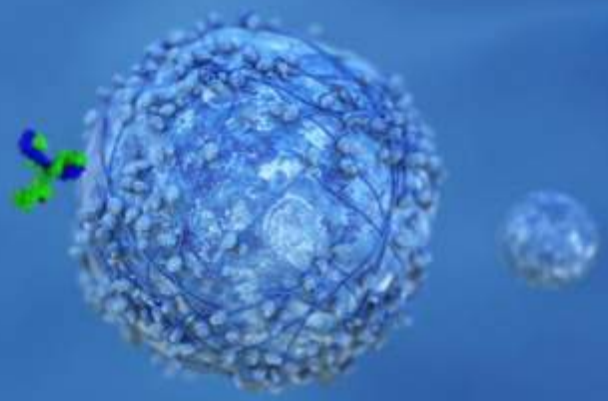

Tumor Targeted *In Situ* Immunization; Off-The Shelf and Systemically Administered

Trevor Hallam CSO

WORLD adc DIGITAL

September 15-18, 2020

SUTRO BIOPHARMA

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, current and future clinical and preclinical activities, timing and success of our ongoing and planned clinical trials and related data, the timing of announcements, 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, competitive position, industry environment and potential market opportunities.
- Forward-looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors. 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 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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- 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.
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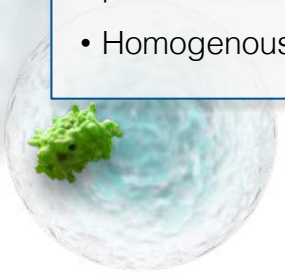
Sutro's Approach

Delivering Potentially Best-in-Class ADCs and Cytokine Conjugates

Widening the Therapeutic Index is Key to Achieving Best-in-Class Performance

The Sutro Advantage

- Rapid iterative design to identify best-in-class product candidates
- Selection of specific sites for conjugation for optimal performance
- Homogenous end-products



XpressCF® — Our Truly Empirical Approach

Proprietary XpressCF® rapid synthesis protein library generation, precision conjugation technology and robust medicinal chemistry to enable:

- Optimization of known product concepts
- Empirical evaluation of unexplored product concepts
- Rapid generation of best-in-class molecules

ADCs, iADCs & Targeted Therapeutics

Precision delivery of active pharmacological entity with optimal attributes is key

Cytokine Receptor Targets

Rapid evolution of optimal attributes to enable systemic administration

Sutro Clinical Pipeline

Owned and Partnered Programs

Program	Discovery	Preclinical	Phase 1/1b	Phase 2/3	Milestone	Commercial Rights
FolRα - Targeting ADC STRO-002	Ovarian and Endometrial Cancer				Updated Clinical Data Expected in 2H 2020 Commence Dose Expansion Phase in 2H 2020	SUTRO BIOPHARMA Worldwide Rights
CD74 - Targeting ADC STRO-001	Lymphomas; DLBCL, Mantle Cell, Follicular Multiple Myeloma (Orphan Drug Designation)				Additional Clinical Data Expected in 2H 2020	
Multiple Oncology Programs including iADCs	Oncology					
BCMA - Targeting ADC CC-99712	Multiple Myeloma				Currently in Phase 1b/2	Bristol Myers Squibb (A)
MUC1-EGFR Bispecific ADC M1231	NSCLC & sqCC (esophageal)				First in Man Projected 1Q21	EMD SERONO (B)
Cytokine Derivatives	Oncology & Autoimmune					MERCK
	Oncology					

A.BMS automatically obtained worldwide rights to the BCMA - targeting ADC---the first collaboration product candidate to achieve IND clearance in the United States.
B.EMD Serono, an affiliate from Merck KGaA, Darmstadt, Germany

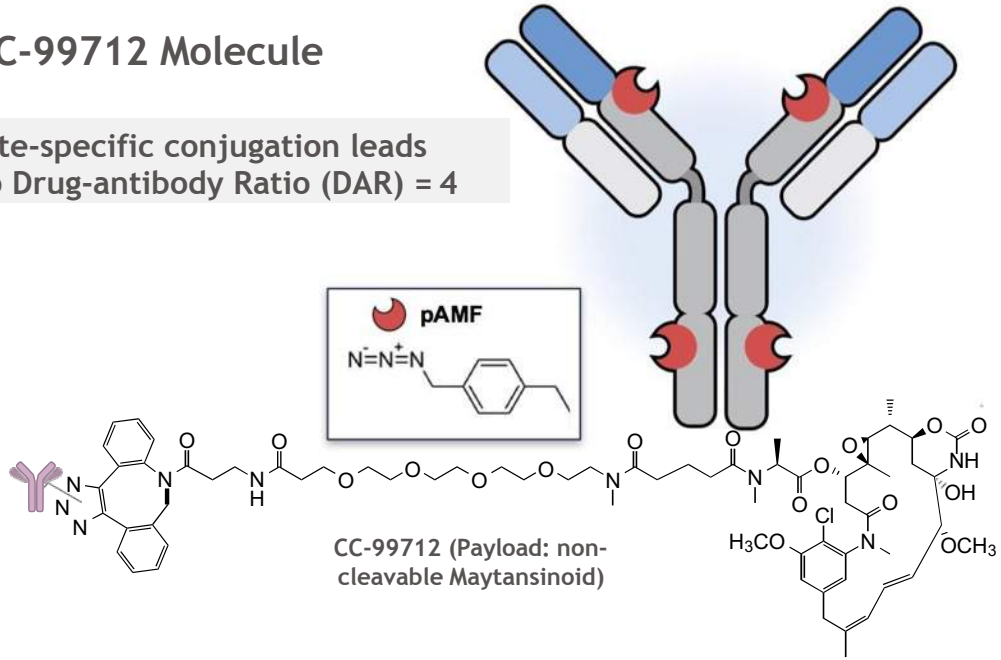
CC–99712 (BCMA-Targeting ADC) Phase 1B/2 Study

Potential for Best-In-Class

Bristol Myers Squibb

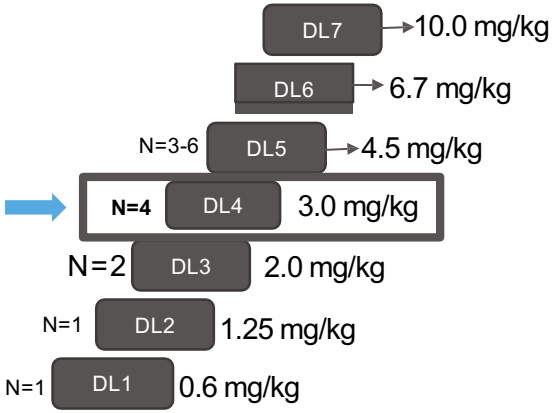
CC-99712 Molecule

Site-specific conjugation leads to Drug-antibody Ratio (DAR) = 4



Control of DAR could be advantageous in terms of patient safety and efficacy

Ongoing Study of Dose Escalation (Q3W)



Dose escalation ongoing. Key data will be the therapeutic index vs competitor.

Source: Bristol-Myers Squibb, Investor Series Day 1, Slide 33, June 2020
https://s21.q4cdn.com/104148044/files/doc_presentations/2020/BMY-Investor-Series-Day1.pdf

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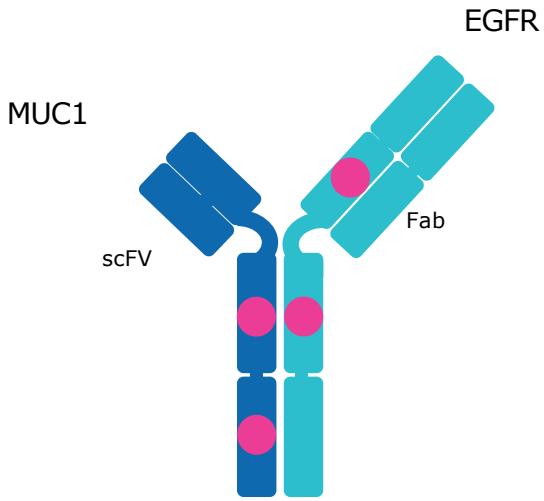
M1231 (MUC1-EGFR Bispecific ADC)

Potential for First-In-Class – 1Q21 First In Man Planned

- First bispecific ADC targeting MUC1 & EGFR
- Combines next generation technologies; stable site-specific conjugation with nnAA, optimized positioning of a proprietary hemiasterlin payload, SEED antibody structure
- Increased uptake into tumor cells, leading to improved preclinical efficacy compared to monospecific variants
- Potentially reduced risk for on-target toxicities based on limited target co-expression in normal tissues
- First in man study planned in 1Q2021 with focus on NSCLC & esophageal squamous cell carcinoma



Sutro's Next Generation Tumor Targeting Immunostimulatory ADC

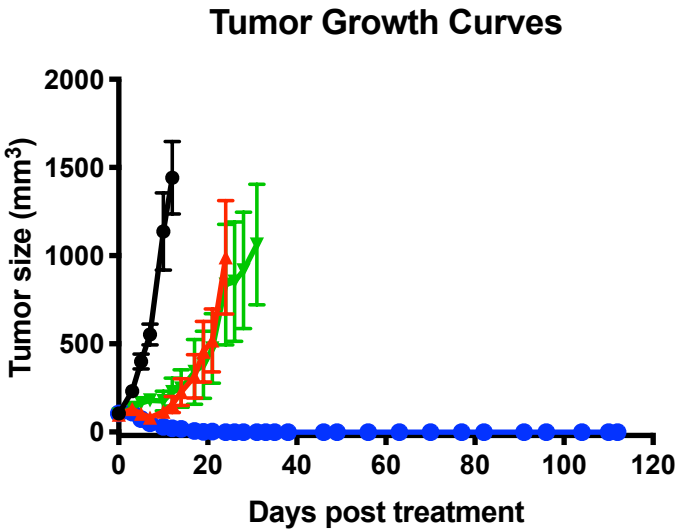
iADC

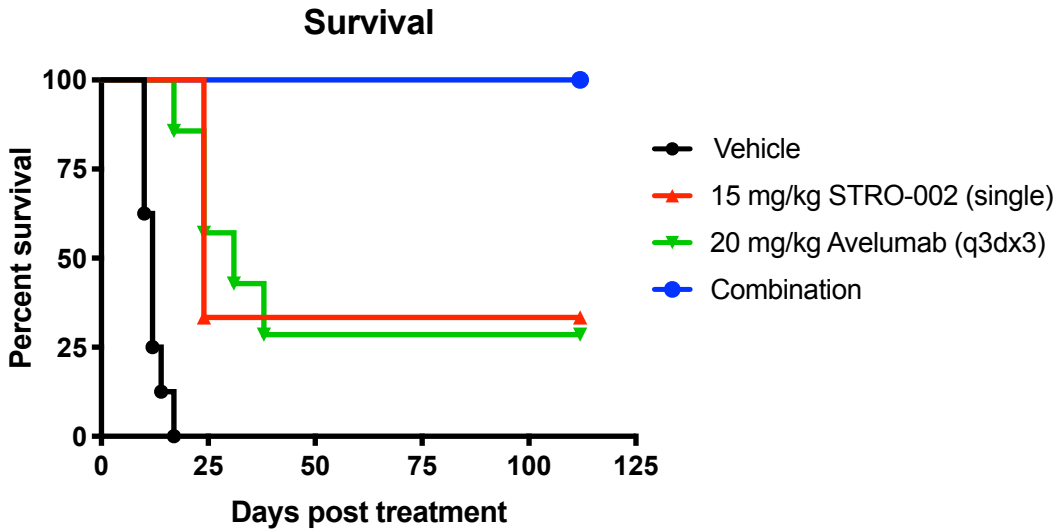
– Off the shelf, systemically administered *in situ* immunization

- Breakthrough technology for dual conjugated immunostimulatory antibody drug conjugate
- Designed and enabled using Sutro's XpressCF+™ platform
- Enables simultaneous and precise tumor targeting of a cytotoxin and a novel toll-like receptor (TLR) agonist with systemic delivery
- Novel design intended to prime an adaptive anti-tumor response in a monotherapy
- Potential to reprogram the patient's tumor microenvironment and generate protective anti-tumor immunity

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

STRO-002 in combination with Avelumab resulted in complete remission of animals bearing MC38-FolRα tumors

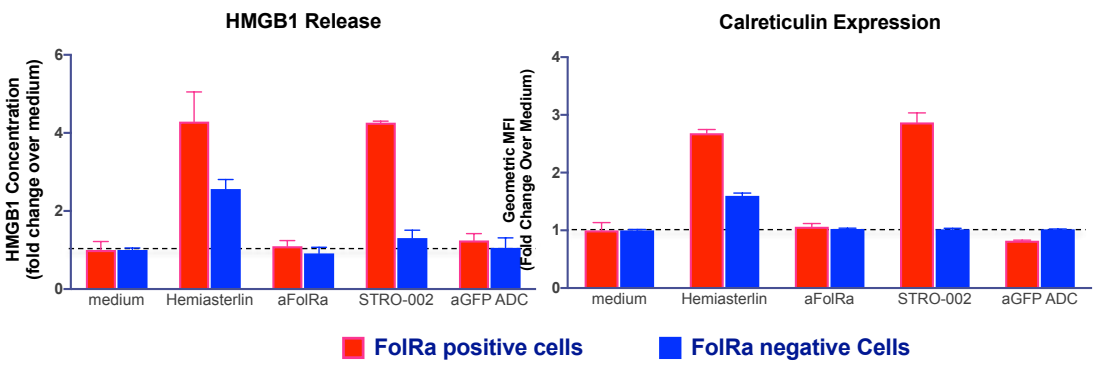




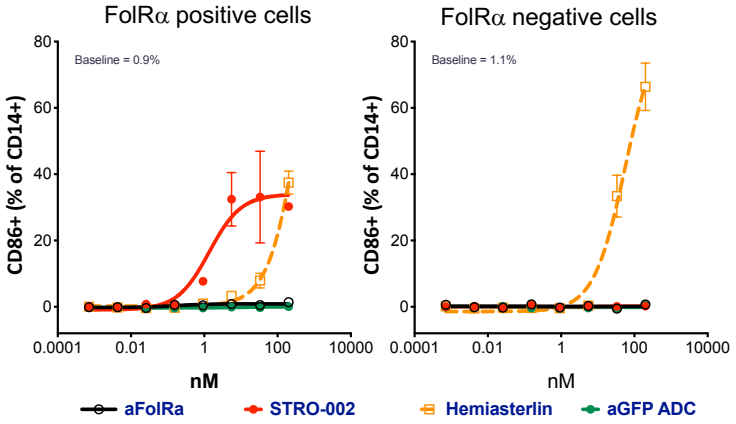
- Markedly enhanced anti-tumor activity observed with combination treatments compared to either single agent alone
- Combination treatment extended median survival compared to single agent therapy
- Combination treatment significantly increased infiltration of CD8+ T Cells into tumor; T cell infiltration not seen with either single agent therapy

STRO-002 Stimulation of The Immune System is Mediated by Hemiasterlin and is FolRα Dependent

STRO-002 Induces Immunogenic Cell Death



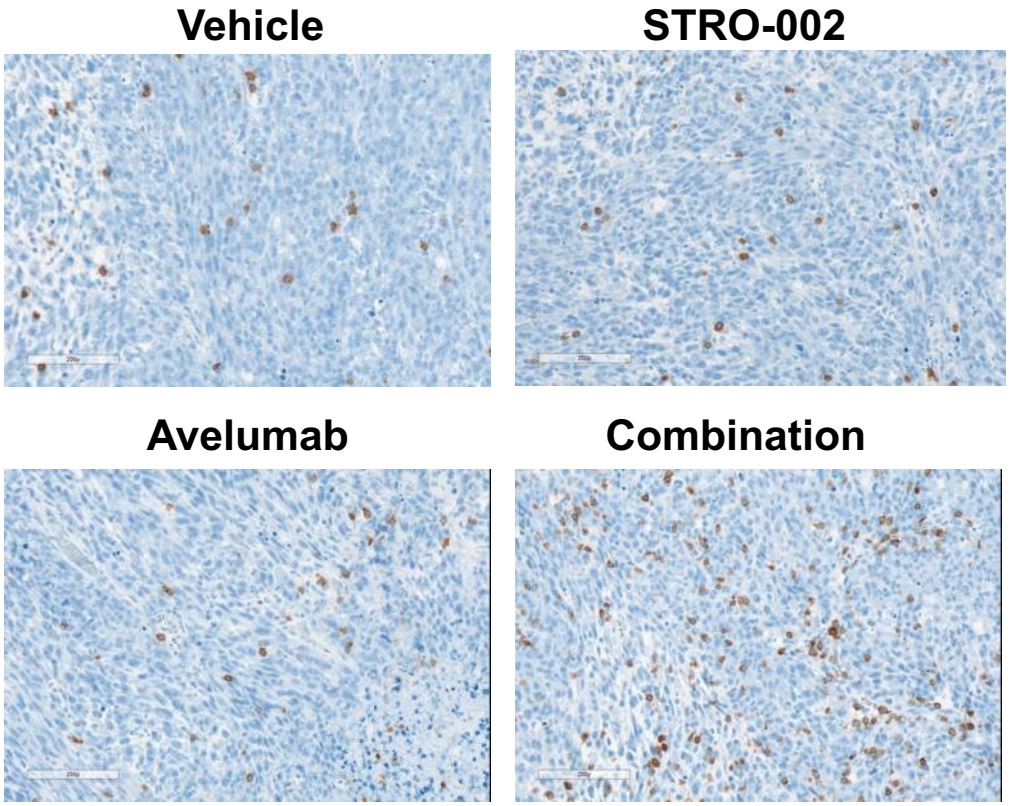
STRO-002 Activates Monocytes

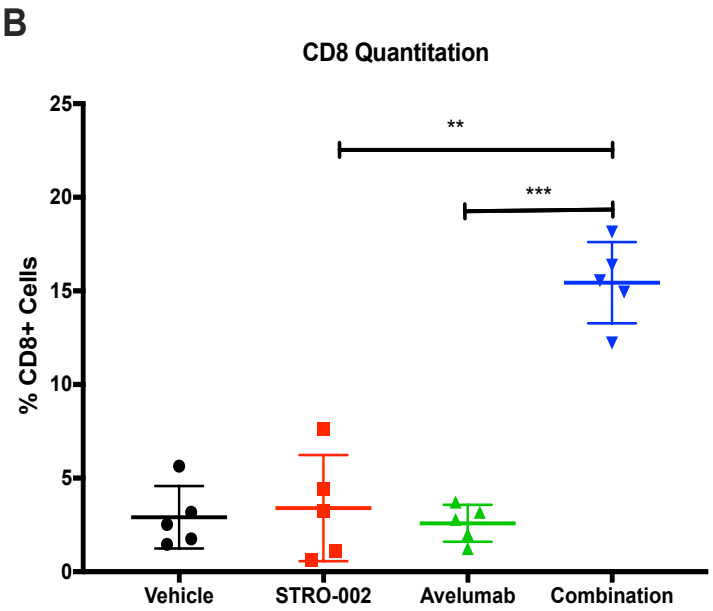


- Tumor targeted immunogenic cell death (ICD) induces activation of monocytes in the tumor microenvironment
- Calreticulin and HMGB1 are markers of ICD and can enhance APC activation, recruitment and tumor antigen uptake
- Tumor ICD promotes innate immune activation and synergy with PD1 checkpoints

STRO-002 Induces ICD Markers only in FolRα Positive Cells

Combination treatment significantly increased infiltration of CD8 T Cells





- Representative images of CD8 staining (brown) with nuclei counterstain (blue) (left) and quantification of percent CD8 positive cells (right).
- Combination treatment resulted in a striking increase in CD8 T cell infiltration into the tumor microenvironment.

18-FR-M2

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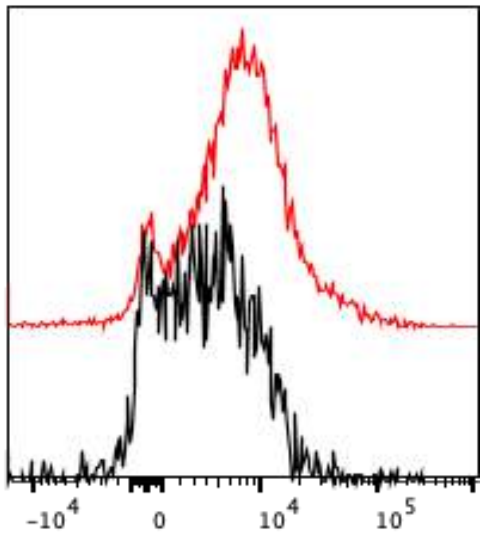
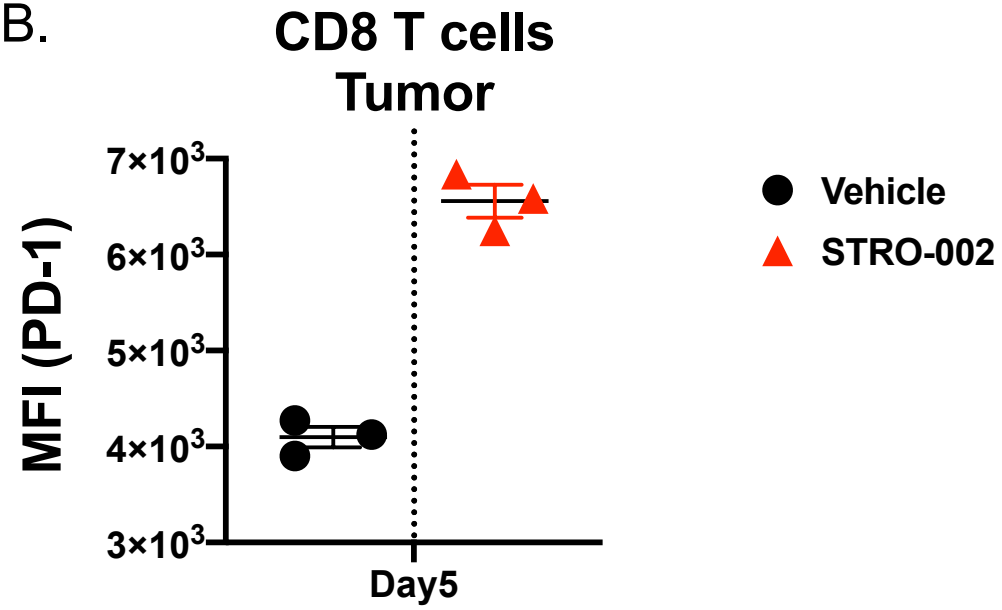
Increased PD-1 expression in response to STRO-002 treatment supports enhanced efficacy with Avelumab

A.

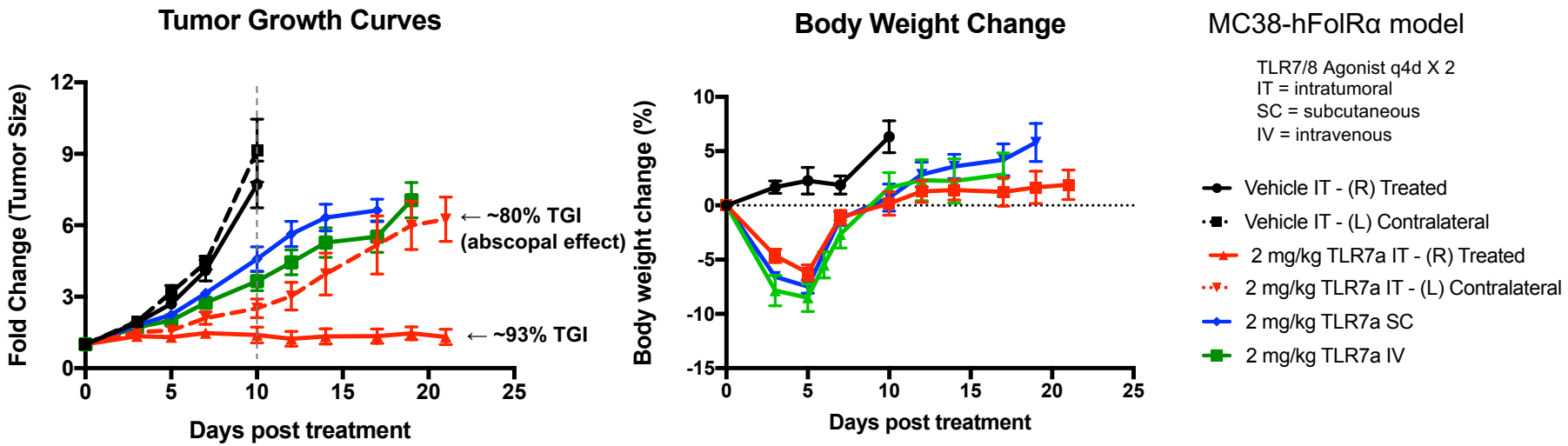


B.



20-FRDC-M1

Systemic Administration of TLR7/8-agonist Resulted in Tumor Growth Inhibition but with Transient BW loss



- Anti-tumor activity of TLR7/8 agonist : IT dosing > IV or SC (systemic) dosing.
- Transient BW loss during 1st week in all treated groups (IT, IV, and SC dosing).

Limitations of IT dosing – leakage and systemic exposure - drive, at least in part, efficacy but also toxicity.

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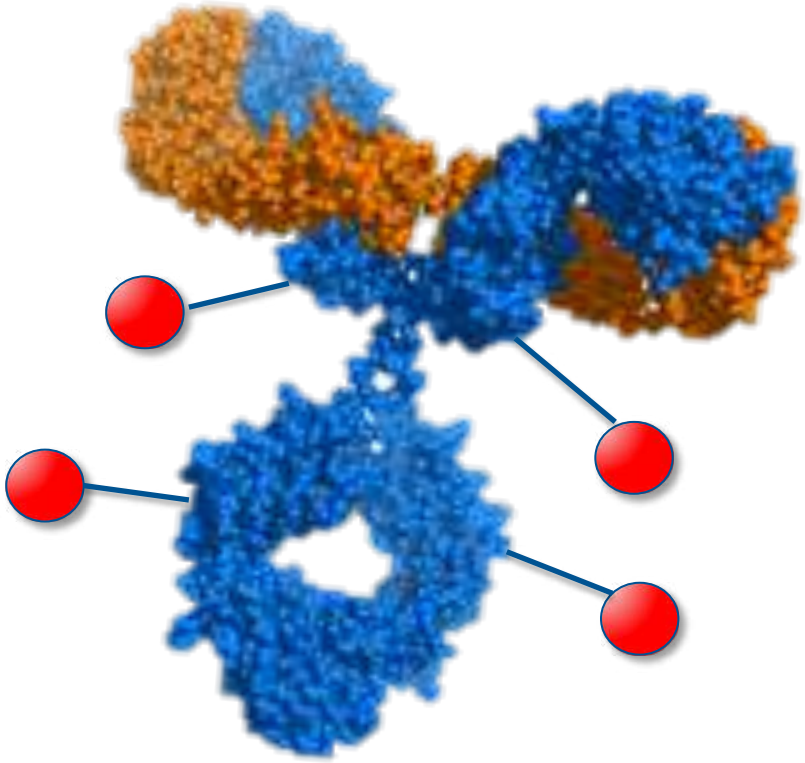
Sutro's FolRα ISAC product concept promises to preserve efficacy and improve tolerability



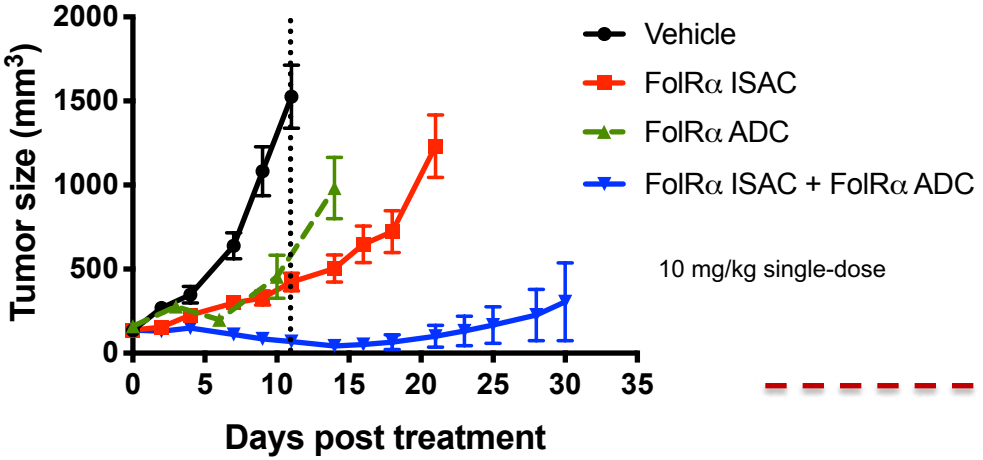
FolRα ISAC
(Immune Stimulator Antibody Conjugate)

FolRα Ab conjugated to TLR7/8 agonist via cleavable linker

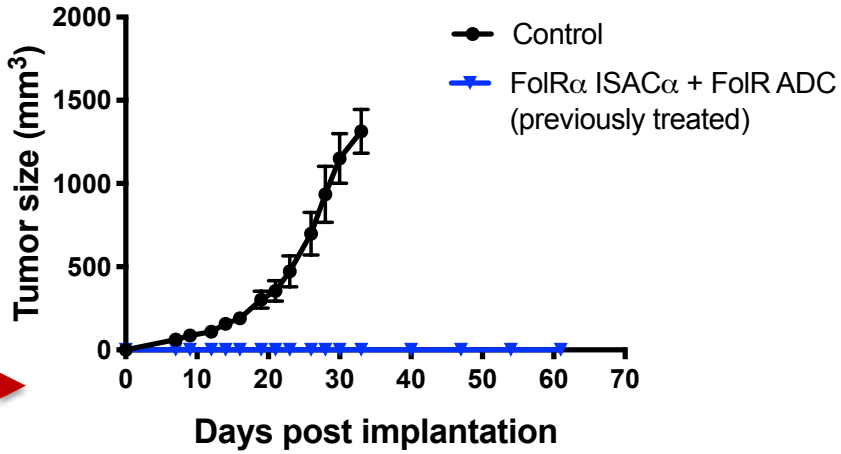
Site-Specific Conjugation Technology Allows For Optimization of Pharmacological Properties

Combination of FolRα ISAC and FolRα ADC Results in Tumor Regressions and No Tumor Growth Upon Re-challenge

Part 1: Evaluation of ISAC/ADC combination

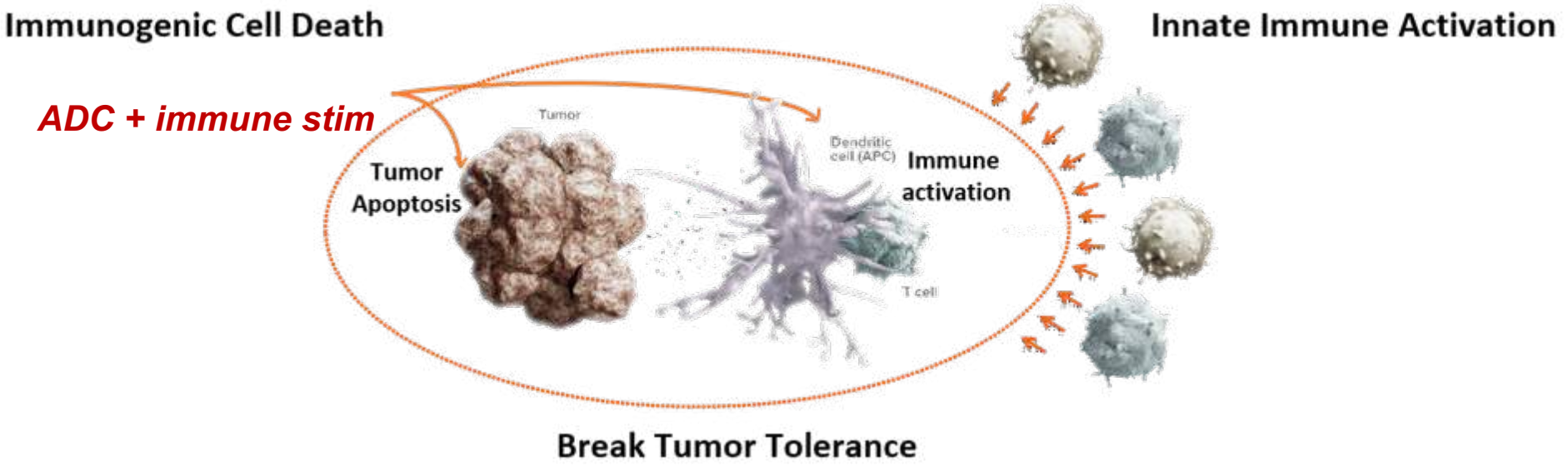


Part 2: Tumor re-challenge in ISAC/ADC tumor-free mice (no additional treatment administered)



- FolR*α* ISAC (immune stimulator antibody conjugate) product concept supported by impressive *in vivo* anti-tumor activity and good tolerability with 1/40th dose of free TLR agonist
- Combination of ADC and ISAC gave greater anti-tumor response with evidence of regressions.
- No tumor re-growth in survivors upon tumor re-implantation, suggest FolR*α* ISAC/ADC-related innate and adaptive immune mechanisms drive anti-tumor response.

Combining ADC and Immune Agonists Can Break Tumor Tolerance and Elicit Protective Immunity in a single therapy

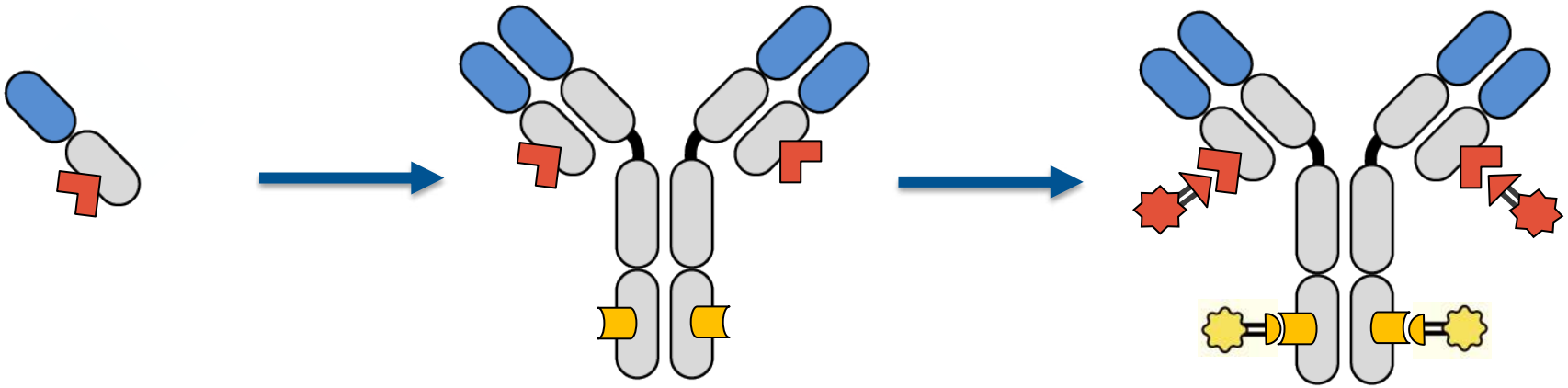


iADC approach can elicit protective tumor immunity by two mechanisms:

1. Tumor targeted ***immunogenic cell death***
   - Induce tumor killing that alerts immune response
2. Directly ***activate immune cells*** (i.e. dendritic cells)
   - Demonstrates tumor immunity in vivo

Some patients will require multiple therapies to enable cancer immunity, an iADC combines multiple MOAs into a single tumor targeted therapy

Double conjugation process; two nnAA species

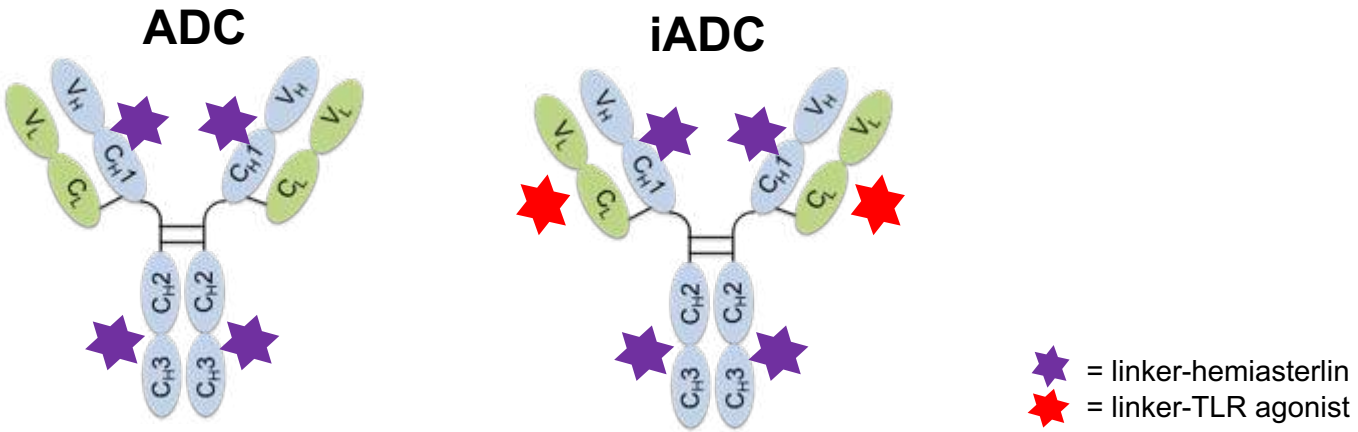


Nonnatural amino acid incorporated into a prefabricated LC

Antibody with 2 different nonnatural amino acids

One-pot conjugation with 2 orthogonal chemistries

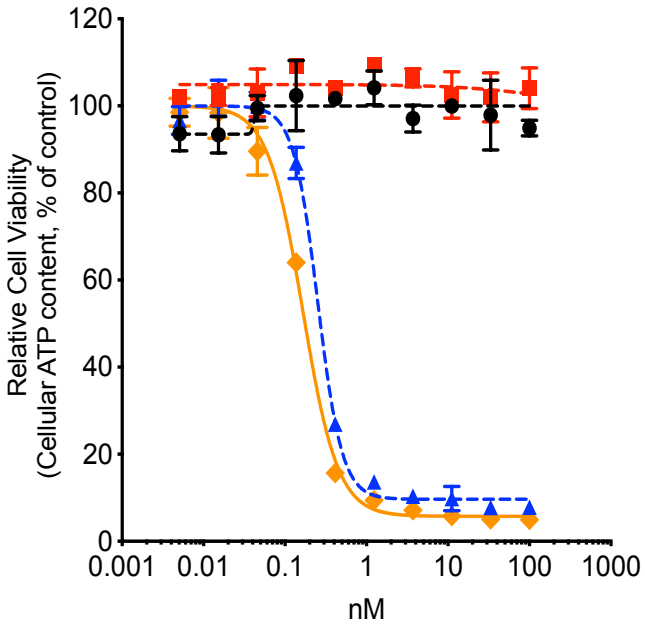
ADC to iADC:
Combining Synergistic Mechanisms in a Single Molecule



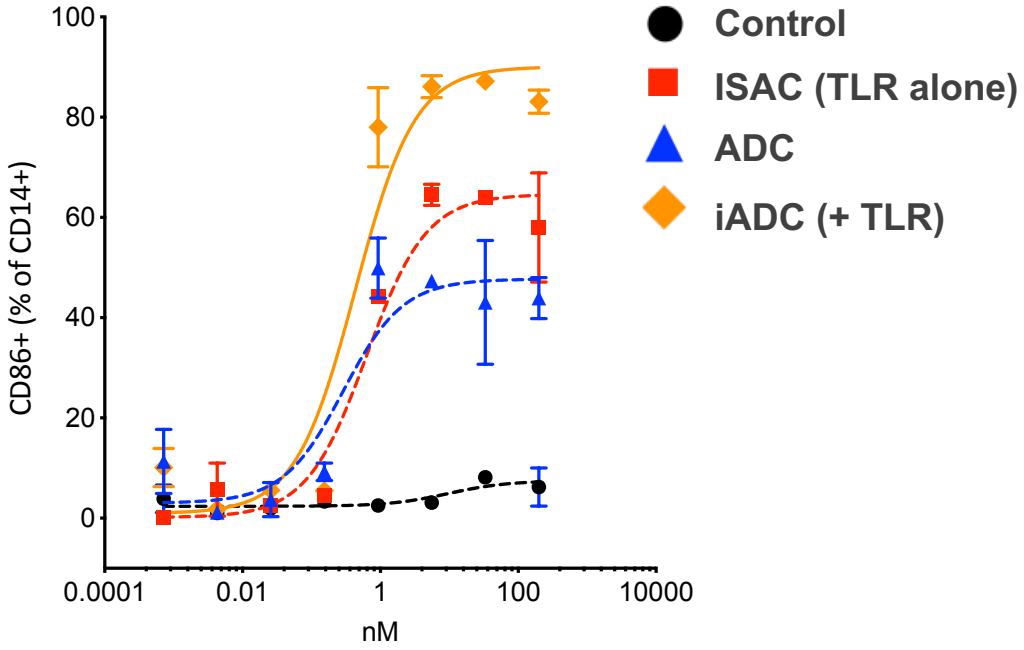
- **Specific conjugations to specifically positioned sites**
  - Optimal stoichiometry (absolute DAR and ratio of each payload)
- **Enables optimal <u>efficacy</u> and <u>tolerability</u>**
- **Process options enabled allowing use of single nnAA or two different nnAAs**
  - Both process paths result in a single molecular species iADC

iADC combination molecule maintains FolR+ cell killing and provides enhanced immune cell activation

Tumor Cell Killing
KB (FolRa positive)

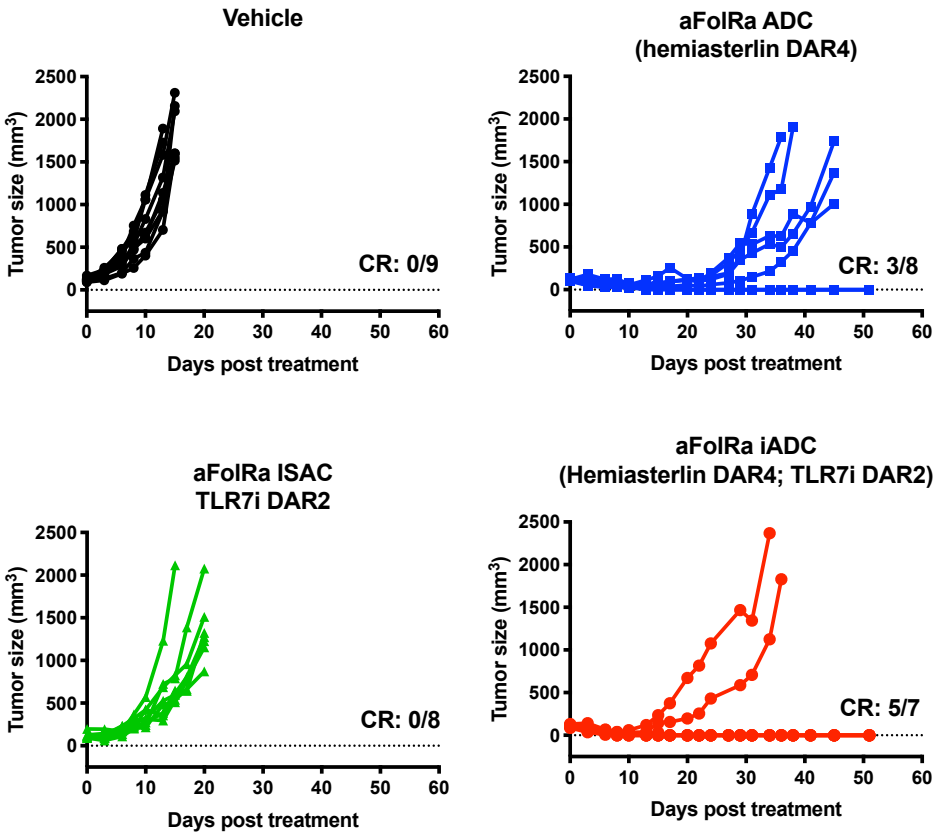


Monocyte Activation
Human immune cells + KB cells

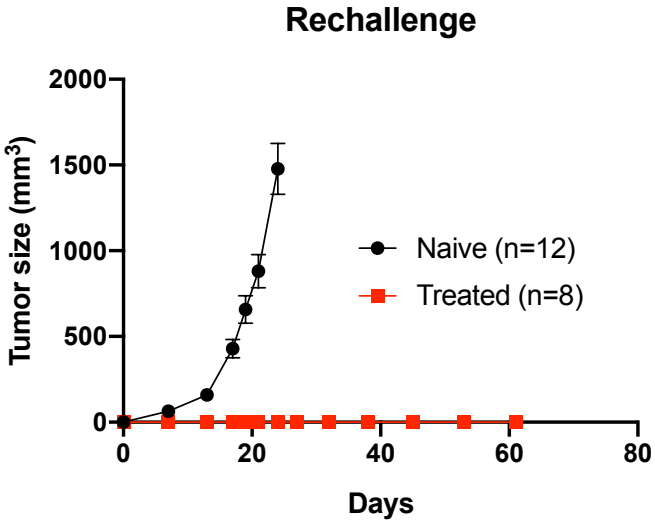


iADC combines targeted tumor killing and innate immune stimulation in a monotherapy

Superior Anti-Tumor Memory Response with Single Dose of a Prototype 4+2 FolRα iADC



All treated animals that achieved CR were re-challenged with MC38-hFolRα cells



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

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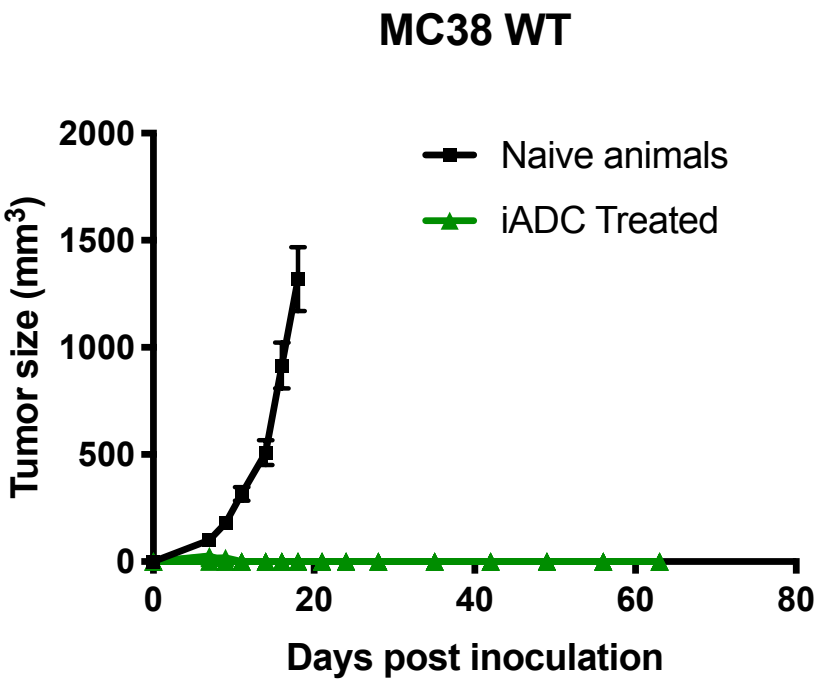
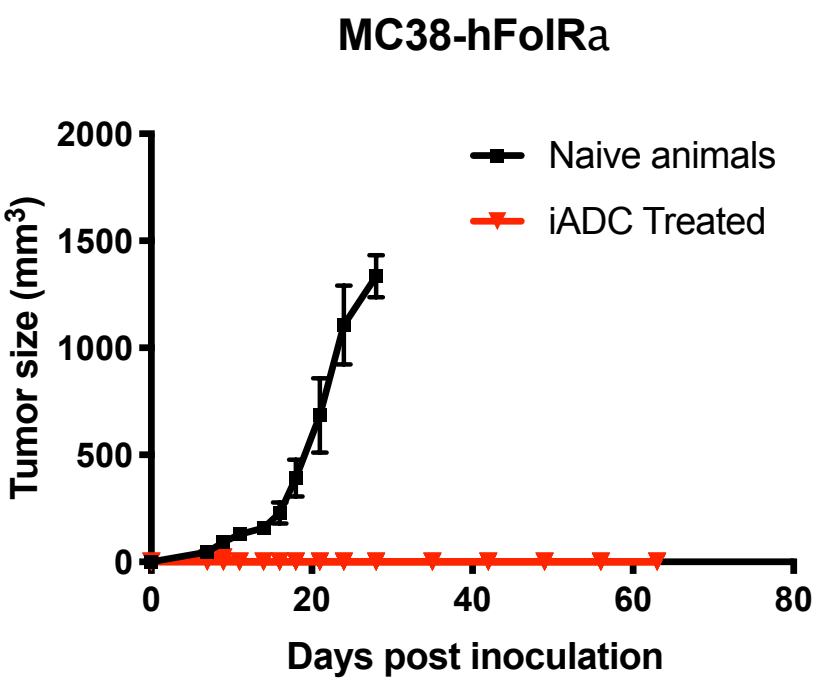
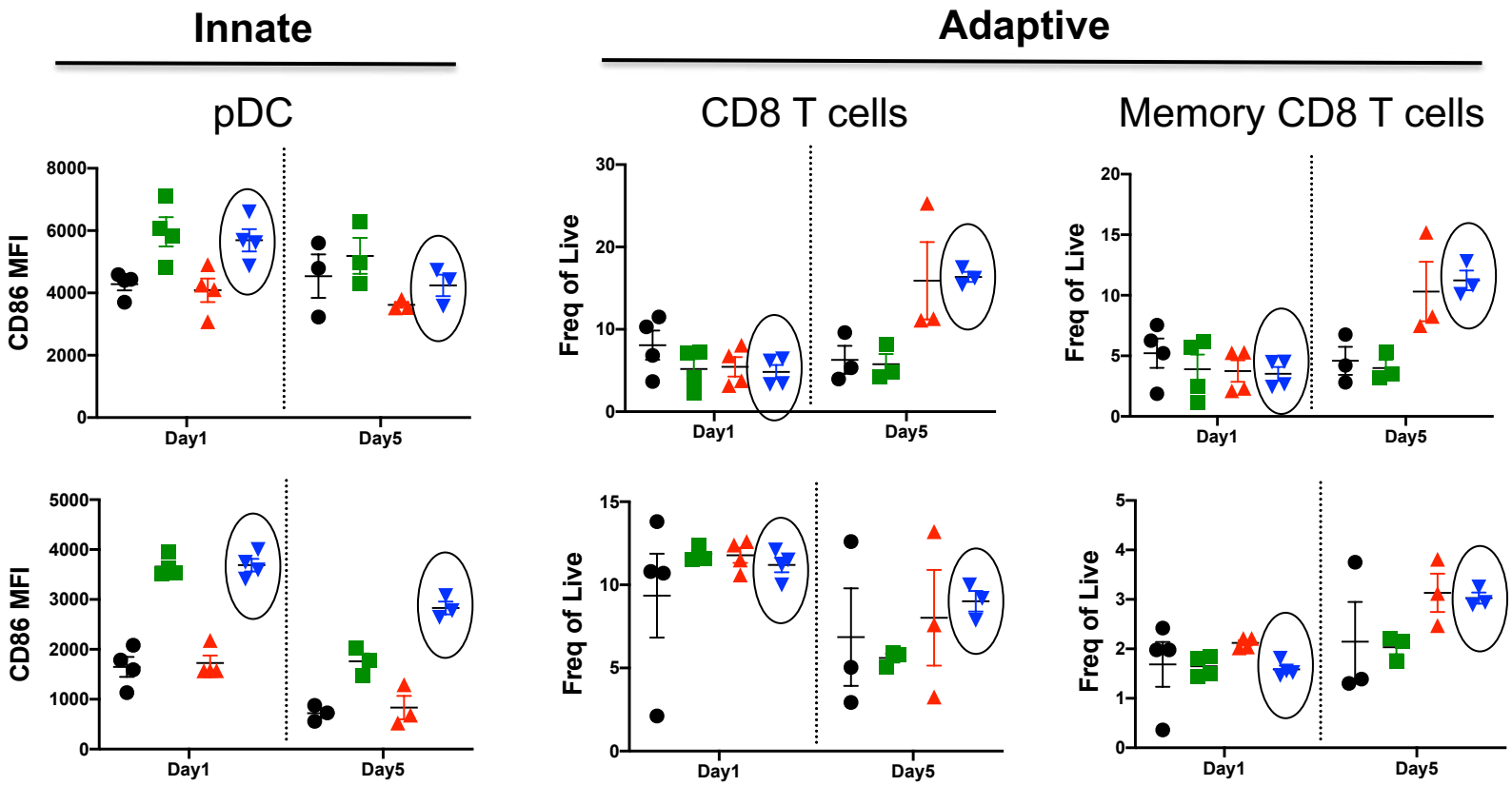
FolRα iADC exhibits durable anti-tumor immunity and evidence of epitope spreading





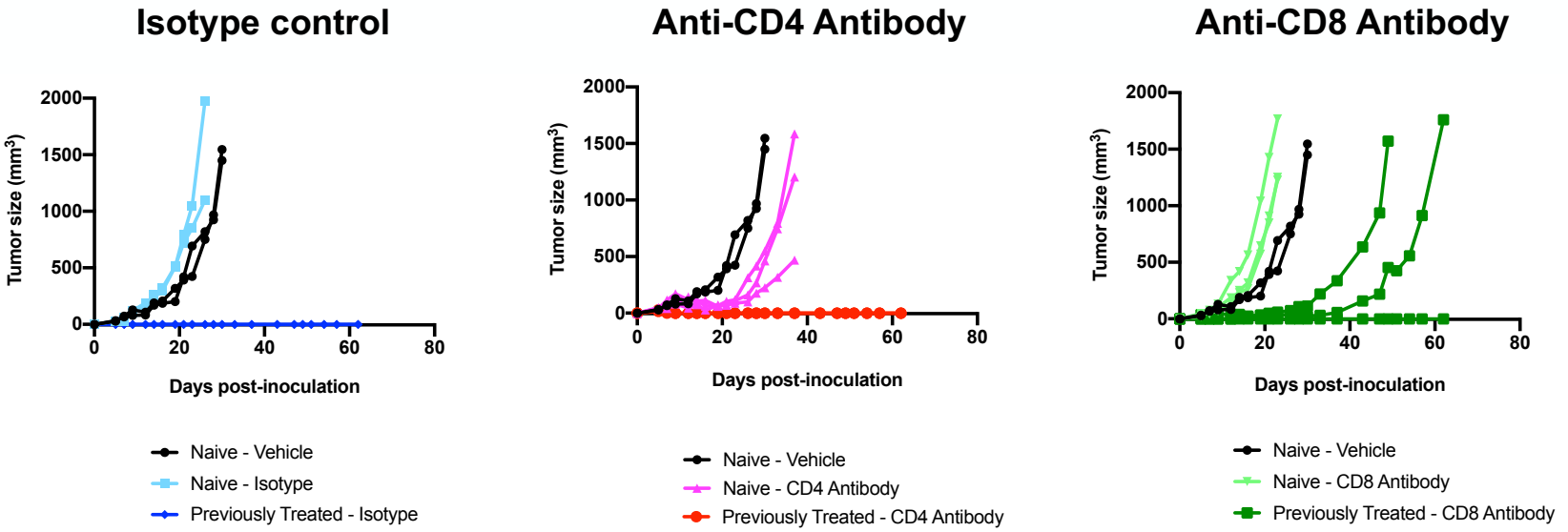
Animals treated with FolRα iADC develop durable anti-tumor immunity against MC38 parent and MC38-hFolRa expressing tumors

FolRα iADC engages innate and adaptive immune compartments in MC38-hFolRα tumor bearing mice



Single 10 mg/kg dose ● Vehicle ■ ISAC ▲ ADC ▼ iADC

Immunodepletion study suggests CD8+ T cells play a key role in mediating FolRα iADC induced anti-tumor immunity

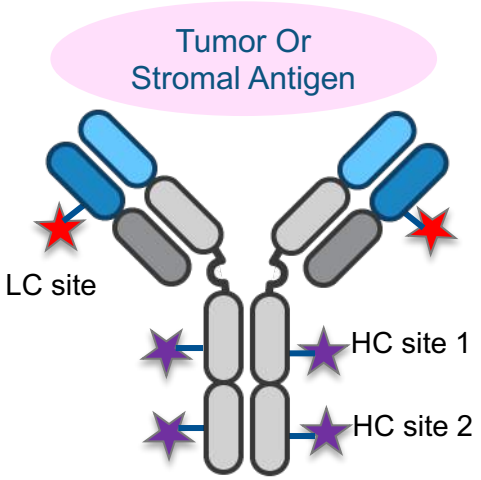


- **Without CD8+ T cells, tumor growth was restored after rechallenge in 2/3 animals previously treated with FolRα iADC**
- **Protective immunity was maintained in previously treated mice that received isotype control and anti-CD4+ blocking antibodies**

Molecular Formats to Target Multiple Mechanisms

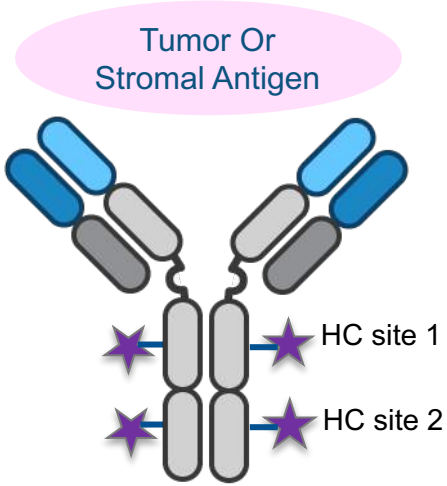
Conjugated Antibody Platform

iADC



Site specific 2+2 or 2+4
dual drug conjugate
Cytotoxic agent + TME Modulator

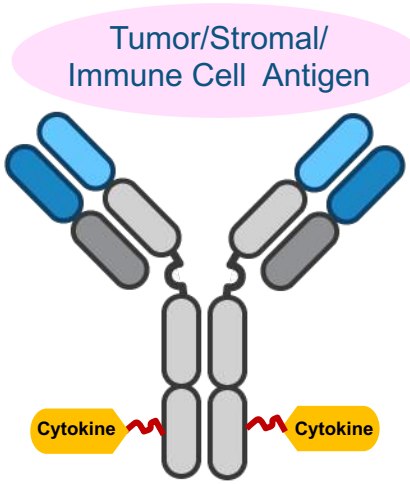
ISAC



Site specific DAR2 or DAR4
drug conjugate with TME
modulator

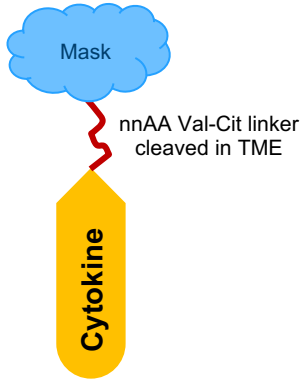
Cytokine Platform

Immunocytokine



Cytokine-antibody fusion or
chemical conjugate targeting
cytokine to TME

Masked Cytokine



Masked cytokine
targeting functional
cytokine to TME

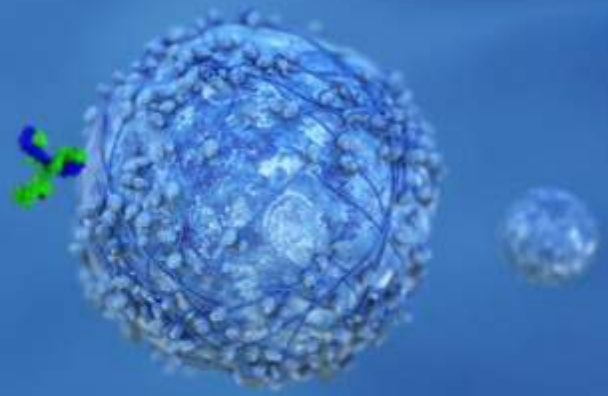
A new precedent

Turning a tumor into a vaccine *in situ*…..

- **TME-targeting of conjugated combination payloads can produce a sustained and robust anti-tumor immune response that bridges innate and adaptive immunity**

- **Hemiasterlin that stimulates immunogenic cell death, provides strong responses as a conventional ADC and synergistic stimulation of memory responses when paired together with TLR agonists**

- **Utilizing ADCs to deliver immune modulators opens a new door to provide systemic and tumor targeted IO molecules**



Thanks!

thallam@sutrobio.com

Headquarters
310 Utah Ave.
Suite 150
South San Francisco, CA 94080
Phone: 650.392.8412
Fax: 650.872.8924
Web: www.sutrobio.com

Manufacturing Plant
870 Industrial Road
San Carlos, CA 94070

Additional Offices
240 E. Grand Ave
South San Francisco, CA 94080

SUTRO BIOPHARMA