

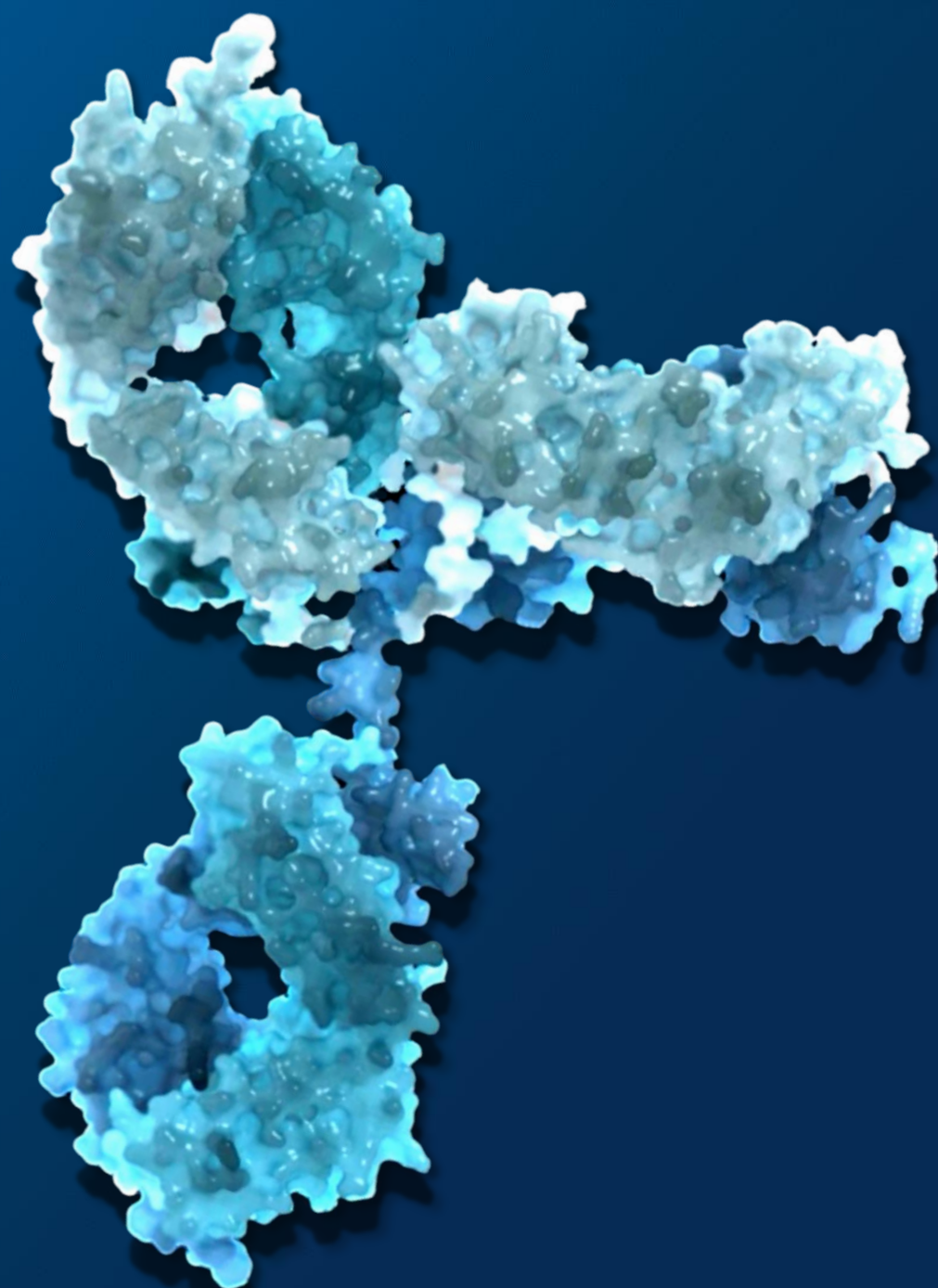
Outlining Predications for Future ADC Innovation

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ADC World, London

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Forward-Looking Statements

This presentation and the accompanying oral presentation contain “forward-looking” statements that are based on our management’s beliefs and assumptions and on information currently available to management. Forward-looking statements include all statements other than statements of historical fact contained in this presentation, including information concerning our future financial performance; business plans and objectives; anticipated preclinical and clinical development activities, including enrollment and site activation; timing of announcements of clinical results, trial initiation, and regulatory filings; outcome of regulatory decisions; our expectations about our cash runway; potential benefits of Iuvelta and our other product candidates and platform; potential expansion into other indications and combinations, including the timing and development activities related to such expansion; potential growth opportunities, financing plans, potential future milestone and royalty payments, competitive position, industry environment and potential market opportunities for our product candidates.

Forward-looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors, including risks and uncertainties related to our cash forecasts, our and our collaborators’ ability to advance our product candidates, the receipt, feedback and timing of potential regulatory submissions, designations, approvals and commercialization of product candidates and the design, timing and results of preclinical and clinical trials and our ability to fund development activities and achieve development goals. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. These factors, together with those that may be described in greater detail under the heading “Risk Factors” contained in our most recent Annual Report on Form 10-K, Quarterly Report on Form 10-Q and other reports the company files from time to time with the Securities and Exchange Commission, may cause our actual results, performance or achievements to differ materially and adversely from those anticipated or implied by our forward-looking statements.

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Prior ADC Development Mostly Focused on Optimizing Potency (2000-2020)

ADC Technology Focus Areas

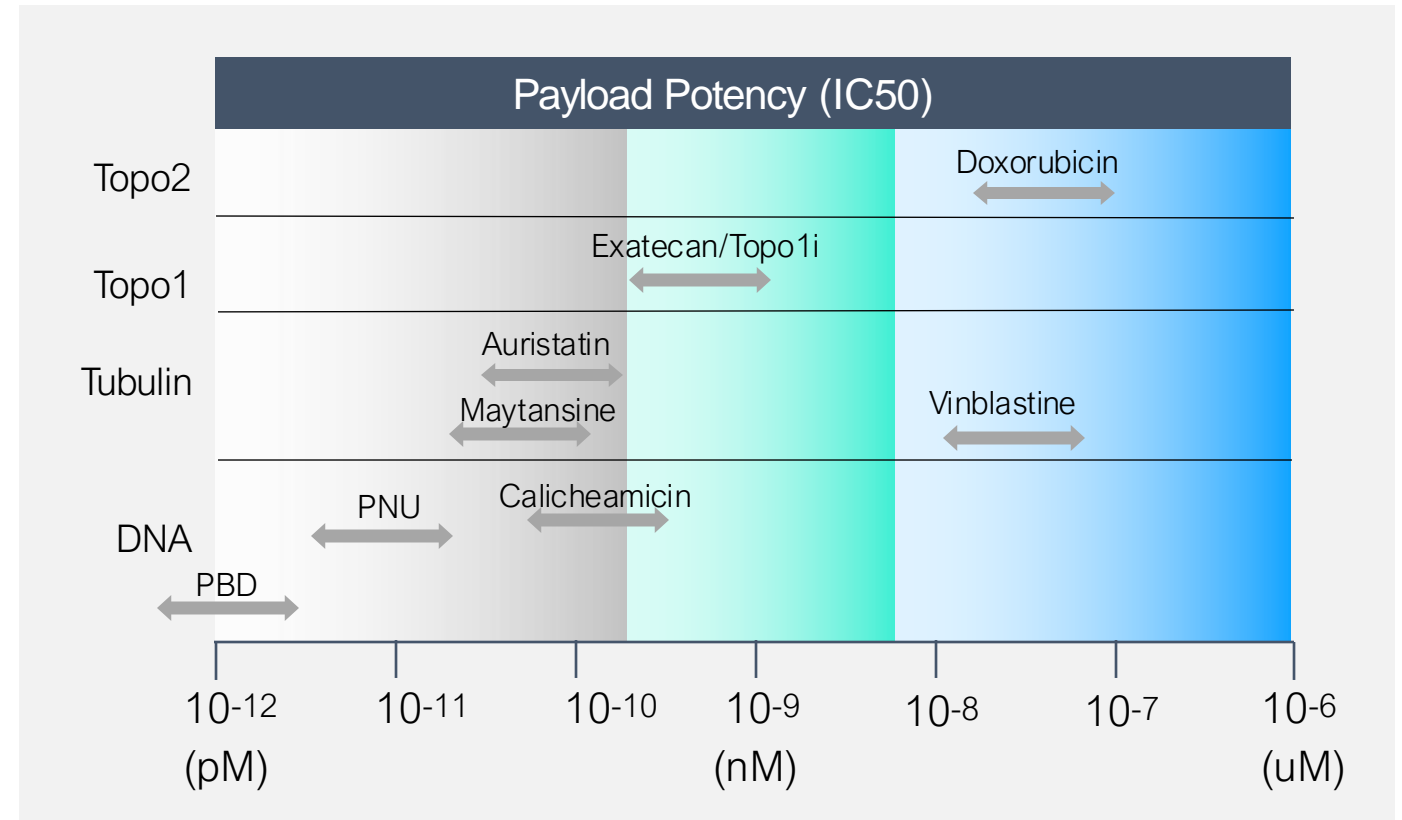
➤ Higher potency payloads

- PBDs, PNUs, etc.

➤ Novel conjugation chemistry

➤ Improved ADC activity

- *In vitro* potency
- *In vivo* xenograft

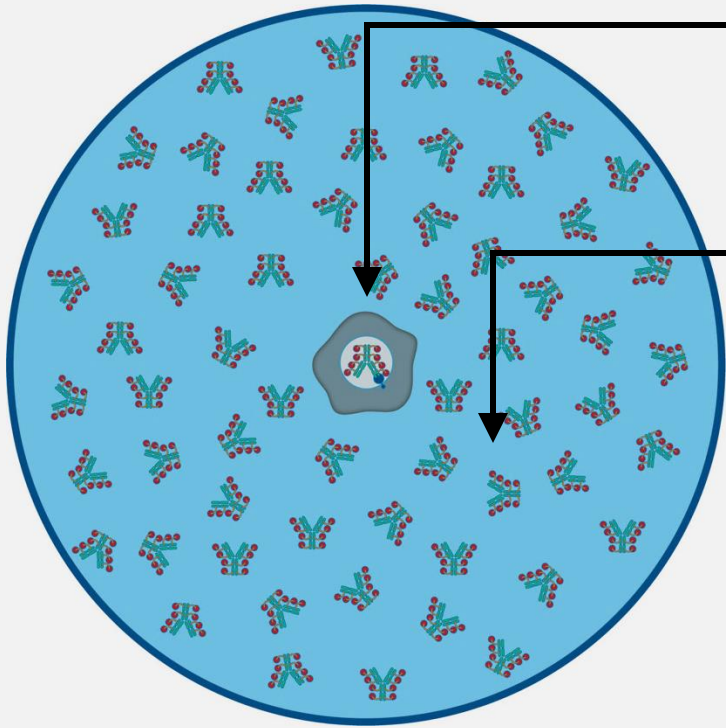


However...

Clinical ADC breakthrough in 2019 with lower potency Camptothecin/Exatecan/Topo1i ADCs

PBD – pyrrolbenzodiazepines; PNU – a highly potent secondary metabolite of nemorubicin belonging to the anthracycline class of natural products; Topo1i – topoisomerase 1 inhibition

Lower Potency Payloads Enable Higher Dosing and Exposure, Which Drives ADC Efficacy



Only 1% of ADCs reach tumors, targeting the tumor effectively when it gets there

99% reside outside tumors, limiting ADC exposure as premature payload release causes platform toxicity

Topo1i ADCs outside the tumor are less toxic to healthy cells:

Reduced
"Platform"
Toxicity



Higher
Dose

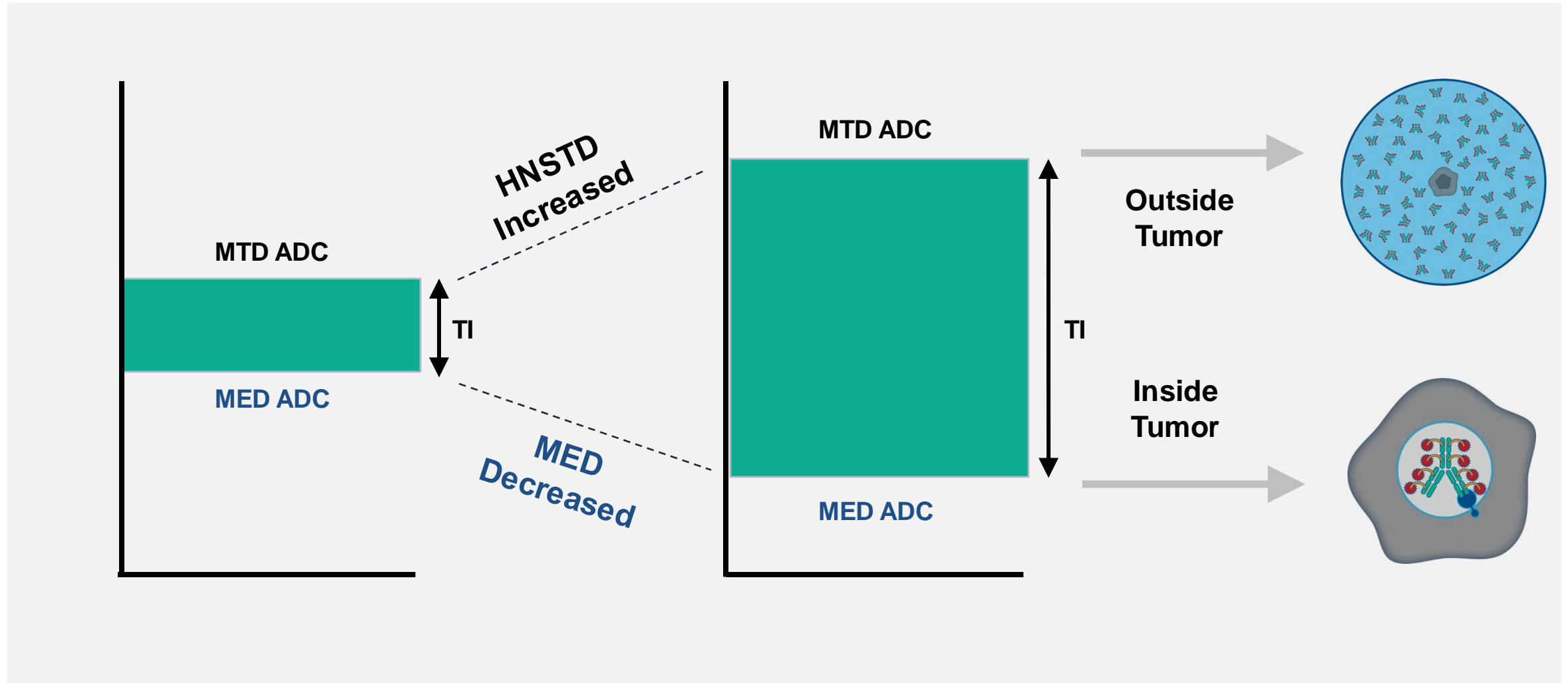


Higher
Exposure



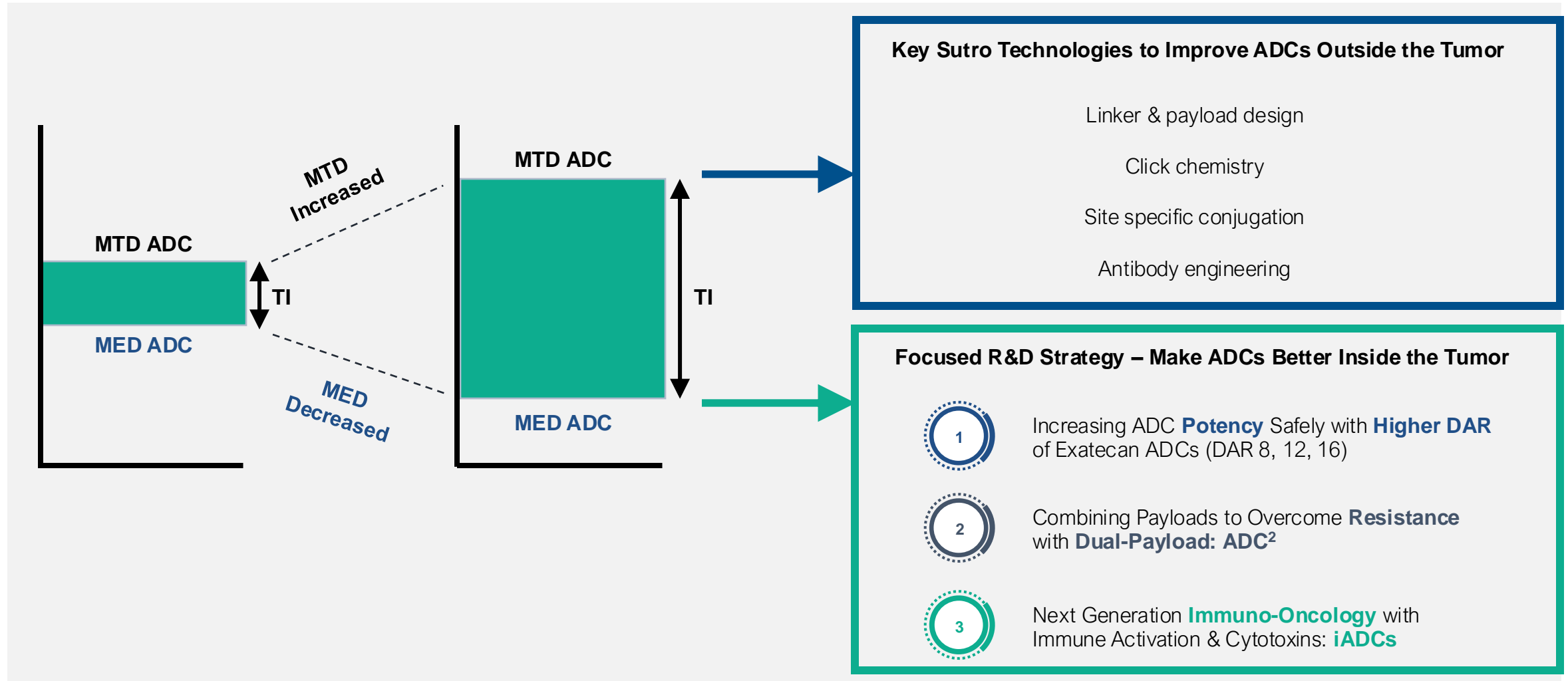
Drives
Efficacy

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

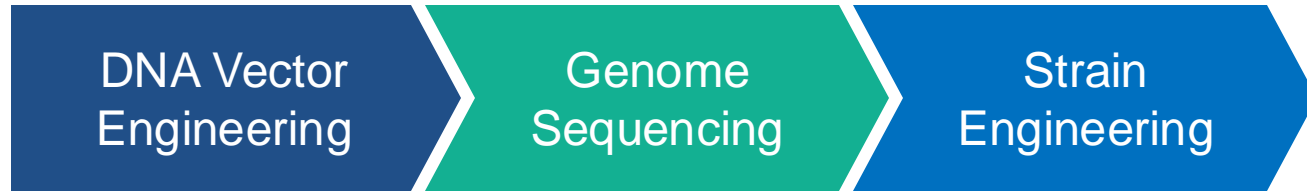
Wider Therapeutic Index Achieved with Sutro's Cell-free ADC Platform



Adapted from Gerber et al, mAbs, 2023

MTD – Maximum Tolerated Dose; MED – Minimum Effective Dose

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



Prokaryotic Cells



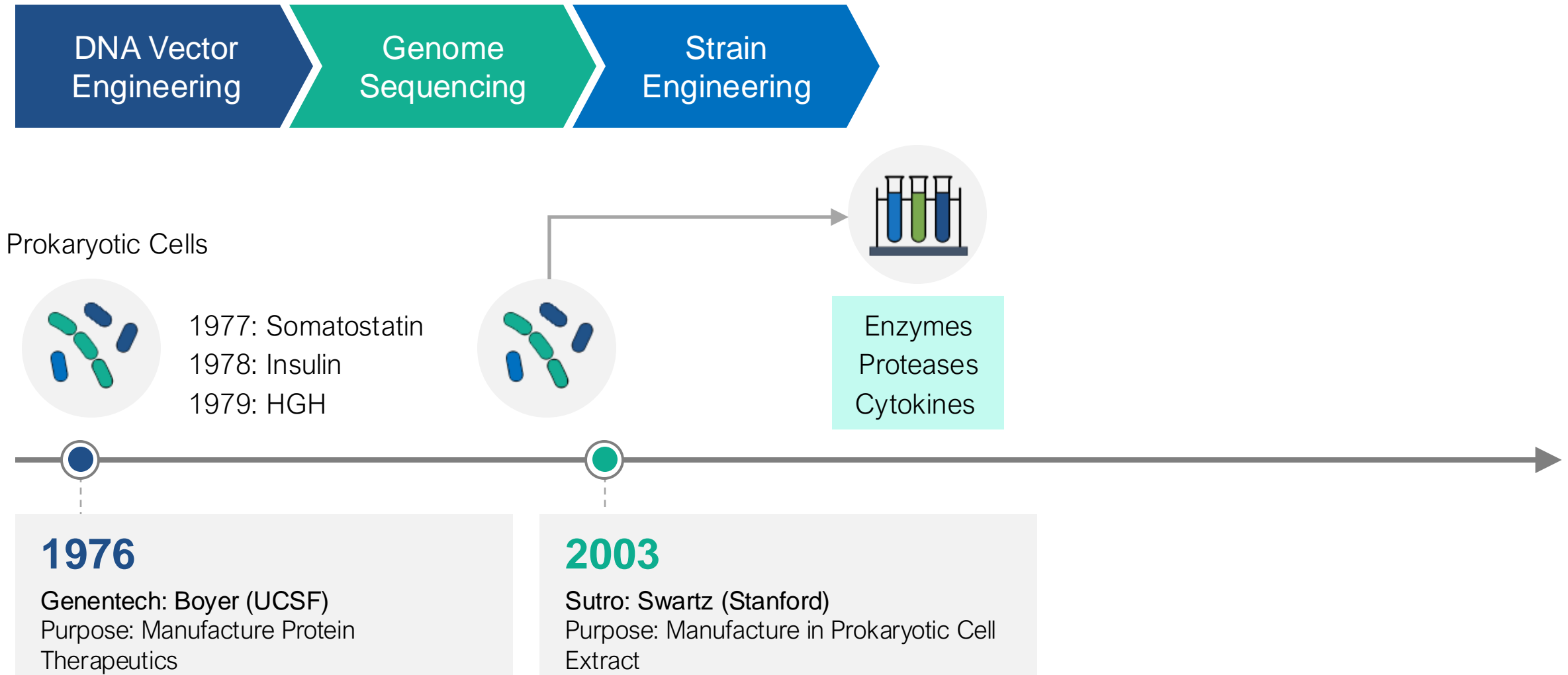
1977: Somatostatin
1978: Insulin
1979: HGH

1976

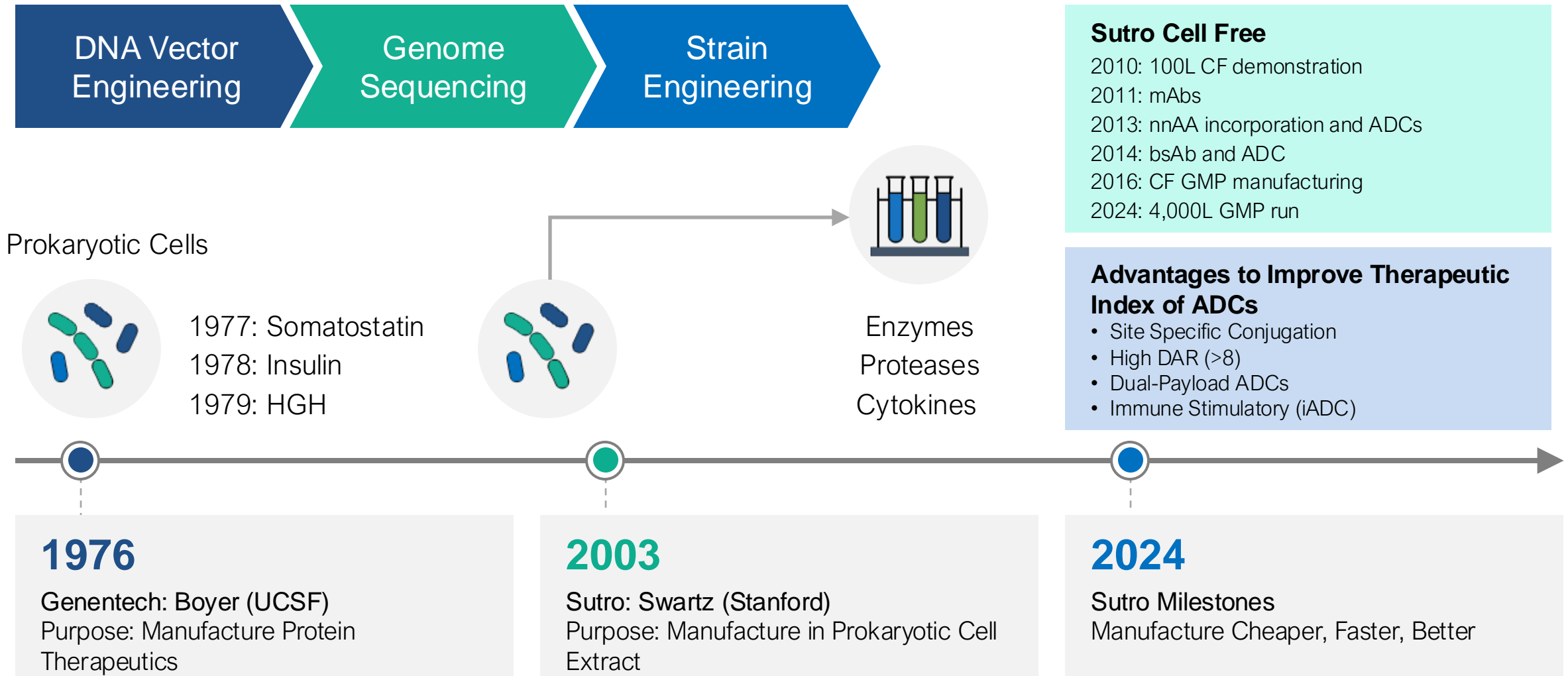
Genentech: Boyer (UCSF)
Purpose: Manufacture Protein
Therapeutics

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


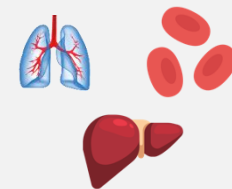
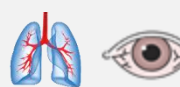
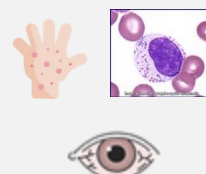
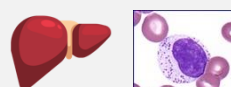
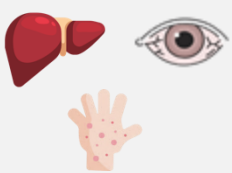


Sutro's ADC Platform is Fundamentally Different: Manufacturing of Proteins in Cell-Free Extracts



nnAA – non-natural amino acids; CF – cell-free; bsAb – bispecific antibody; GMP – good manufacturing practice

Sutro Technologies Enabled by CF Manufacturing Improve ADCs Outside the Tumor

	ADC	mAb	mAb	Linker	Conjugation Chemistry	Payload
MOA inducing Tox	Untargeted Pinocytosis	Impaired FcRn recycling	FcγR uptake	Cleavage outside tumor	De-conjugation	Catabolism "Detox"
Toxicity Types						
Sutro Technology	Linker design & mAb eng.	Site specific conjugation	Lack of FcγR engagement	Linker design & chemistry, site selection	Click chemistry	Payload & chemical engineering

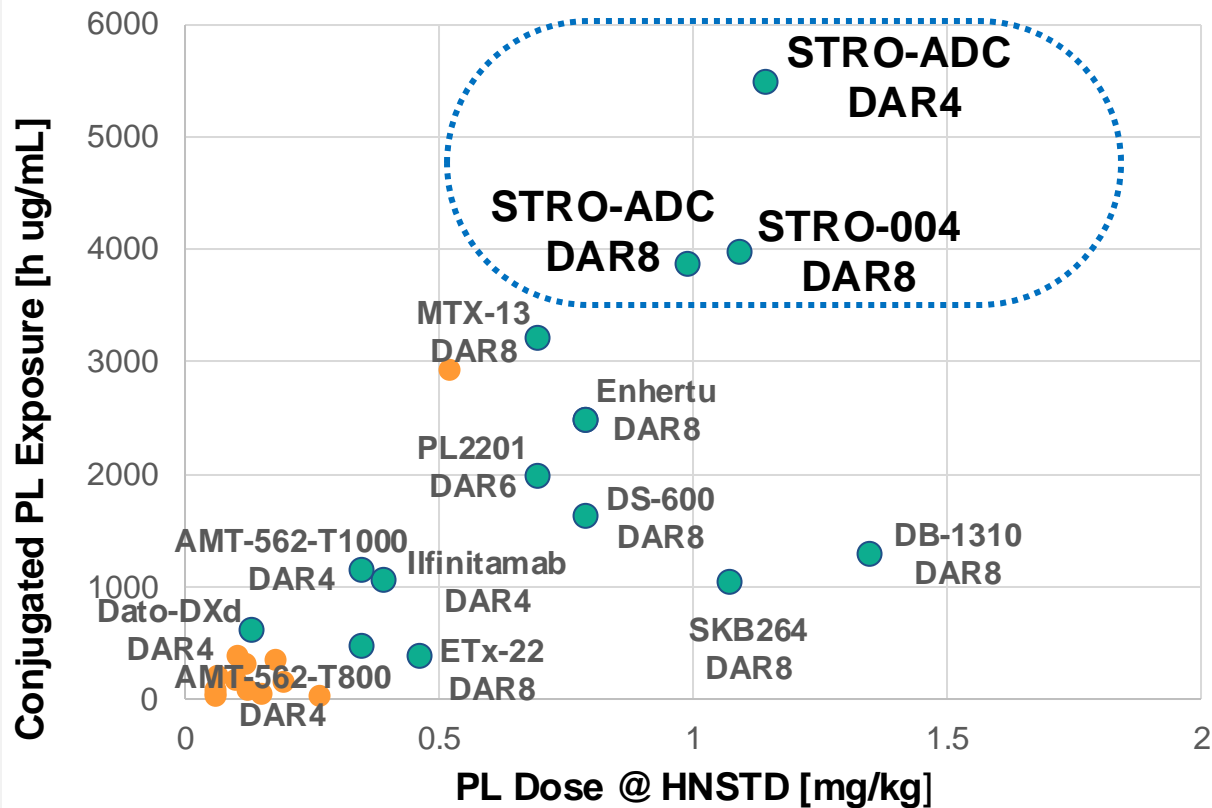
Success Criteria: Improved PK (Higher ADC Exposure, Longer Half Life, Higher Dose)

PK – pharmacokinetics

Sutro Cell-Free Approach Enables Industry-Leading ADC Exposure



Comparison of Exposure Levels in NHPs at Highest Non-Severely Toxic Dose (HNSTD) Levels in DAR Equivalents

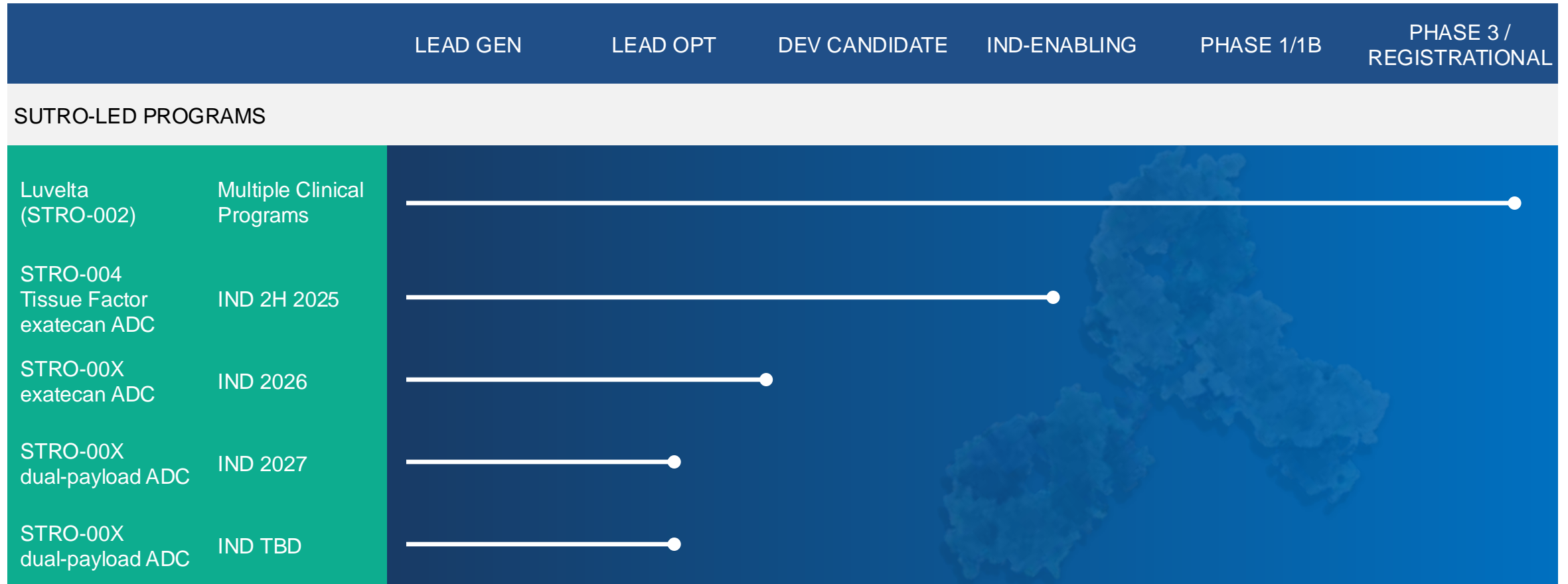


Why does it matter?

- For ADCs, exposure drives efficacy
- Based on PK data, our exatecan ADCs are positioned to be differentiated on safety and efficacy versus on-market ADCs

● Exatecan/Topo1i ADCs ● Tubulin inhibitor ADCs

Our Current ADC Portfolio with Three Expected INDs by 2027

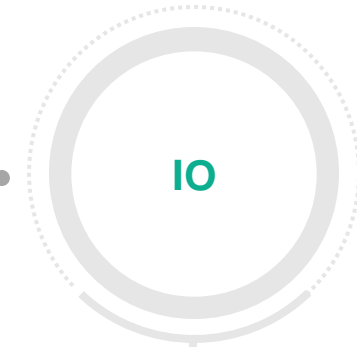


STRO-003 – Ipsen has an exclusive global license to STRO-003 (ROR1 ADC)

iADC – Sutro has a strategic collaboration with Astellas to develop two iADCs

IND – investigational new drug application

Our Focused R&D Strategy: Make ADCs Better Inside the Tumor with Higher DAR



**Higher DAR of Exatecan ADCs
(DAR 8, 12, 16)**

Increasing ADC
Potency Safely

Dual-Payload: ADC²

Combining Payloads
to Overcome
Resistance

**Immune Activation &
Cytotoxins: iADCs**

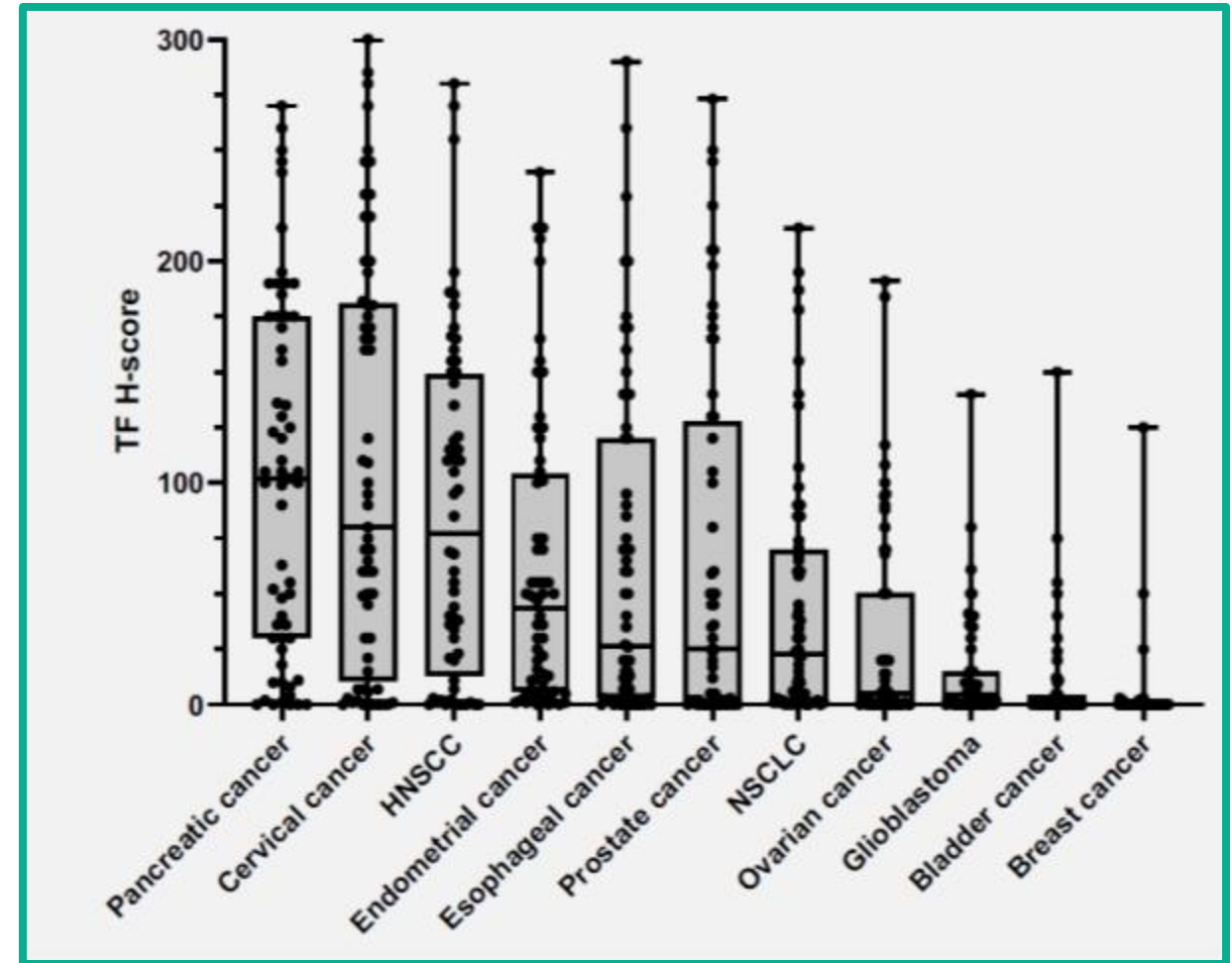
Next Generation IO

Unique advantage of non-natural amino acid incorporation by Cell-free XpressCF®
IO – immuno-oncology

Tissue Factor is Broadly Expressed Across Multiple Solid Tumor Indications, Presenting Opportunity for Pan-Tumor Targeting

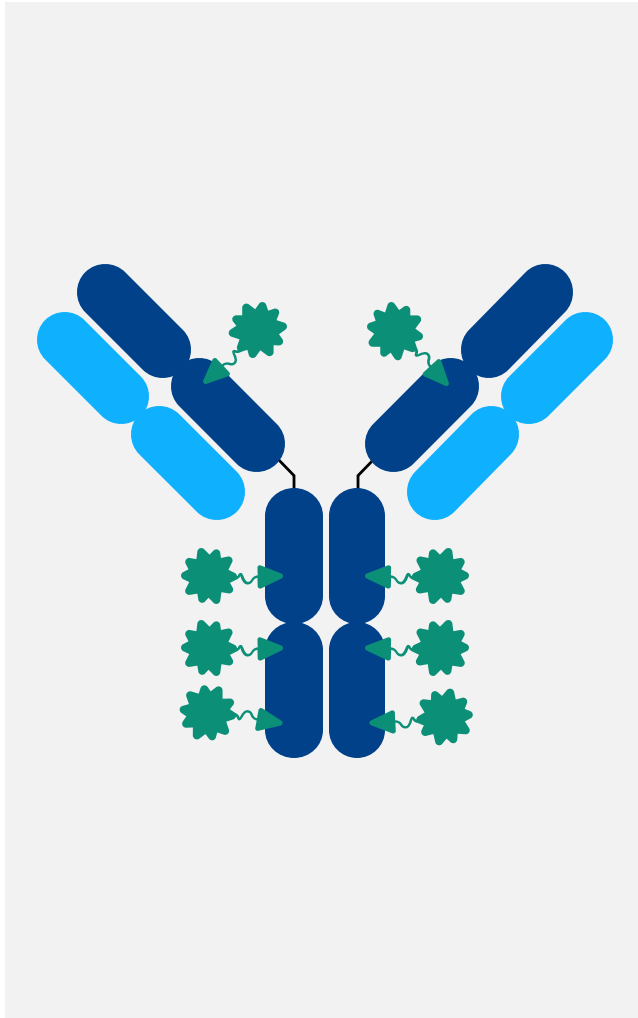
Broad Opportunity for TF in Many Solid Tumors of Significant Unmet Need

- TF expression has been associated with poor disease prognosis and increased metastatic properties
- Clinical validation of TF in cervical cancer, along with early signs of activity in HNSCC, pancreatic cancer, and multiple other solid tumors with significant unmet needs

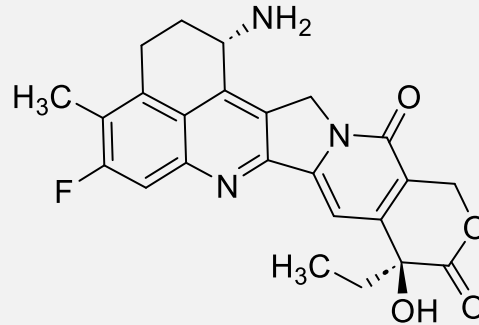


HNSCC – head and neck squamous cell carcinoma
NSCLC – non-small cell lung cancer

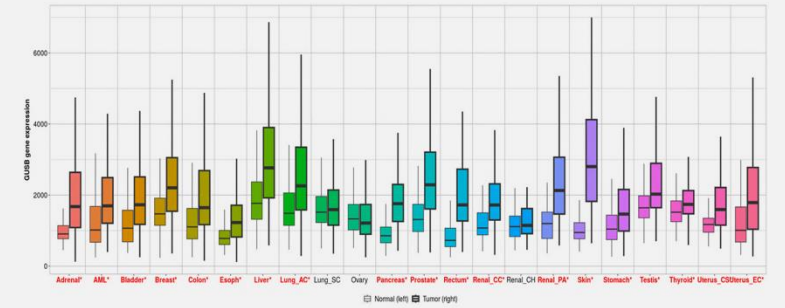
STRO-004: DAR8 Exatecan Payload ADC Designed for Enhanced Stability, Potency and Tumor Selectivity



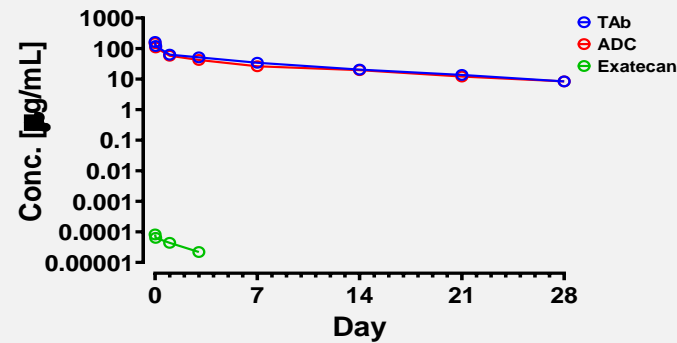
Potent exatecan topo1 inhibitor



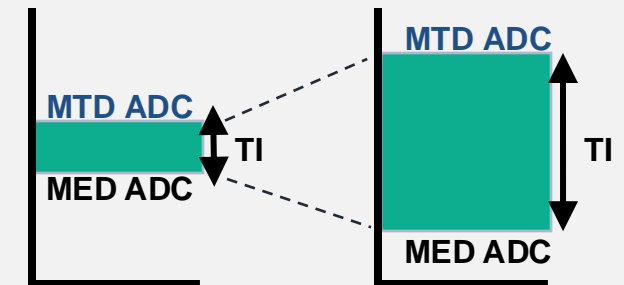
β -glucuronidase upregulated in tumor



Hydrophilic design for optimal PK



Enhanced therapeutic window



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

Objective:

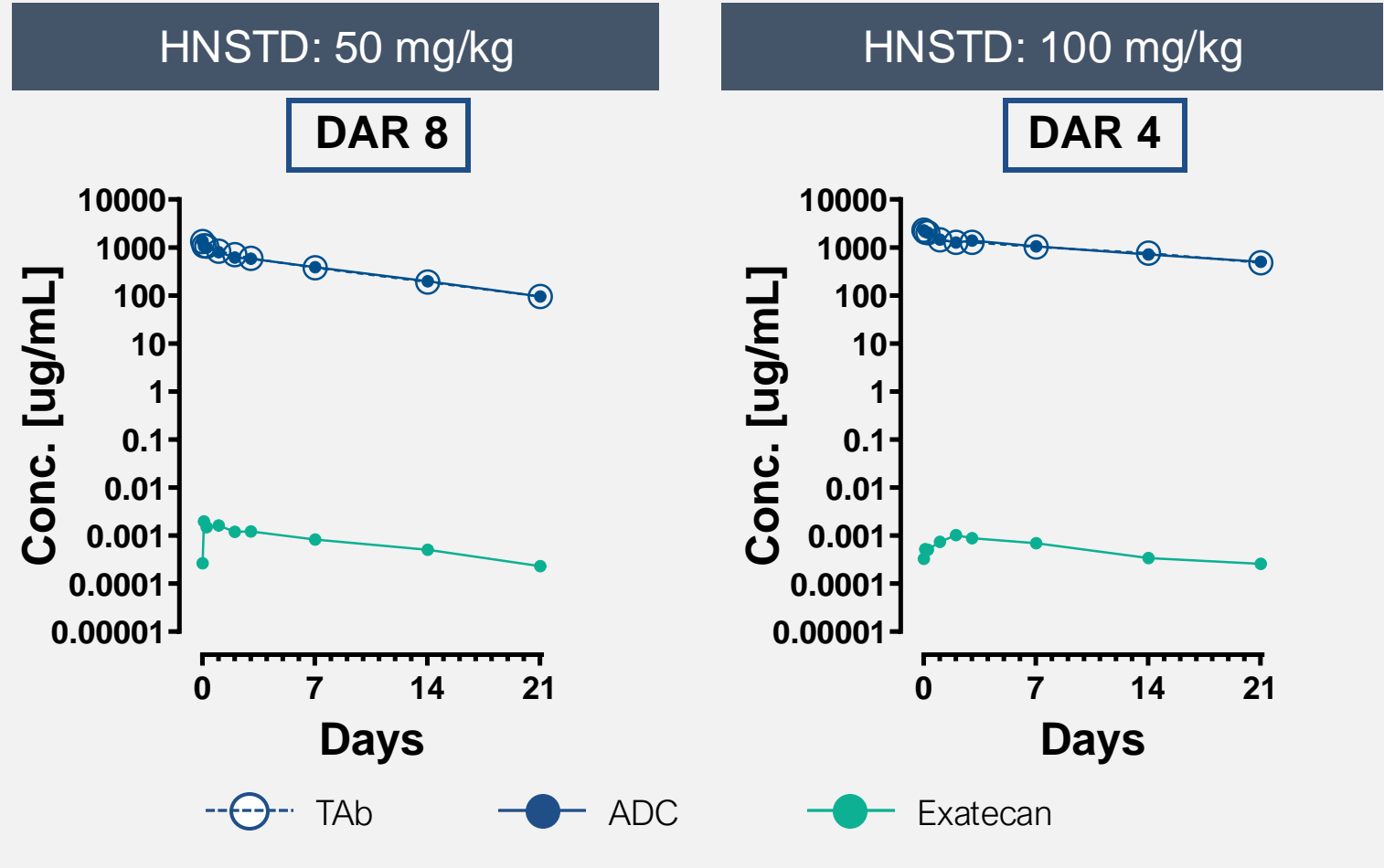
Compare nonclinical safety of DAR4 and DAR8 TF exatecan-ADC

Study:

Dosed twice, three weeks apart, payload-matched doses

Findings:

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



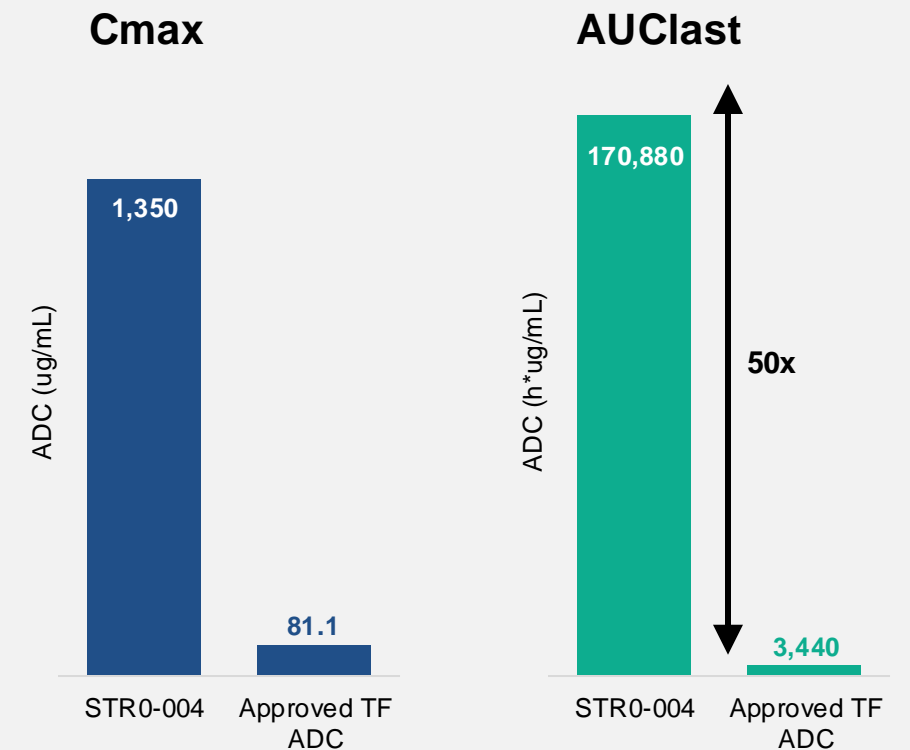
TAb – Total Antibody

STRO-004: Next Generation Tissue Factor-Targeting Exatecan/Topo1 ADC with Enhanced Therapeutic Potential

Optimally Designed for Improved Clinical Benefits, Enhanced Stability, Potency and Tumor Selectivity

- **Exatecan payload:** Clinically validated with potent activity, bystander and reduced susceptibility to resistance
 - Improved potency to reach low copy number patients
- **β -glucuronidase linker:** Engineered for enhanced tumor selectivity and hydrophilicity
- **Optimized drug performance:** High DAR8 and improved conjugation positioning
- **Widened therapeutic/safety index:** Driving higher drug exposure and efficacy than 1st gen TF ADCs; designed to minimize interference with coagulation cascade
 - Optimized to reduce risk of neutropenia, bleeding, and ocular toxicities

Increased Tolerability Leads to Enhanced Drug Exposure



IND filing and first-in-human studies planned for 2H 2025

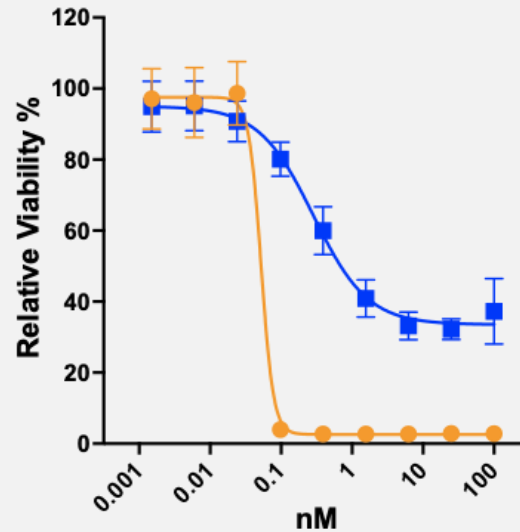
STRO-004 Demonstrated Reduced Platform and On-target Toxicity Due to Site Specific Conjugation and Beta Glu Linker-Payload Technology

STRO-004 Tolerability Profile vs. Approved aTF ADC



Eye Inflammation

Human Corneal Epithelial Cells

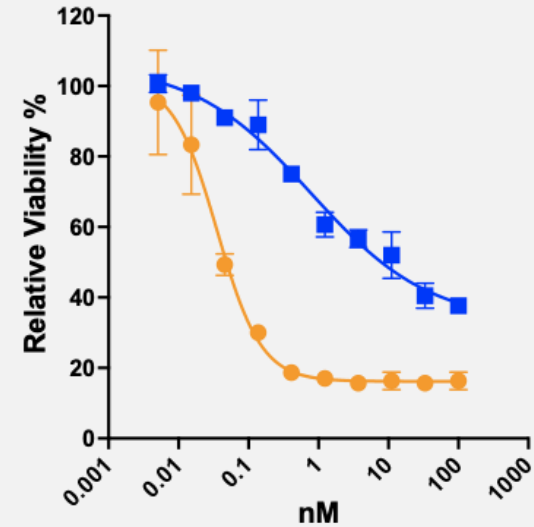


■ STRO-004 (DAR8-exatecan)



Skin Toxicities

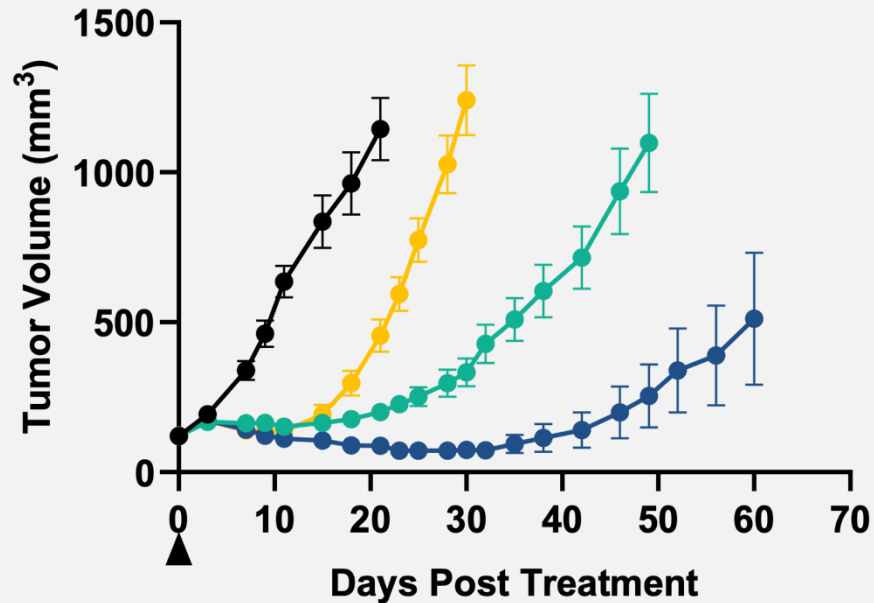
Human Keratinocyte



■ Approved aTF ADC (DAR4-MMAE)

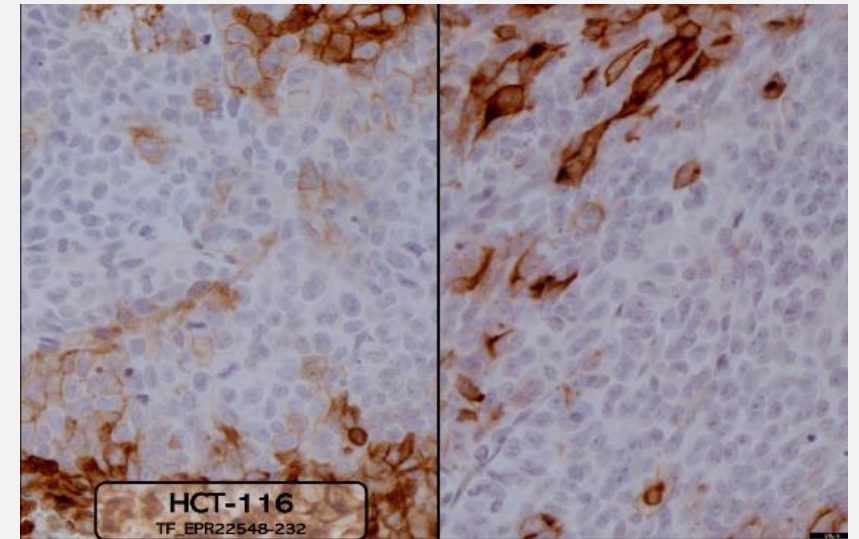
Selected DAR8 ADC Delivers More Payload to Low-TF Expressing Tumors Corresponding to Greater Anti-Tumor Response

STRO-004 (DAR8 TF ADC)
Improves Anti-Tumor Activity at a Lower Dose



- Vehicle control
- aTF DAR8-exatecan (STRO-004), 7.5 mg/kg
- aTF DAR4-MMAE, 15 mg/kg
- aTF DAR4-exatecan, 15 mg/kg (approved)

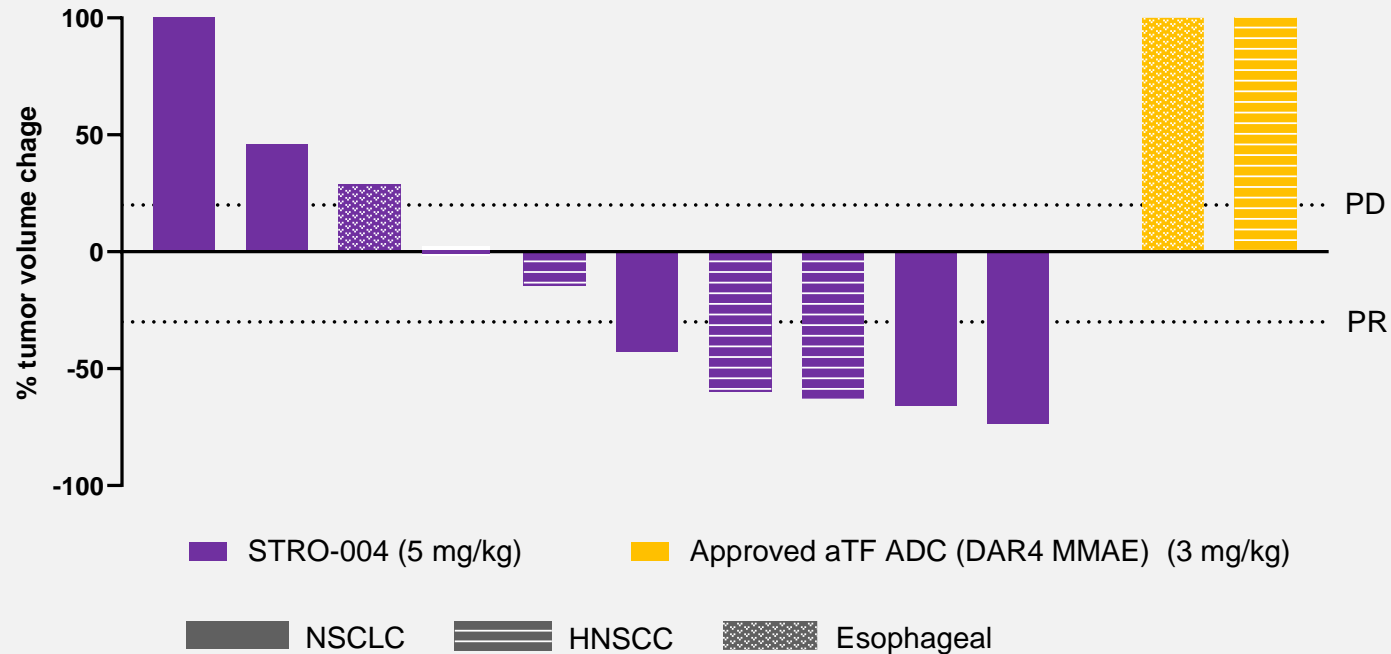
HCT-116
(colorectal model, TF – low)



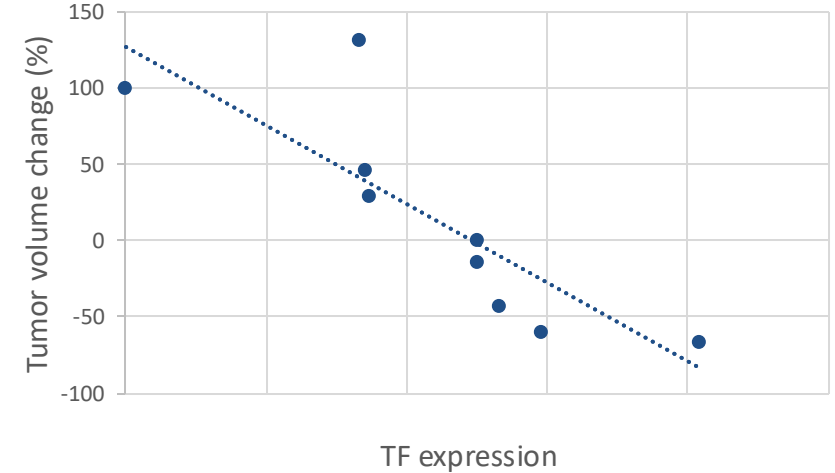
STRO-004 Shows Promising Anti-tumor Activity In TF Positive PDX Models of HNSCC, NSCLC, and Esophageal Cancer

> 50% of Tumors Respond to STRO-004 at Low Dose

% Best response from baseline



STRO-004 Best response vs TF expression



Our Focused R&D Strategy: Make ADCs Better Inside the Tumor with Dual-Payloads



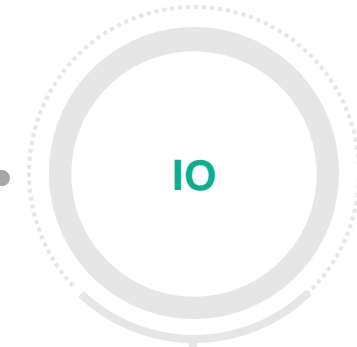
**Higher DAR of Exatecan ADCs
(DAR 8, 12, 16)**

Increasing ADC
Potency Safely



Dual-Payload: ADC²

Combining Payloads
to Overcome
Resistance

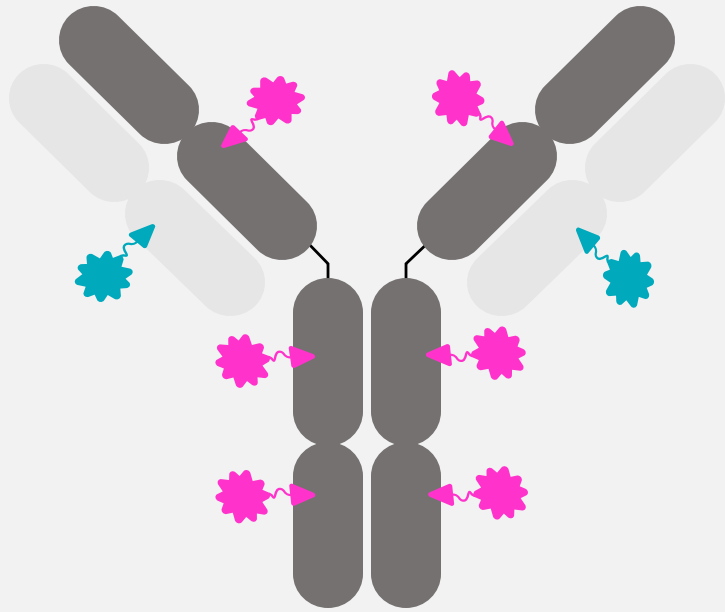


**Immune Activation &
Cytotoxins: iADCs**

Next Generation IO

Unique advantage of non-natural amino acid incorporation by Cell-free XpressCF®
IO – immuno-oncology

Potential Advantages of Dual-Payload ADC Approach



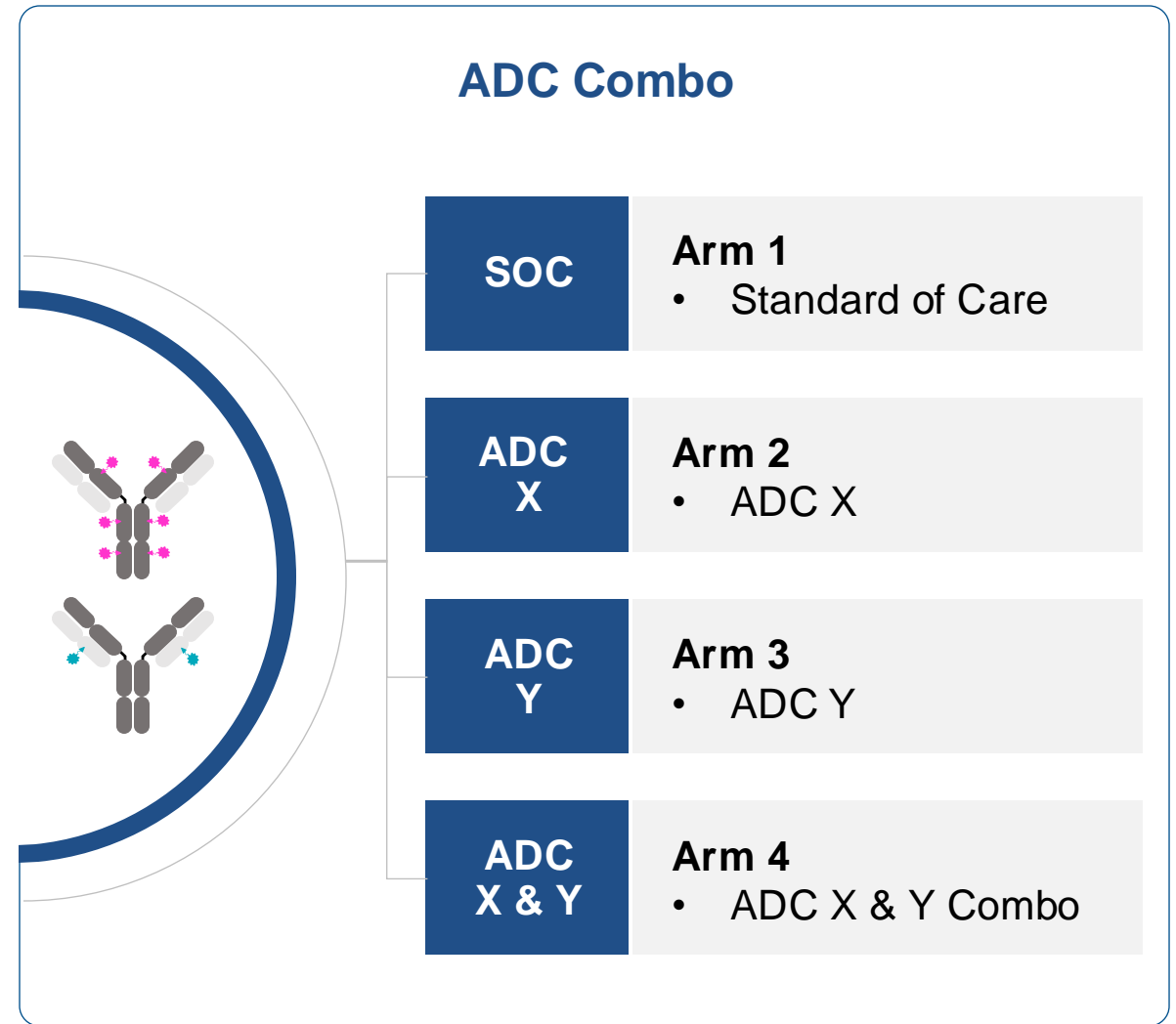
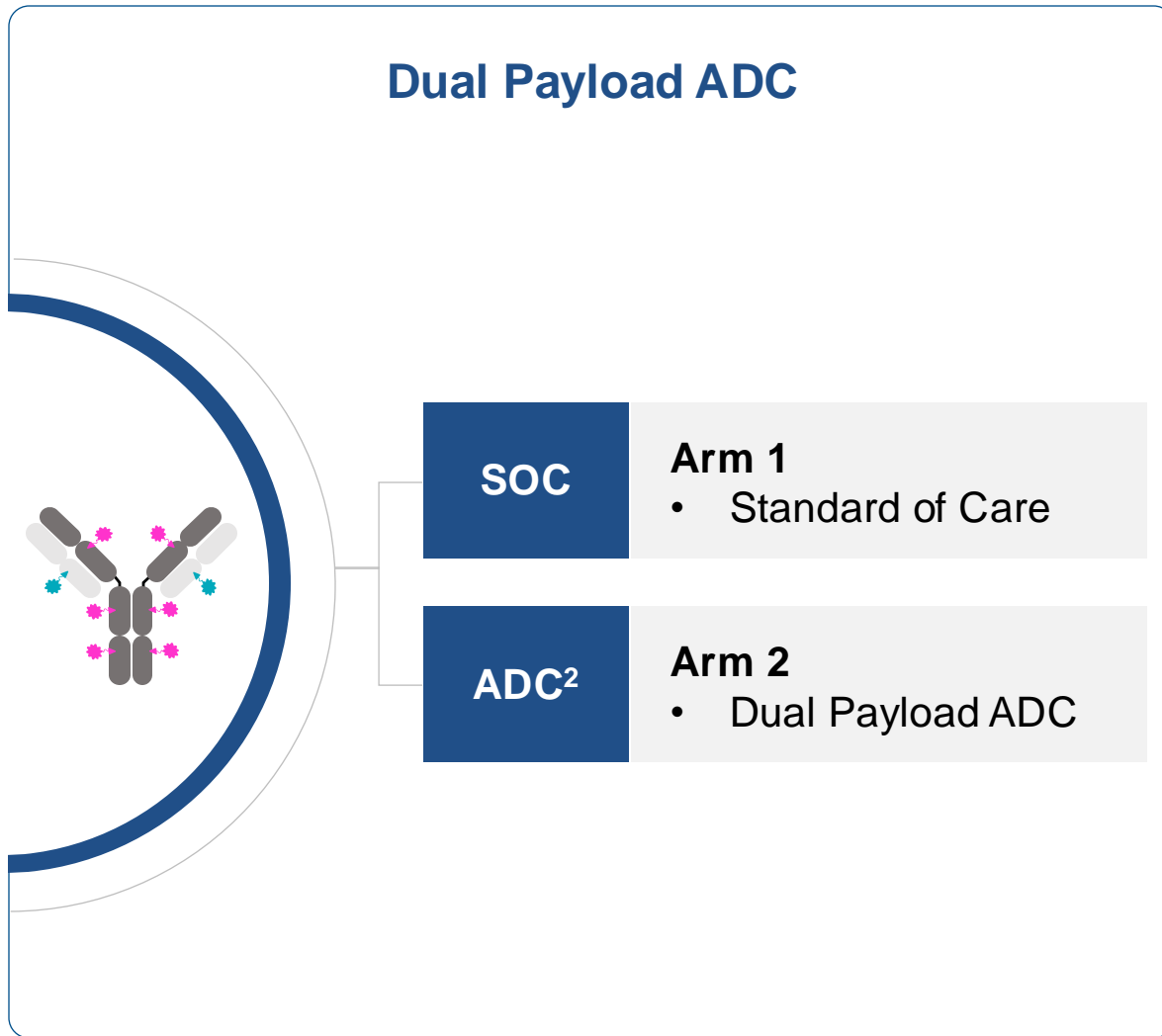
- Reduced Toxicity
- Reduced Clinical Complexity
- Simultaneous Payload Delivery
- Overcome Resistance Mechanisms

Dual Payload ADCs: Innovative Method for Delivering Targeted Combination Therapy

	ADC + Chemo	ADC + ADC	Dual Payload ADC	Potential benefits of a dual payload ADCs for targeted combination therapy
Safety (Compared to small molecule combinations)	<p>Greater SAEs reported for ADC + chemo vs ADC^{1,2}</p>			Improved tolerability Through reduced systemic payload exposure
Efficacy (Control over delivery of drugs to same cell)		<p>Binding competition impacts efficiency of delivery (for same target)³</p>		Greater control over delivery Both payloads delivered to the same cell at the same time
Regulatory Simplicity				Reduced clinical complexity Single agent regulatory data package, standard monotherapy dose escalation design
Combination Study Simplicity			<p>Combo with modalities such as ICI⁴ that have shown improved outcomes with ADCs⁴</p>	Reduced cost Potential for combination benefit in one product

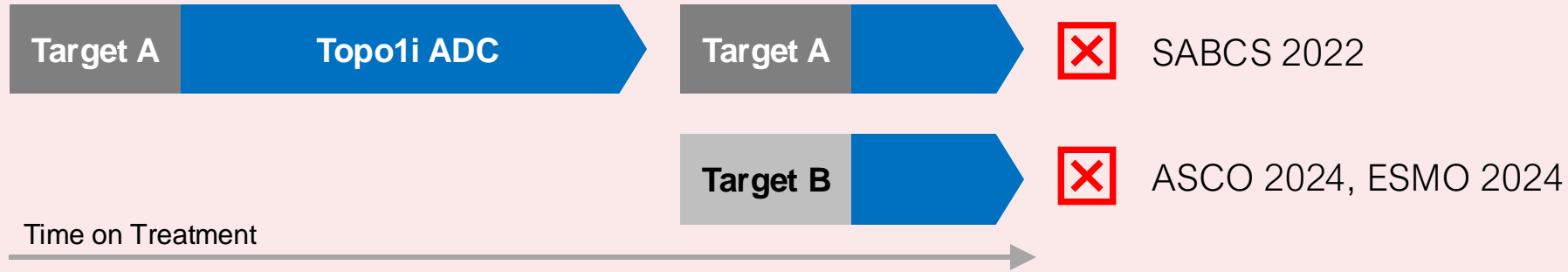
Sources: 1. PMID: [27052654](#); 2. PMID: [23020162](#); 3. PMID: [34112795](#); 4. PMID: [36041086](#); ICI – Immune checkpoint inhibitor; TGI – Tumor growth inhibition; SAE – Severe adverse event

Regulatory Advantages of Dual Payload ADCs vs ADC Combination Trials

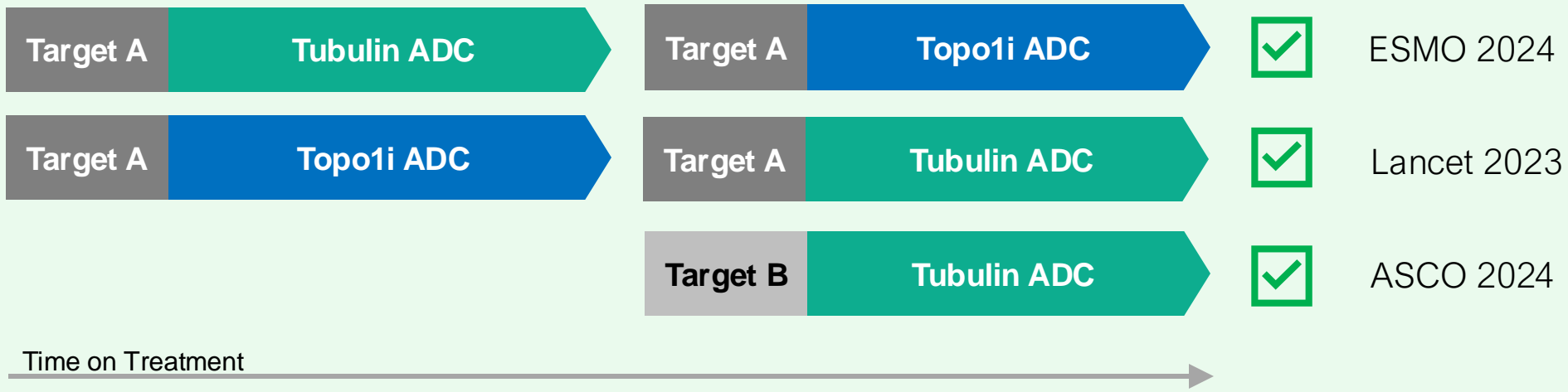


Dual Payload ADCs Overcome Emerging Resistance to Single Payload ADCs

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

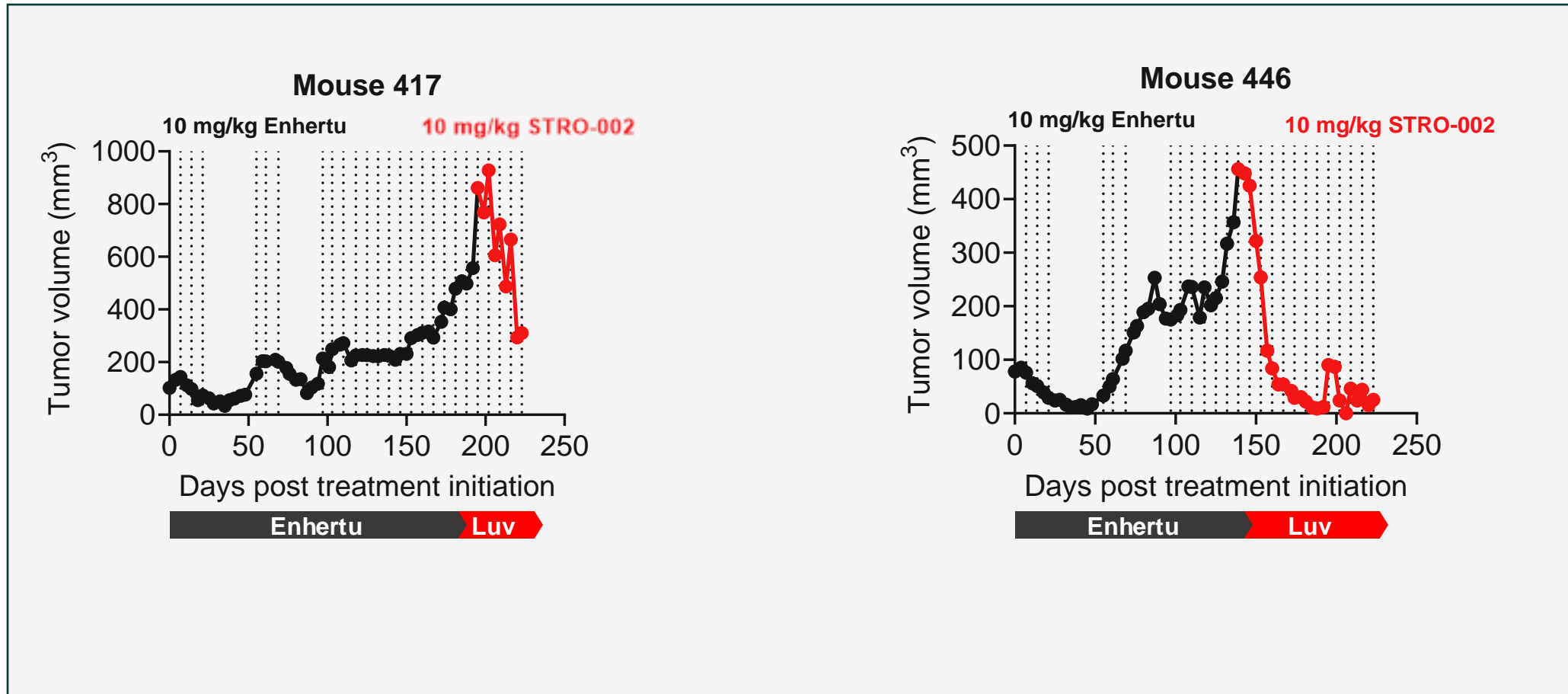


Switching Payload Class Maintains ADC Efficacy, Irrespective of the Target Antigen



SABCS – San Antonio Breast Cancer Symposium; ASCO – American Society of Clinical Oncology; ESMO – European Society for Medical Oncology

Enhertu/Topo1i ADC Resistant Cell Lines Are Responsive to Tubulin ADC Treatment



Target A Topo1i ADC

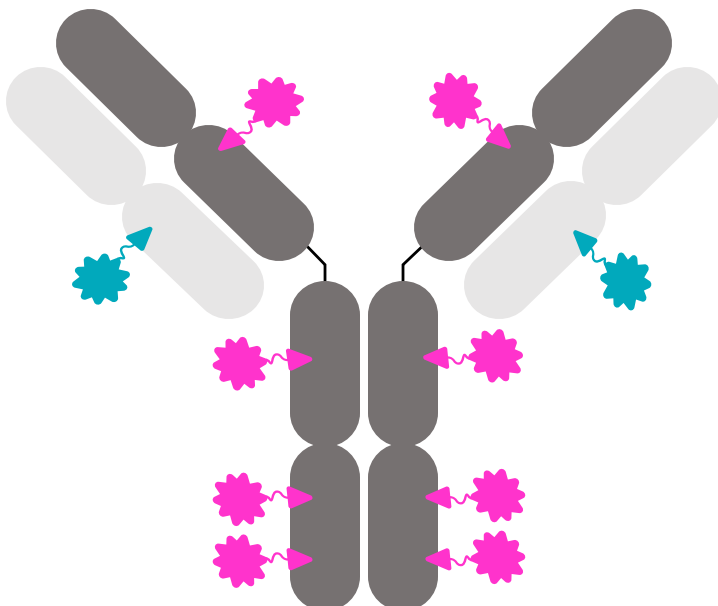
Enhertu

Target B Tubulin ADC

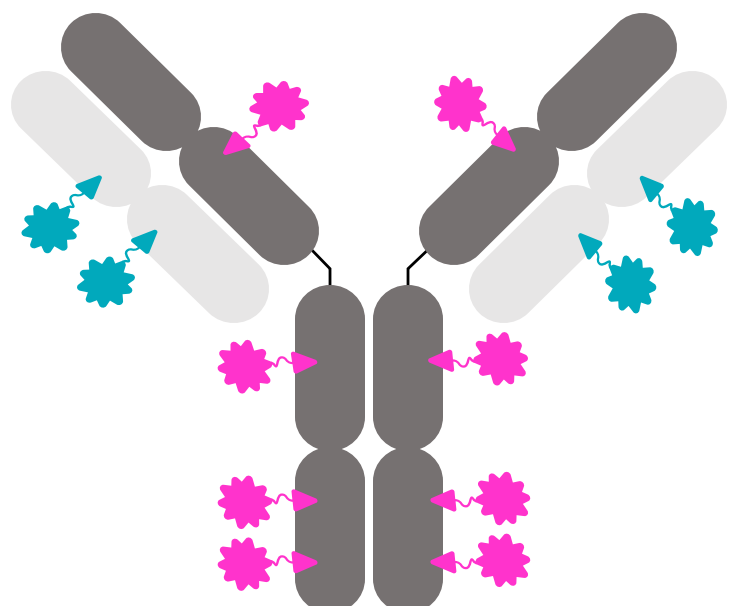
Luvelta



Optimization of Dual-Payload ADC Design (Topo1i + anti-Tubulin)

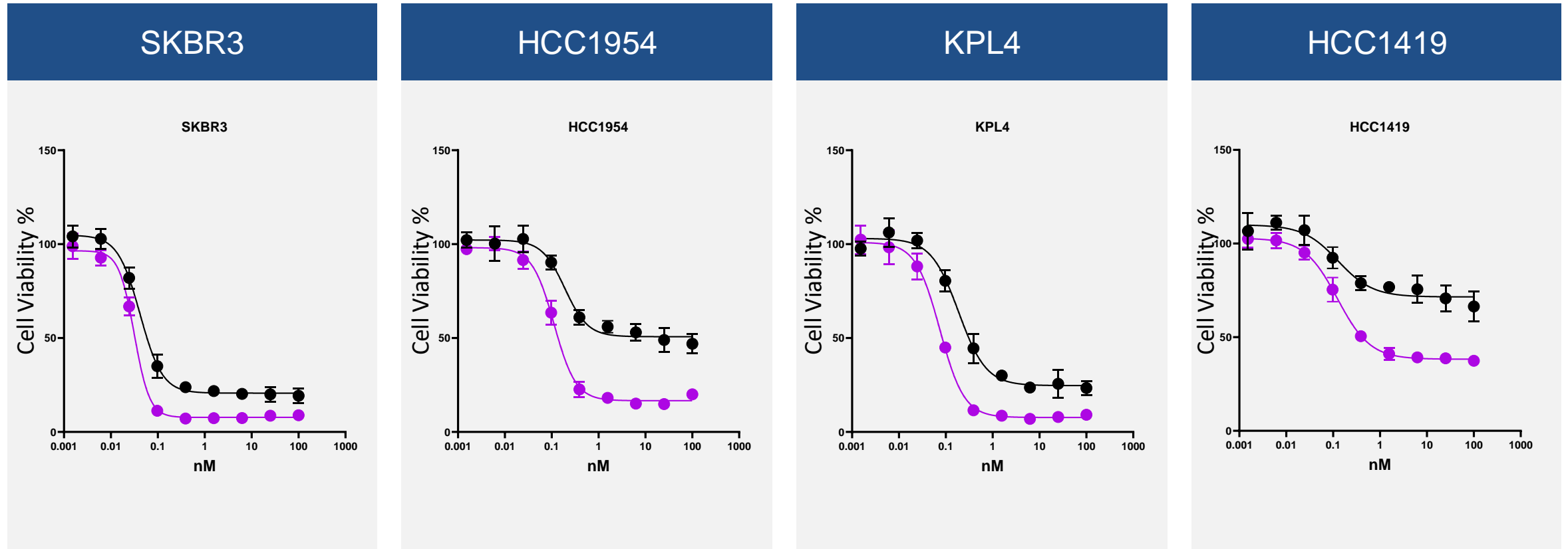


8+2



8+4

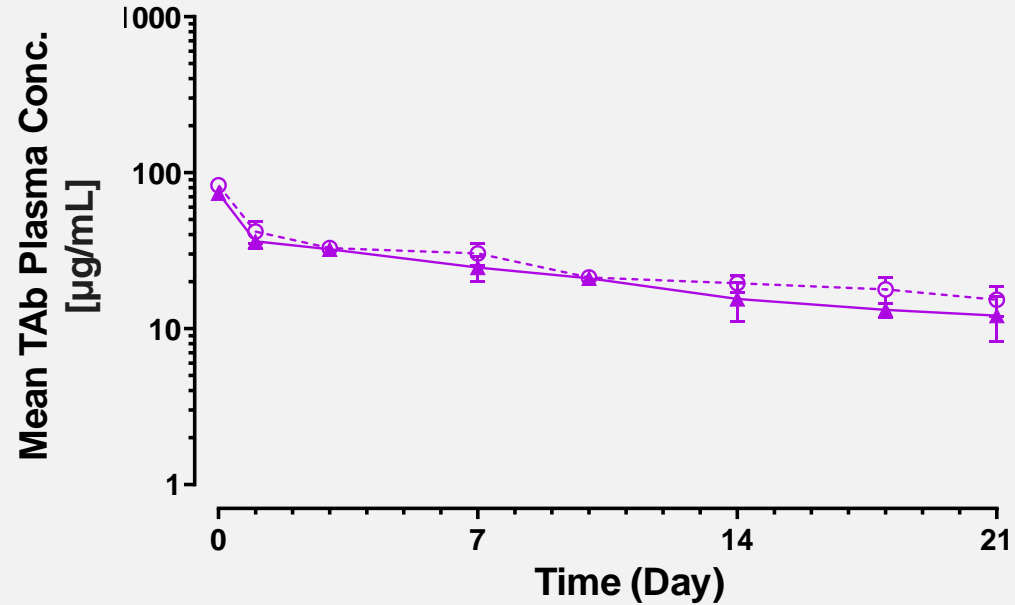
Improved *In Vitro* Activity of Dual-Payload ADC



● Enhertu

● Trastuzumab DAR8 Topo1i + DAR2 MMAE

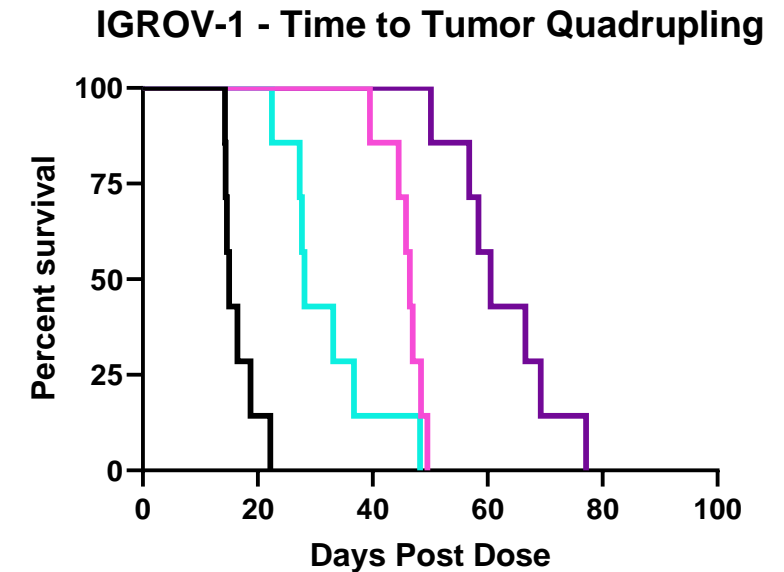
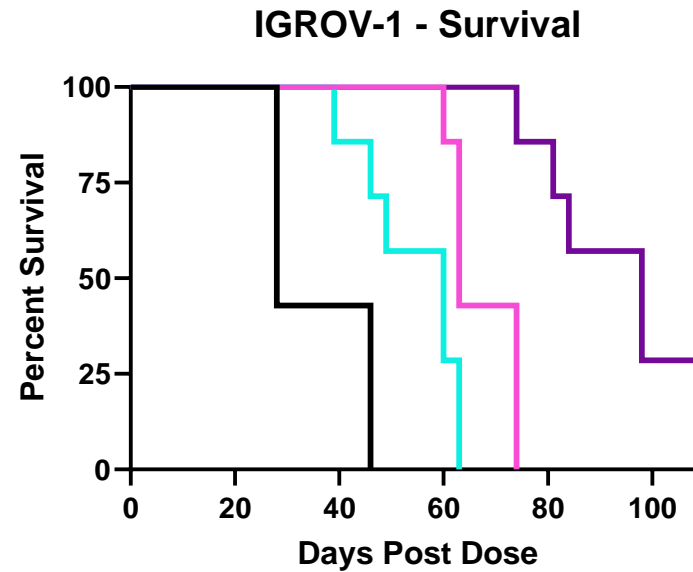
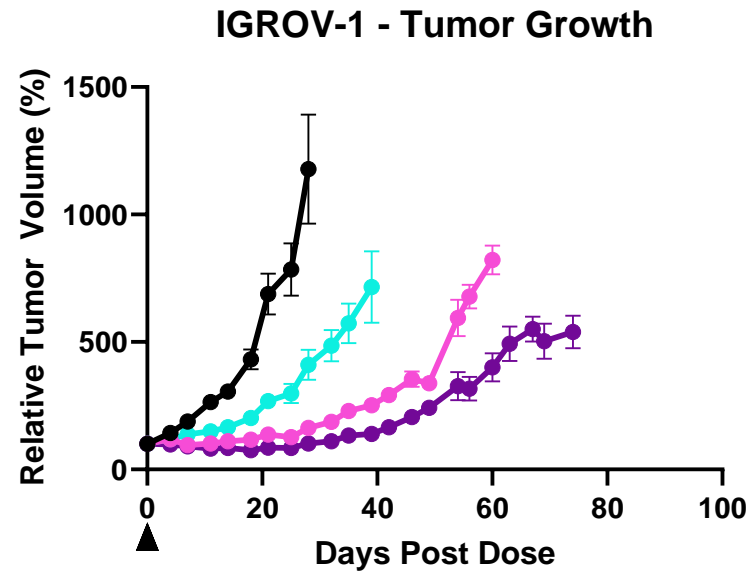
Dual-Payload ADC Displays Desirable Preclinical Mouse PK



	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

Cl_{obs} – observed clearance; V_{ss} – volume of distribution at steady state; $t_{1/2}$ – half-life

Dual Payload ADC (Topo1i + anti-Tubulin) Display Enhanced *In Vivo* Efficacy in Ovarian Cancer

















Vehicle control

Trastuzumab DAR4 MTI ADC (5 mg/kg)

Trastuzumab DAR8 Topo1i ADC (5 mg/kg)

Trastuzumab DAR8 Topo1i + DAR4 MTI dpADC (5 mg/kg)

Sutro is Primed to Become a Leader in Dual Payload ADCs

Company	Targets	Payloads	DAR	Single Payload Clinical	Target IND
	Her2/ND	Topo 1 x MTIs	8:2  8:4 	MTI: Ph3	2027
	Her2/TF/ND	Topo 1 x PARPi	8:2  8:8 	Topo1: 2025 IND	TBD
	ND	Topo 1 x IO	ND	IO: IND ND	iADC Astellas
	Trop2	Topo 1 x TKI	ND	Topo1: Ph3	-
	Her3	Topo 1 x IO	ND	IO, TKI: No	-
	Her2	Topo 1 x ATR	1:1 ratio 	No	-
	NaPi2b	Topo 1 x Topo 1	ND	No	-
	Her2	DXd x MTI	4:4 	No for MMAF	-
	Her2	DXd x TLR7	ND	No	-
	B7H3	MTI x TLR7	3-4: 7-14 	No	-

Lack of Preclinical Reports from Pharma on Dual Payload ADCs

* Hanson Wade: Nov 2024 ADC; Digest: Dual Payload ADCs; ND = Nondisclosed; MTI = Microtubule inhibitor

Acknowledgements

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Jeff Hanson

Miao Wen

Cuong Tran

Robert Yuan

CMC

Judy Hsii

Upstream Process Development

Downstream Process Development

Analytical Development

MSAT Team

Manufacturing Team

SMT

Jane Chung

David Pauling

Barbara Leyman

Venkatesh Srinivasan

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