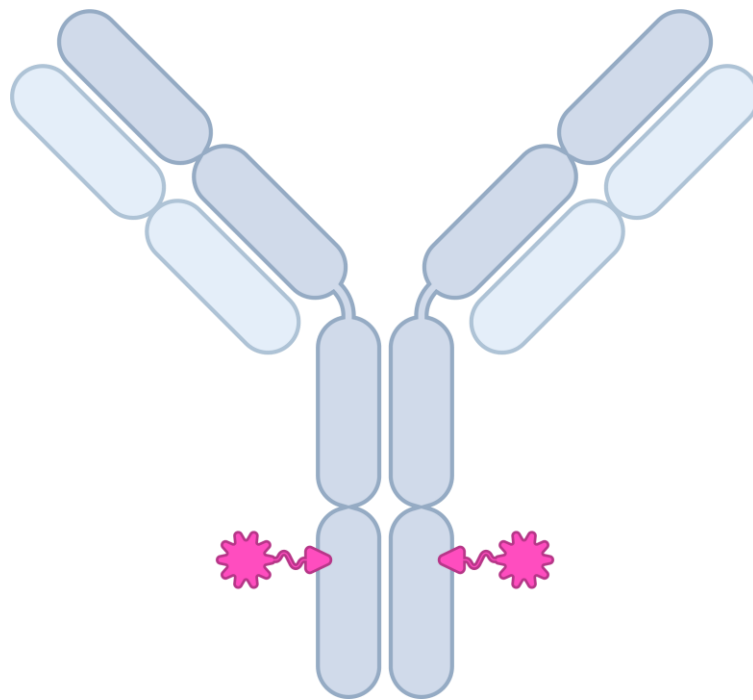
STRO-227: PTK7-Targeted Dual-Payload ADC

Sutro Cell-Free Platform Allows Precise Tuning of Linker-Payloads



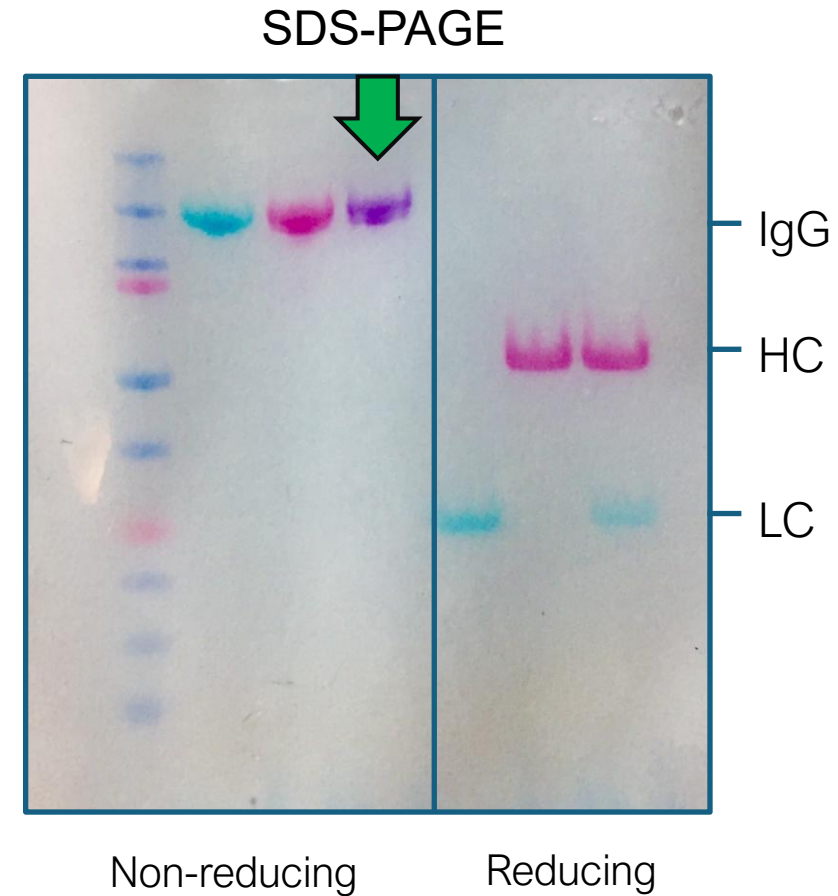
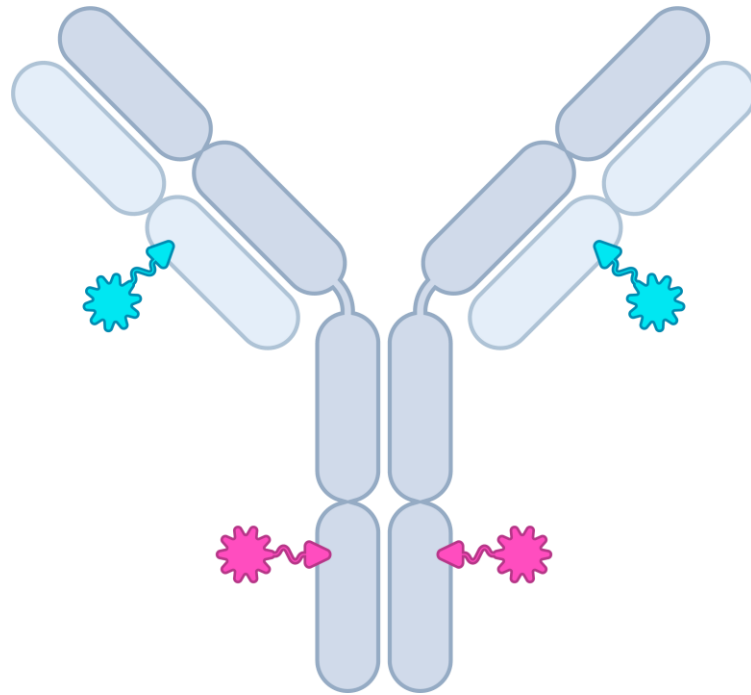
Wen M, Yu A, Park Y, Calarese D, Gerber HP, Yin G. Homogeneous antibody-drug conjugates with dual payloads: potential, methods and considerations. *MAbs*. 2025;17(1):2498162. doi:10.1080/19420862.2025.2498162

Sutro Cell-Free Platform Allows Precise Tuning of Linker-Payloads



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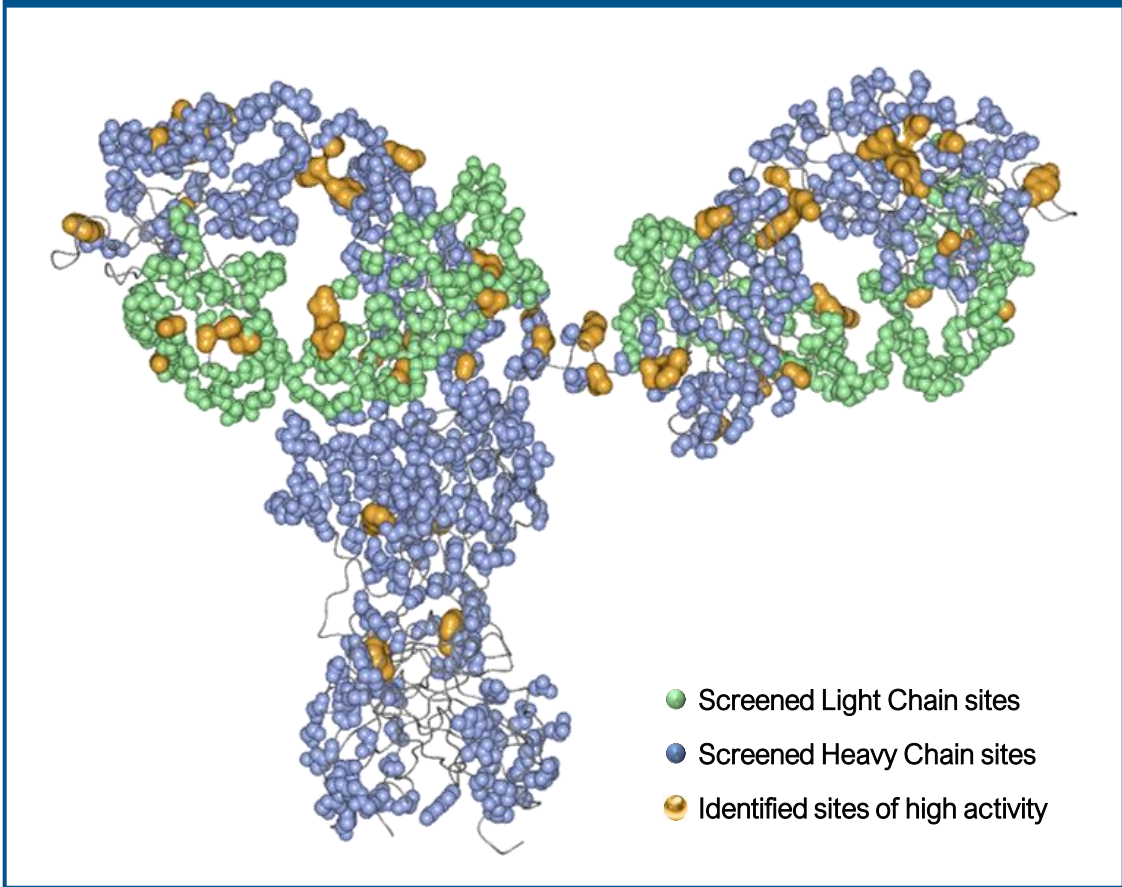
Sutro Cell-Free Platform Allows Precise Tuning of Linker-Payloads



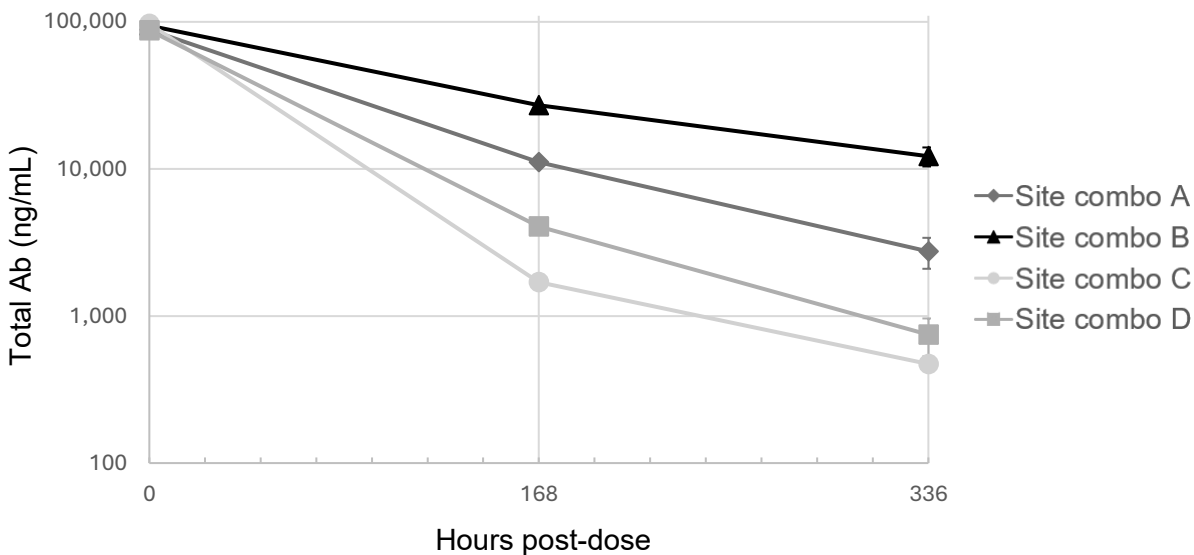
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Sutro Cell-Free Manufacturing Platform Enables Site-Selective ADCs with Superior Exposure and Design Flexibility

Surface Sites Screened on an IgG



DAR16 ADCs



Choosing the right combination of sites can result in optimized pharmacokinetics



Better PK



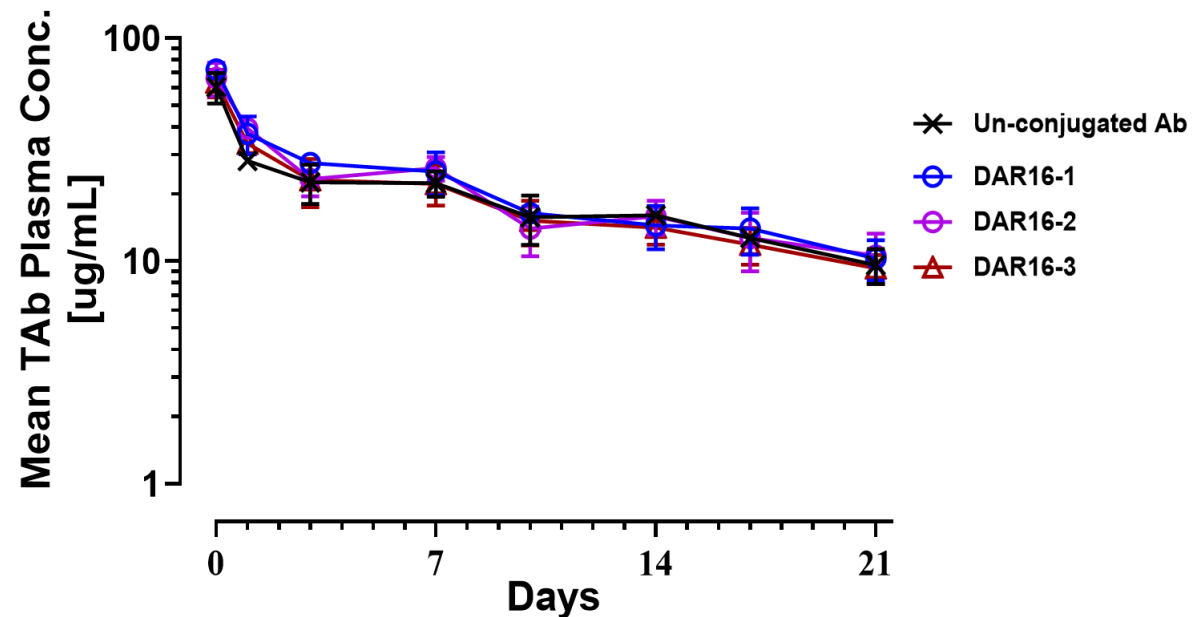
Less ADC Clearance



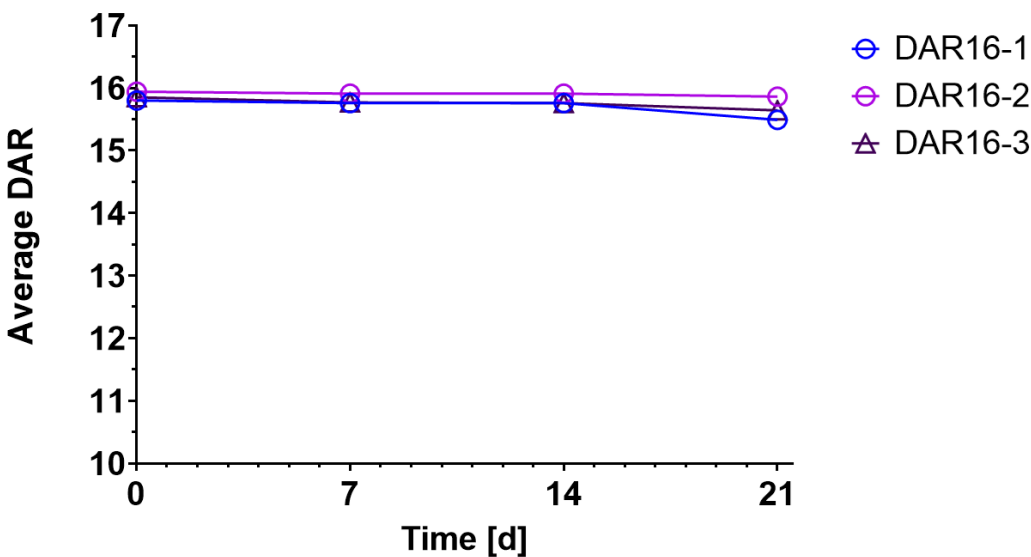
Less Systemic Toxicity

Sutro Cell-Free Manufacturing Platform Enables Site-Selective ADCs with Superior Exposure and Design Flexibility

PK of DAR16 ADCs in C57BL/6 mice



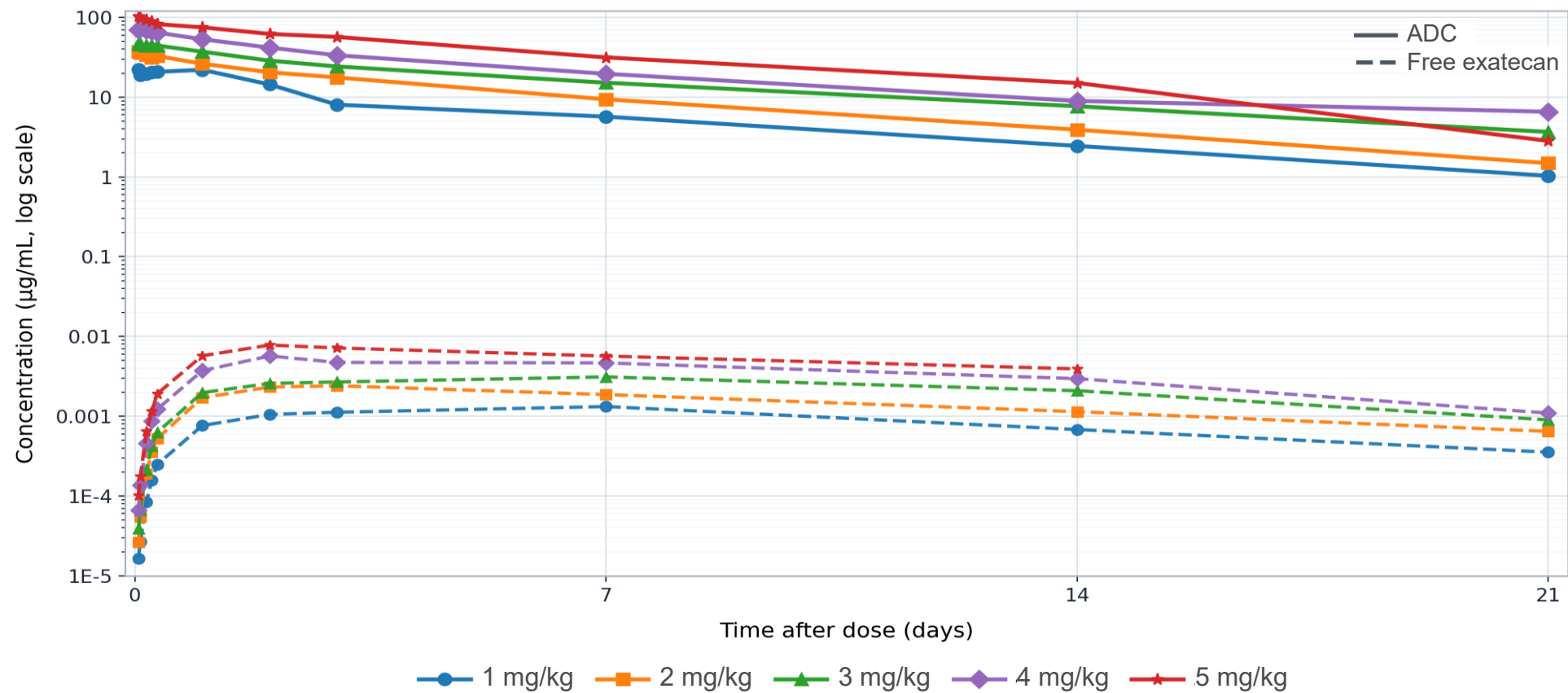
In Vivo DAR Stability



	DAR	CL_{obs} ($\text{mL}\cdot\text{d}^{-1}/\text{kg}$)	$T_{1/2}$ (d)
Unconjugated Ab	0	5.07	14.6
DAR16-2	16	4.67	14.6

STRO-004 Clinical PK Shows Sustained ADC Exposure with Low Free Payload C_{max}

Long half-life of nearly 7 days, maintains 98% DAR8 configuration



Cycle 1 geometric mean concentration by dose level; same dose color/symbol is used for both analytes; ADC uses solid lines and free exatecan uses dashed lines. PK – Pharmacokinetics; TI – Therapeutic Index

STRO-004 Favorable Tolerability Profile: Mostly Low-Grade AEs with Limited On-Target and Platform Toxicity

All-grade TRAEs ≥10% of Subjects and All Gr 3+ Events; Low Discontinuation Rate Due to AEs of 6%

Dose Level (n)	1 mg/kg (2)		2 mg/kg (10)		3 mg/kg (13)		4 mg/kg (16)		5 mg/kg (8)		Overall (49)	
Median Prior LoT (Range 1-7)	3.0		3.0		3.0		2.5		4.0		3.0	
	All Gr	Gr 3+	All Gr	Gr 3+	All Gr	Gr 3+	All Gr	Gr 3+	All Gr	Gr 3+	All Gr	Gr 3+
Any subject with a TRAE: n (%)	1 (50)	0 (0)	5 (50)	0 (0)	10 (77)	3 (23)	13 (81)	5 (31)	7 (88)	4 (50)	36 (73)	12 (24)
Nausea	1 (50)		2 (20)		3 (23)		5 (31)		5 (63)	1 (13)	16 (33)	1 (2)
Fatigue			2 (20)		7 (54)		3 (19)		2 (25)		14 (29)	
Anemia					2 (15)	2 (15)	5 (31)	3 (19)	2 (25)	2 (25)	9 (18)	7 (14)
Vomiting			1 (10)		2 (15)		2 (13)		2 (25)		7 (14)	
Diarrhea			1 (10)				4 (25)		1 (13)		6 (12)	
Epistaxis			1 (10)		1 (8)		3 (19)		1 (13)		6 (12)	
Decreased appetite					2 (15)		3 (19)				5 (10)	
Stomatitis							2 (13)		3 (38)	1 (13)	5 (10)	1 (2)
ALT increased					1 (8)		2 (13)	1 (6)	1 (13)		4 (8)	1 (2)
AST increased					1 (8)		2 (13)	1 (6)	1 (13)		4 (8)	1 (2)
Mucosal inflammation					1 (8)		2 (13)		1 (13)	1 (13)	4 (8)	1 (2)
Conjunctivitis					2* (15)	1 (8)			2 (25)		4* (8)	1 (2)
Neutrophil count decreased							1 (6)	1 (6)	2 (25)	2 (25)	3 (6)	3 (6)
Platelet count decreased							1 (6)		2 (25)	1 (13)	3 (6)	1 (2)
Blood bilirubin increased							1 (6)	1 (6)			1 (2)	1 (2)
Embolism							1 (6)	1 (6)			1 (2)	1 (2)
Febrile neutropenia									1 (13)	1 (13)	1 (2)	1 (2)
Hypokalaemia									1 (13)	1 (13)	1 (2)	1 (2)
Lymphocyte count decreased							1 (6)	1 (6)			1 (2)	1 (2)
White blood cell count decreased									1 (13)	1 (13)	1 (2)	1 (2)

Data cutoff date: July 24, 2026; All grade 3+ events were grade 3, except for one grade 4 neutrophil count decrease in the 5 mg/kg cohort

* Count increased by 1 manually to capture single event of Gr 3 keratoconjunctivitis

Gr – Grade; TRAE – Treatment related adverse events; LOT – Lines of therapy; ALT – Alanine aminotransferase; AST – Aspartate aminotransferase; AE – Adverse event; TF – Tissue Factor; DLT – Dose limiting toxicity; CRC – colorectal cancer; EGC – esophageal/gastric cancer

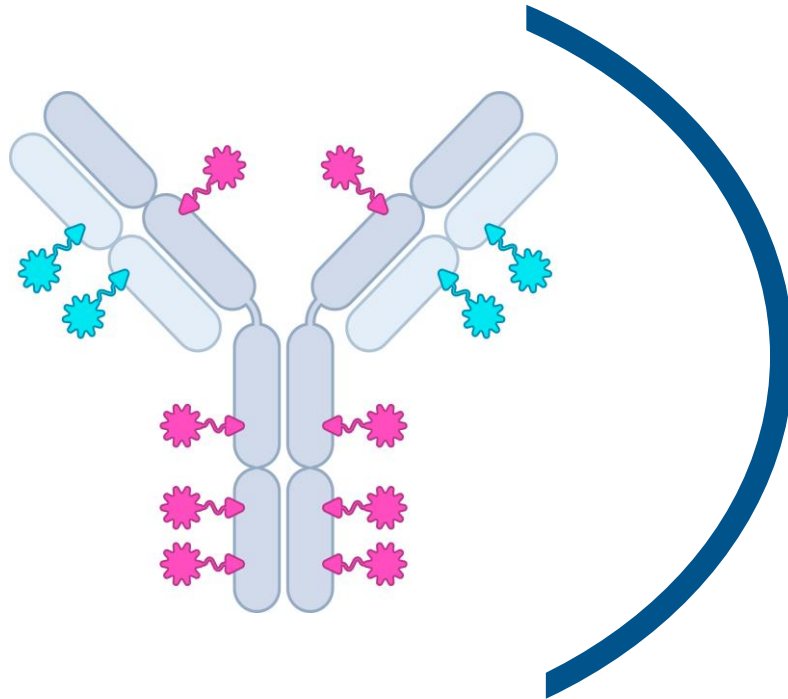
- ▶ All-grade TRAEs >15% were nausea (33%), fatigue (29%), anemia (18%)
- ▶ Other TRAEs of note that occurred in >5% of patients included:
 - ▶ Hematologic events: neutrophil count decreased (6%), platelet count decreased (6%)
 - ▶ On-target TF-related events: epistaxis (12%), stomatitis (10%), mucosal inflammation (8%), conjunctivitis (8%), dry eye (7%); these events were predominantly Grade 1-2
 - ▶ Grade 3+ events: anemia (14%)
- ▶ DLTs occurred only in CRC/EGC subjects (4-7 Prior LoT) and only at 5 mg/kg, driven by target-related toxicity; no discontinuations
 - ▶ Gr 2/3 stomatitis +/- neutropenia, Gr 2 conjunctivitis

Pipeline of Next-Generation Single- and Dual-Payload ADCs

On track to deliver three programs into the clinic in two years

	PROGRAM	MODALITY/TARGET	INDICATION	DISCOVERY	PRECLINICAL	PHASE 1/1B	PHASE 2	PHASE 3/ REGISTRATIONAL	PARTNER
ONCOLOGY PROGRAMS	STRO-004	Tissue Factor ADC	Solid Tumors						
	STRO-006	Integrin $\alpha\beta 6$ ADC	Solid Tumors						
	STRO-227	DUAL PAYLOAD ADCS	PTK7						
	STRO-00Y		Undisclosed						
	ASP2998		TROP2*						
	2nd iADC		Undisclosed*						
NON-ONC	VAX-31	31-Valent Conjugate Vaccine	Invasive Pneumococcal Disease						
	VAX-24	24-Valent Conjugate Vaccine	Invasive Pneumococcal Disease						

*Dual Payload Immunostimulatory ADC (iADC)



1

Sutro Site-Selective ADC Platform

2

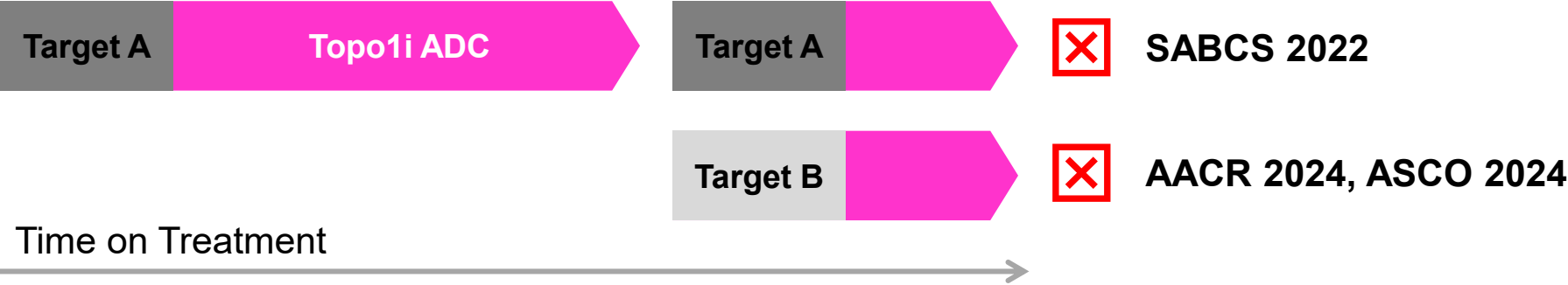
Topo1i x MTI Dual-Payload Proof of Concept

3

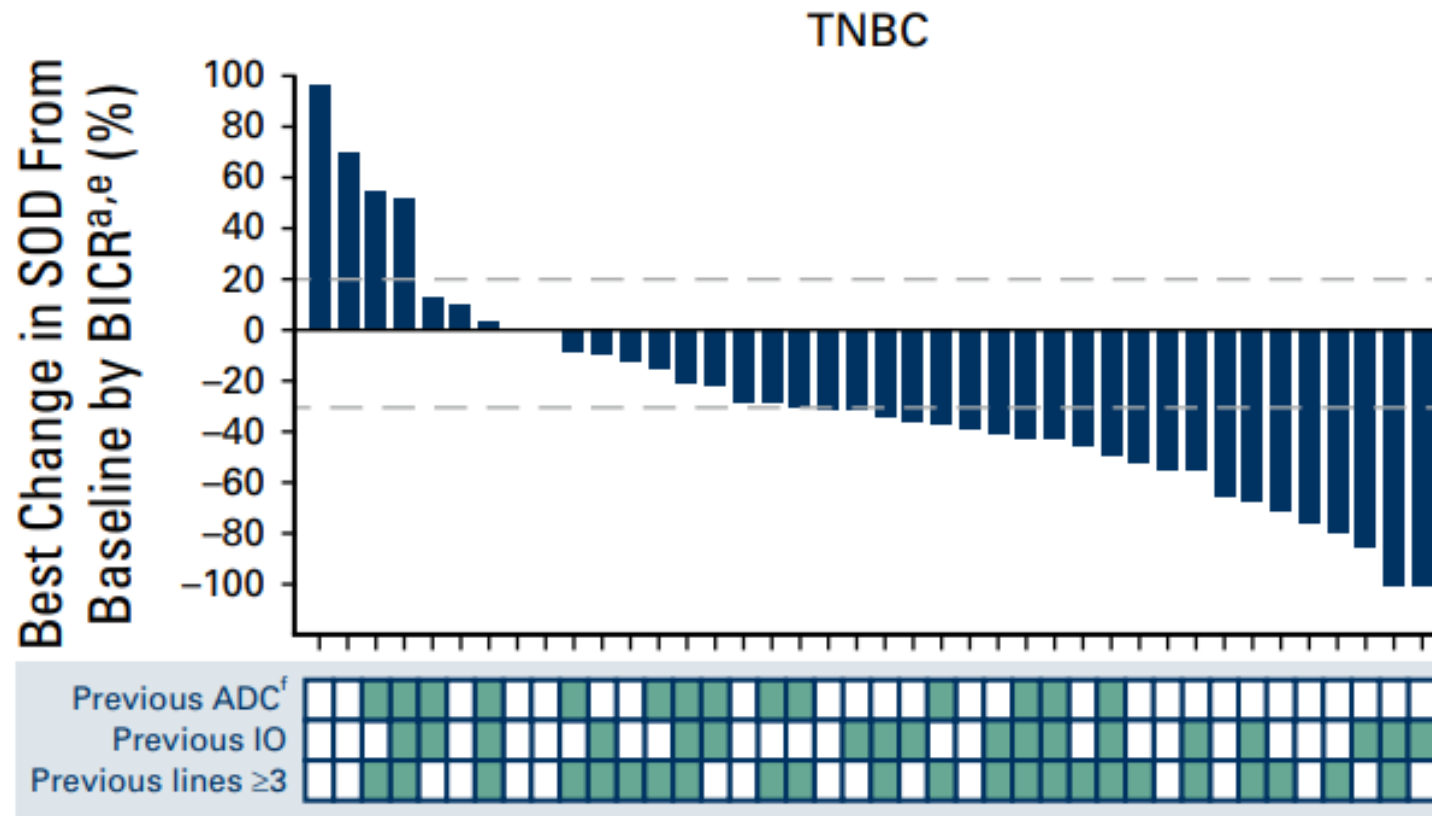
STRO-227: PTK7-Targeted Dual-Payload ADC

Emerging Clinical Challenge: Payload Resistance Limits ADC Efficacy

Payload Resistance to Topo1i Limits ADC Efficacy, Irrespective of the Target Antigen



Emerging Clinical Challenge: Payload Resistance Limits ADC Efficacy



TROPION-PanTumor01

Dato-DXd in TNBC

14 patients had received prior
Topo1 ADC: 11 SG, 2 T-DXd, 1
HER3-DXd

Confirmed overall response rate
of **40%** (12/30) in Topo1-Naïve
vs **14%** (2/14) in patients with
prior Topo1 ADC

Figure reproduced from Bardia A, Krop IE, Kogawa T, et al. Datopotamab Deruxtecian in Advanced or Metastatic HR+/HER2- and Triple-Negative Breast Cancer: Results From the Phase I TROPION-PanTumor01 Study. *J Clin Oncol*. 2024;42(19):2281-2294 under the creative commons license (<https://creativecommons.org/licenses/by-nc-nd/4.0/>). No changes were made.

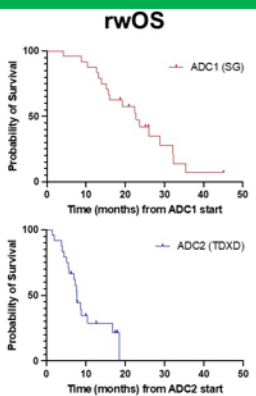
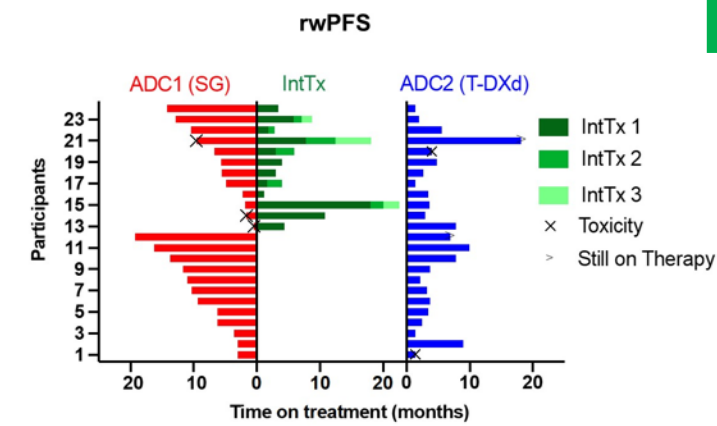
Emerging Clinical Challenge: Payload Resistance Limits ADC Efficacy

HR+/HER2-low Efficacy Data (n=56)

SG → T-DXd (n=24, 42.9%)

- Median lines of therapy for MBC prior to SG:
 - Median lines chemo: **2.0** (range 0-7)
 - Median total lines therapy: **3.0** (range 0-9)
- IntTx between ADCs: 50.0%

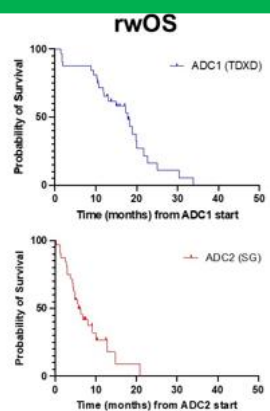
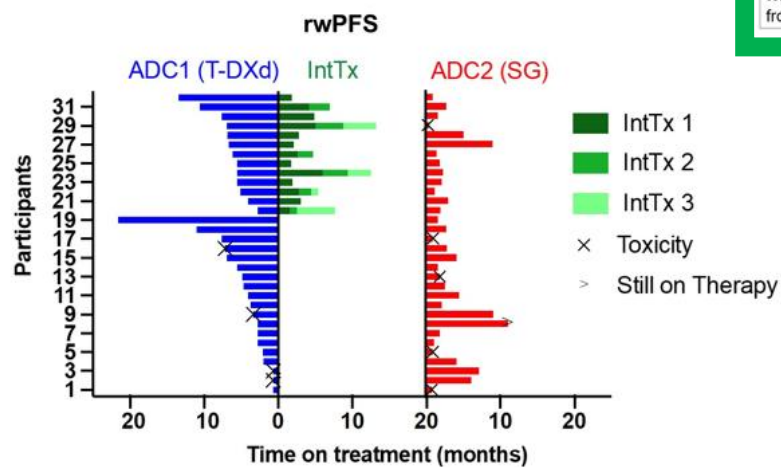
	ADC1 (SG)	ADC2 (T-DXd)
Median rwPFS from time of each ADC start, months	6.5	3.6
Median rwOS from time of each ADC start, months	20.1	7.7



T-DXd → SG (n=32, 57.1%)

- Median lines of therapy for MBC prior to T-DXd:
 - Median lines chemo: **2.0** (range 0-6)
 - Median total lines therapy: **4.5** (range 2-10)
- IntTx between ADCs: 40.6%

	ADC1 (T-DXd)	ADC2 (SG)
Median rwPFS from time of each ADC start, months	5.3	2.1
Median rwOS from time of each ADC start, months	15.1	5.6



While there are patients that see significant benefit to a second Topo1i-payload ADC, there is significantly shorter PFS regardless of ADC sequence (SG, Enhertu in mBC)

Figure was adapted from Laura Ann Huppert et al., Multicenter retrospective cohort study of the sequential use of the antibody-drug conjugates (ADCs) trastuzumab deruxtecan (T-DXd) and sacituzumab govitecan (SG) in patients with HER2-low metastatic breast cancer (MBC): Updated data and subgroup analyses by age, sites of disease, and use of intervening therapies. *JCO* **42**, 1083-1083(2024)

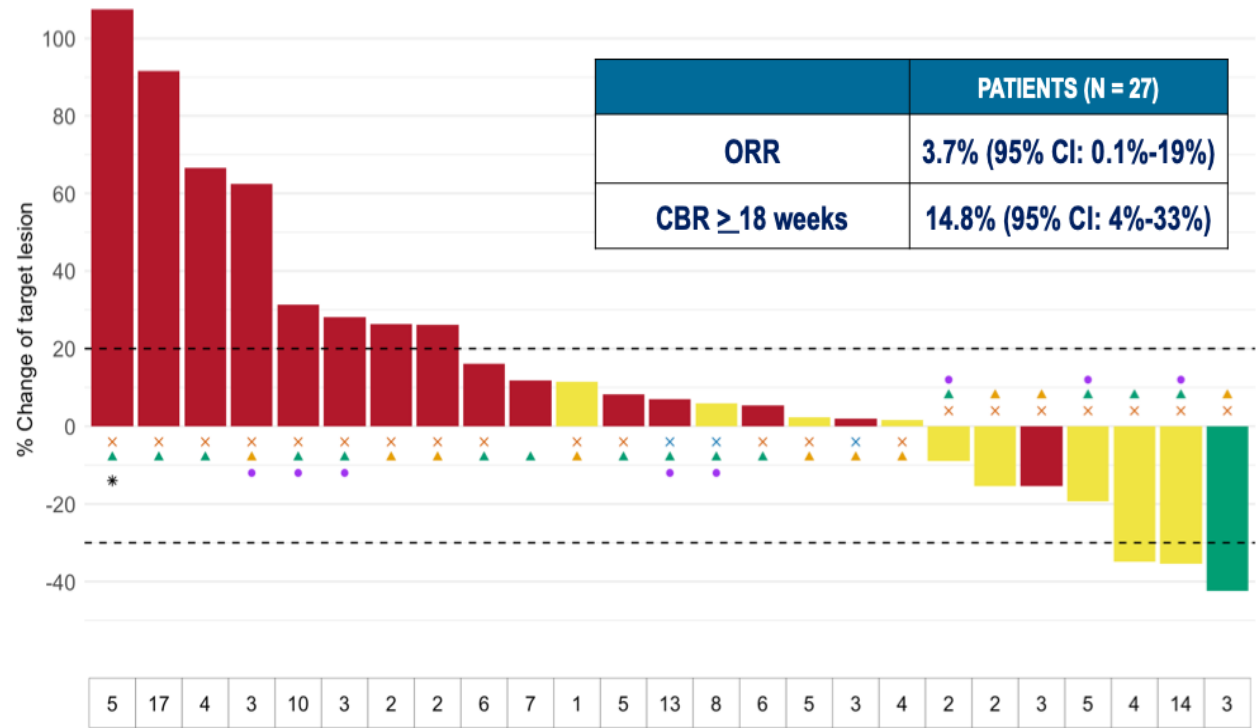
Emerging Clinical Challenge: Payload Resistance Limits ADC Efficacy

SATEEN: Phase 2, investigator-initiated, multicenter trial

- Advanced **HER2+** cancer
- Prior **taxane**, **trastuzumab** and **T-DXd** in any setting
 - ✓ Progression on T-DXd not required
 - ✓ T-DXd not required to be the immediate prior line
 - ✓ Patients ineligible for T-DXd allowed to enroll
- No prior anti-Trop2 ADC
- ≤ 5 prior lines of chemo/ADC *
- Brain metastases allowed[#]



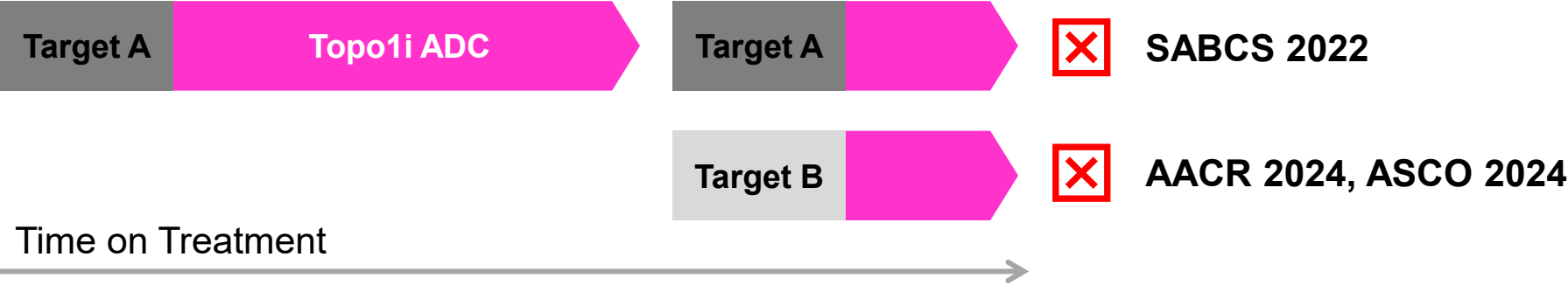
**Sacituzumab
govitecan
10 mg/kg IV D1,8
Q21D
+
Trastuzumab
Q3W (IV or SC)**



Tarantino P. et al. ESMO Breast 2026

Emerging Clinical Challenge: Payload Resistance Limits ADC Efficacy

Payload Resistance to Topo1i Limits ADC Efficacy, Irrespective of the Target Antigen



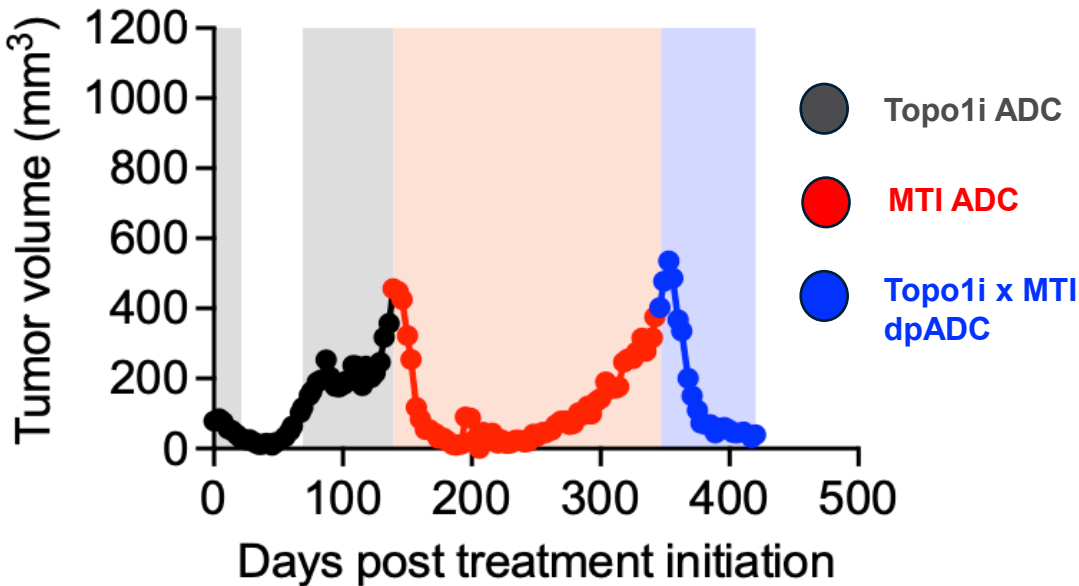
Switching Payload Class Maintains ADC Efficacy, Irrespective of the Target Antigen



SABCS – San Antonio Breast Cancer Symposium; ASCO – American Society of Clinical Oncology

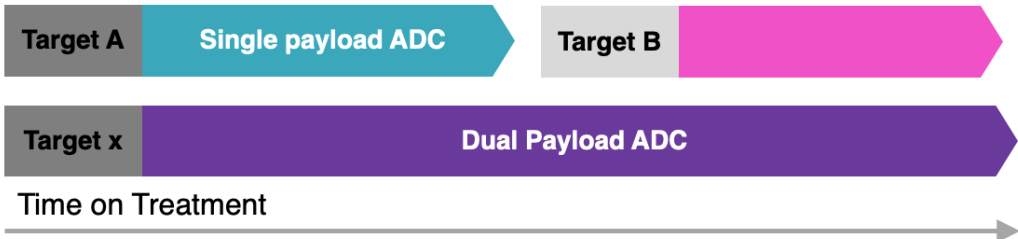
Dual-Payload ADCs Have Potential to Overcome Resistance and Expand Clinical Opportunities

Tumors Resistant to both Topo1i and MTIs respond to dpADC

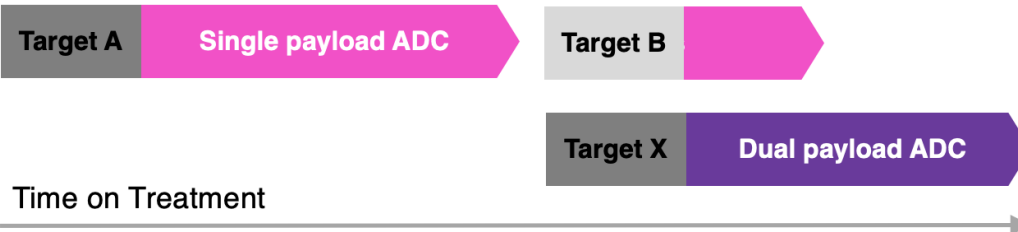


Clinical Development Opportunity: Relapse to Front-Line

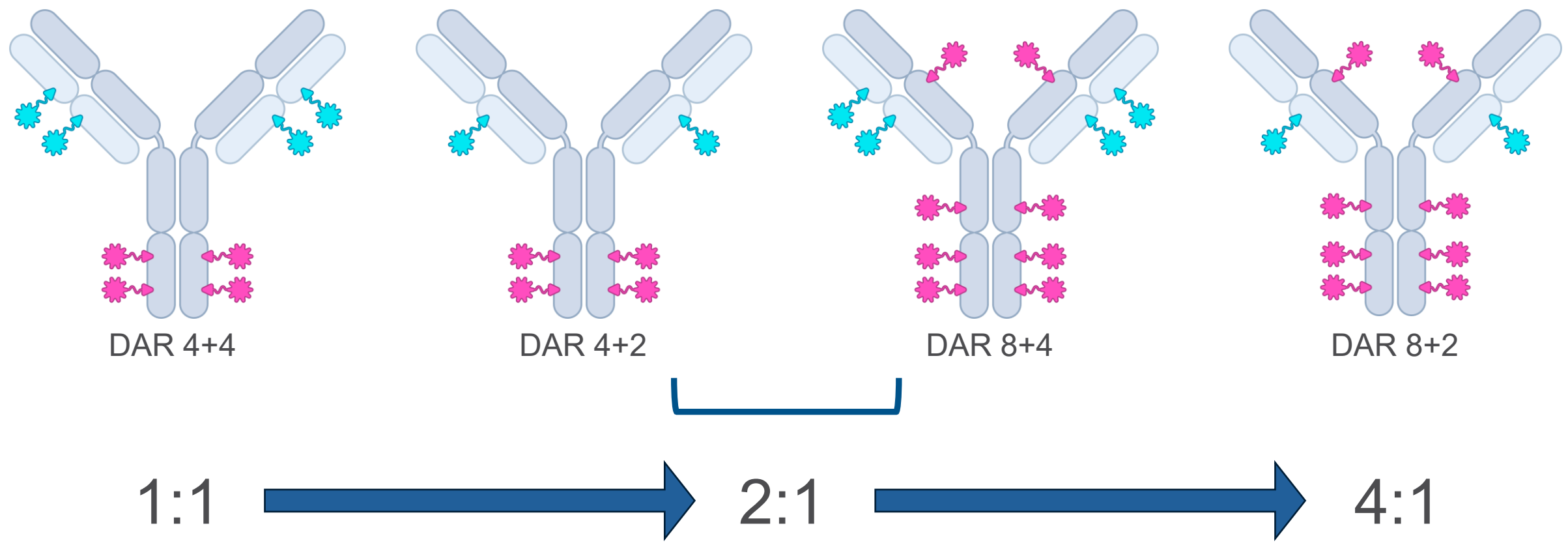
Early Line: Instead of two sequential spADCs



Late Lines: dpADC after relapse from spADC



Cell-Free Platform Enables Site-Specific Tuning of Payload Ratios



Sutro Dual-Payload ADC Portfolio

Topo1 x Tubulin

Combination of clinically validated payloads to improve efficacy

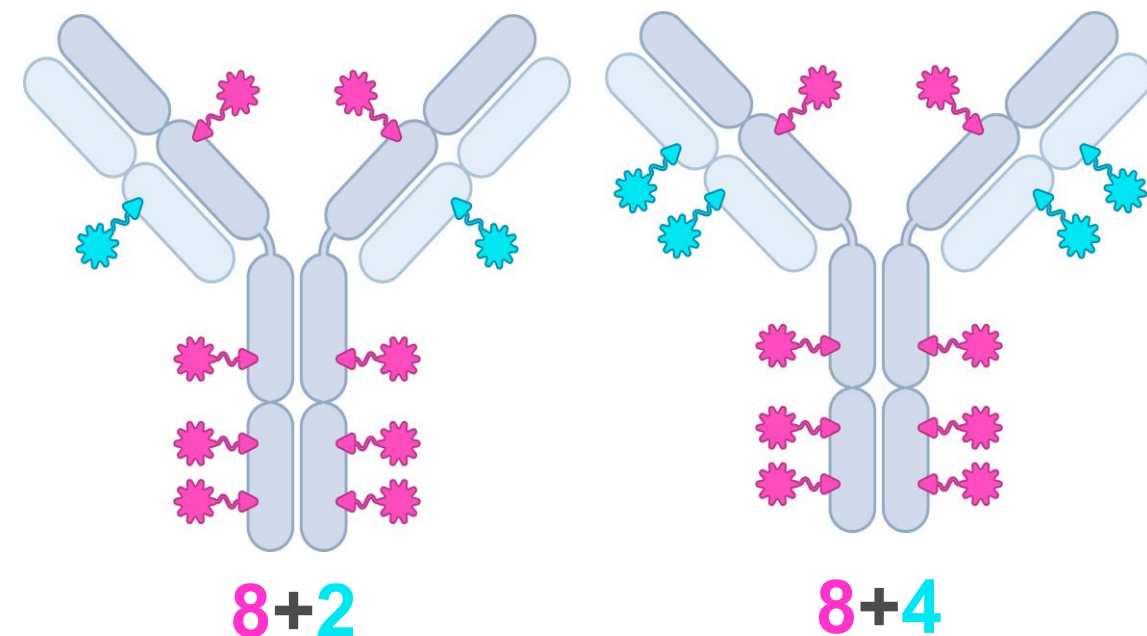
Topo1 x STING

Engaging immune activation to make tumors hotter

Topo1 x DDRi

Leveraging DDRi synergy to enhance Topo1i activity

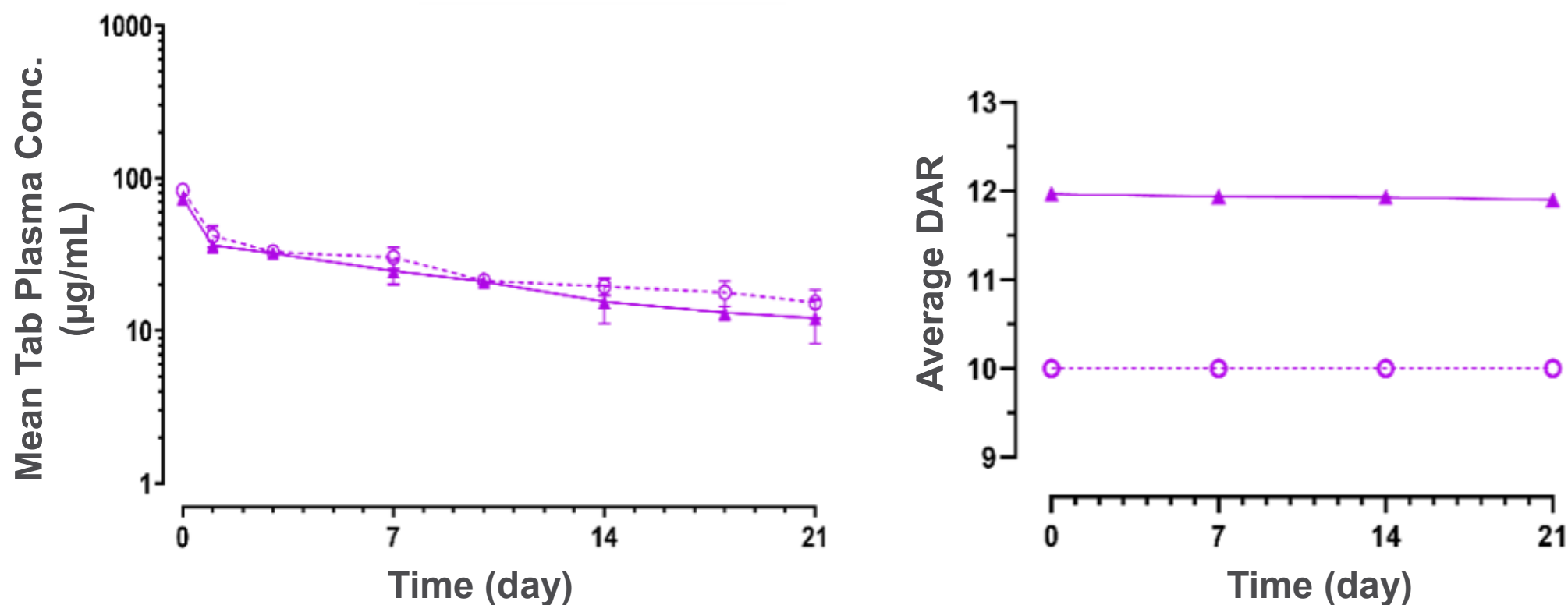
Anatomy of Topo1i + MTI Dual-Payload Her2-ADC: Designed to Deliver Superior Efficacy and Safety



 DAR8: TOPO1i
 DAR2: MTI

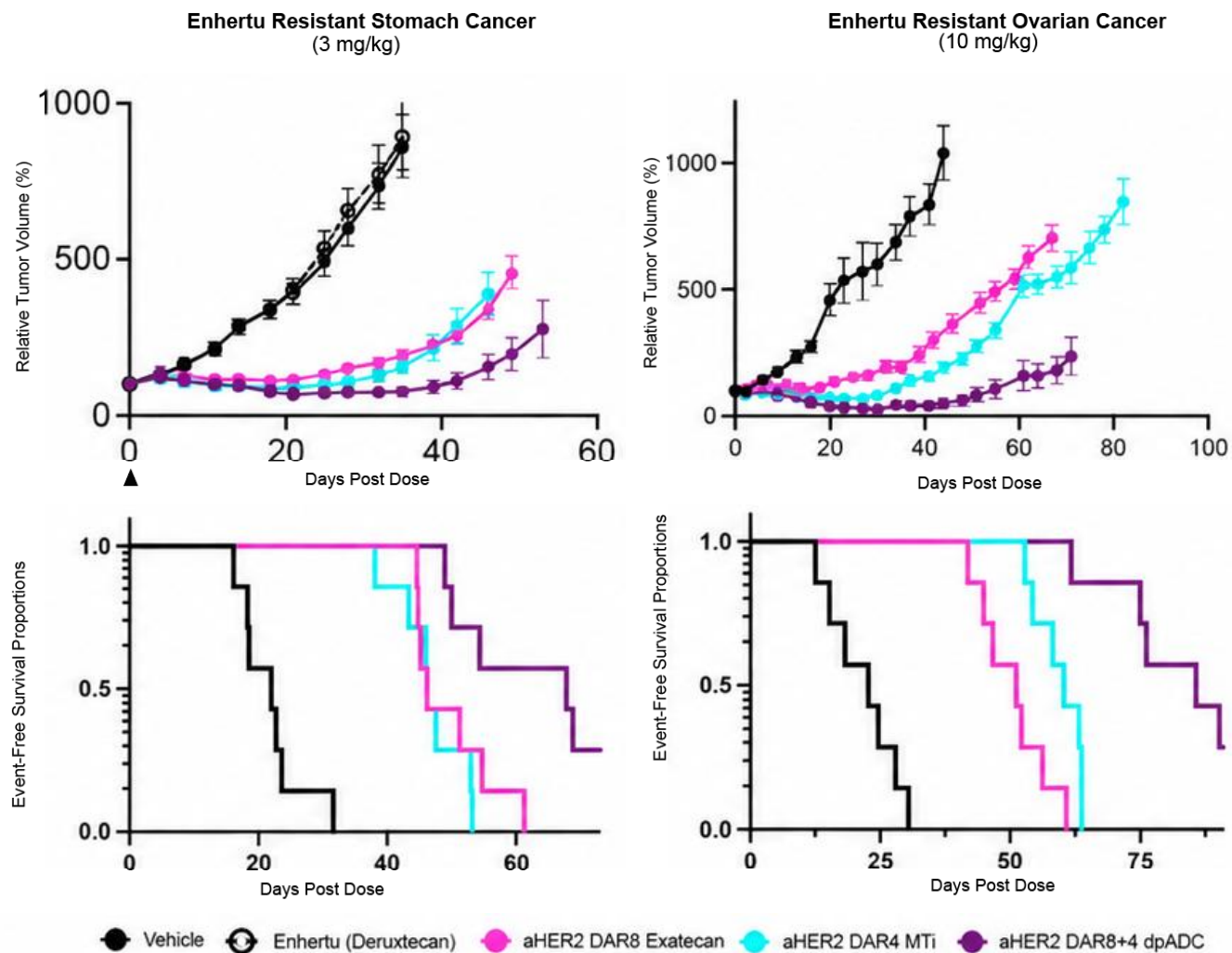
- 1 **Optimally positioned non-natural amino acids**, p-azidomethyl-L-phenylalanine (pAMF), combined with ultra stable click chemistry
- 2 **β -glucuronidase cleavable linkers** with tumor selective cleavage, strong stability while in circulation, and added hydrophilicity led to **best-in-class PK**
- 3 **Exatecan payload causing DNA disruption** and potent tumor cell killing, with high bystander activity, and immunogenic cell death (ICD)
- 4 **MMAE payload causing Tubulin disruption** and potent tumor cell killing, with high bystander activity, and immunogenic cell death (ICD)
- 5 **Lack of Fc γ R interactions** limits uptake by alveolar macrophages, reducing risk of interstitial lung disease (ILD)

Dual-Payload ADCs have Desirable *In Vivo* PK and Stability

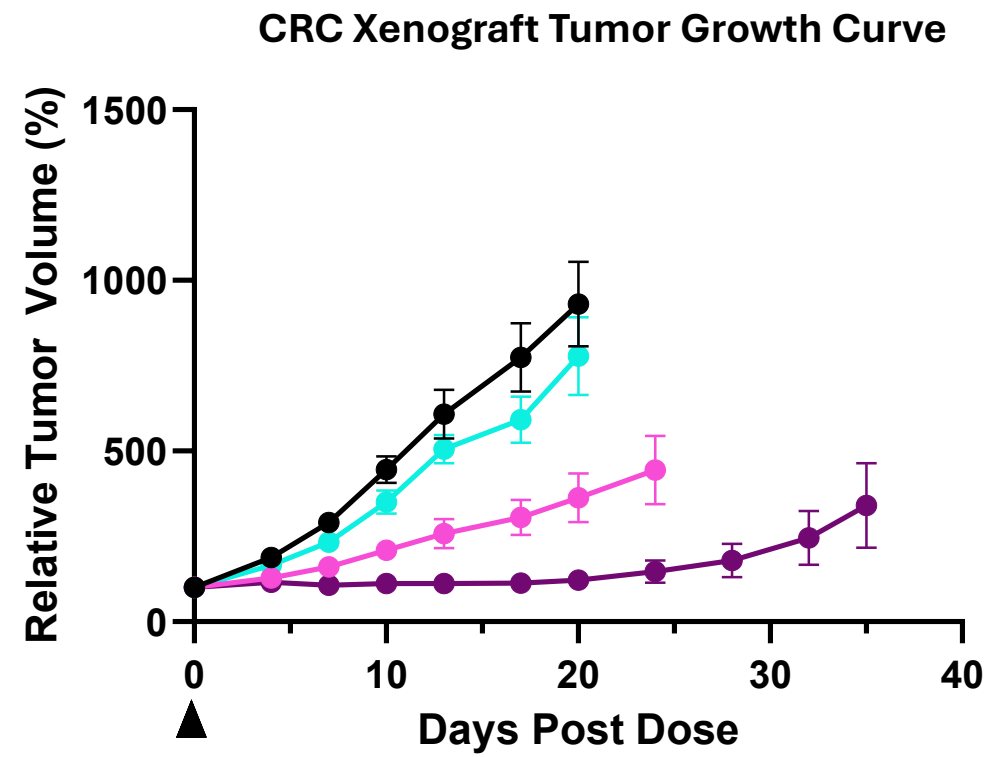


	DAR		Cl_{obs} (mL·d ⁻¹ /kg)	V_{ss} (mL/kg)	$t_{1/2}$ (days)
	Topo1i	MMAE			
	8	2	3.3	75.8	16.3
	8	4	4.2	81.4	14

Topo1i x MTI Proof-of-Concept: Dual-Payload ADC is More Effective in Enhertu-Resistant CDX

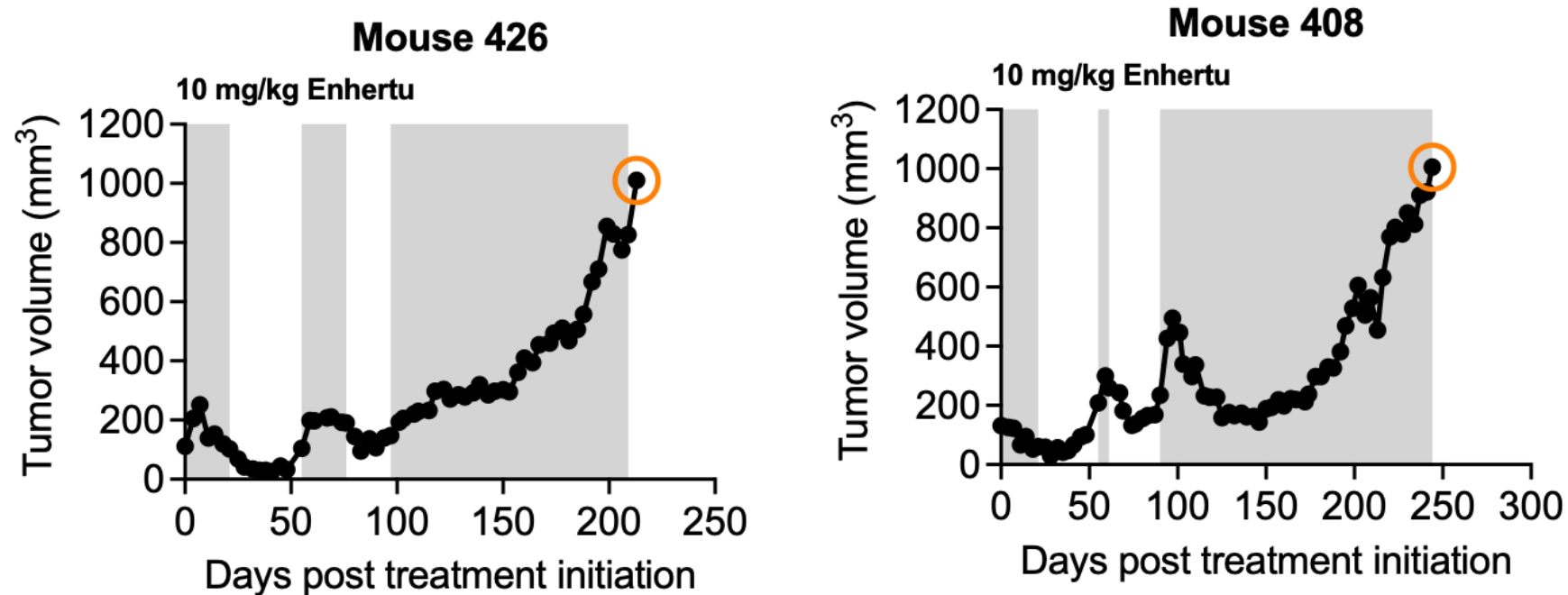


Dual-Payload ADCs Show Improved *In Vivo* Efficacy in an MTI-Resistant CRC Xenograft Model



- Vehicle control
- Trastuzumab DAR4 MTI (MMAE) ADC (5 mg/kg)
- Trastuzumab DAR8 Topo1i ADC (5 mg/kg)
- Trastuzumab DAR(8+4) Topo1i + MTI dpADC (5 mg/kg)

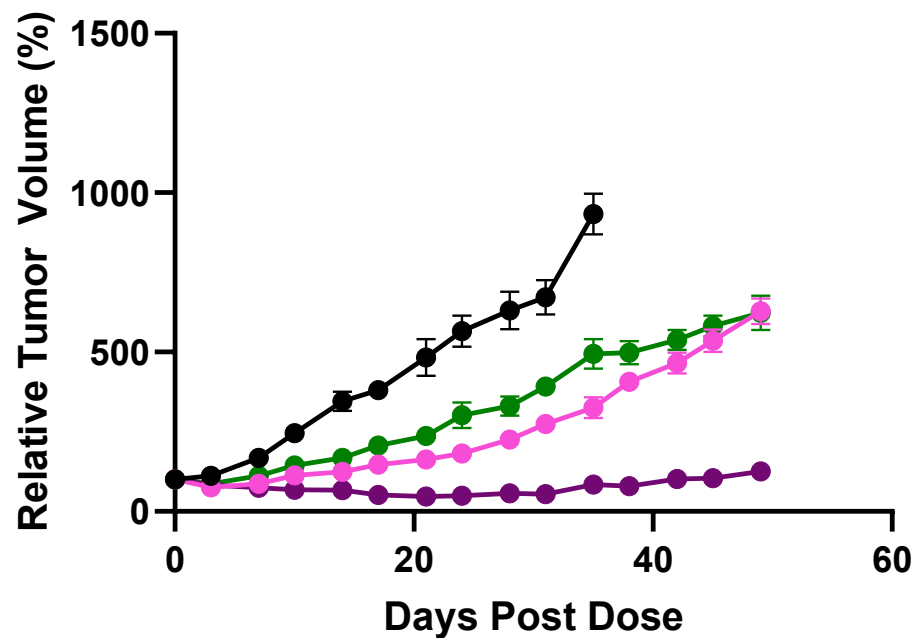
In Vivo Selection of Enhertu-Resistant Ovarian Cancer Cell Lines



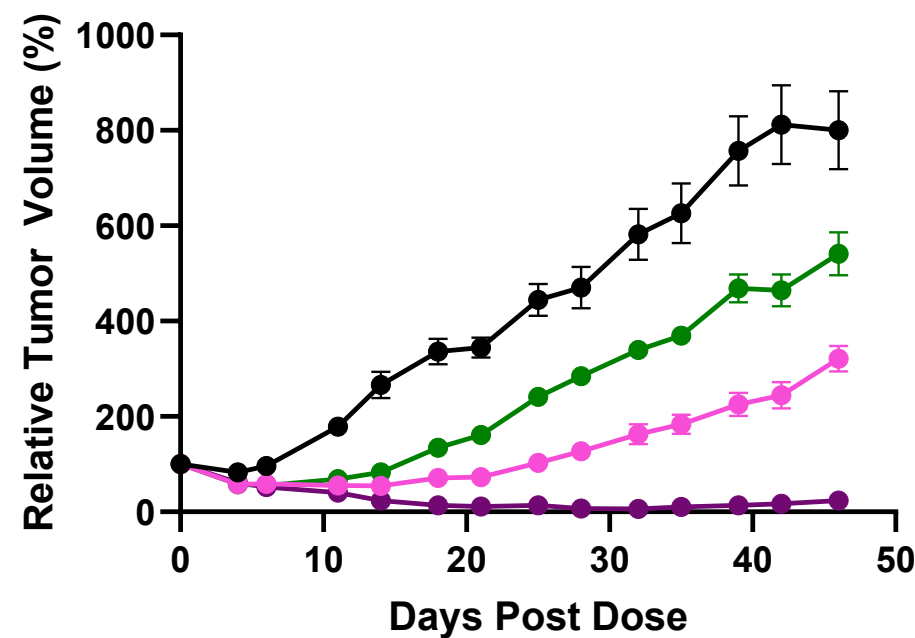
Upon reaching ~1,000 mm³ during continuous weekly treatment with Enhertu, tumors were harvested to establish resistant cell lines

Dual-Payload ADCs Display Improved *In Vivo* Efficacy in Ovarian Cancer Models With Reduced Enhertu/Topo1 Sensitivity

OvCa-ENR1 Tumor Growth Curves

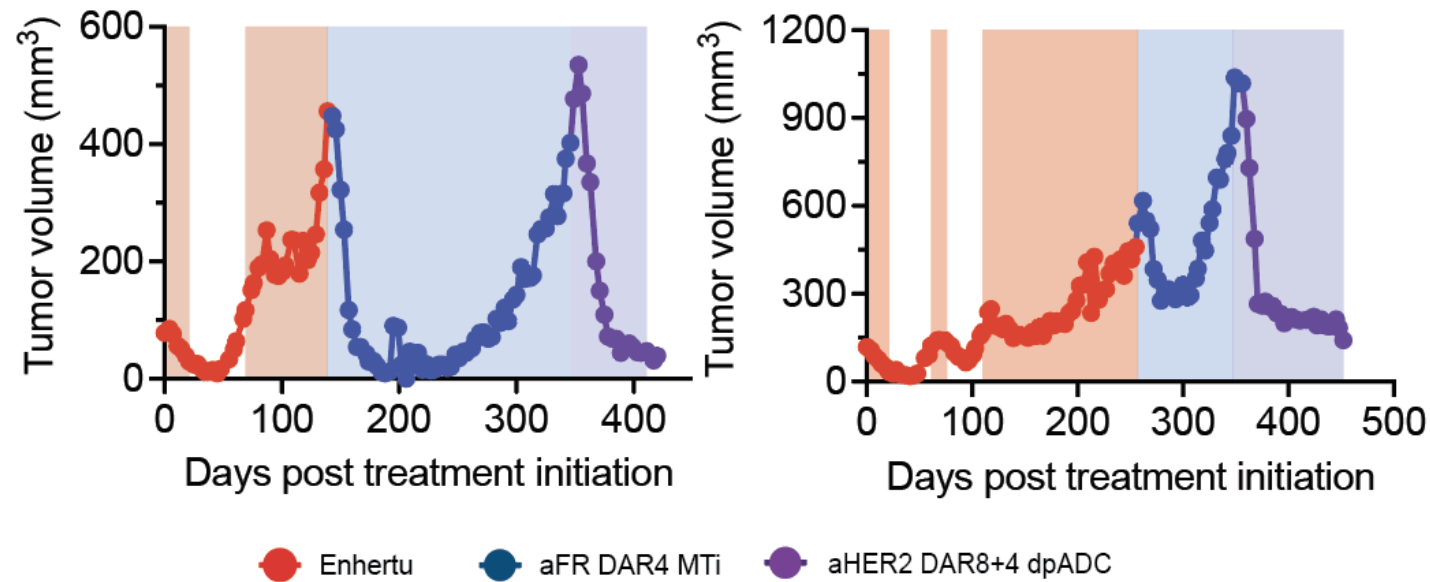
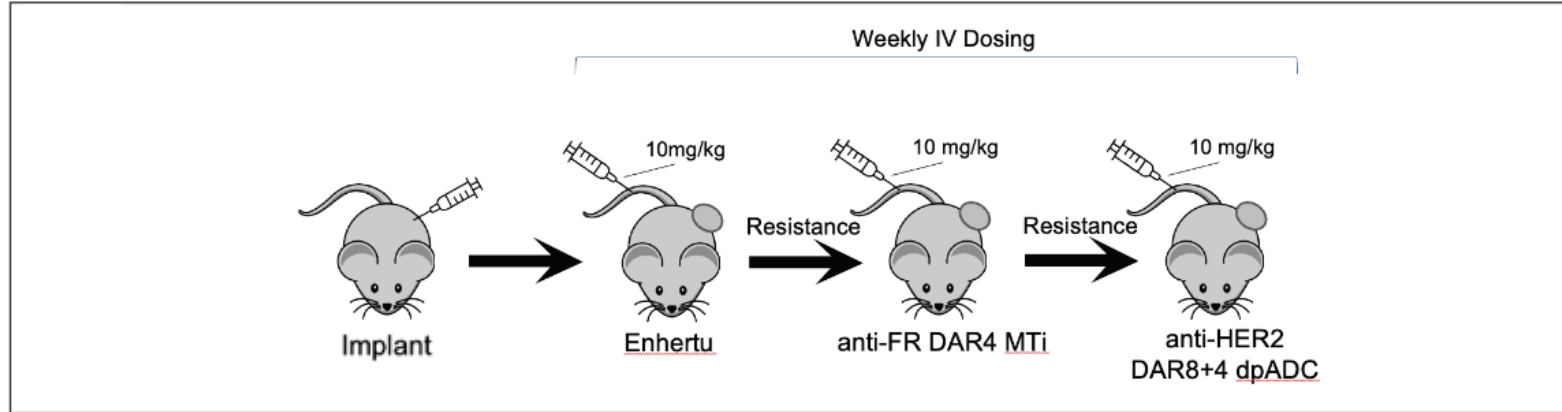


OvCa-ENR3 Tumor Growth Curves

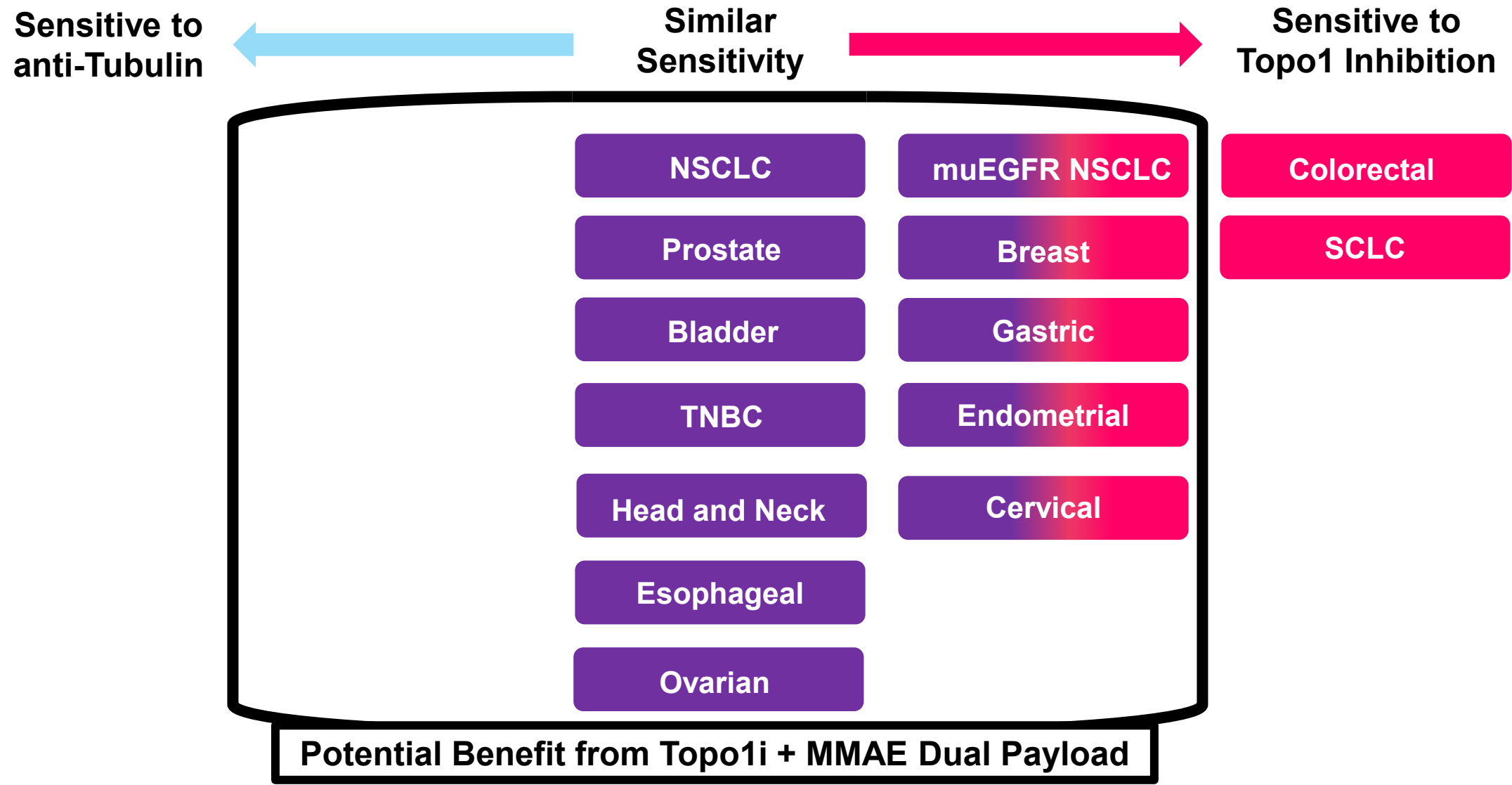


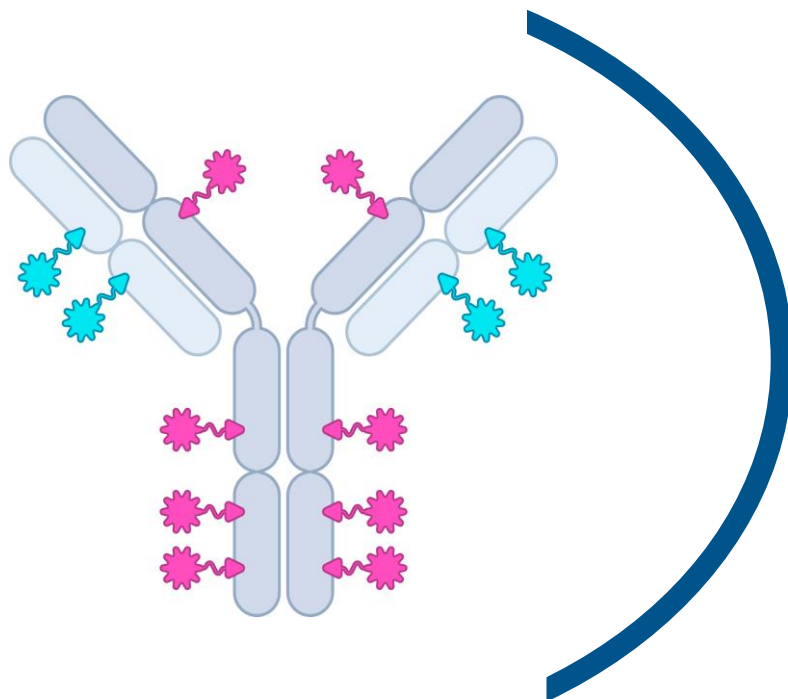
Vehicle control
Trastuzumab DAR8 Topo1i ADC (10 mg/kg)
Trastuzumab DAR(8+4) Topo1i + MTI (MMAE) dpADC (10 mg/kg)
Enhertu (10 mg/kg)

Topo1i x MTI Proof-of-Concept: Dual-Payload ADC Overcomes Sequential Topo1i and MTI ADC Resistance



Indications Poised to Benefit from Topo1i + MTI Dual-Payload ADCs





1

Sutro Site-Selective ADC Platform

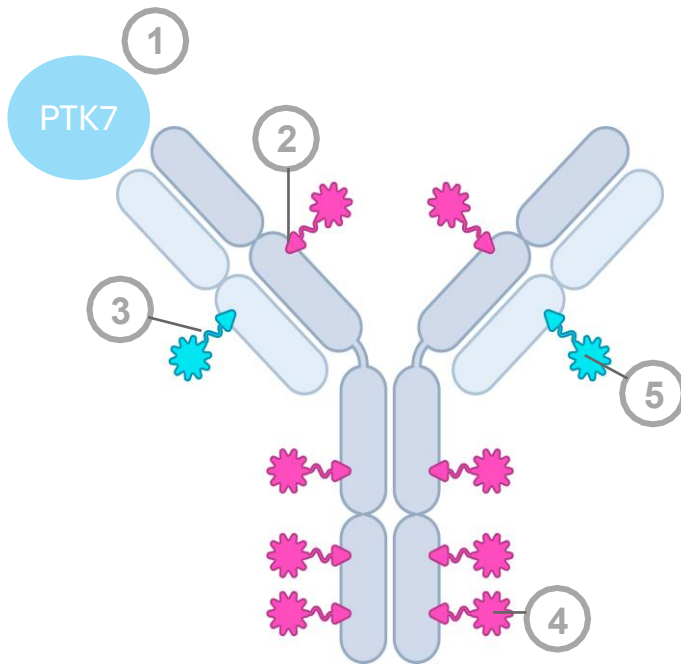
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Topo1i x MTI Dual-Payload Proof of Concept

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STRO-227: PTK7-Targeted Dual-Payload ADC

STRO-227, Dual-Payload Topo1i x MTI ADC Targeting PTK7

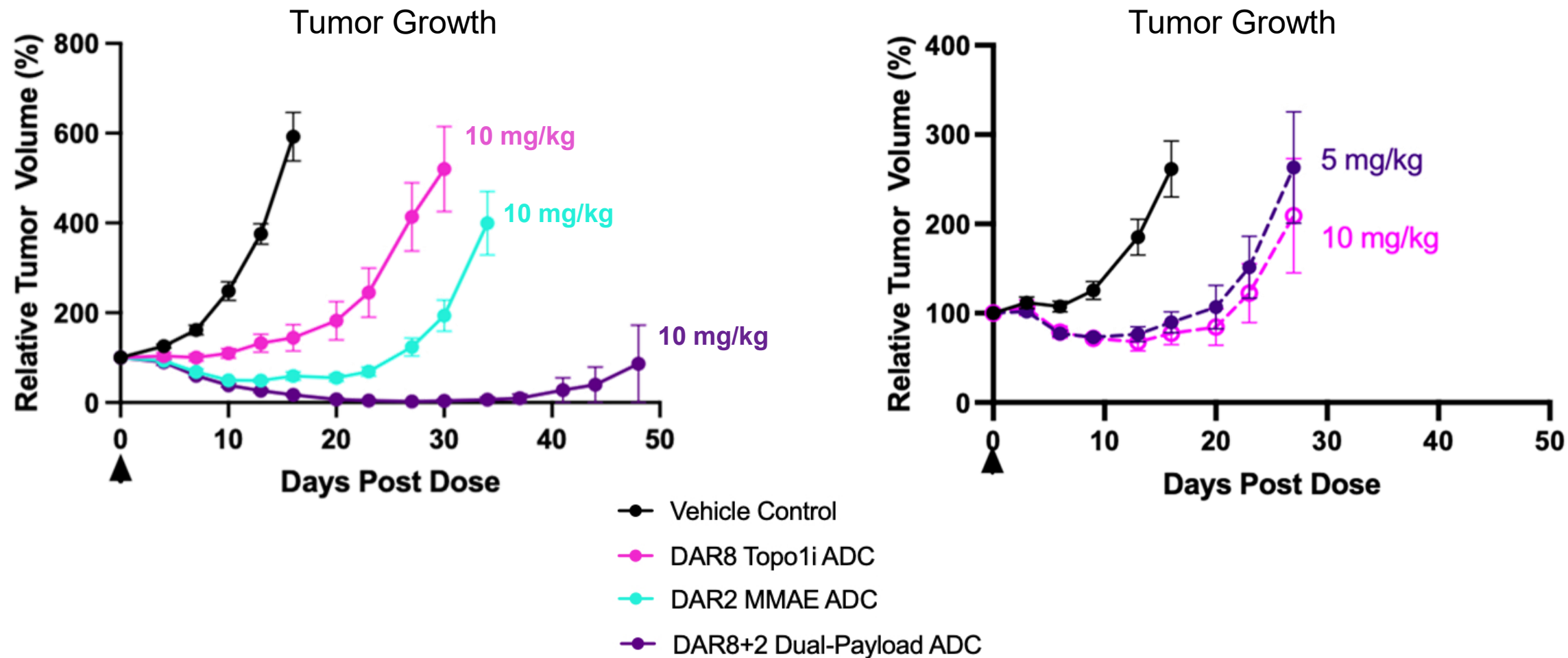


 DAR8: TOPO1i
 DAR2: MTI

- 1 **PTK7** is a pan-tumor target enriched on tumor-initiating cells. Its expression is correlated with poor prognosis in multiple solid tumors
- 2 **Optimally positioned non-natural amino acids**, p-azidomethyl-L-phenylalanine (pAMF), combined with ultrastable click chemistry
- 3 **β -glucuronidase cleavable linkers** with tumor selective cleavage, strong stability while in circulation, and added hydrophilicity led to **best-in-class PK**
- 4 **Eight exatecan payloads causing DNA disruption** and potent tumor cell killing, with high bystander activity, and immunogenic cell death (ICD)
- 5 **Two MMAE payloads causing Tubulin disruption** and potent tumor cell killing, with high bystander activity, and immunogenic cell death (ICD)

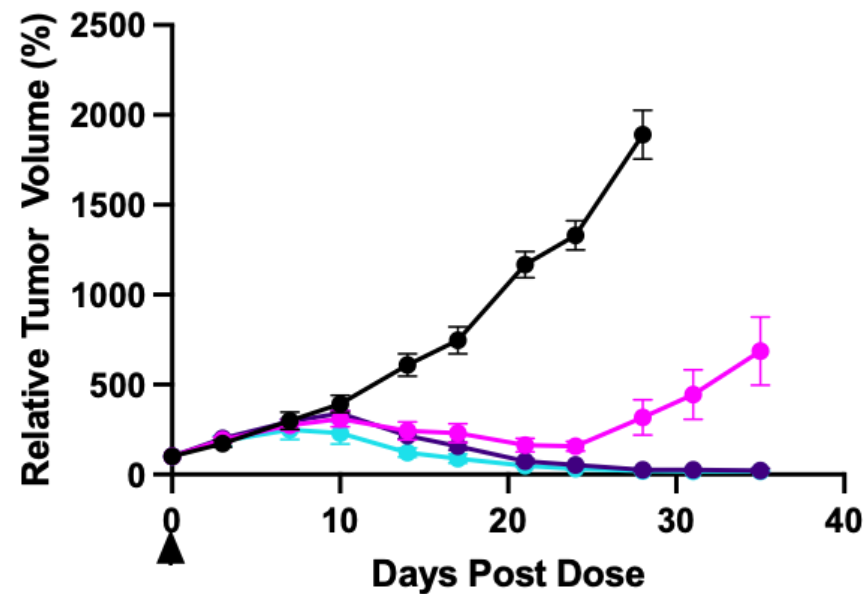
Better Together: STRO-227 Outperforms Single-Payload ADCs

Breast Cancer Xenograft Model

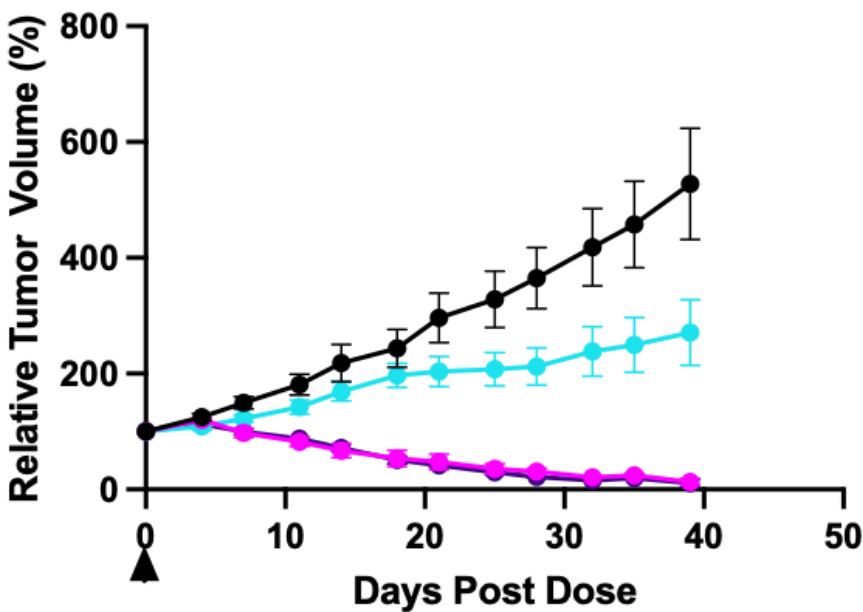


STRO-227 PDX Activity in Models with Different Payload Sensitivity

TNBC PDX Model

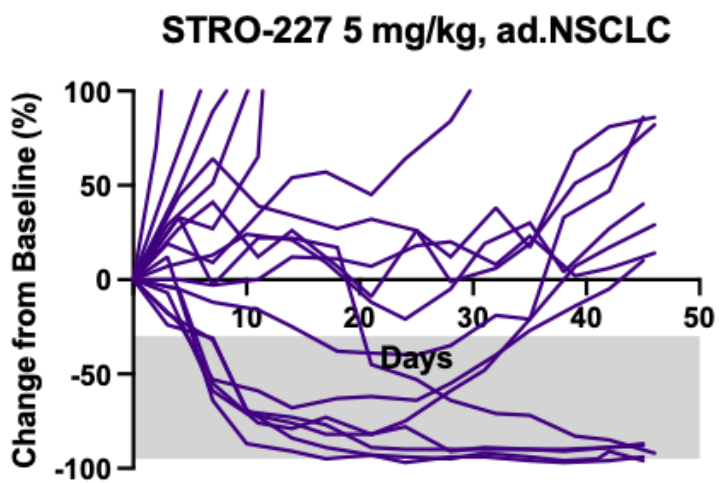
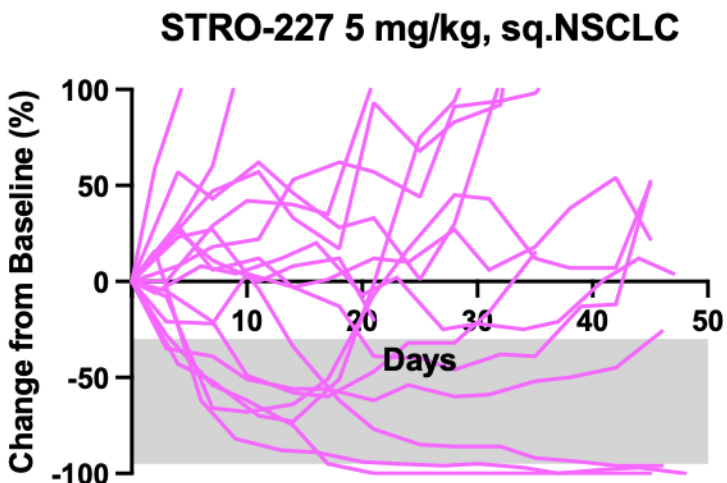
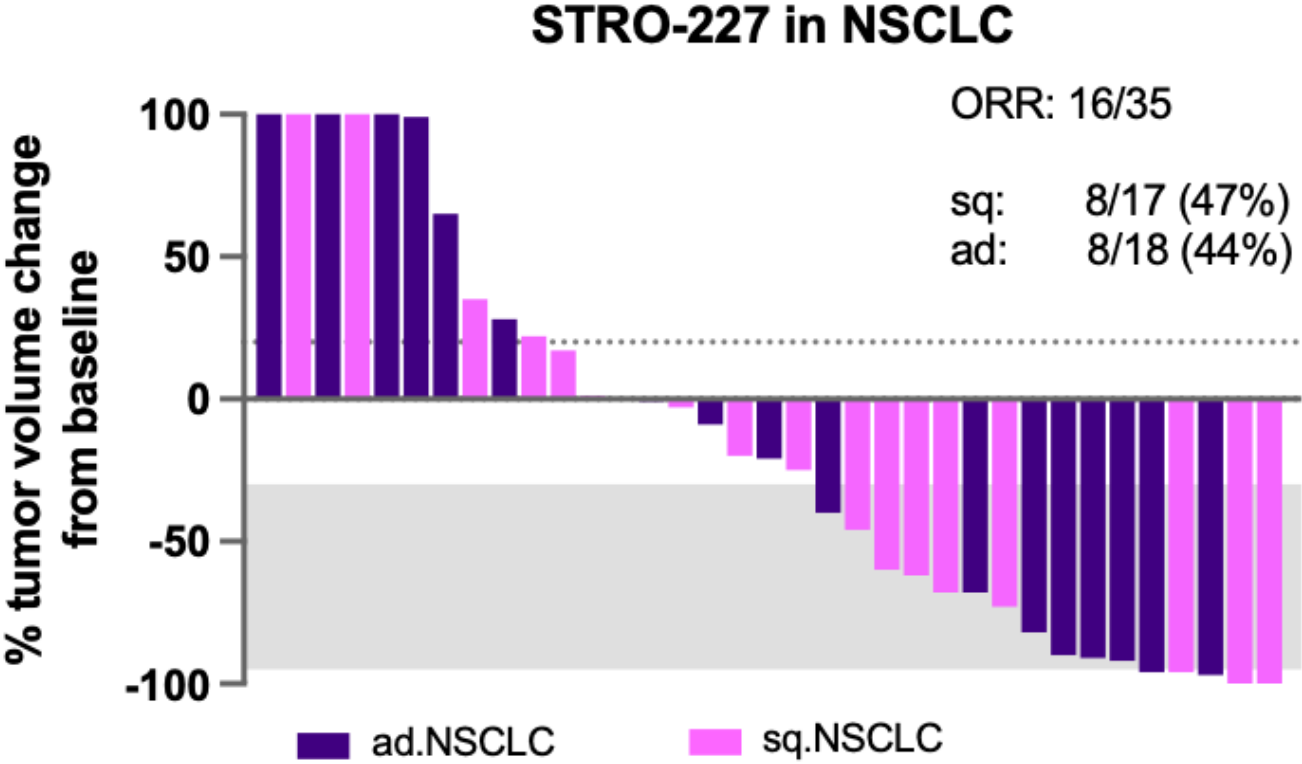


Ovarian Cancer PDX Model

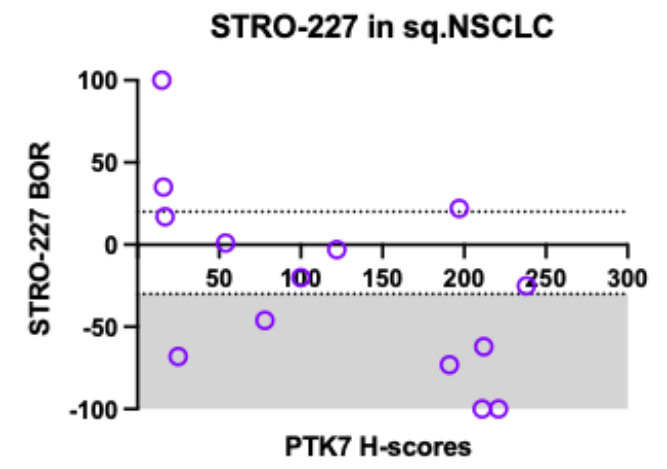
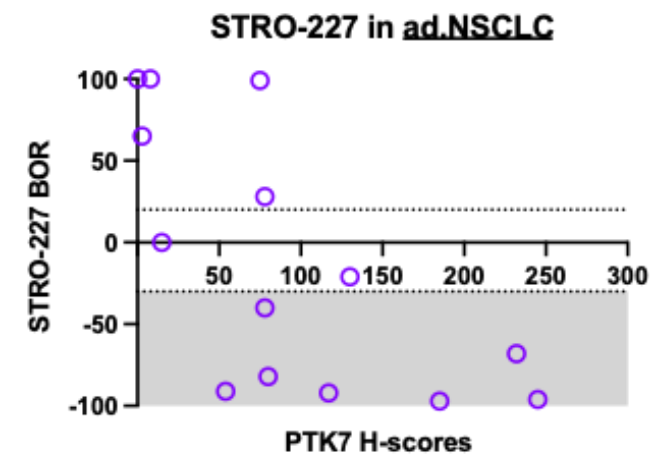
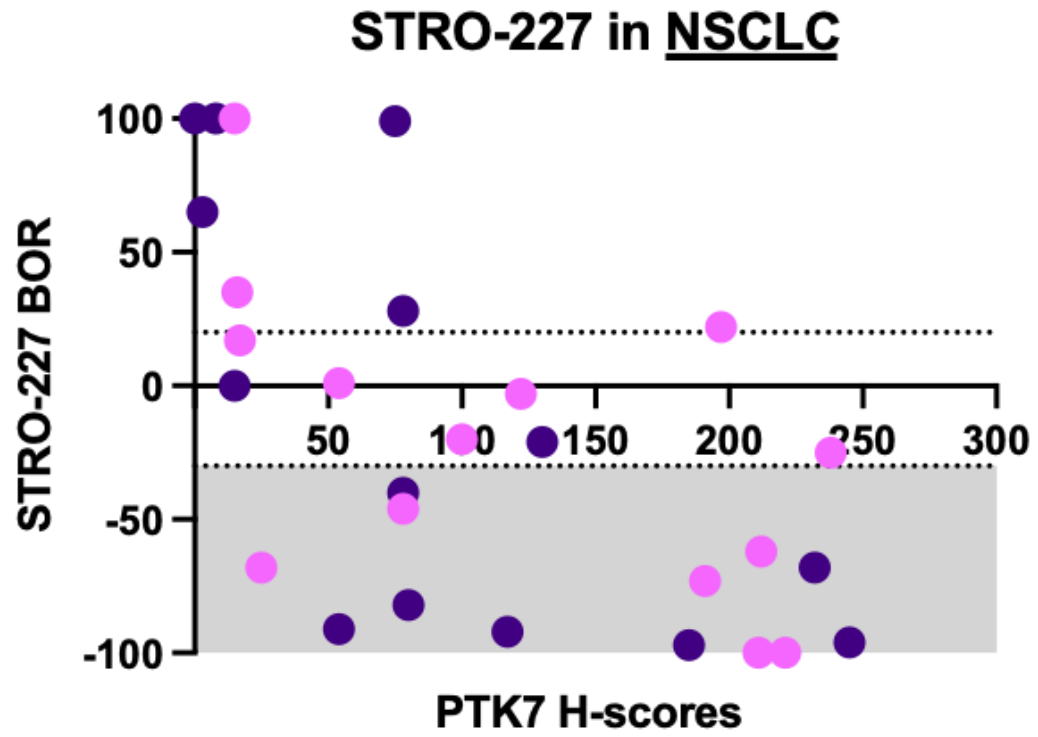


- Vehicle
- DAR2 MMAE ADC (5 mg/kg)
- DAR8 Topo1i ADC (5 mg/kg)
- STRO-227 (5 mg/kg)

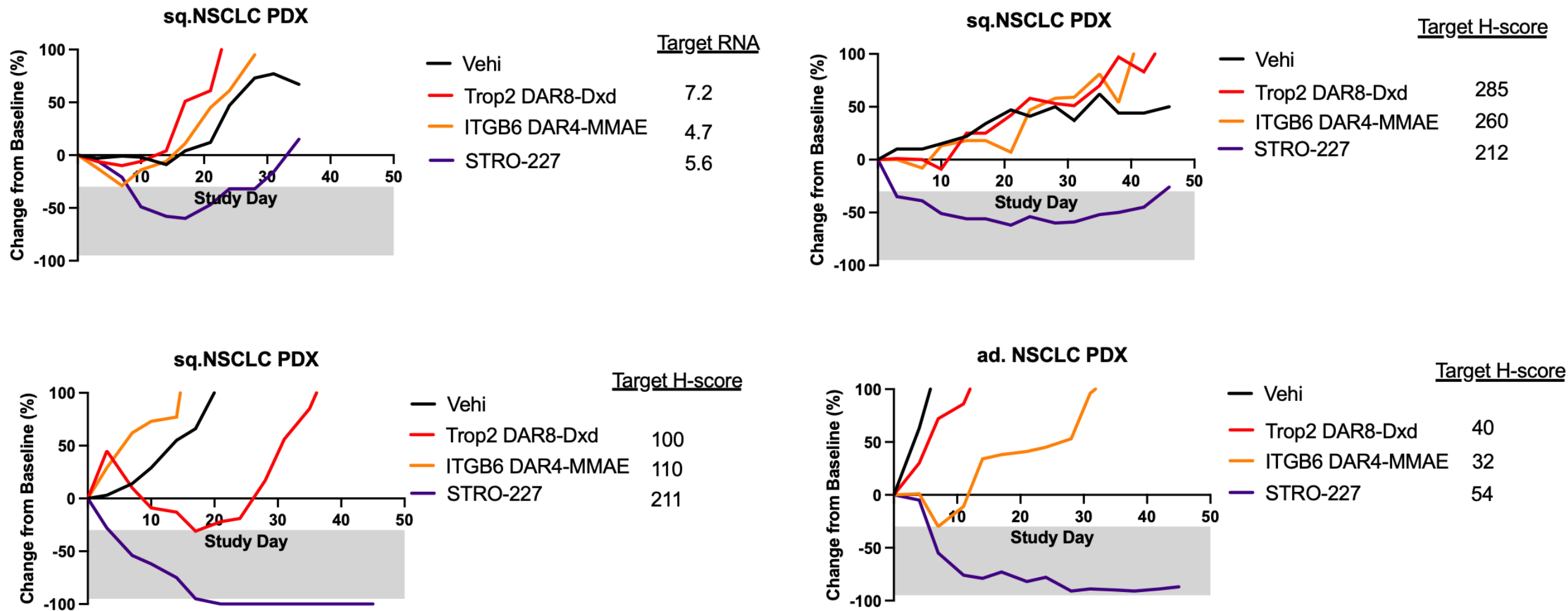
STRO-227 Activity in Non-Small Cell Lung Cancer PDX Models



STRO-227 Activity Tracks with PTK7 Expression in PDX Models

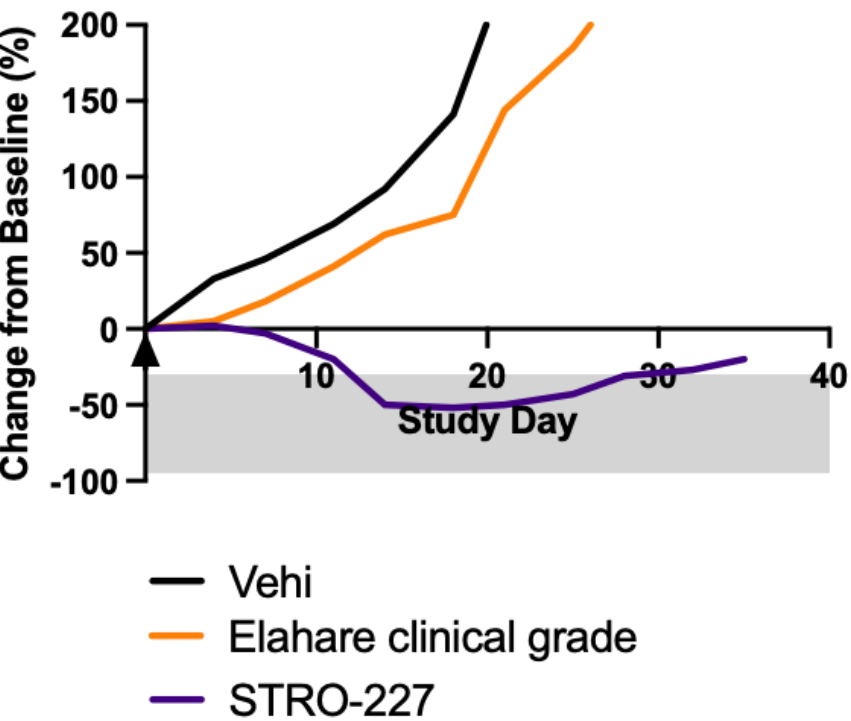


STRO-227 Achieves Deeper Responses Than Single-Payload Benchmarks in Selected NSCLC PDX Models

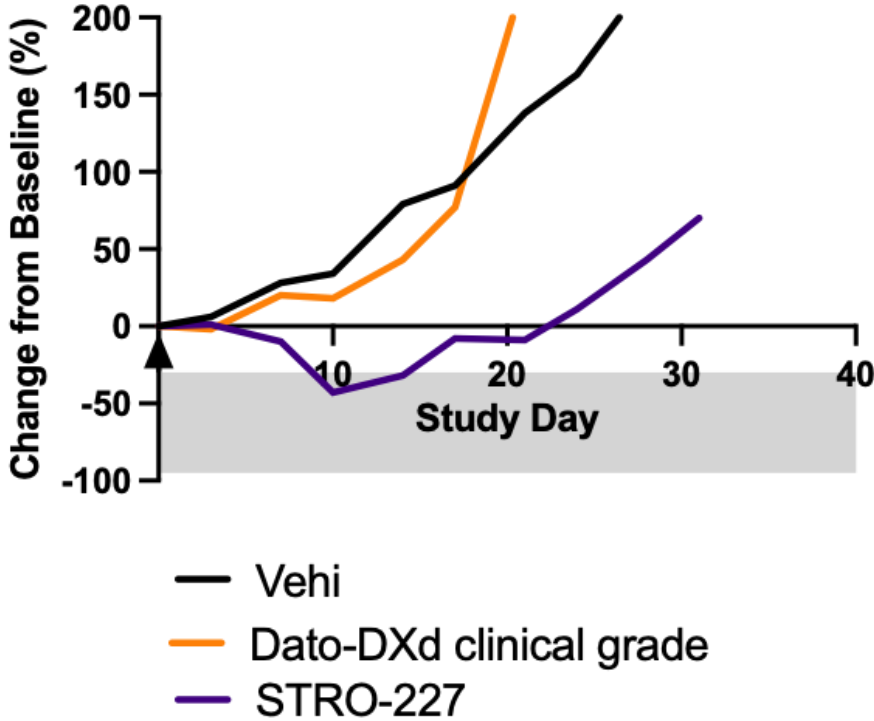


STRO-227 Drives Regressions in PDX Models Derived After Clinical Progression on Single-Payload ADCs

Ovarian Cancer PDX
Patient Progressed on an MTI ADC

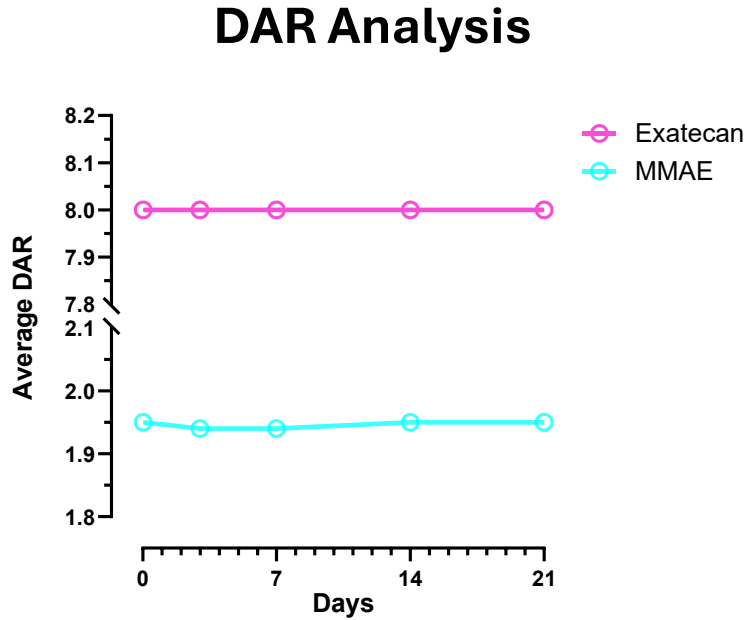
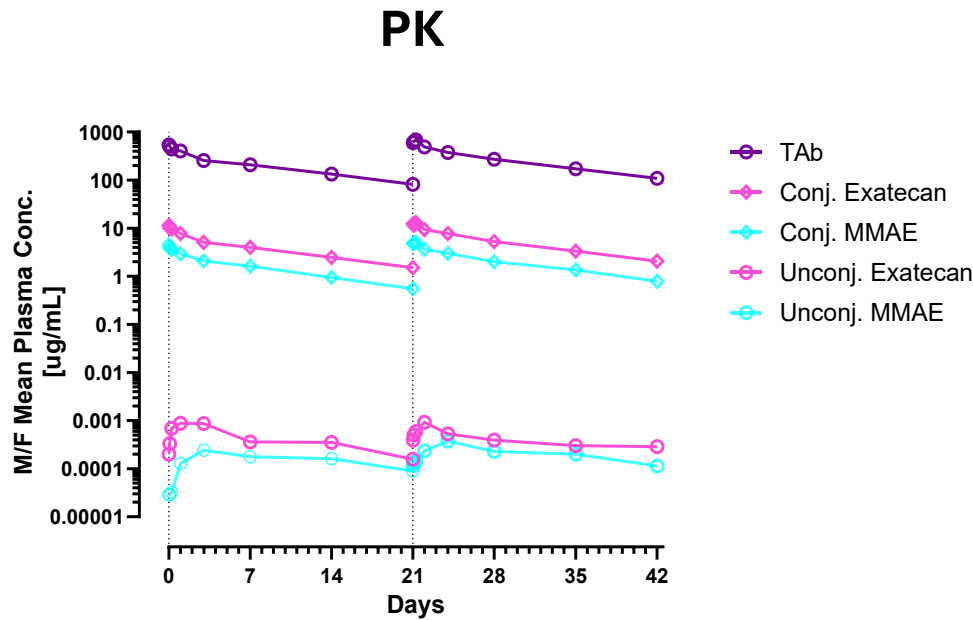


TNBC PDX
Patient Progressed on a Topo1i ADC



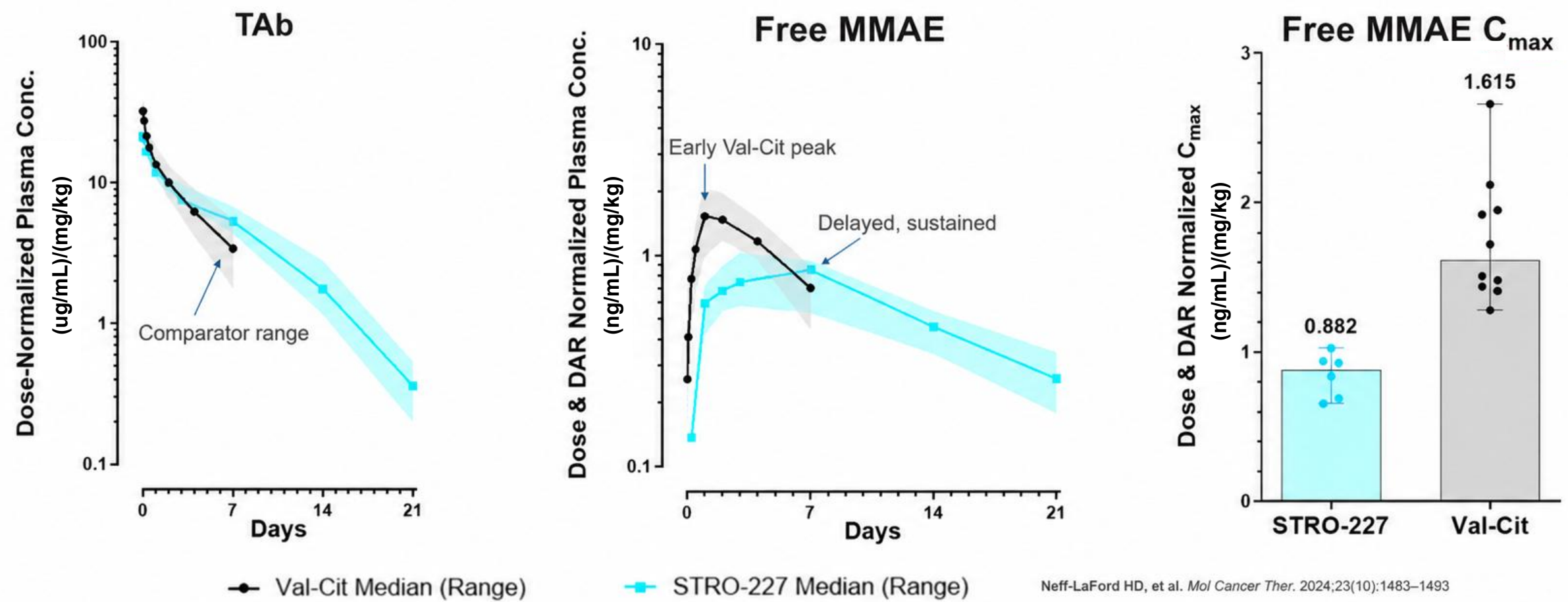
Encouraging PK and Safety Profile for STRO-227 (PTK7) in NHP

25 mg/kg 8+2 PTK7 dpADC (Q3Wx2)



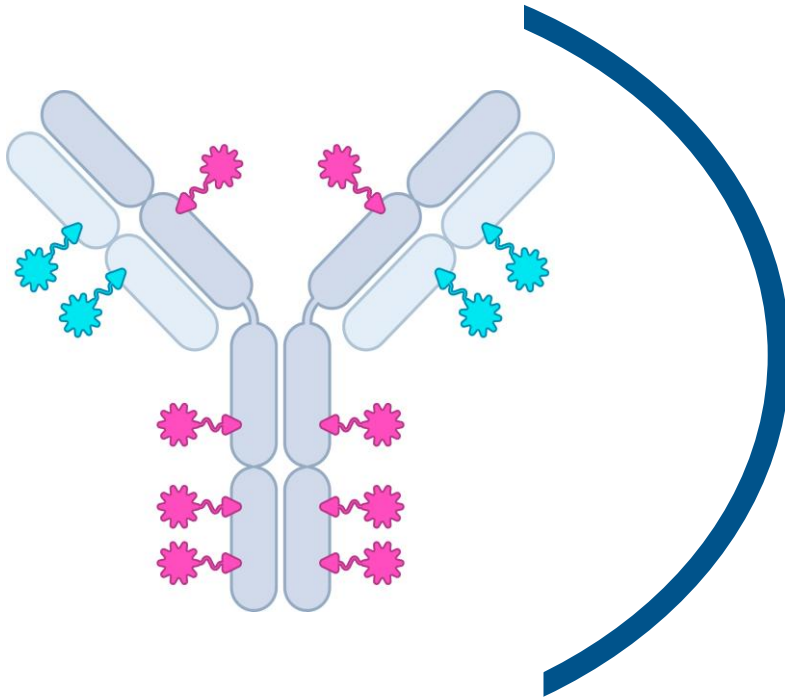
Dose (mg/kg)	Analyte	C _{max} (ug/mL)		AUC _{last} (d · ug/mL)		CL (mL/d/kg)	V _{ss} (mL/kg)	t _{1/2} (d)	
		C ₁	C ₂	C ₁	C ₂	C ₁	C ₂	C ₁	C ₂
25 (MF Mean)	TAb	541	684	3940	5220	4.89	70.5	10.3	10.8

STRO-227 Preclinical NHP PK Shows Delayed MMAE Appearance and Lower Free MMAE C_{max} vs Published Val-Cit MMAE ADCs



STRO-227 Has a ~45% Lower Normalized MMAE C_{max} Compared to Val-Cit MMAE ADCs in NHP

Differentiation by Design: Sutro Dual-Payload ADC Platforms



Precise Design: Optimization of conjugation sites, linker stability, and payload stoichiometry

Clinical Validation: STRO-004 demonstrates sustained ADC exposure, low circulating free payload, and low platform toxicity

Pipeline Translation: STRO-227 combines two clinically-validated payloads

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