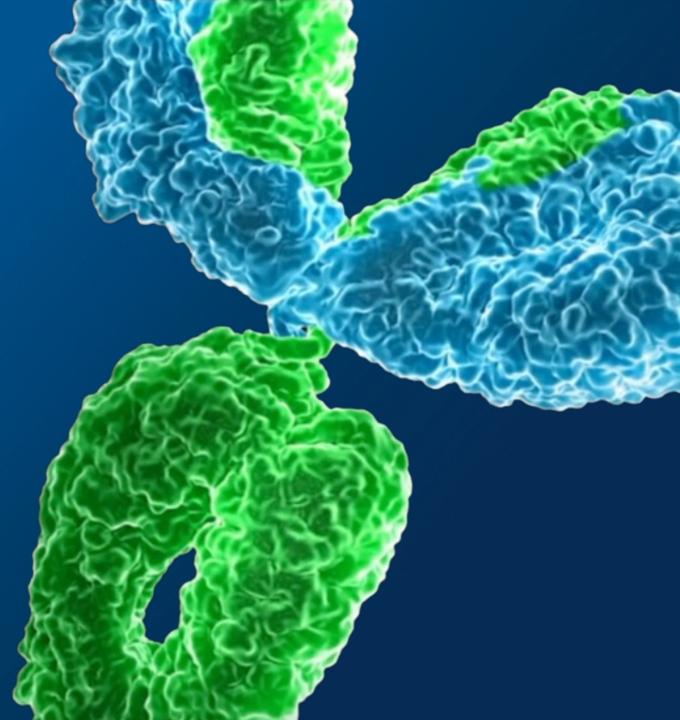


### **Virtual Research Forum:**

## Sutro's Next-Generation Innovations in ADCs

July 20, 2022



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, current and future clinical activities, timing, design and success of our ongoing and planned clinical trials and related data, updates and results of our clinical trials and related data, timing and success of our planned development activities, our ability to obtain and maintain regulatory approval, the potential therapeutic benefits and economic value of our product candidates, potential growth opportunities, financing plans, potential future milestone and royalty payments, competitive position, industry environment and potential market opportunities for the Company's 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, the design, timing and results of preclinical and clinical trials, and the expected impact of the COVID-19 pandemic on our operations. 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.

You should not rely upon forward-looking statements as predictions of future events. Although our management believes that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances described in the forward-looking statements will be achieved or occur. Moreover, neither we nor our management assume responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to publicly update any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations, except as required by law.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.



**Bill Newell** Introduction Chief Executive Officer **STRO-003 Emerging Research Portfolio** Trevor Hallam, Ph.D. President of Research and Chief Scientific Officer **Product & Process Design Integration** CMC and Supply Chain Strategies Summary and Q&A **Bill Newell** Kristin Bedard, Ph.D. Chief Executive Officer Vice President, Discovery Venkatesh Srinivasan, Ph.D. Trevor Hallam, Ph.D. President of Research and Chief Scientific Officer

> Shabbir Anik, Ph.D. **Chief Technical Operations Officer**

Senior Vice President, Process & Analytical Development



### Six Product Candidates in Clinical Development are Enabled by Sutro's Platform

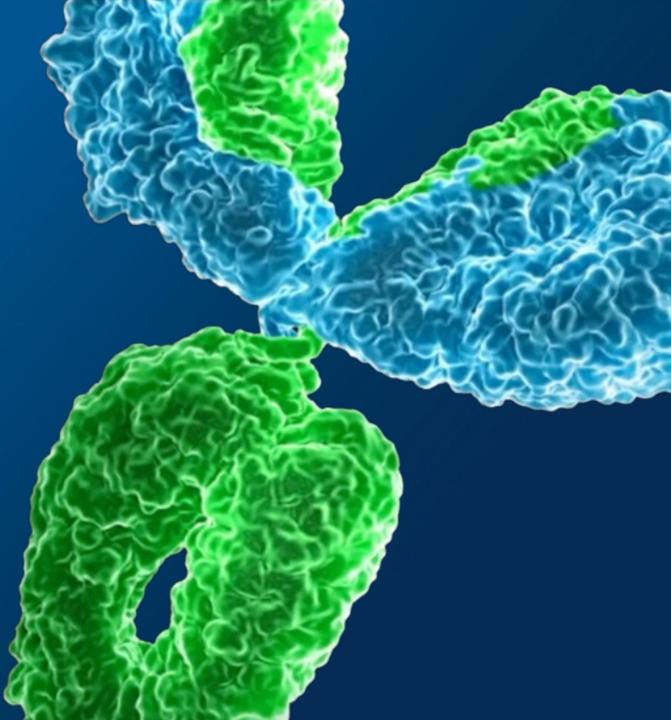
Unique engineering prowess in the field of precisely conjugated biologics, including next-gen ADCs

Modality	Program	Target(s)	Indication	Discovery	Preclinical	Phase 1/1b	Phase 2/3	Partner		
	STRO-002	FolRa	Ovarian Cancer	Fast Track Designation						
			Ovarian Cancer (bevacizumab combo)					会で見たした。 (Greater China)		
			Endometrial Cancer							
			NSCLC/Non-Gyn Cancers	C/Non-Gyn Cancers						
Antibody-Drug	STRO-001	CD74	Lymphoma					日本 (Greater China)		
Conjugate (ADC)			Multiple Myeloma	Orphan Drug De	esignation					
	CC-99712	ВСМА	Multiple Myeloma	Orphan Drug De	esignation			ller in a su		
			Multiple Myeloma (GSI combo)					ull Bristol Myers Squibt رالل Bristol Myers Squibt		
	STRO-003	ROR1	Cancer							
	Other Early- Stage ADCs	Tissue Factor	Cancer							
Bispecific ADC	M1231	MUC1-EGFR	NSCLC & Esophageal Cancer					EMD (1) SCROND		
Immunostimulatory ADC (iADC)	Undisclosed	3 Undisclosed Targets	Cancer					<b>X</b> astellas		
Cytokine	MK-1484	Undisclosed	Advanced or Metastatic Solid Tumors					S MERCK		
Vaccine	VAX-24	24-Valent Conjugate Vaccine	Invasive Pneumococcal Disease					Vaxcyte		

(1) EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt Germany in the U.S.



## STRO-003: ROR1 Targeting ADC



### STRO-003: A Novel ROR1 Targeted ADC is Designed for Purpose

### Ø

## ROR1 biology makes it an attractive ADC target

ROR1: **Role in cancer progression** and expressed in tumor and tumorinitiating cells

Low potential for on-target toxicity due to **restricted normal tissue expression and clinical safety validation** 

Expansive indication space in oncology

Clinical validation of ROR1 in hematological malignancies and broad potential opportunity in solid tumors, including large indications such as NSCLC and breast cancer



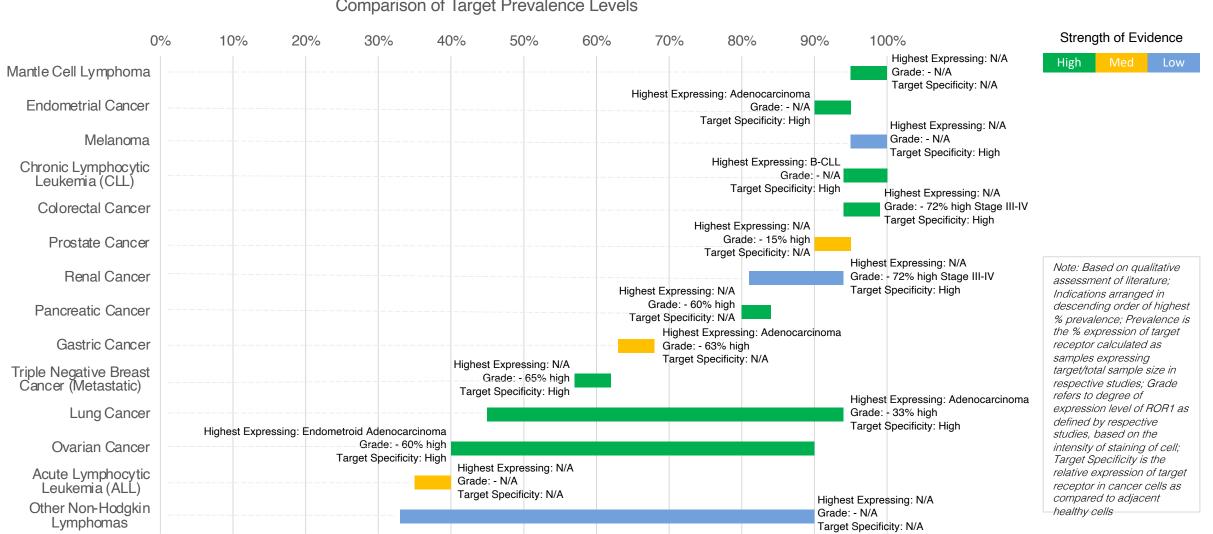
## Potential for attractive clinical performance

Low copy number and heterogeneous expression of ROR1 antigen in tumors favors potent ADCs with great tolerability

STRO-003's optimized linker design and payload selection—along with precise positioning of 8 linker-payloads per antibody—provides **potent efficacy** in low antigen expressing human tumors (PDX) and has been tolerable in preclinical studies



### ROR1 Target is Broadly and Differentially Expressed Across Wide Range of Solid and Hematologic Tumors

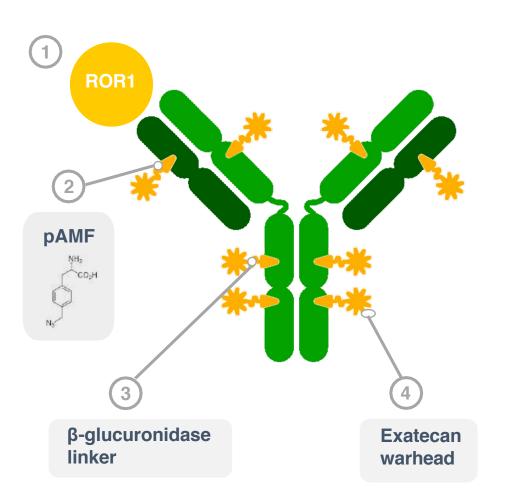


**Comparison of Target Prevalence Levels** 



**STRO 003** 

### Our Innovative Design: STRO-003 is a Novel Optimized ROR1 ADC, Featuring TOPO-1 Inhibitors Linked with β-Glucuronidase Cleavable Linkers, DAR 8



STRO-003 is a single homogeneous antibody drug conjugate (ADC) with a drug-antibody ratio (DAR) of 8, targeting ROR1 tumor antigen

2

cancers including hematological and solid tumor indications Precisely positioned non-natural amino acids,

Targeted ROR1 epitope is overexpressed in diverse

p-azidomethyl-L-phenylalanine (pAMF), **to enable DAR8** and optimal conjugation sites for enhanced performance and stability

3

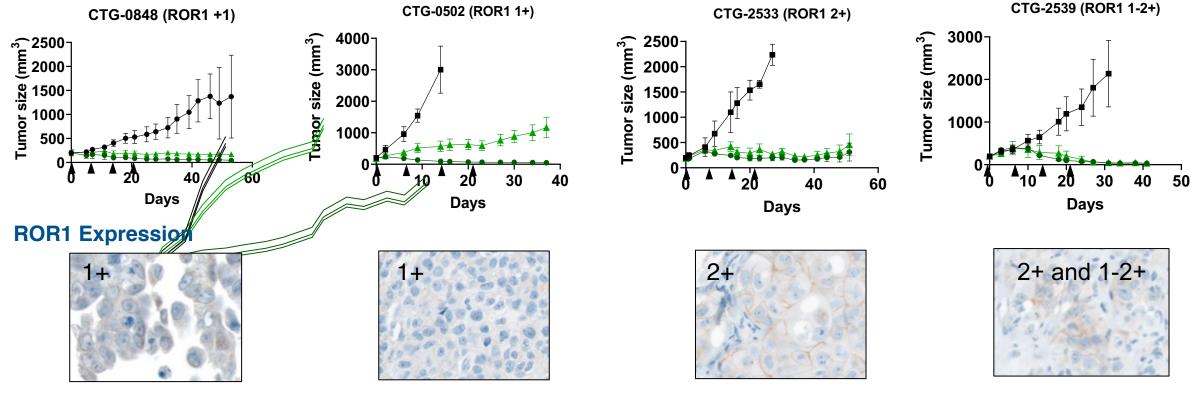
Stable β-glucuronidase cleavable linkers demonstrate tumor specificity and encouraging preclinical tolerability. Preclinical data has shown marked improvement over CatB linkers regarding neutropenia and lung tolerability issues seen with tubulin and TOPO-1 inhibitors in the clinic

**Exatecan warhead inhibits TOPO-1 causing DNA disruption**. It elicits potent tumor cell killing, bystander activity and immunogenic cell death



# STRO-003 Demonstrated Complete Regression of Human Patient-Derived NSCLC STRO 003 Xenografts Expressing *Low and Heterogeneous* ROR1 Antigen Levels in Preclinical Studies

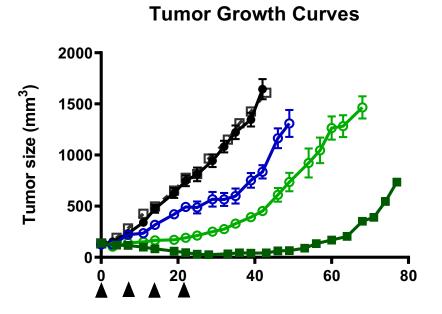




- Vehicle
- STRO-003(β-glu exatecan)
- Alternative Design (CatB exatecan)
- ROR1 ADC variants (STRO-003 and Alternative Design featuring CatB exatecan) are efficacious in the PDX models (10 mg/kg qw x4)
- β-glu linker validates PDX models for release of exatecan catabolite and potent activity

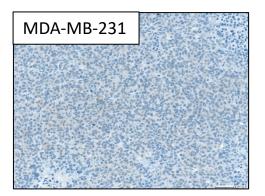


## DAR8 β-Glu Exatecan is Potent in MDA-MB-231 Breast Cancer Model with Moderate ROR1 Expression



Days post treatment

	Description	Dose (qw x4)	% TGI (Day 42 or 43)
-	DAR8 β-glu exatecan (STRO-003 Linker-Payload*)	5 mg/kg	106%
<b>+</b>	DAR8 CatB exatecan (Alternative Linker Design)	5 mg/kg	79%
<b>+</b>	DAR4 CatB MMAE (VLS-101 Linker-Payload)	5 mg/kg	53%
	Vehicle		
-D-	Vehicle*		

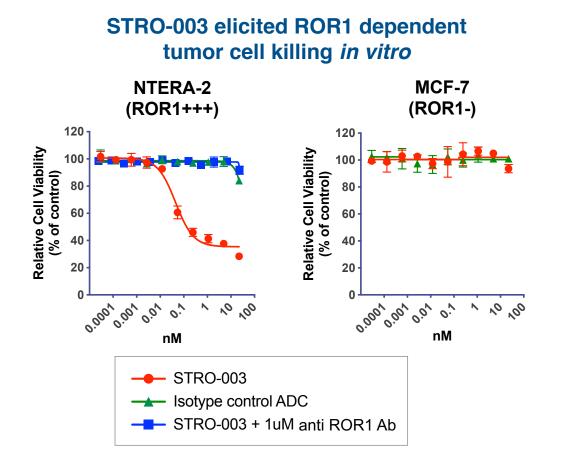


Medium/Moderate ROR1 protein expression by IHC

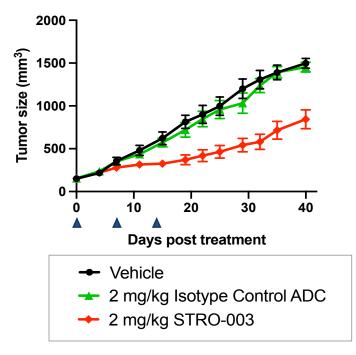


SUTR:

### STRO-003 Demonstrated Potent and ROR1 Dependent Tumor Killing



## STRO-003 elicited ROR1 dependent tumor growth inhibition *in vivo*



#### MDA-MB-231 (ROR1+)

- Potent cell killing of ROR1 positive cells, no activity on ROR1 negative cells
- STRO-003 cell killing activity can be blocked with a competing anti-ROR1 antibody



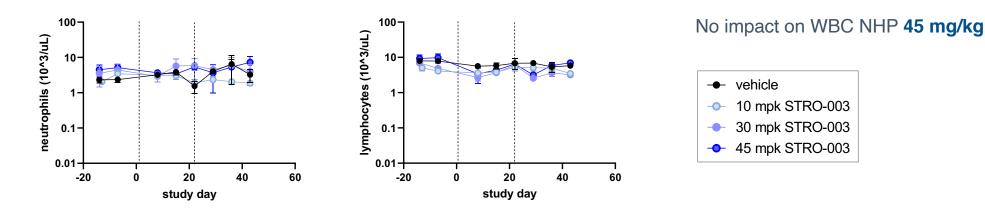
### STRO-003 Demonstrated a Wide Safety Window in Multiple Cross-Reactive Species

STRO-003 was cross-reactive and well tolerated in rat at high doses

No observed neutropenia, no elevation of liver enzymes at high doses (60 mg/kg)

STRO-003 was cross-reactive and well tolerated in a multi-dose non-GLP NHP study

• No observed neutropenia or thrombocytopenia, well tolerated up to 45 mg/kg, no changes observed in WBCs



#### Additionally, no lung toxicities observed at 45 mg/kg STRO-003 in NHPs;

- Note: In this same preclinical NHP study, a ROR1 ADC with Cathepsin B linker exatecan ADC was studied and generated lung findings consistent with developing pneumonitis (and ILD) at 45 mg/kg
- Possible that improved tolerability with STRO-003 is driven by use of new β-glucuronidase linker
- Other CatB-linker exatecan ADCs, including Enhertu, are associated with significant rates of clinical pneumonitis/ILD



#### **Expansive indication space**

• Clinical validation of ROR1 in hematological indications and opportunity in broad solid tumors, including NSCLC and breast cancer

#### STRO-003: Designed for significantly superior clinical performance

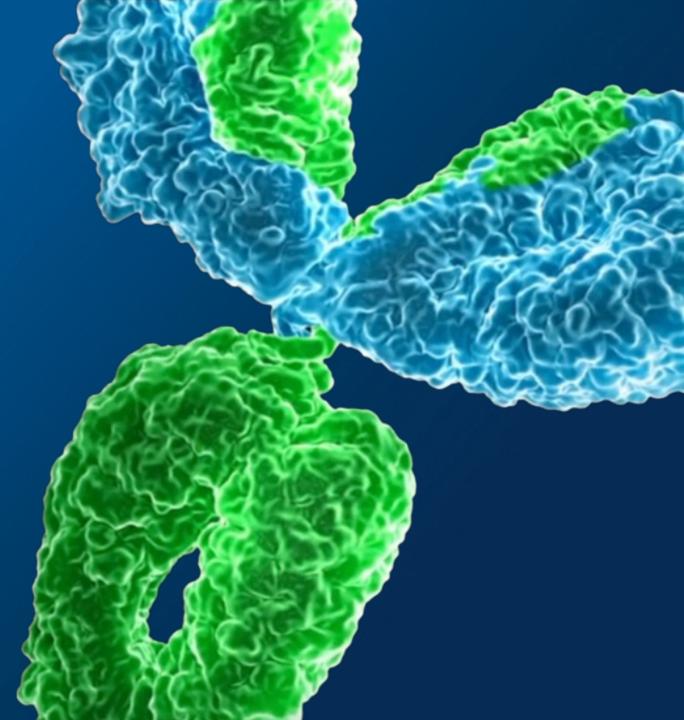
- Optimal molecule to deliver efficient tumor killing with every antigen binding and internalization event
- High potency DNA targeting TOPO-1 inhibitor payload with compelling clinical validation
- Optimized novel linker design-payload combination improves tumor selectively to increase therapeutic index and provide significant safety window
- High DAR8, clinically precedented, but now with optimized conjugation positioning, to maximize payload delivery to tumor cell

We believe that STRO-003's design elements appear to demonstrate impressive efficacy while potentially reducing lung and neutropenia tolerability concerns associated with TOPO-1 class payload ADCs





## Sutro's Emerging Research Portfolio Including iADCs



#### Sutro's precision design can drive potential best-in-class differentiation

- Precise conjugation sites and their combination in a homogeneous ADC can greatly improve efficiency of killing and tolerability
- Positioning of conjugation sites matter
- Bispecific targeting of co-localized tumor antigens can improve tumor selectivity over healthy tissue, e.g. M1231, Muc1/EGFR ADC

#### Sutro has enabled novel TOPO-1 inhibitor linker payloads and new cleavable linker chemistries

- Best performing ADCs in clinic are those with DNA disruptors
- · Sutro deployed new cleavable linker chemistries to improve stability, selectivity for tumor and tolerability

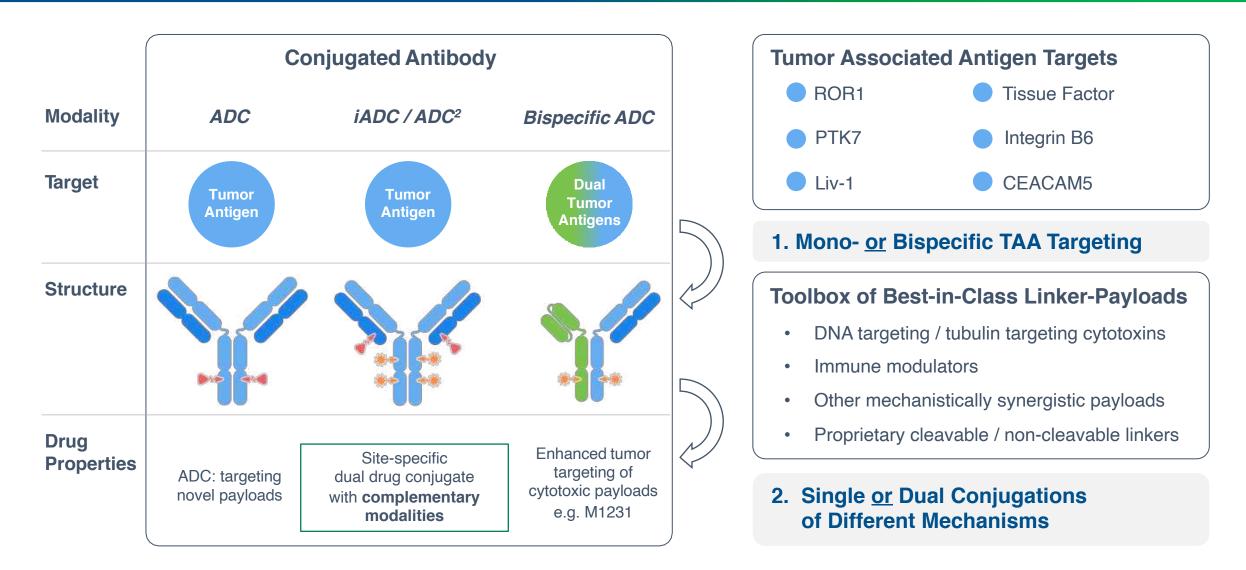
#### High DAR (8 and above) ADCs now in play with Sutro's unique technical advantage

- Homogeneous (positionally optimized, site-specific)
- Flexibility to find new space (not limited by having to co-opt Cys and being limited to their native positioning)

#### Unique precise dual conjugations to take us beyond best-in-class to first-in-class

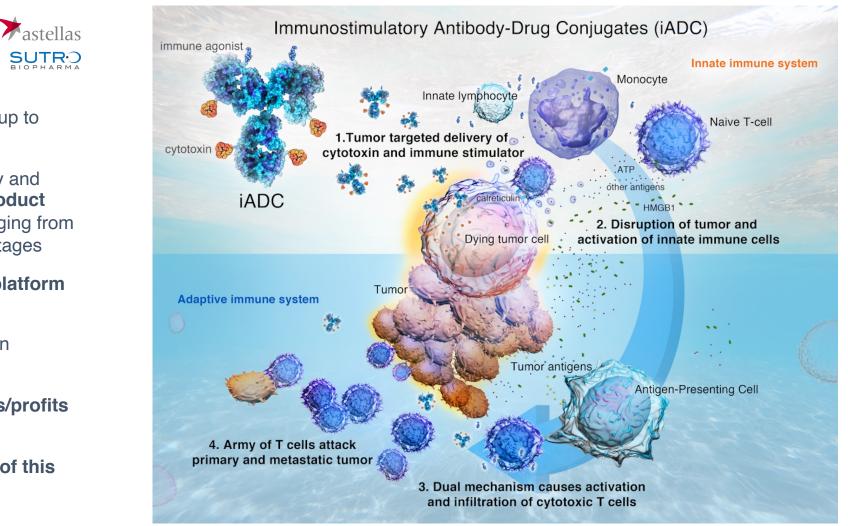
- Combination of targeted mechanisms to engage immune system and offset resistance
- iADCs moving to a more "complete" therapeutic; dual payloads for mechanistic synergy
- ADC<sup>2</sup> dual mechanisms to offset resistance

Drug Discovery Platform Enables the Opportunity for Best-in-Class or First-in-Class Molecules Precise novel design to enhance efficacy and safety across multiple modalities and targets





New Modality for Cold Tumors: Immunostimulatory Antibody Drug Conjugate (iADC) Featuring dual drug conjugation technology with both cytotoxin and immune modulator





 \$90M upfront to develop iADCs for up to three targets

Strategic iADC Collaboration

June 27, 2022

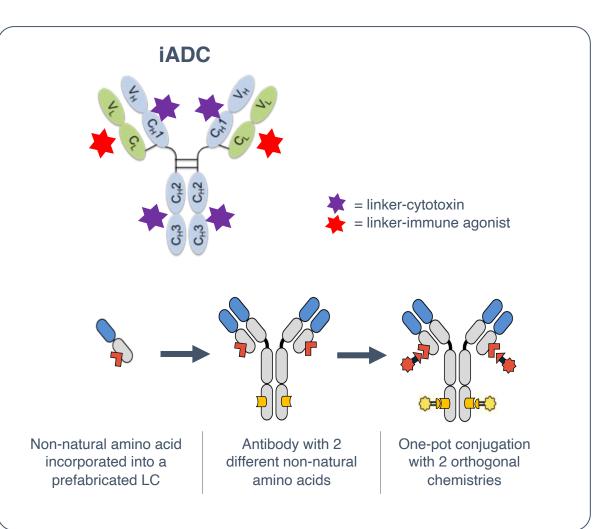
- \$422.5M in development, regulatory and commercial milestones for each product candidate, plus tiered royalties ranging from low-double digit to mid-teen percentages
- Builds on success of Sutro's ADC platform and engineering expertise
- Leverages Astellas' primary focus on
  immuno-oncology
- Sutro has the **option** to share **costs/profits** for U.S. product development
- Sutro can develop iADCs outside of this collaboration in other targets

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### Sutro's Next-Generation Tumor Targeting Immunostimulatory ADC

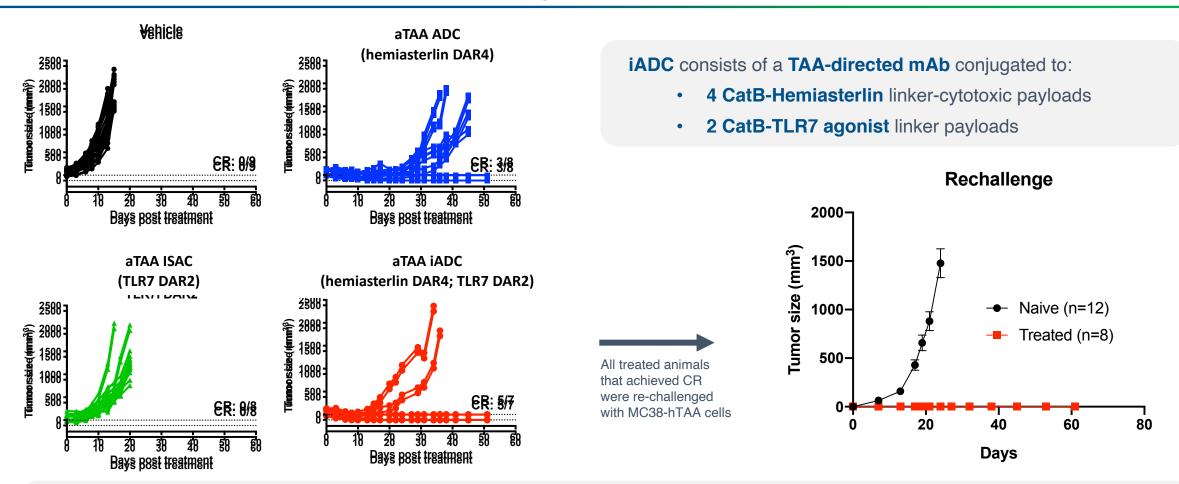
A systemically administered monotherapy that drives anti-tumor immunity

- Precision technology for dual conjugated immunostimulatory antibody drug conjugate
- POC molecule enables simultaneous and precise tumor targeting of a cytotoxin and a novel toll-like receptor (e.g. TLR) agonist with **systemic delivery**
- Novel design intended to prime an adaptive antitumor response in a systemic monotherapy
- Potential to reprogram the patient's tumor microenvironment and generate protective antitumor immunity



Data Presented at the World ADC Meeting in London, 3/2020

### Superior Anti-Tumor Response with Single Dose of iADC

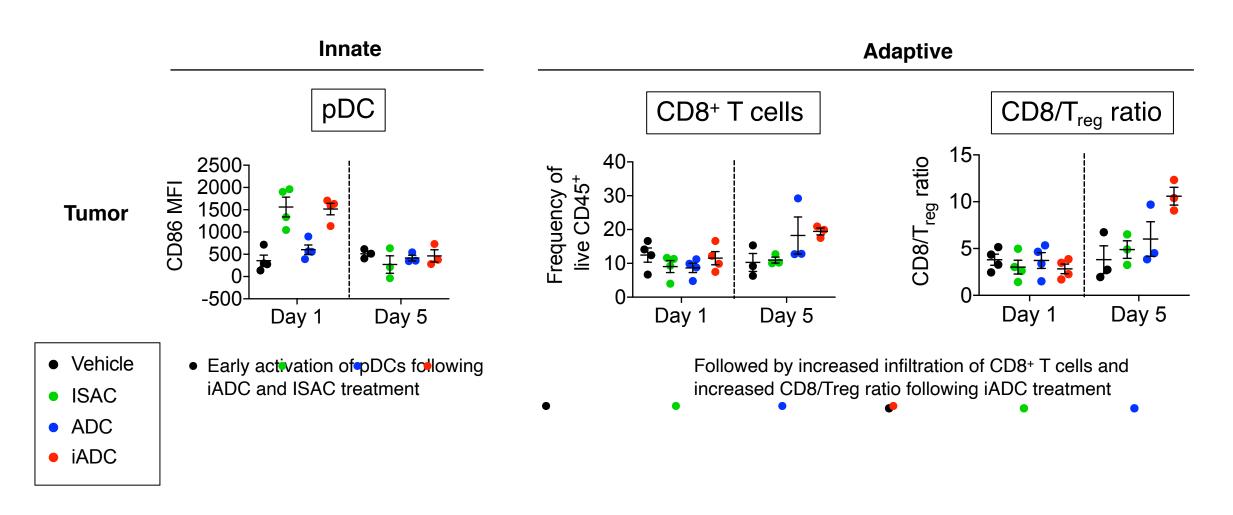


iADC showed enhanced activity vs. ADC alone based on higher number of animals with complete responses and durable anti-tumor immunity

Data Presented at FOCIS Meeting June 2022

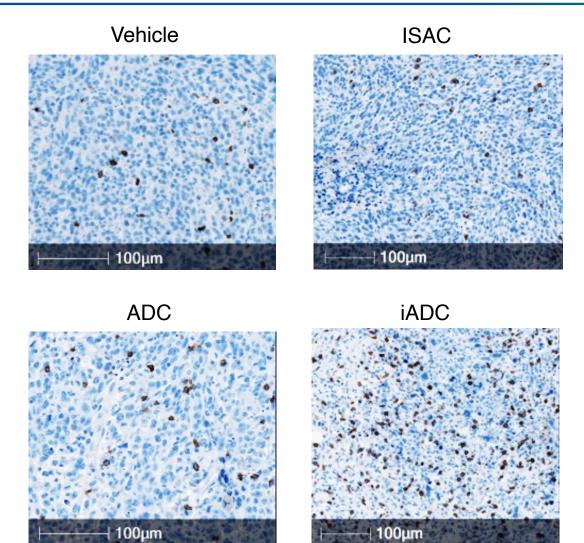
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### iADC Engaged Both Innate and Adaptive Immune Compartments in hTAA-MC38 Tumor Bearing Mice



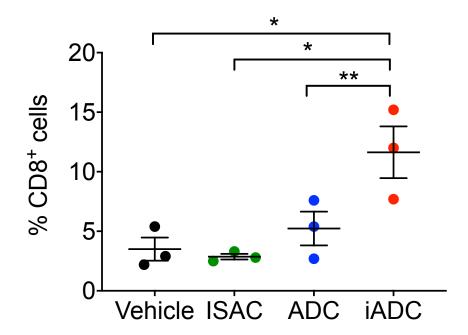
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### iADC Increased CD8+ T cells in Tumor Microenvironment



Data Presented at FOCIS Meeting June 2022

CD8<sup>+</sup> quantitation





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### Novel Mechanism of Action Differentiates iADC from Other Immunotherapies

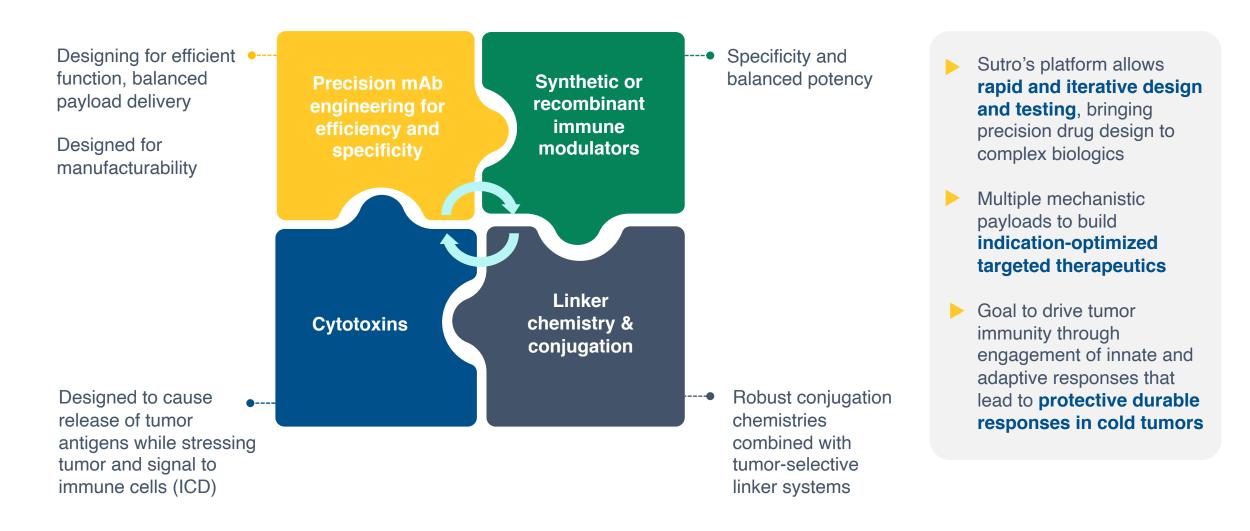
			Sutro iADC	ISAC	Vaccine	PD-1 /PDL-1	CAR-T cells	STING
		Molecule	Targeted and homogeneous	Mixed ADC	Biologic	Ab	Biologic	Nucleic acid
		Opportunity: Risk	Combine ICD with innate agonists (TLR, Sting, etc.)	TLR 7/8- requires Fc effector	Ag selection challenge	Limited tumor types	Safety concerns	Non-targeted, issues with TI
		Direct tumor cell killing						
S		Tumor antigen presentation	-					
		Priming and activation of Antigen Presenting Cells	-	•	•			•
		T-cell recruitment to tumor		•		•	•	•

Mechanisms to achieve anti-tumor immunity

Sutro iADCs bridge innate and adaptive immunity to provide broad protection in a single molecule



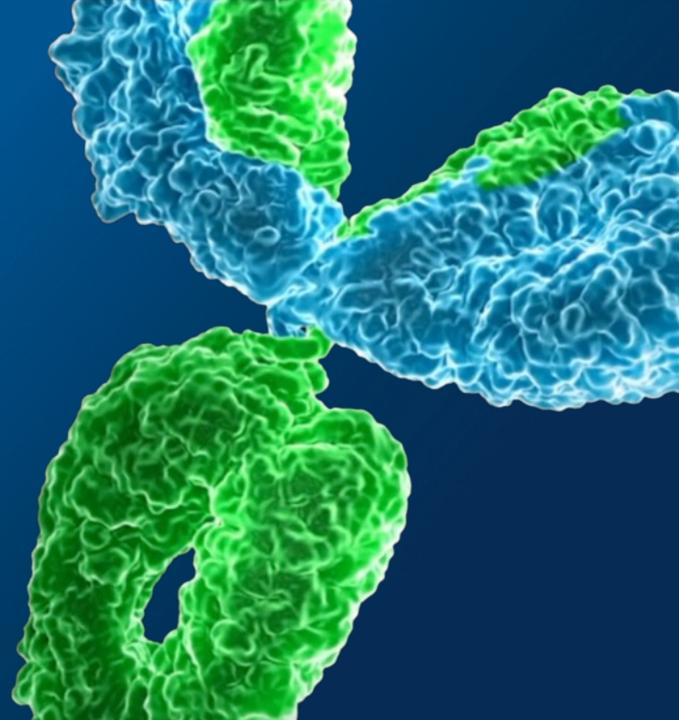






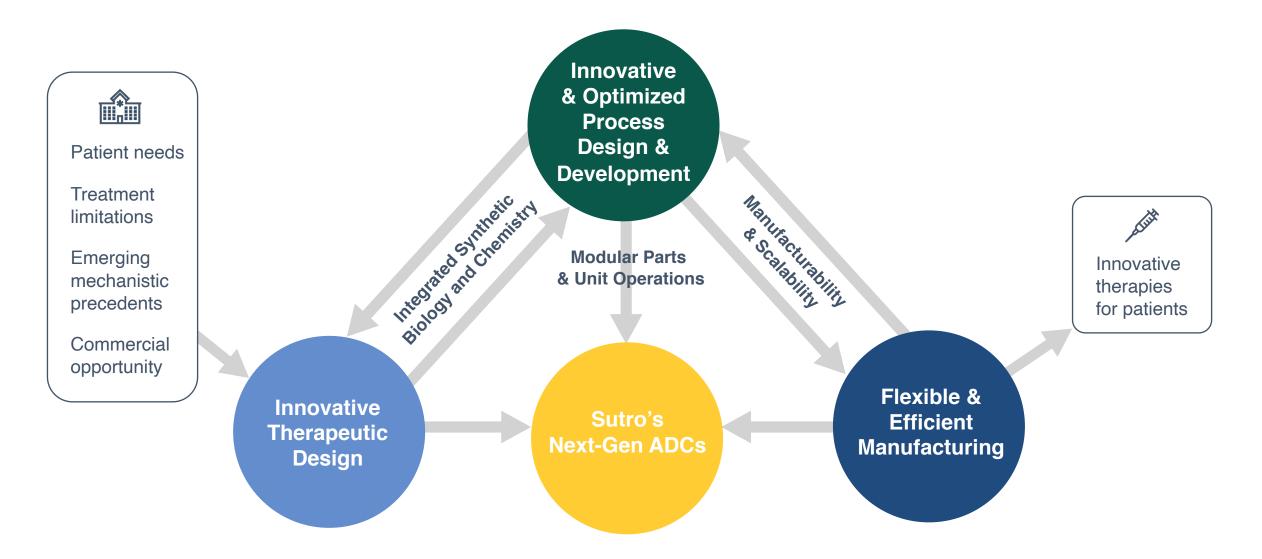
### SUTR: BIOPHARMA

## Product and Process Design Integration Drives Efficient and Predictable Manufacturability



### Sutro's Cell-Free Synthetic Biology and Medicinal Chemistry Platform

Integrating developability and manufacturability into product design





## ADCs are complex molecules where the ultimate clinical profile depends on multiple molecular features in the parent antibody and the placement and stability of the conjugated payload

#### These attributes can be compromised in conventional cell-based ADC manufacturing

• Can often impose molecular changes to product between preclinical stage and commercial scale; due to scale-up, or tech transfer related issues

Preserving the integrity of the product profile from early clinical through commercial manufacturing avoids costly comparability challenges and potential delays in regulatory acceptance

Sutro's cell-free production process allows seamless scalability from mL scale to thousands of liters – the process is the same with no formatting changes



#### Cell-free reaction can be quickly deployed to produce a new molecule within days - on-demand

#### "Component concept" facilitates rapid process development

- core cell-free product-agnostic manufacturing process
- "off-the shelf" (OTS) extract and reagents
- stock-piled cGMP-ready PFLCs (where common LCs are used)
- linker-payloads
- modularized process options by selecting from a menu of pre-tested unit operations

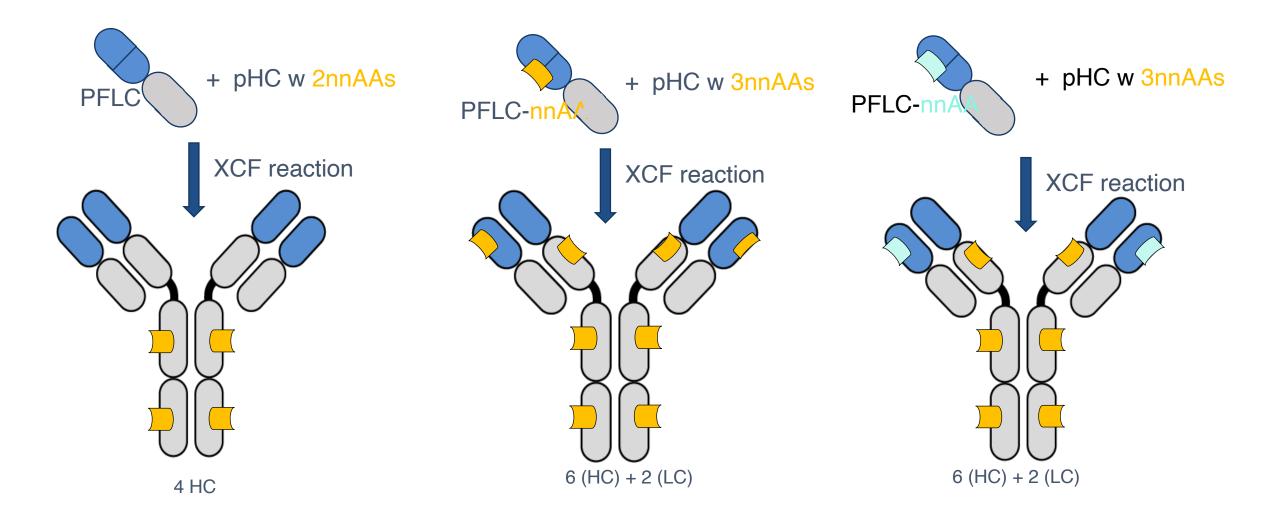
#### Individual components and processes can be independently optimized for greater process efficiency

#### Standardized control strategy

• provides familiar and predictable CMC packages for health authority review

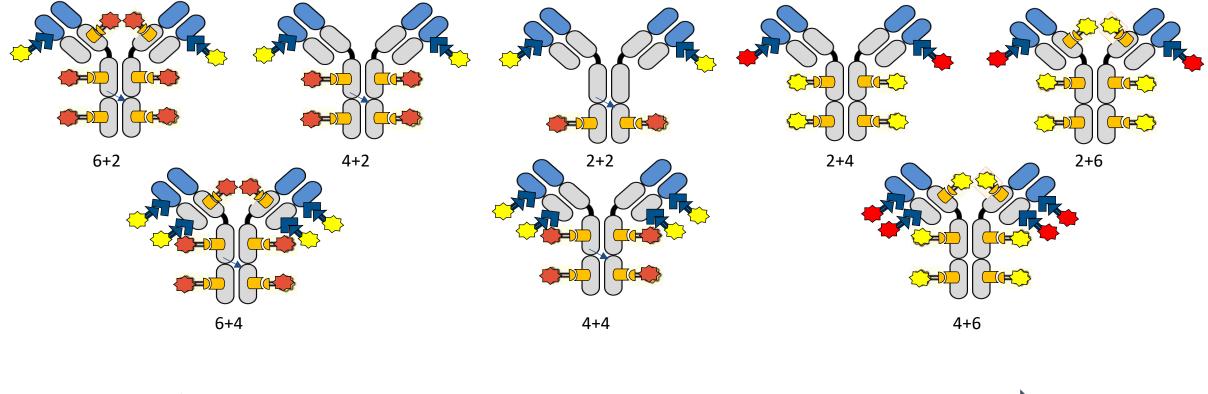


### Use of Prefabricated Light Chain (PFLC) for Modular Production Processes





## Sutro Advantage: Precision Dual Conjugation Enables (>) 9-Fold Range of Payload Ratio Critical for Optimal Synergy of Two Mechanisms of Action

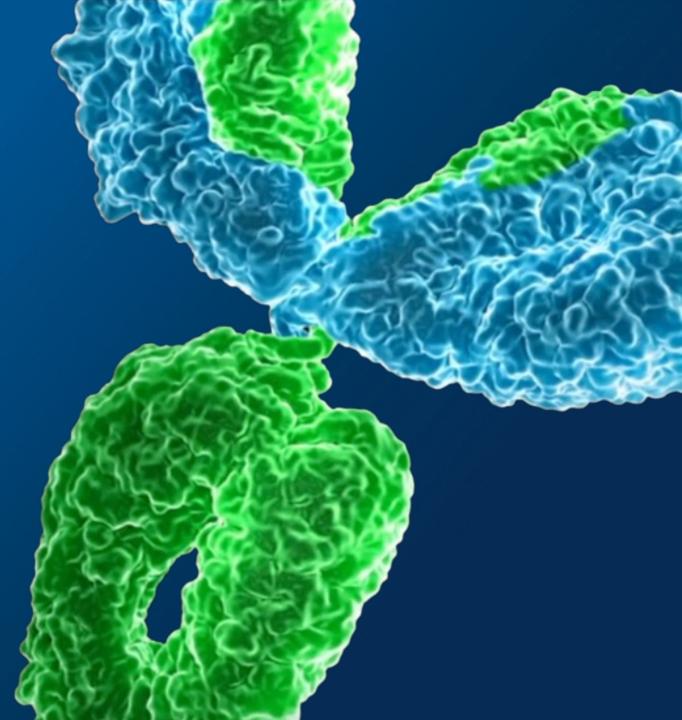








CMC and Supply Chain Strategies for Fast-to-Clinic and Commercialization



## Sutro's GMP manufacturing facility has enabled the development of 6 product candidates into clinical trials

• 3 monospecific ADC's, a bispecific ADC, a Cytokine bio-conjugate (and a conjugate vaccine)

## Establishing a robust external supply chain for clinical supplies which can be rapidly adapted and deployed for new programs

- linker-warhead process chemistry and GMP manufacture
- ADC and bio-conjugate drug substance (conjugation)
- drug product in vials
- clinical packaging

Extract and custom reagents create a common platform for rapid application to antibody-based and cytokine product development and manufacturing



## Establishing a CMO network for each component that delivers scalability, facilitates inventory build and minimizes risk to product availability for clinical studies and commercial launch

- Extract
  - Dry powder formulation
  - Scalability in progress (10X relative to Sutro's San Carlos facility)
  - GMP batches 2H 2022
- Custom Reagents
  - Large-scale GMP batches manufactured
- Pre-Fabricated Light Chain
  - Large-scale GMP batches manufactured
- XCF
  - CMO selected, GMP batches in 4Q 2023

#### Supply chain will produce >250kgs of Ab intermediate annually

**Opportunities to expand production capacities in the future** 





#### Convergent Optimization of Product Design

We know which drug linker combination needs to placed where in the molecule for optimal clinical developability

## Modular Process Development



#### Scalable Manufacturing

Independent Manufacturing of Partnered Products

Use the core open format production platform to integrate components and pretested unit operations to accelerate process development Outsourcing capability, scalability, on-demand, flexible location of product manufacturing possible (U.S., EU, Japan, China) Technology readily transferrable to partners allowing them to control their own CMC schedule



## SUTR: BIOPHARMA

## Q&A

