

DESIGNED

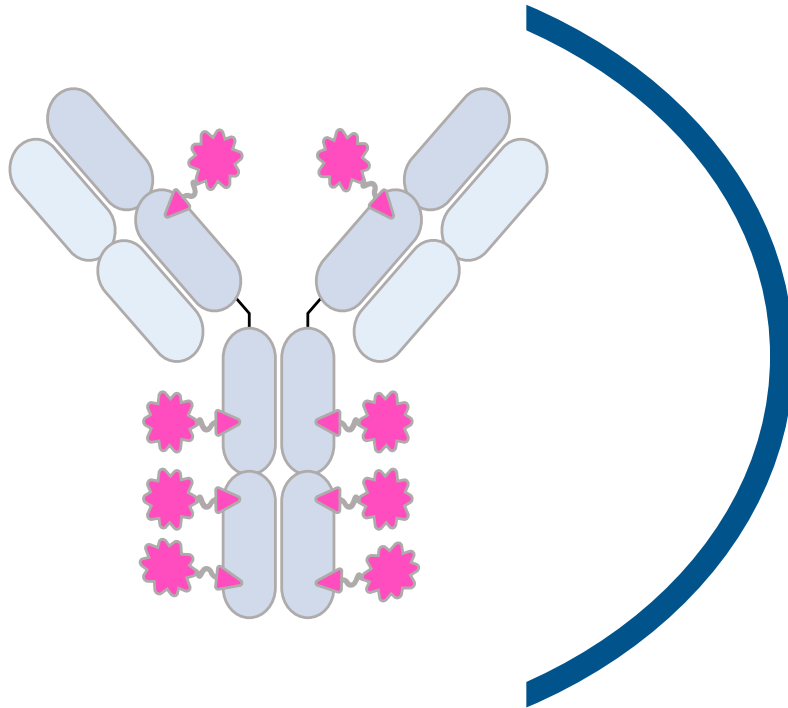
TO DELIVER

**STRO-004 Clinical
Learnings:
How ADC Design
Shapes Safety and
Efficacy**

Daniel Calarese, PhD

SUTRO
BIOPHARMA

World ADC 2026, San Diego
October 13, 2026



1

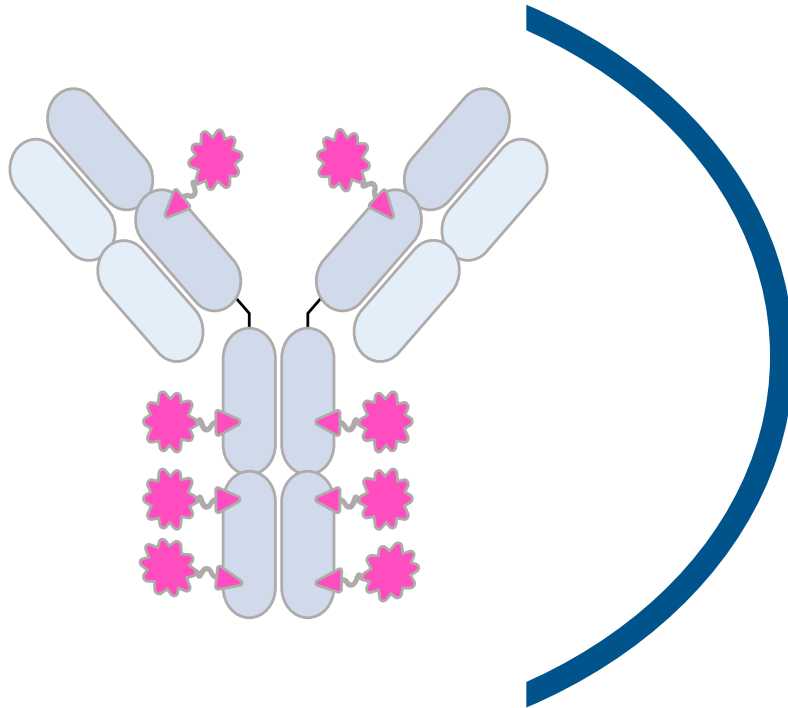
Sutro Site-Selective ADC Platform

2

STRO-004 Preclinical-to-Clinical Translation

3

Platform Expansion Across Targets and Payloads



1

Sutro Site-Selective ADC Platform

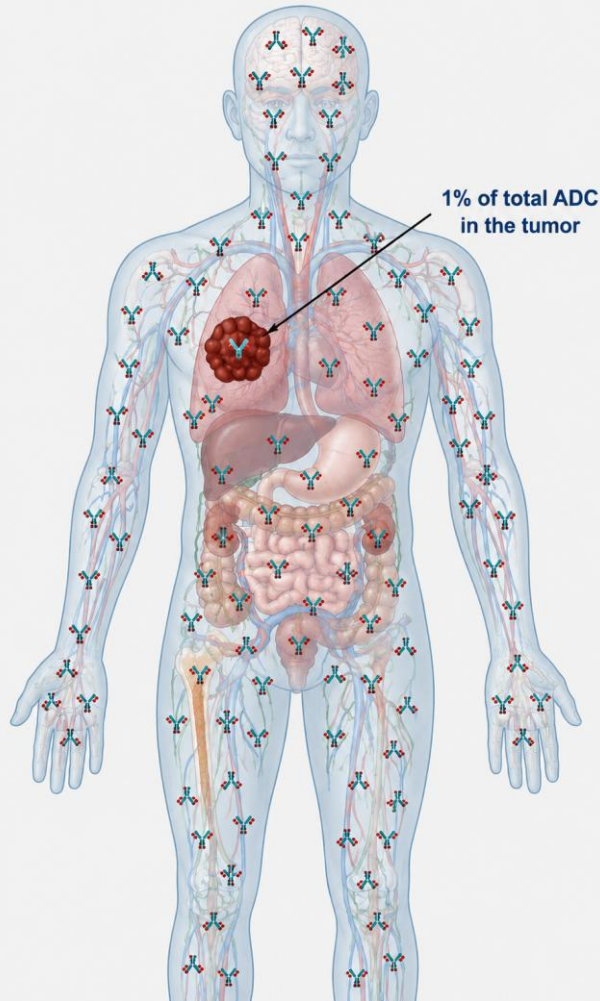
2

STRO-004 Preclinical-to-Clinical Translation

3

Platform Expansion Across Targets and Payloads

Higher ADC Dose and Exposure Drive Efficacy



Only 1% of ADCs reach tumors

99% reside outside tumors

Stable ADCs limit free payload exposure to healthy tissues

Reduced
"Platform
Toxicity"



Higher
Dose

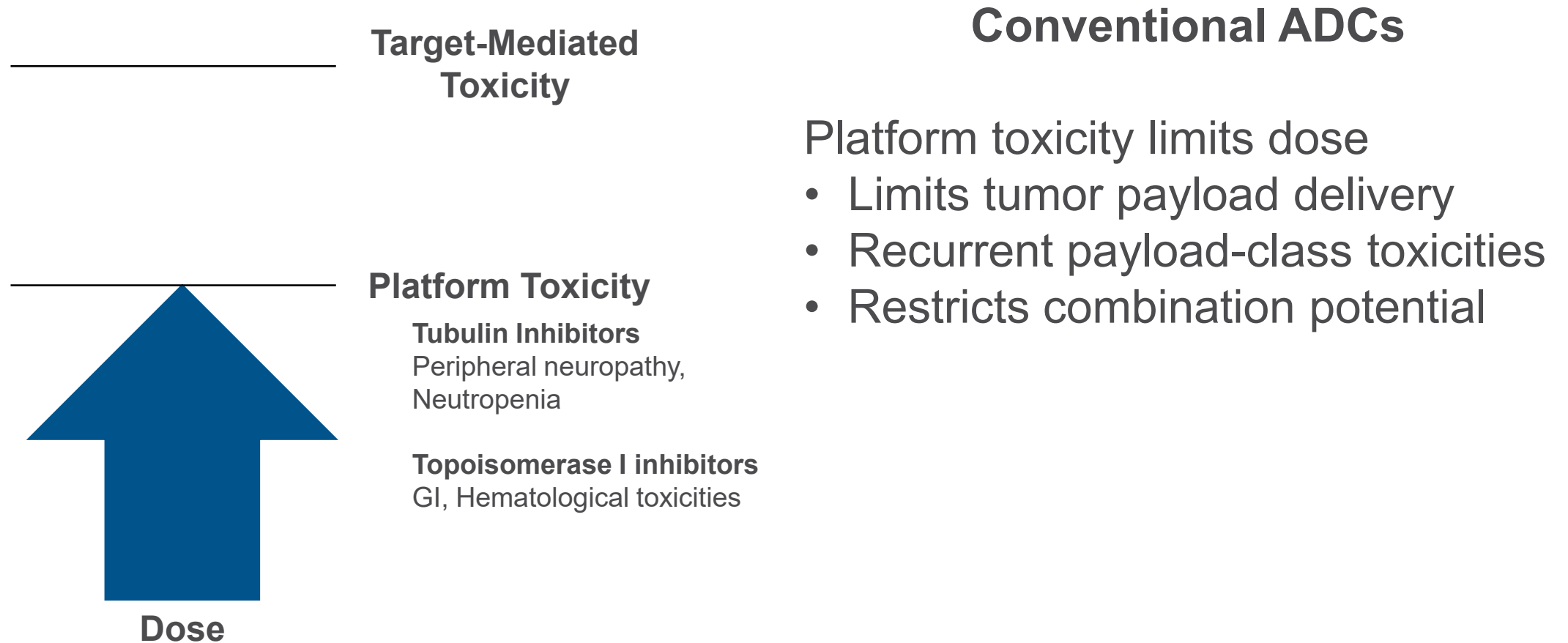


Higher
Exposure

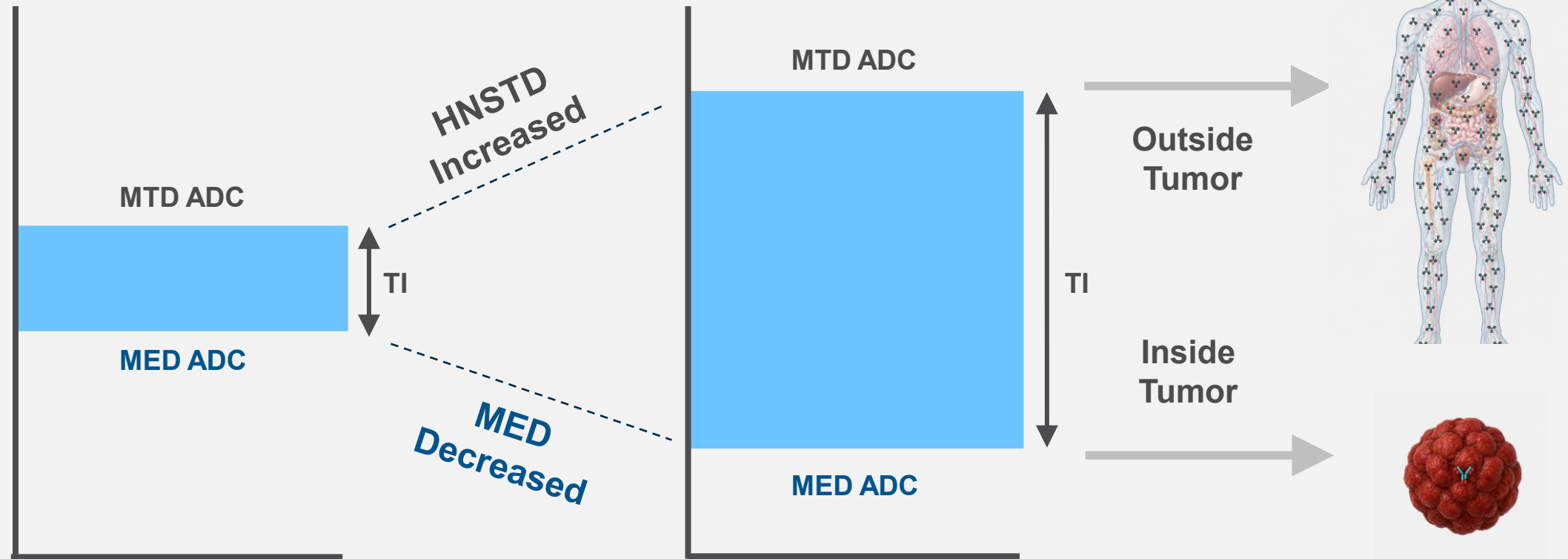


Drives
Efficacy

Conventional ADCs Are Often Limited by Platform Toxicity



Enhancing ADCs Inside and Outside the Tumor With Sutro's Platform Technologies Leads to a Higher Therapeutic Index



Adapted from Gerber et al, mAbs, 2023

Sutro's ADC Platform is Fundamentally Different: Manufacturing of Proteins in Cell-Free Extracts



Prokaryotic Cells



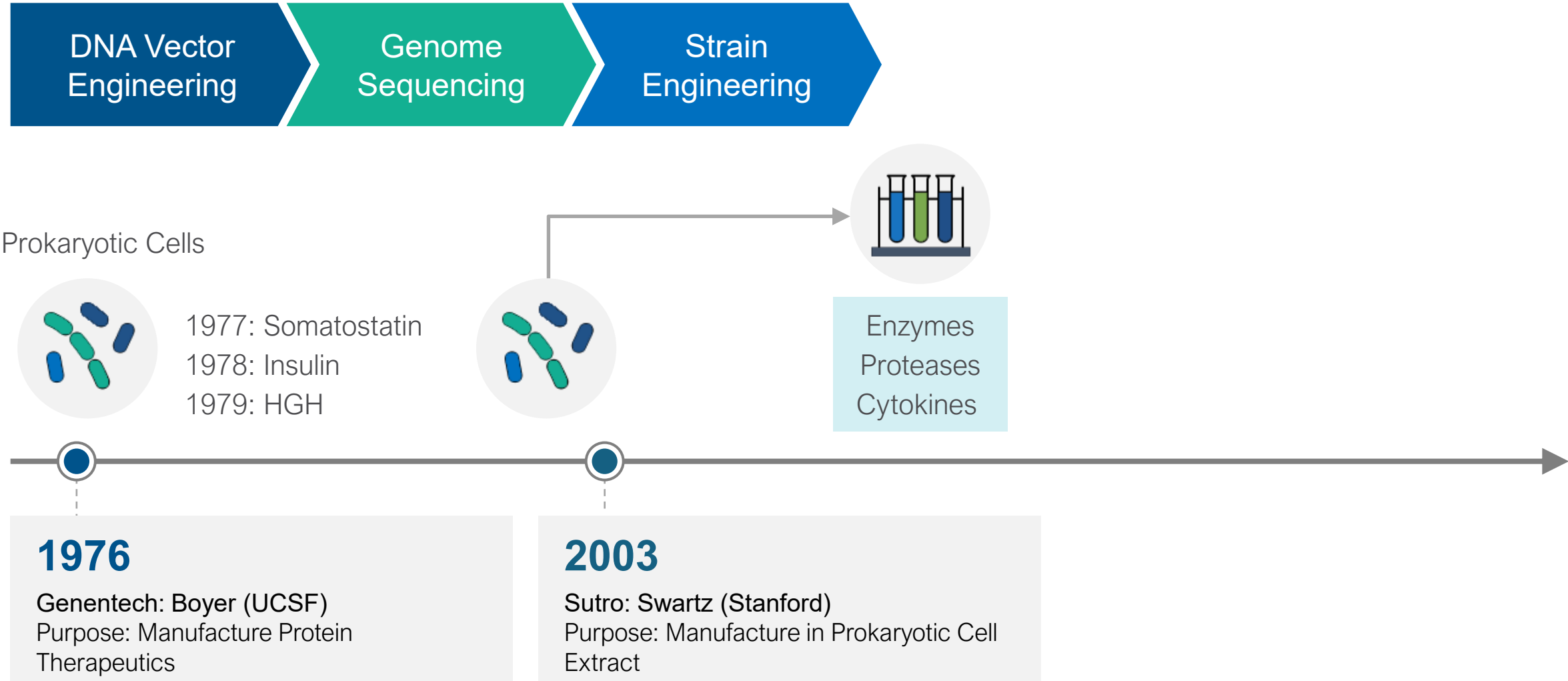
1977: Somatostatin
1978: Insulin
1979: HGH



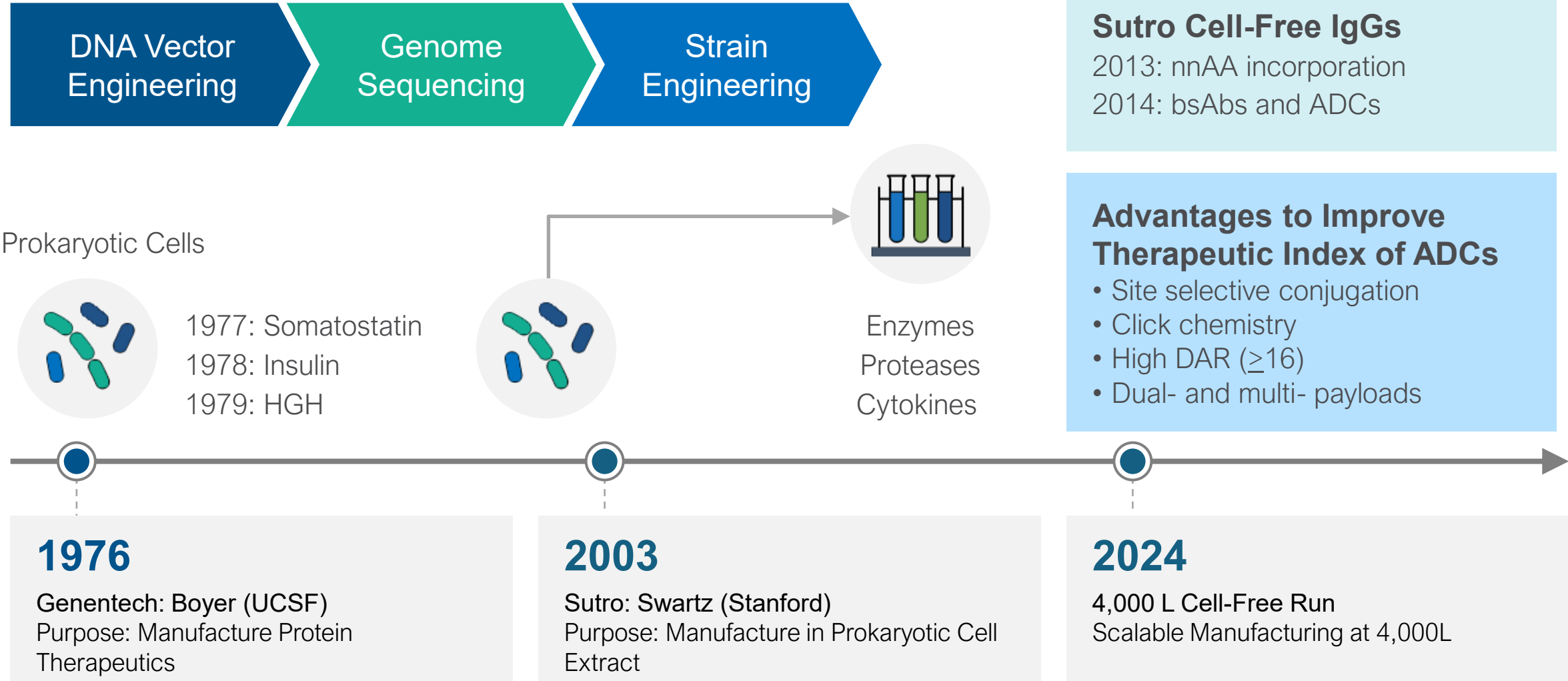
1976
Genentech: Boyer (UCSF)
Purpose: Manufacture Protein
Therapeutics

DNA - deoxyribonucleic acid; HGH – human growth hormone; UCSF – University of California, San Francisco

Sutro's ADC Platform is Fundamentally Different: Manufacturing of Proteins in Cell-Free Extracts



Sutro's ADC Platform is Fundamentally Different: Manufacturing of Proteins in Cell-Free Extracts



nnAA – non-natural amino acids

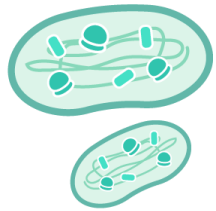
Industry-Leading Cell-Free Protein Synthesis Platform

Enables Rapid Make/Test Cycle for Empirical Selection of Optimal Leads

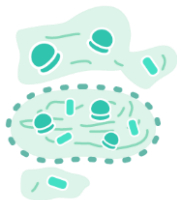


The extract is readily available, eliminating the need to establish a new cell line or strain for discovery or manufacturing

Stockpiled Extract



Grow Cells from *E. Coli*



Cell Lysis



Cellular Extract



Biophysical Properties



Functional Activity



Potency



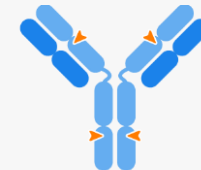
Pharmacology



Rapid make/test cycle to optimize protein design



Cell-Free Protein Synthesis



IgG with Non-Natural Amino Acids



Linker-Payload Click Chemistry



Homogeneous ADC

1

2

3

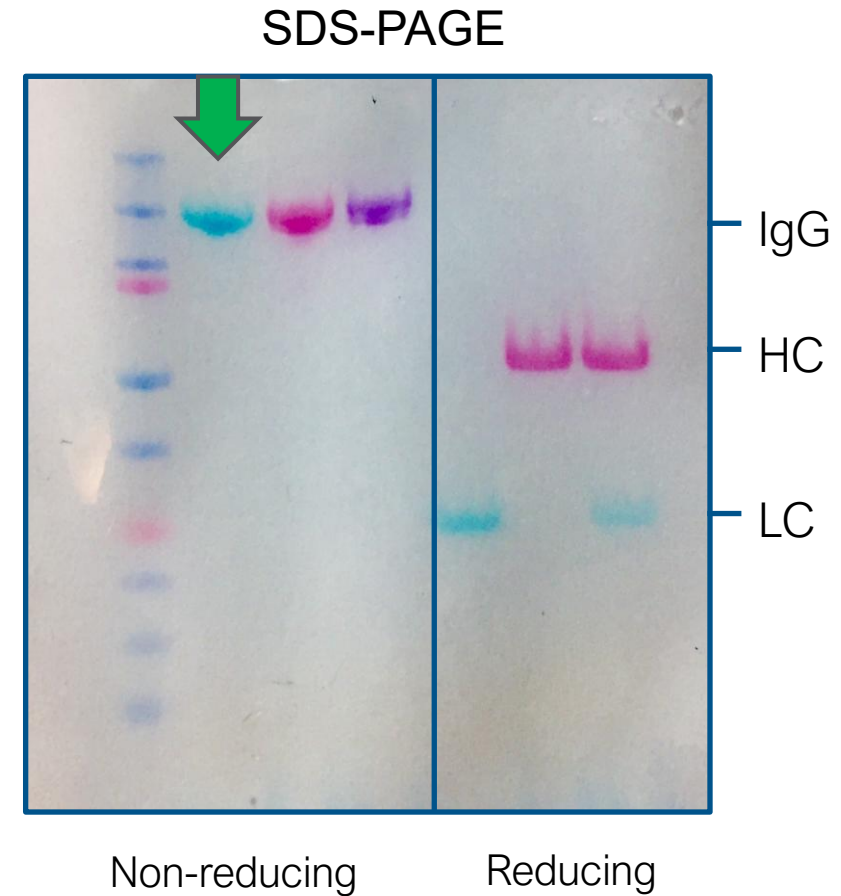
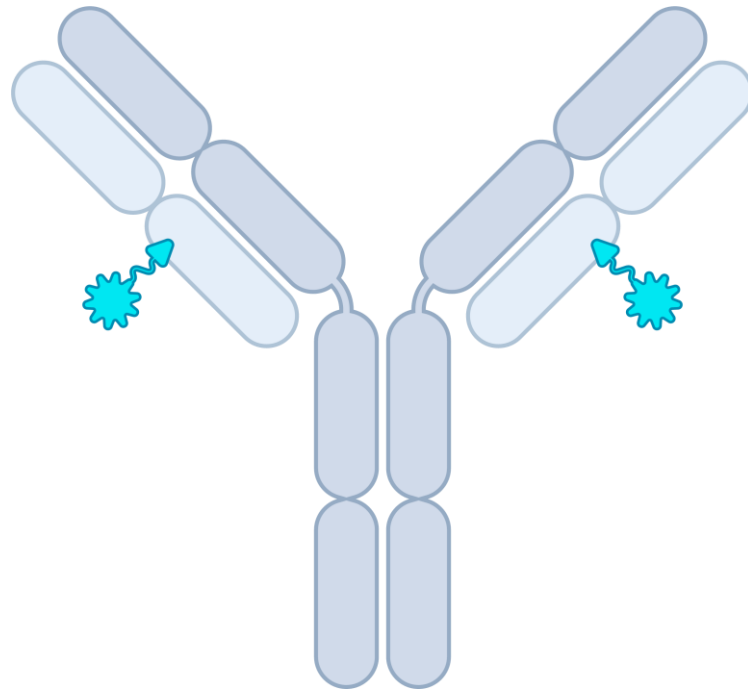
4

5

6

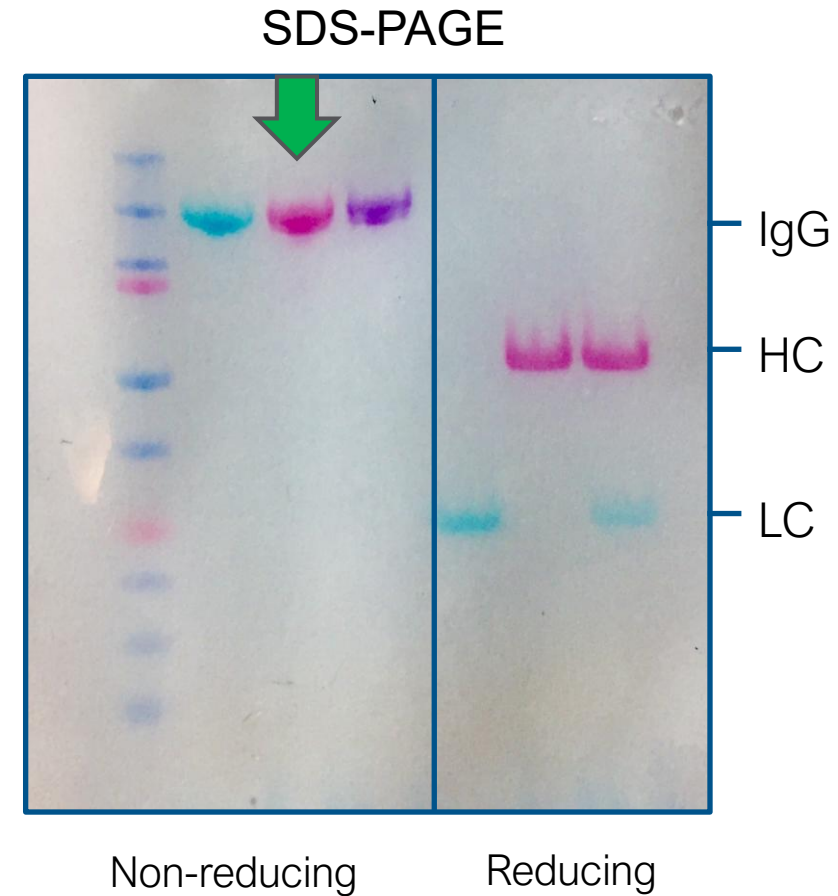
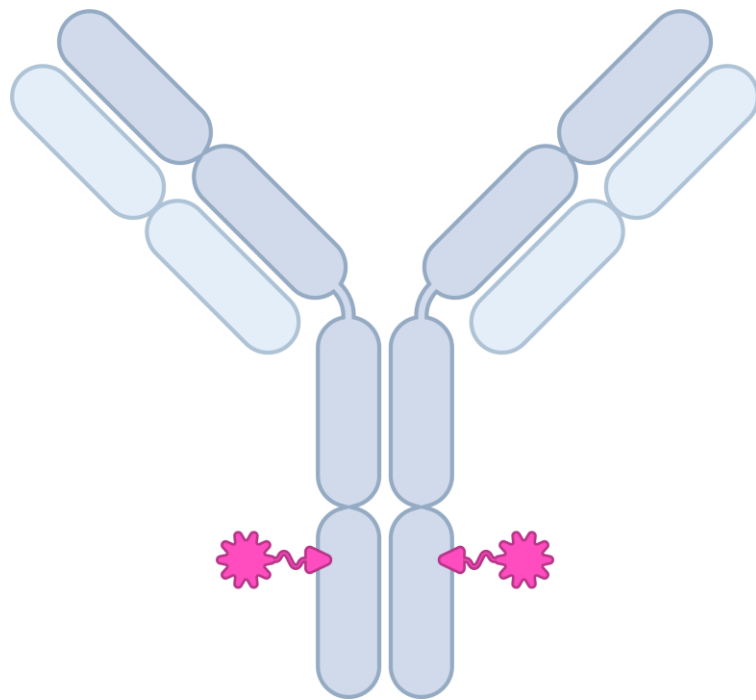
7

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



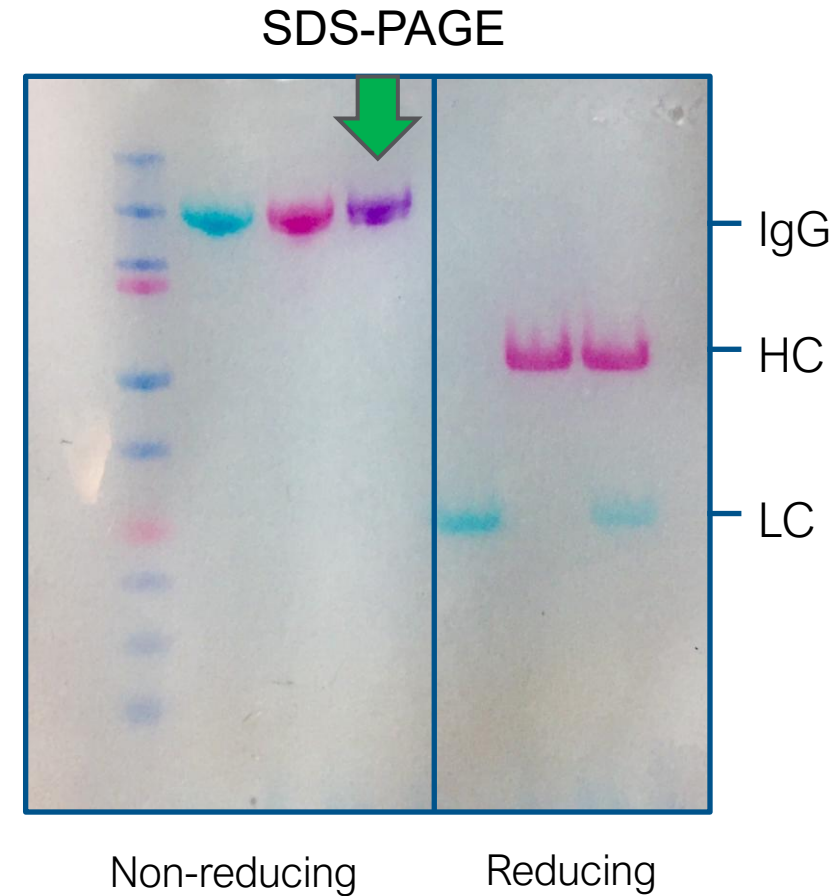
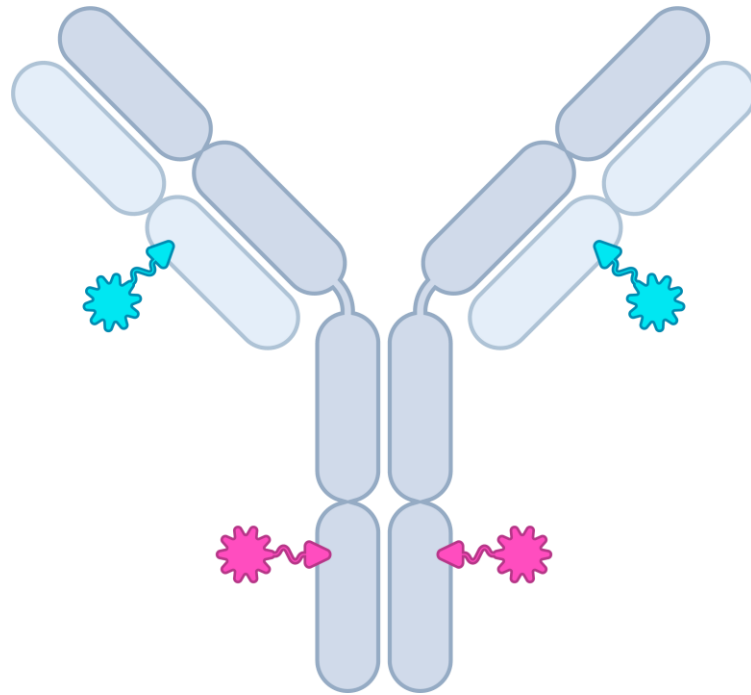
Wen M, Yu A, Park Y, Calarese D, Gerber HP, Yin G. Homogeneous antibody-drug conjugates with dual payloads: potential, methods and considerations. *MAbs*. 2025;17(1):2498162. doi:10.1080/19420862.2025.2498162

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



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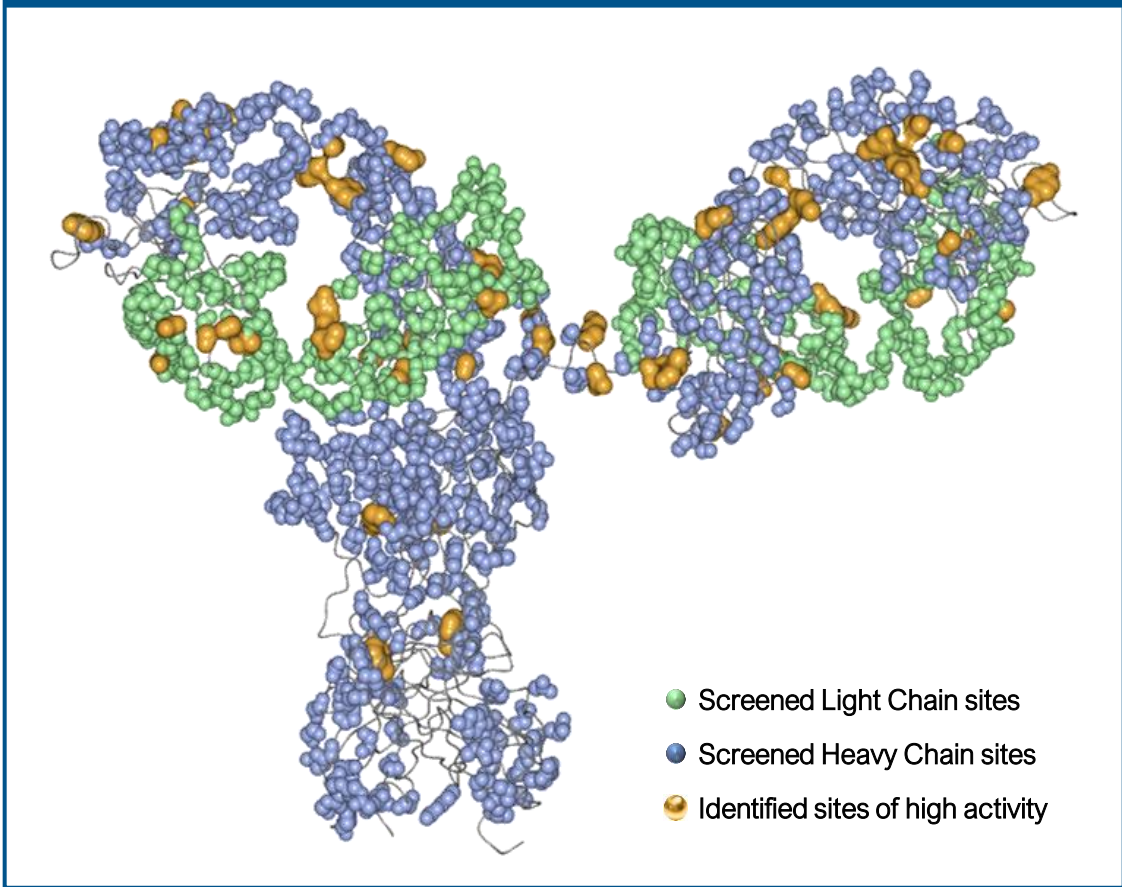
Sutro Cell-Free Platform Allows Precise Tuning of Linker-Payloads



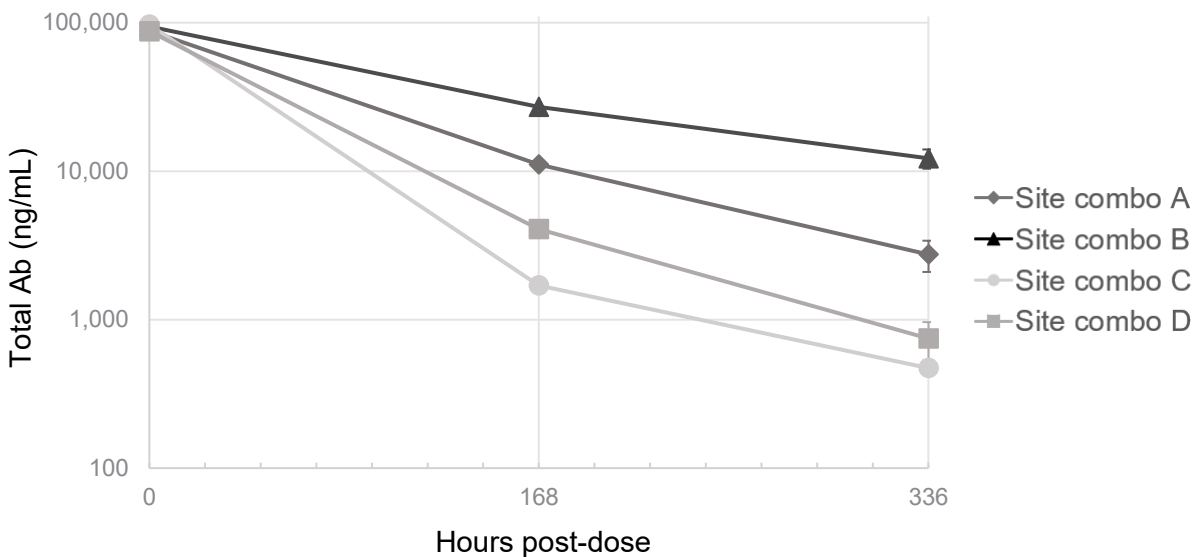
Wen M, Yu A, Park Y, Calarese D, Gerber HP, Yin G. Homogeneous antibody-drug conjugates with dual payloads: potential, methods and considerations. *MAbs*. 2025;17(1):2498162. doi:10.1080/19420862.2025.2498162

Sutro Cell-Free 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



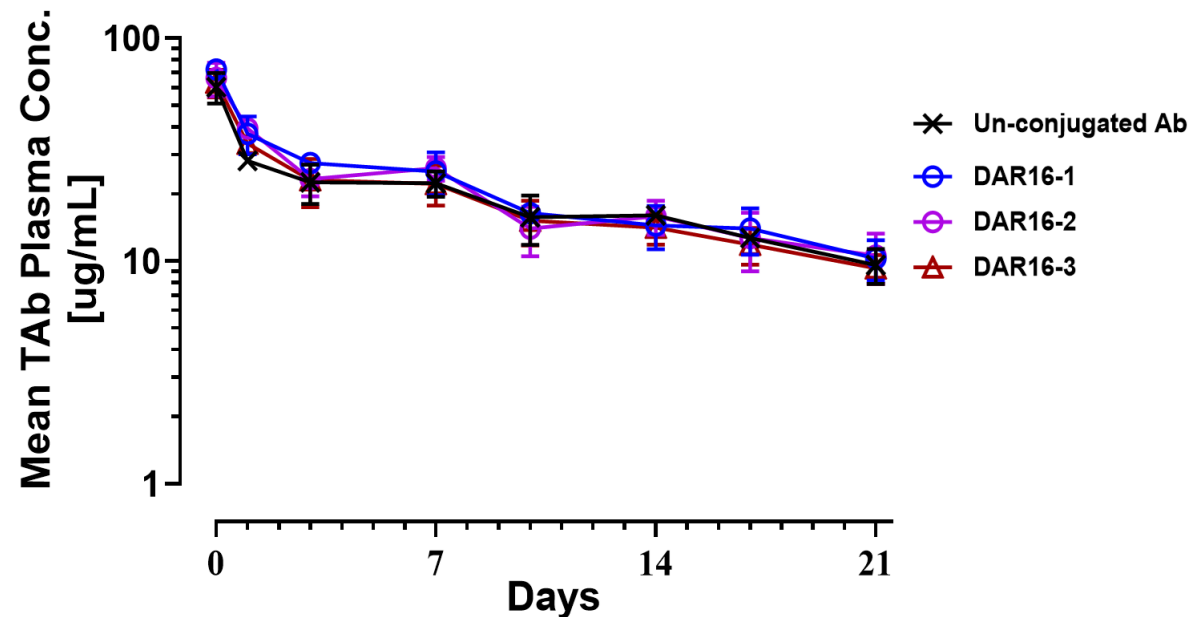
Less ADC Clearance



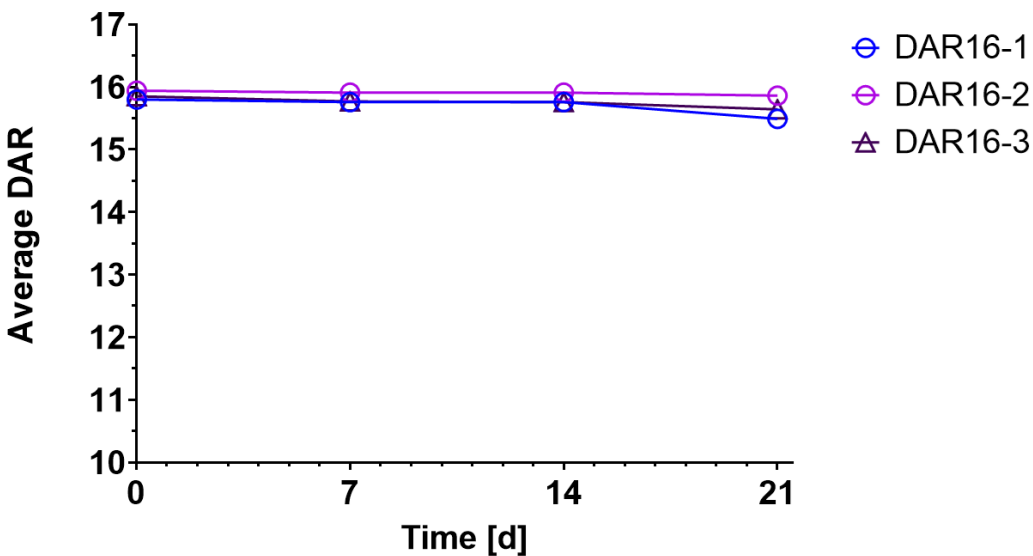
Less Systemic Toxicity

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

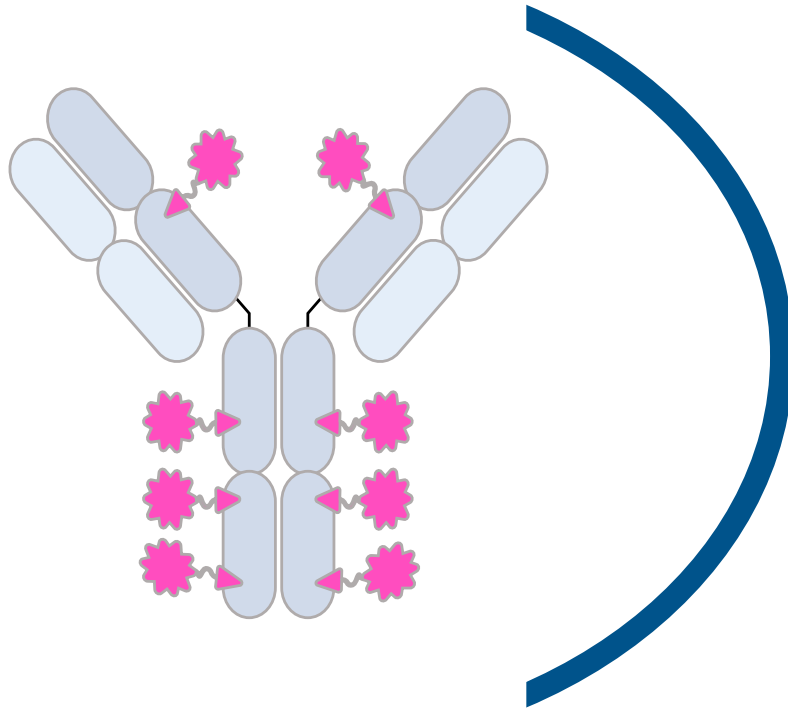
PK of DAR16 ADCs in C57BL/6 mice



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



1

Sutro Site-Selective ADC Platform

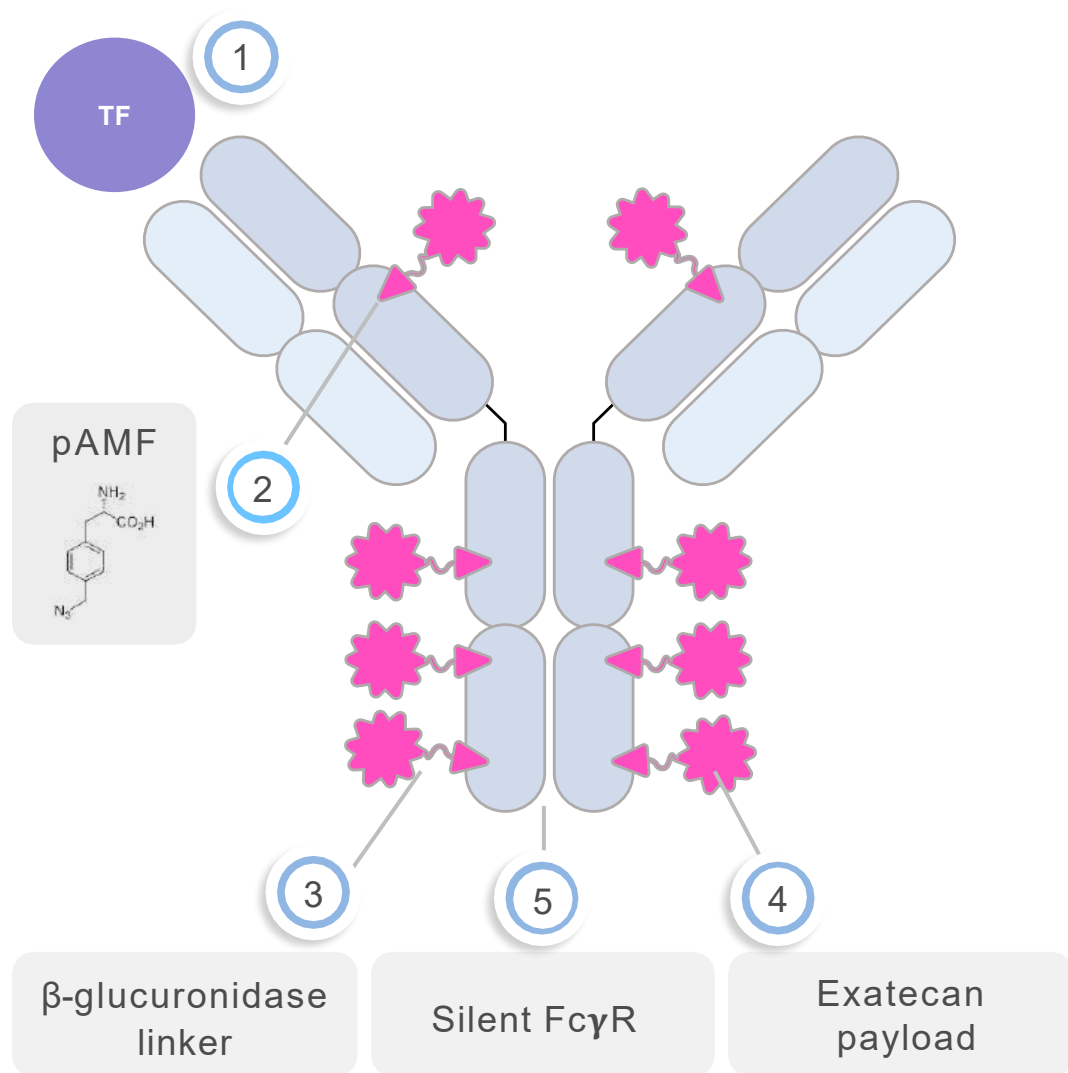
2

STRO-004 Preclinical-to-Clinical Translation

3

Platform Expansion Across Targets and Payloads

STRO-004 Anatomy: Next-Generation TF-Targeting Exatecan/Topo1 ADC Engineered for Enhanced Therapeutic Index



STRO-004 is a homogeneous antibody drug conjugate (ADC) with a drug-antibody ratio (DAR) of 8, targeting TF



1

Enhanced mAb with high affinity, internalization; reduced bleeding risk

2

Optimally positioned non-natural amino acids, p-azidomethyl-L-phenylalanine (pAMF), combined with ultrastable click chemistry results in lowest levels of unconjugated payloads

3

β -glucuronidase cleavable linkers with tumor selective cleavage, strong stability while in circulation, and added hydrophilic element led to best-in-class PK

4

Exatecan payload causing DNA disruption and potent tumor cell killing, with high bystander activity, and immunogenic cell death (ICD)

5

Lack of FcR interactions limits uptake by alveolar macrophages, reducing risk of interstitial lung disease (ILD)

STRO-004 Well-Tolerated in NHP up to 50 mg/kg

Preclinical Prediction: Sustained Intact ADC Exposure with Limited Systemic Payload Toxicity

Objective:

Nonclinical safety of DAR8 TF exatecan-ADC

Study:

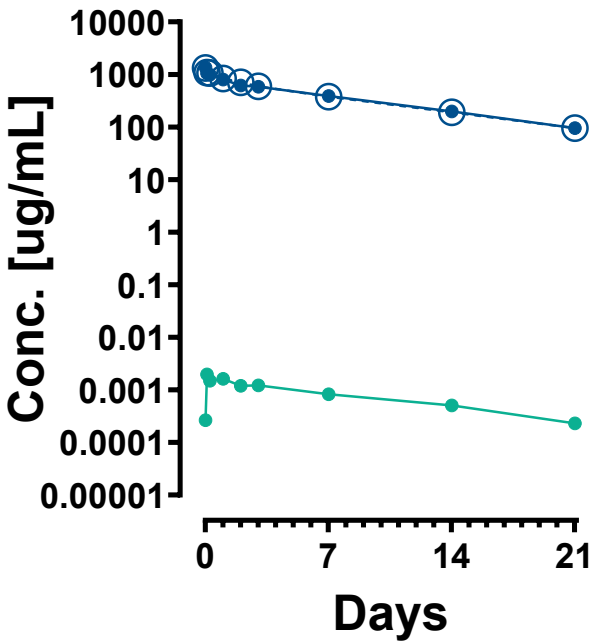
Dosed twice, three weeks apart

Findings:

- DAR4 and DAR8 ADCs were well-tolerated up to 100 and 50 mg/kg, respectively
- No evidence of eye toxicity
- No significant hematologic toxicities
- Mild skin toxicity

HNSTD: 50 mg/kg

DAR 8



---○--- TAB

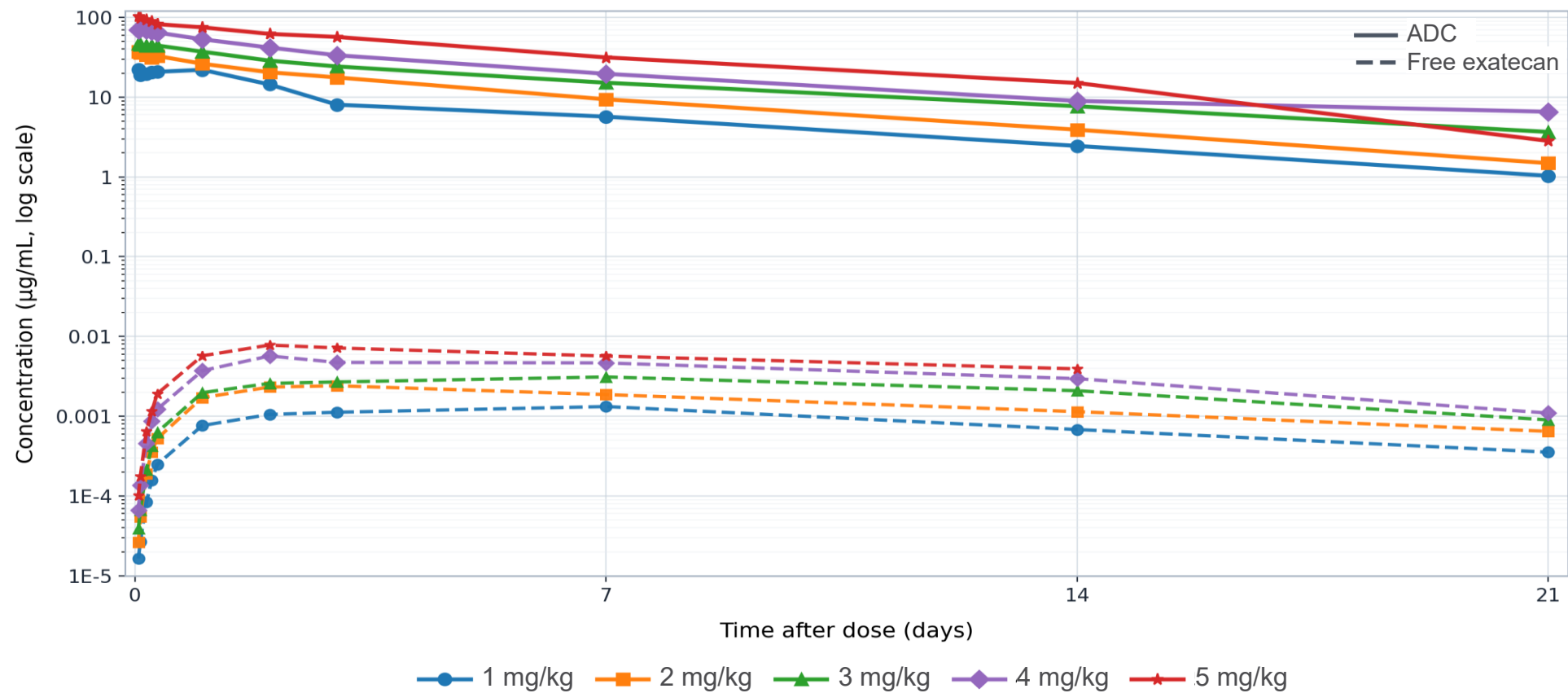
—●— ADC

—●— Exatecan

TAB – Total Antibody

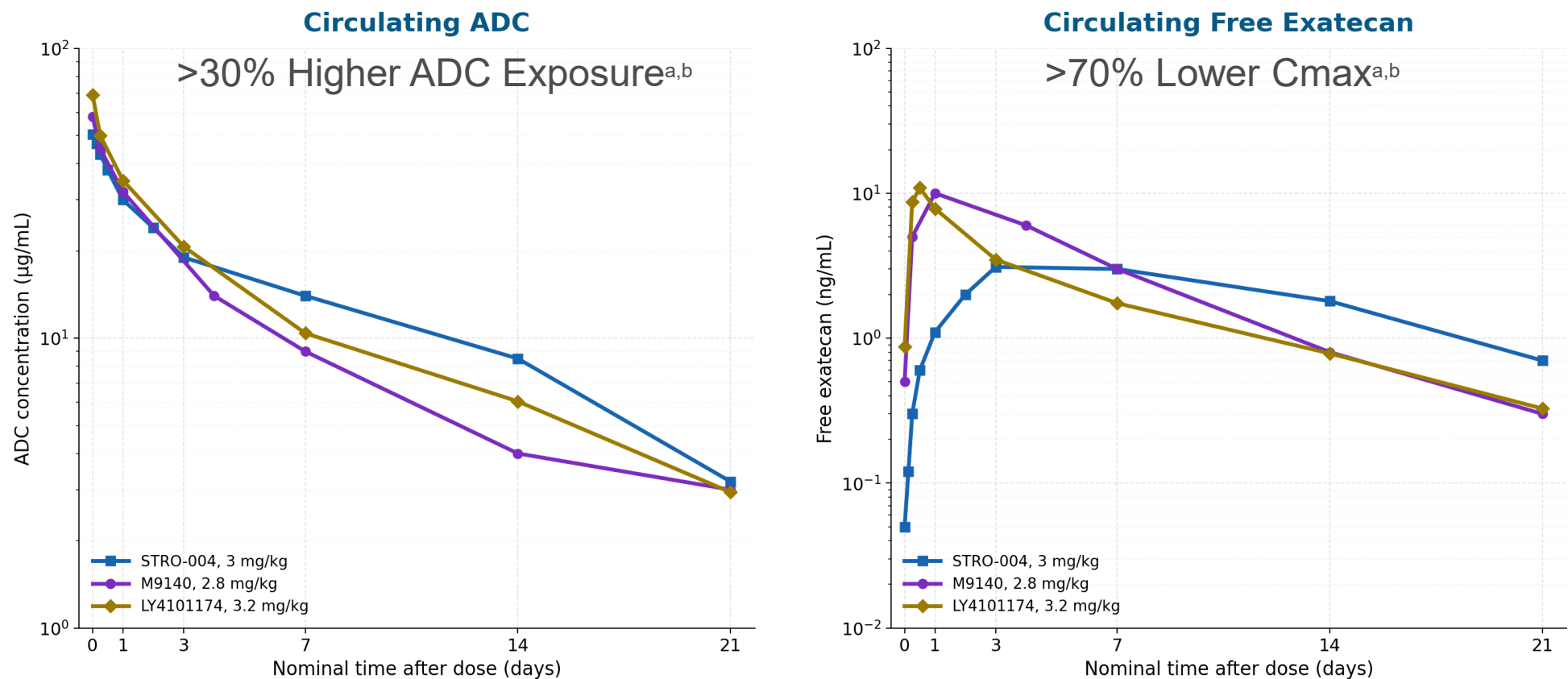
STRO-004 Clinical PK Shows Sustained ADC Exposure with Low Free Payload C_{max}

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 Shows Higher ADC Exposure and >70% Lower Free Exatecan C_{max} vs Clinical β-Glu Exatecan ADCs



Stable ADC in Circulation → Lower Free Payload → Lower Platform Toxicity

^aKopetz, Nature Medicine 2025 ^bGao, ASCO 2026. C_{max}: Tang et al. *Cancer Metastasis Rev.* 2025;44:18; Nguyen, Bordeau & Balthasar. *Cancers.* 2023;15:713.

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

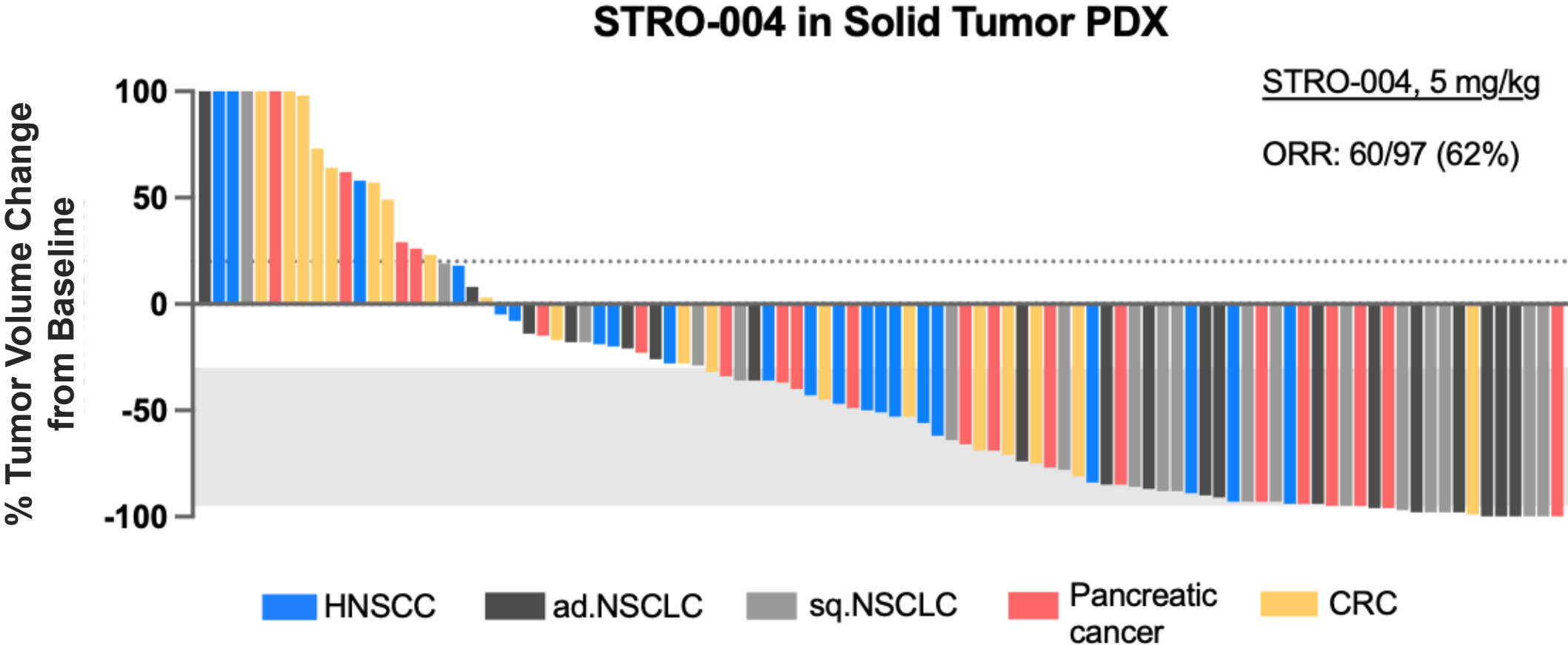
* Count increased by 1 manually to capture single event of Gr 3 keratoconjunctivitis

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

Does STRO-004's Favorable PK and Tolerability Translate into Anti-Tumor Activity?

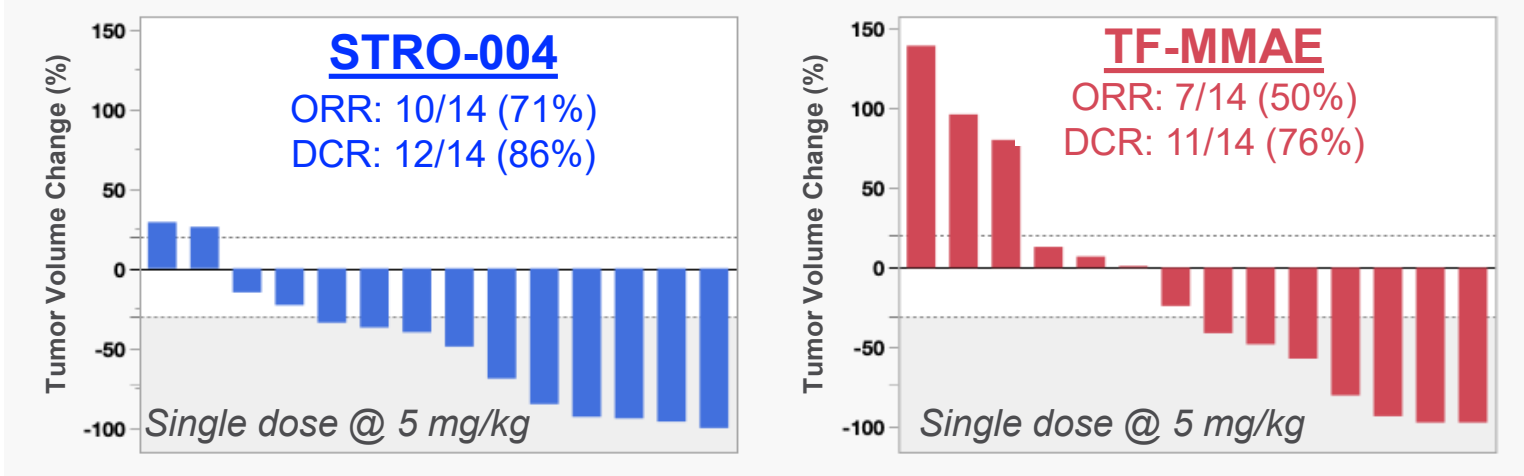
STRO-004 Demonstrates Robust Anti-Tumor Activity Across Multiple Solid Tumor PDX Models



ORR – Objective Response Rate; DCR – Disease Control Rate

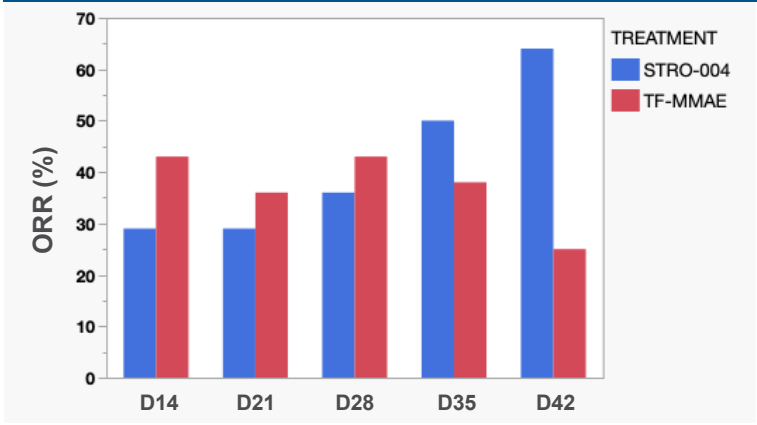
PDAC: STRO-004 Outperforms TF-MMAE Across Response and Survival Endpoints in Preclinical PDX

Best % Change in Tumor Volume

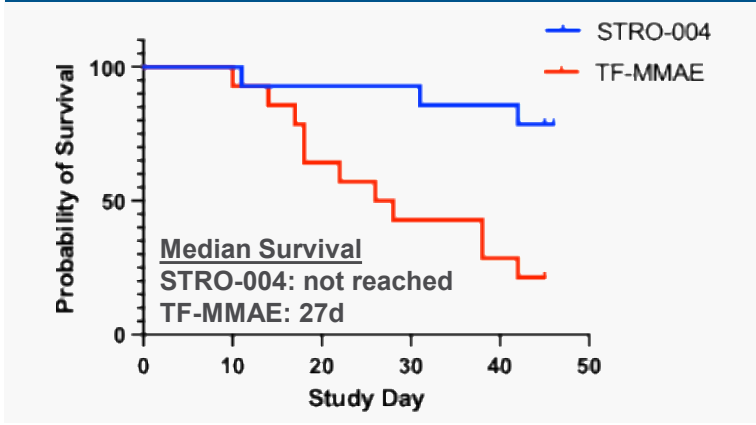


- Higher ORR vs. TF-MMAE (71% vs. 50%)
- Deeper and more consistent tumor regression across models
- Sustained survival benefit (median NR vs. 27 days)

Landmark ORR



Progression-Free Survival



Ph1/2: MRG004A (TF-MMAE) in PDAC
33% ORR @ 2 mg/kg Q3W

ASCO 2024

STRO-004 Preliminary Clinical Conclusions

Higher ADC exposure vs conventional β -Glu Exatecan ADCs preclinical and clinical

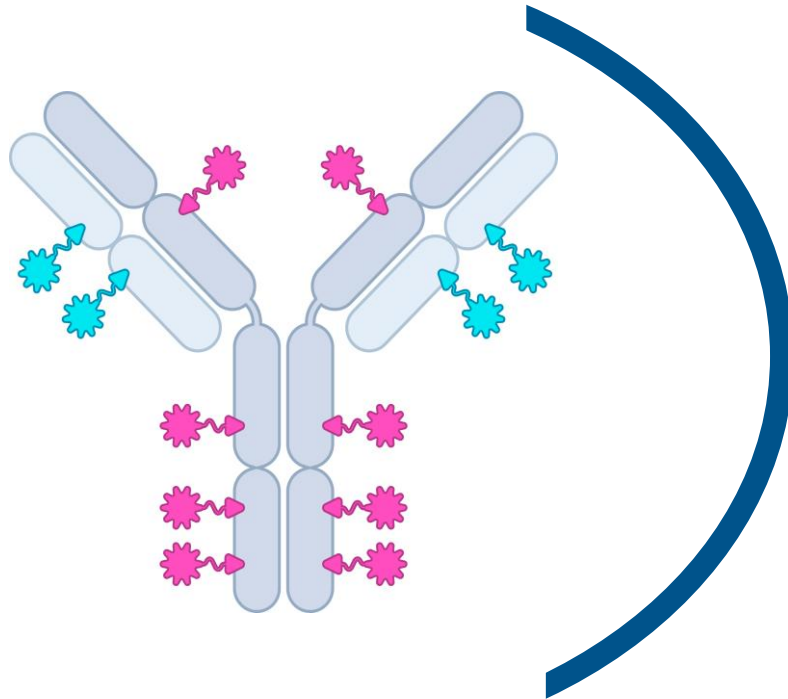
- Clinical activity observed across all dose levels, including responses in NSCLC, PDAC, and HNSCC

Lower circulating free exatecan $C_{\max}$ preclinical and clinical

- Limited hematologic toxicity consistent with low systemic payload exposure
- DLTs occurred only at 5 mg/kg and were predominantly target-related

Clinical PK and Safety Validate ADC Platform

- Low systemic toxicity may preserve headroom for combination therapies
- No treatment-emergent ADA observed to date
- Shared technology supports read-through across ADC pipeline



1

Sutro Site-Selective ADC Platform

2

STRO-004 Preclinical-to-Clinical Translation

3

Platform Expansion Across Targets and Payloads

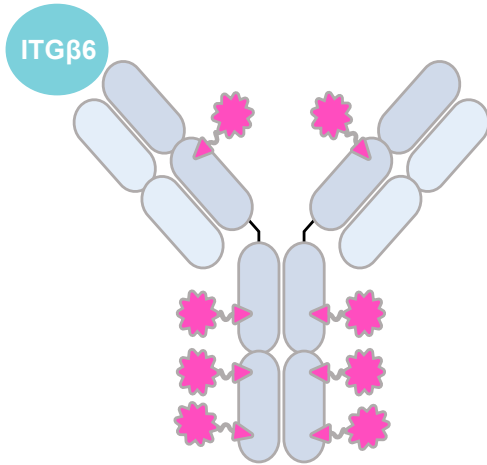
Pipeline of Next-Generation Single- and Dual-Payload ADCs

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)

STRO-006 Applies the Clinically Validated ADC Platform to ITGB6



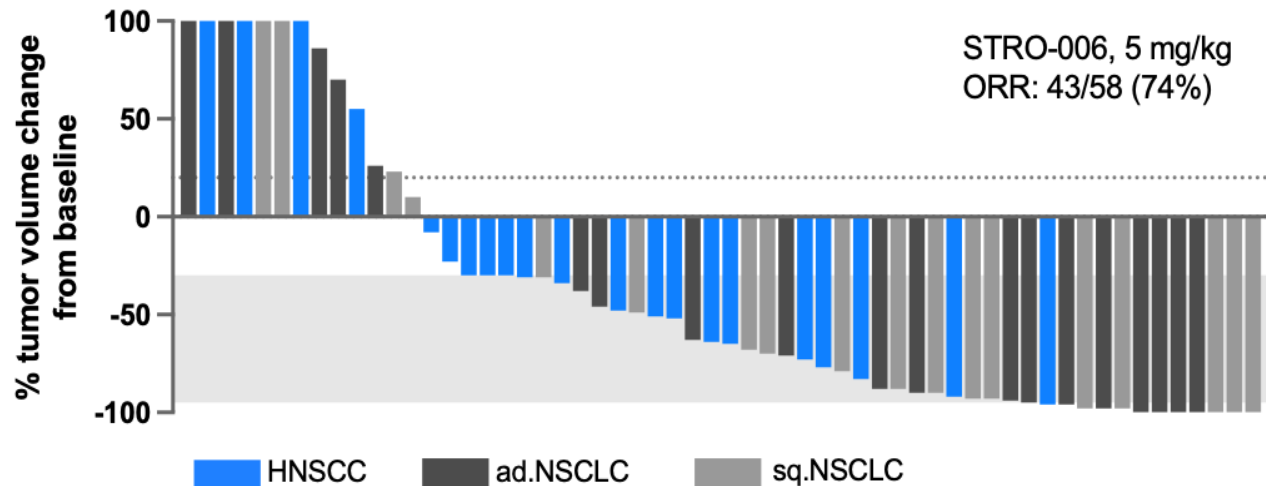
Entered clinic Q3 2026

DAR8 hydrophilic β -Glu exatecan

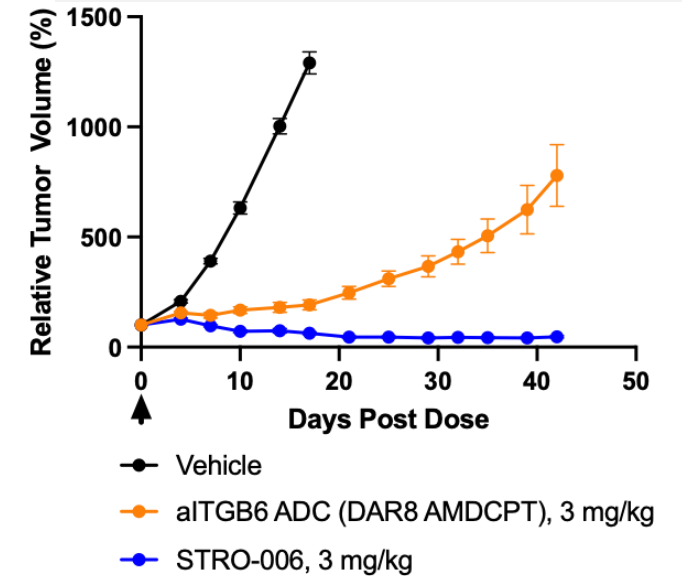
High affinity, specificity, and tumor selectivity

Alice Yam, PhD
Tues 10/13 Noon
Preclinical Track

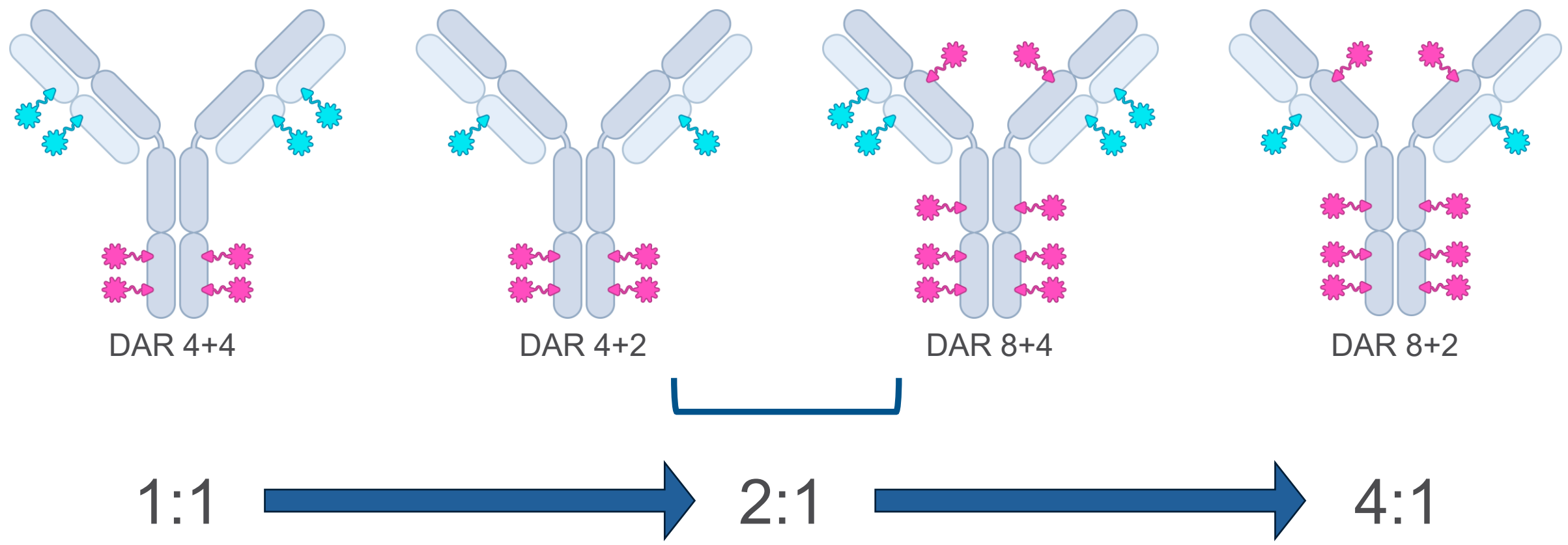
Broad Tumor Response in Mouse PDX Clinical Trial



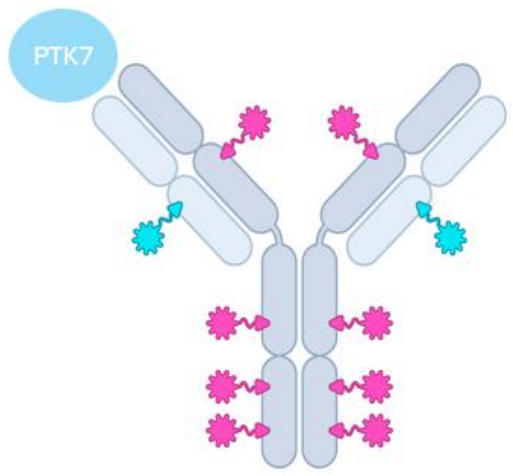
Superior Efficacy Compared to ITGB6 DAR8-AMDCPT ADC



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



STRO-227, DAR10 Dual-Payload Topo1i x MTI ADC Targeting PTK7



DAR10: 8 Exatecan + 2 MMAE

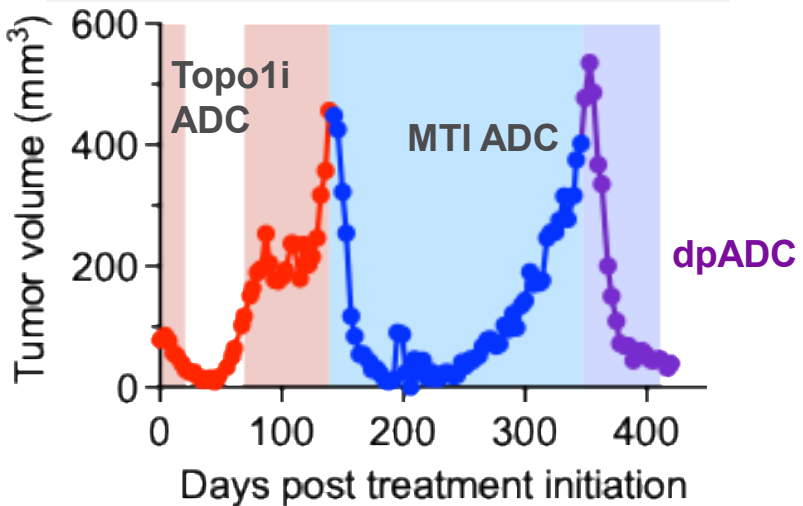
25 mg/kg HNSTD (Q3W X 2) in pilot NHP

Favorable NHP PK ($t_{1/2}$ = ~10.5 days)

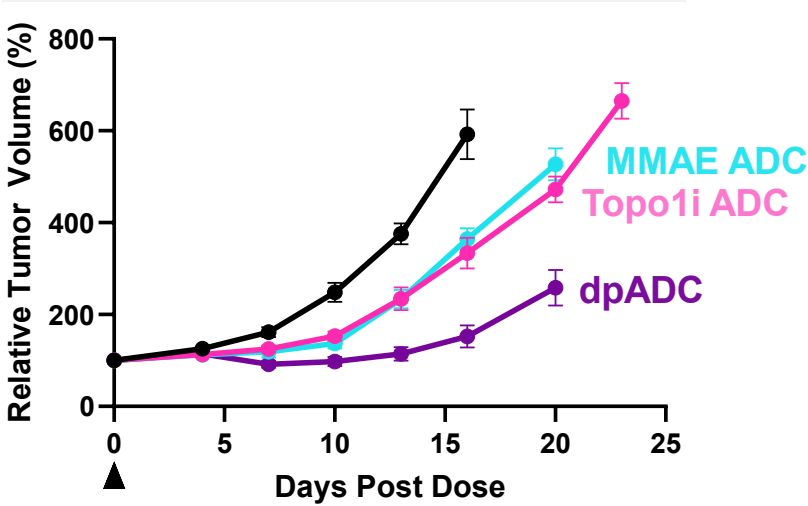
Anticipated IND in Q4 2026

Daniel Calarese, PhD
Wed 10/14 2:30
Preclinical Track

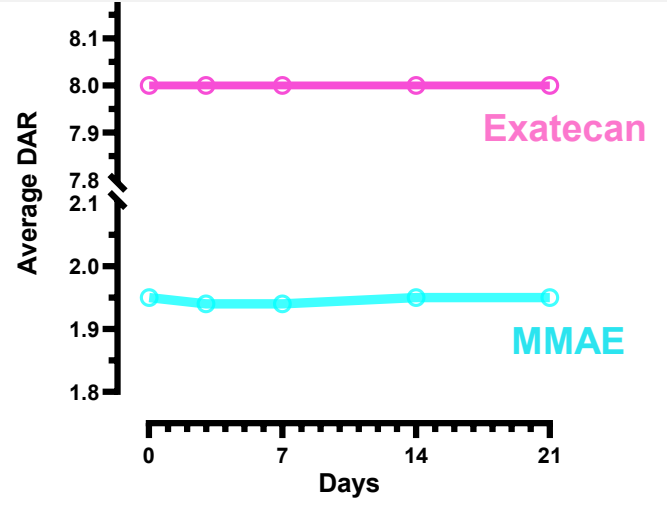
Overcome Resistance
Ovarian Cancer CDX



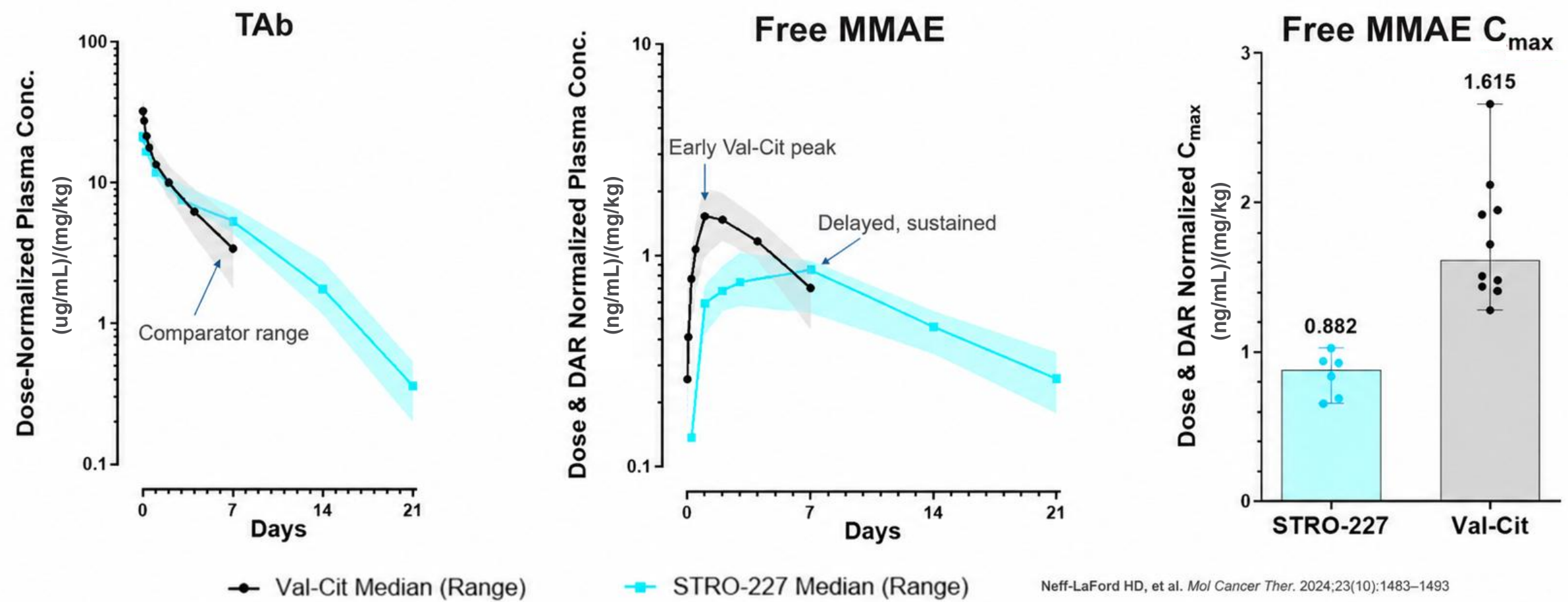
Superior to Single-Payload ADC
Breast Cancer CDX



DAR Stability in NHP

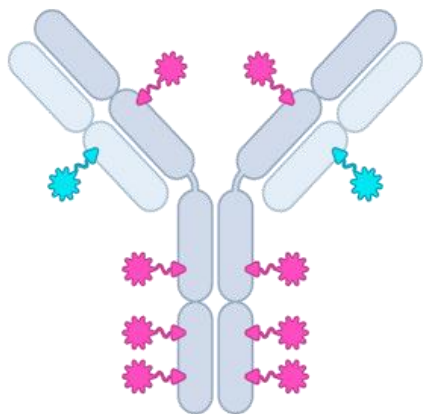


STRO-227 Preclinical NHP PK Shows Delayed MMAE Appearance and Lower Free MMAE C_{max} vs Published Val-Cit MMAE ADCs



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

DAR10 Topo1i x STING Dual-Payload Immunostimulatory ADC



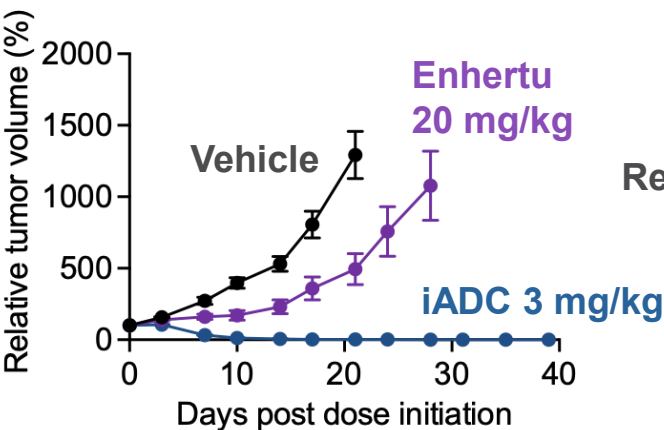
DAR10: 8 exatecan + 2 STING agonist

STING potentiates Topo1i activity and stimulates immune system

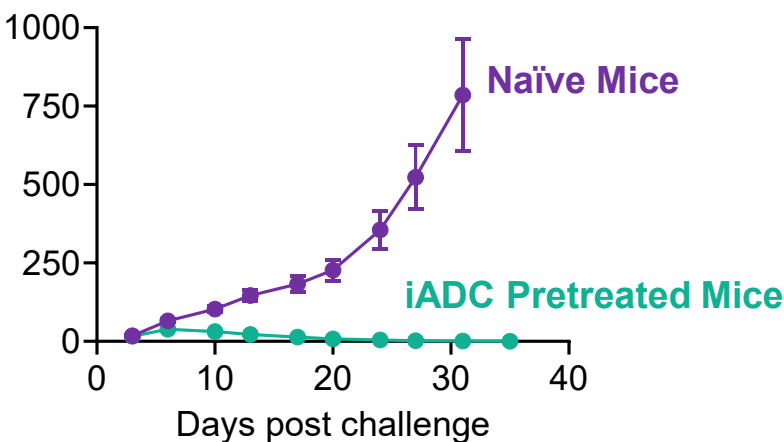
25 mg/kg HNSTD (Q3W X 2) in NHP. Comparable to single-payload Topo1i ADC

Favorable NHP PK ($t_{1/2}$ = ~9.5 days), stable DAR, and limited systemic payload exposure

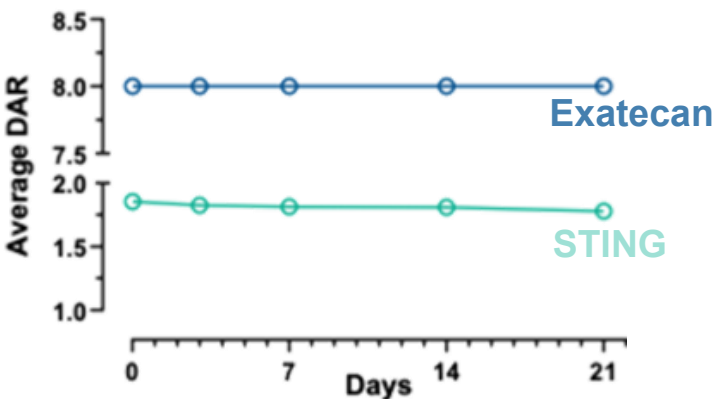
Dual-Payload iADC Induces Complete Responses and Immunological Memory
MC38 Syngeneic Mouse Model



Tumor
Rechallenge

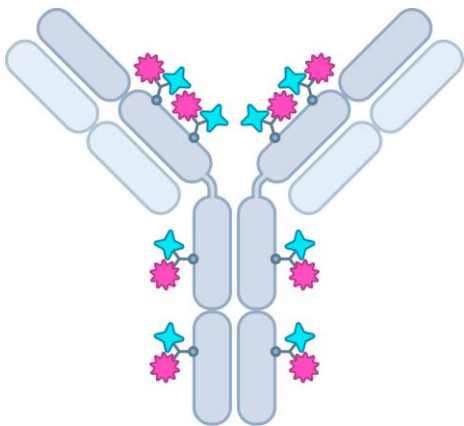


DAR Stability in NHP



DAR16 Topo1i x PARPi Dual-Payload ADC

Krishna Bajjuri, PhD
Mon 10/12 2:30
ADCs in Combination



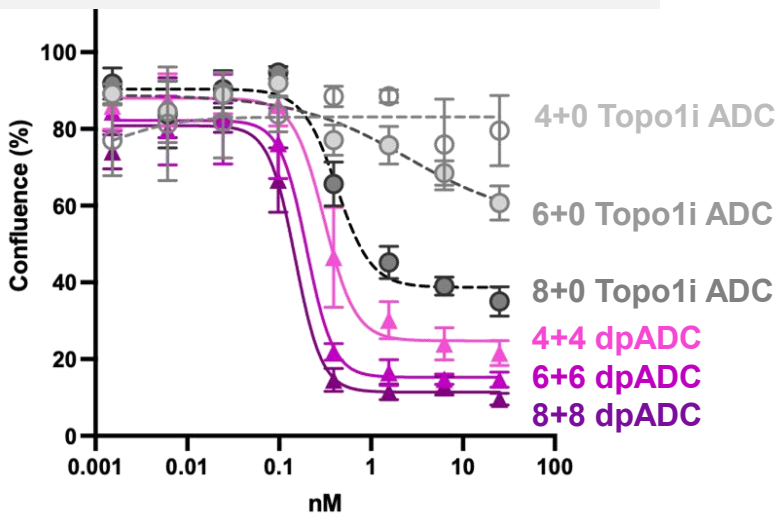
DAR16: 8 exatecan + 8 PARPi

Proprietary potent pan-PARP inhibitor that is not a drug efflux substrate

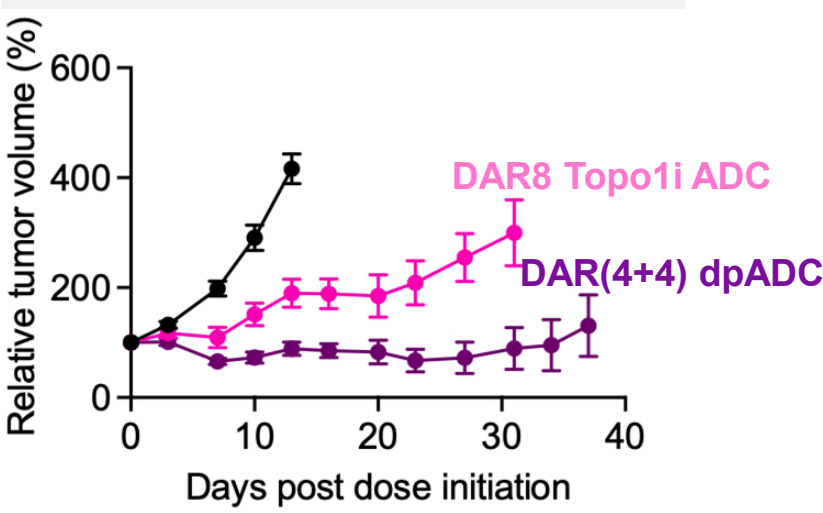
Combination effects of Topo1i and PARPi *in vitro* and *in vivo*

Favorable PK ($t_{1/2}$ = ~13 days) and DAR stability in mice

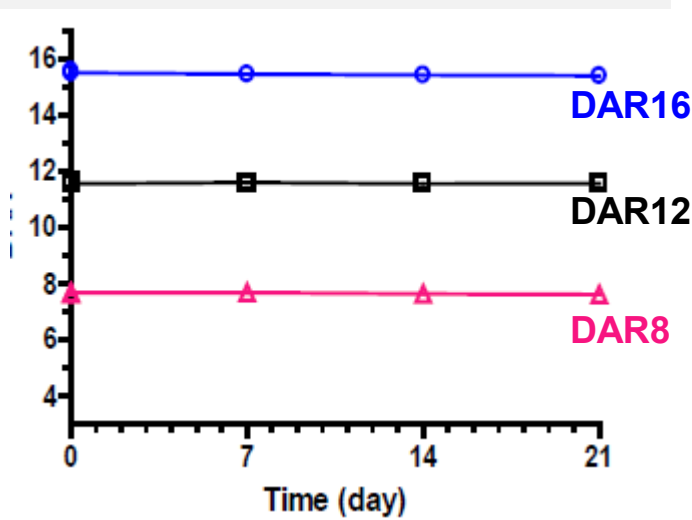
Superior to Single-Payload ADC
In Vitro Cell Viability



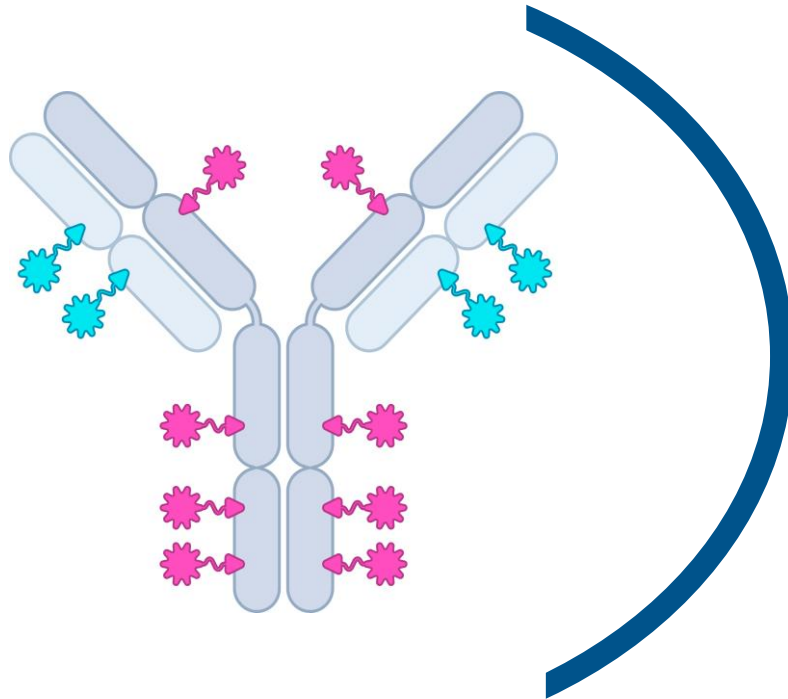
Superior to Single-Payload ADC
Breast Cancer CDX



DAR Stability in Mice



Differentiation by Design: Sutro Site-Selective ADC Platform



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: Shared technology across targets, payloads, and single- and dual-payload ADCs

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