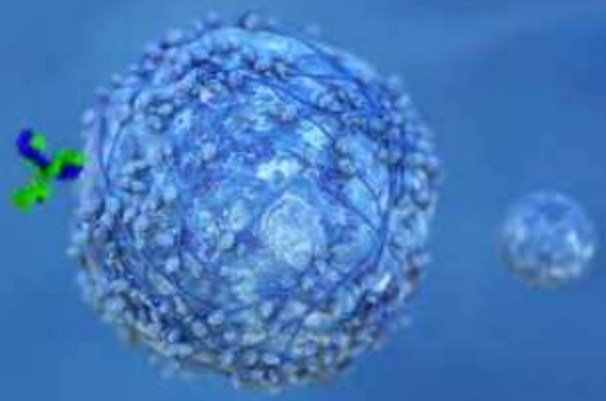

Tumor Targeted Immunostimulants; A Promising Approach to *In Situ* Immunization

Trevor Hallam CSO

March 4, 2020

10th ANNUAL WORLD adc LONDON 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.
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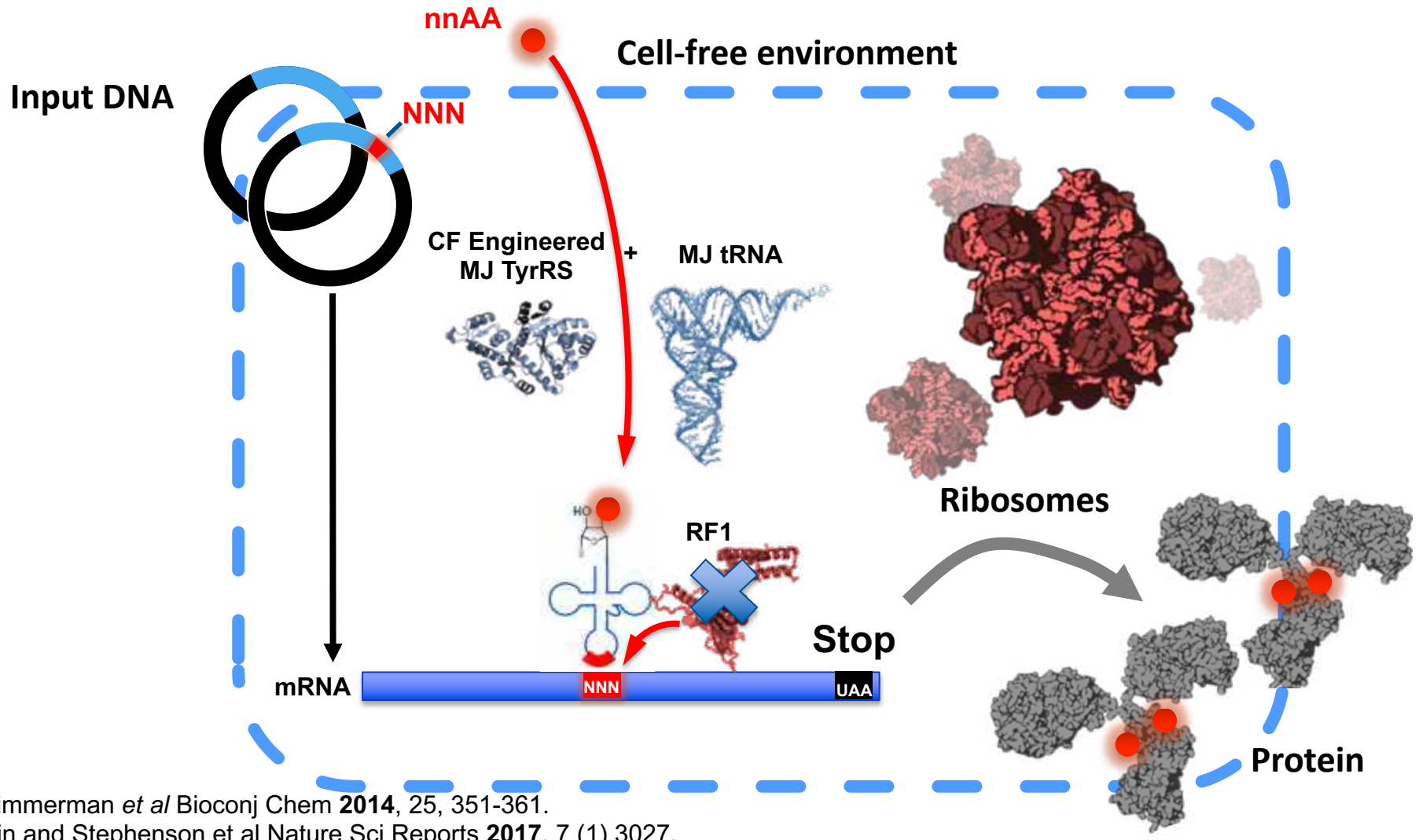
Sutro Clinical Pipeline
Owned and Partnered Programs

PROGRAM	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2/3	MILESTONE	COMMERCIAL RIGHTS
FolRα - targeting ADC STRO-002			Ovarian and Endometrial Cancer		Additional Clinical Data Expected in 1H20	SUTRO BIOPHARMA Worldwide Rights
CD74 – targeting ADC STRO-001			Multiple Myeloma (Orphan Drug Designation); Lymphomas: DLBCL, Mantle Cell, Follicular		Additional Clinical Data Expected in 1H20	
Multiple Oncology & I/O Programs			Oncology			
BCMA – targeting ADC CC-99712			Multiple Myeloma		Trial Enrolling BMS Worldwide Rights	Bristol-Myers Squibb Company (a)
Bispecific ADC			Oncology		GMP supply in process	EMD SERONO (b)
Cytokine Derivatives			Oncology & Autoimmune			MERCK
			Oncology			
PD1-LAG3			ImmunoOncology			SUTRO BIOPHARMA (a)
BCMA-CD3			Multiple Myeloma			
PD1-TIM3			ImmunoOncology			Bristol-Myers Squibb Company

(a) BMS automatically obtained worldwide rights to the BCMA - targeting ADC---the first collaboration product candidate to achieve IND clearance in the United States. Additionally, there are three programs to which BMS currently has ex-U.S. rights and Sutro currently has U.S. rights. Sutro is eligible for milestones and royalties on each of the four product candidates.

(b) EMD Serono is the U.S. healthcare business of Merck KGaA, Darmstadt, Germany.

Sutro's XpressCF+™ Platform: Incorporation of Non-natural Amino Acids



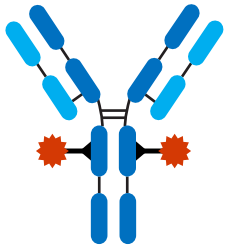
Zimmerman *et al* Bioconj Chem **2014**, 25, 351-361.
Yin and Stephenson et al Nature Sci Reports **2017**, 7 (1) 3027.

Wholly Owned Manufacturing Advantage – XpressCF™

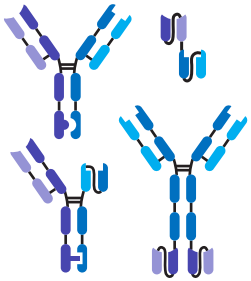
Accelerating the development of potential best-in-class protein therapeutics

Potential Best-in-Class Protein Therapeutics

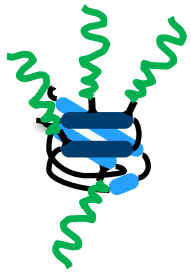
- Rapid generation of diverse protein structures enables empirical assessment and selection of optimal candidates
- Can accelerate time to IND by 9 - 15 months compared to conventional technologies
- Homogeneous drug products generated precisely according to specifications



ADCs



Bispecifics



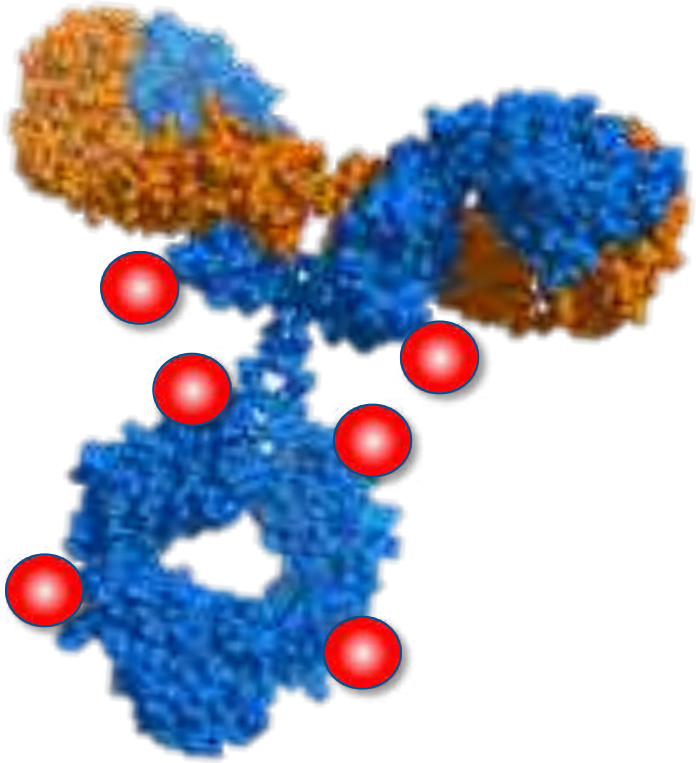
Cytokine-based I/O Therapeutics

Differentiated Attributes of XpressCF™

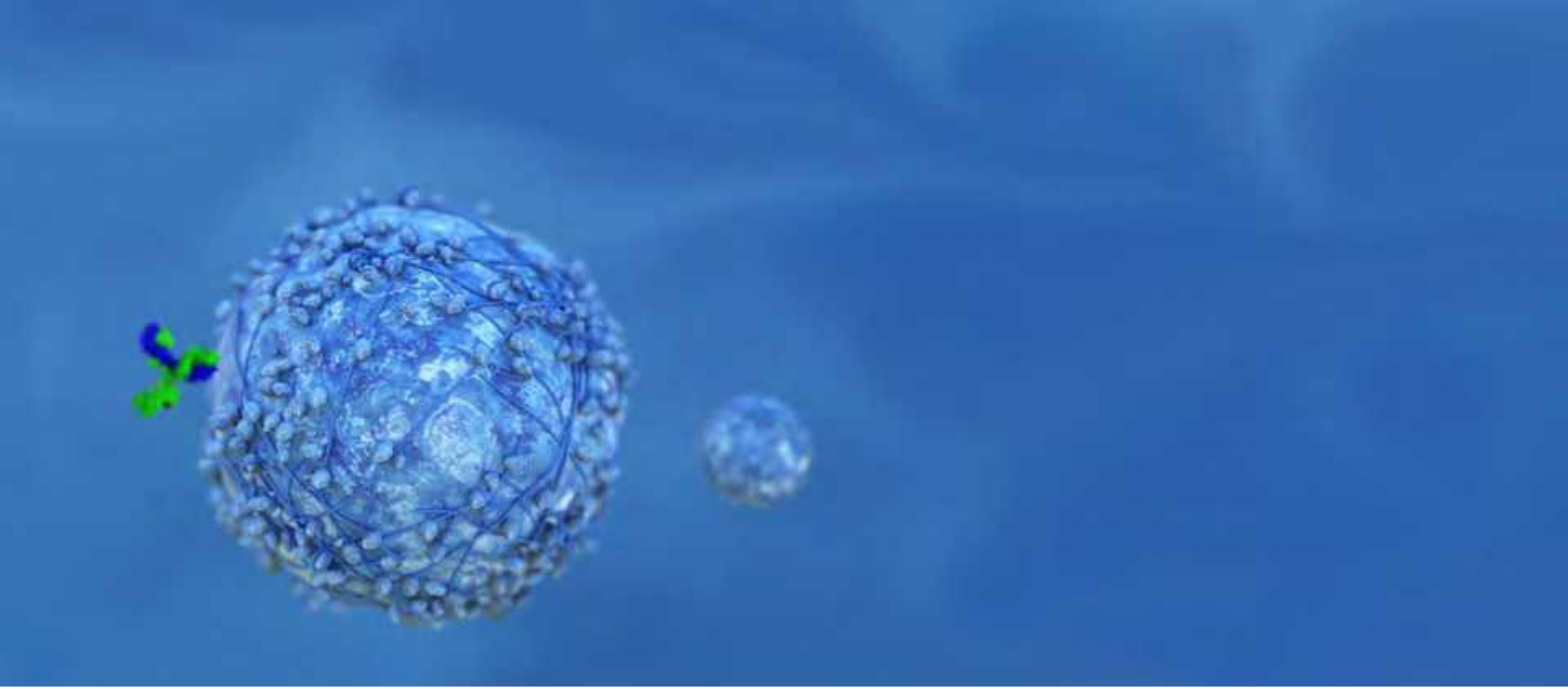
- Cell-free protein production process generates homogenous products from DNA sequences in <24 hours
- Consistent production method used across scale-up — from discovery to commercial manufacturing
- Enables site-specific, efficient and complete conjugation to non-natural amino acids

Sutro Platform Enables Rapid & Precise Optimization of single species ADCs

- **ADCs produced in a few days**
- **Structure-Activity optimization allows screening for**
  - Optimal Antibody discovery
  - Sites of drug-linker attachment
  - Optimal combination of sites
  - Precise Drug/Antibody Ratio
  - Refinement of linker and warhead attributes
- **Good product stability**



Specific Conjugation-Optimized Sites Drives Superior Therapeutic Index with First and Best-in Class potential



STRO-002: FolRα ADC

Potential Best-in-Class ADC for Ovarian and Endometrial Cancers

STRO-002: Overcoming Therapeutic Window Limitations of 1st Generation ADCs

STRO-002 Properties	Implications for Best-in-Class Potential
• Homogeneous ADC product generated from Sutro's XpressCF™ platform.	• Potential for improved therapeutic index through homogeneous delivery of cytotoxin to tumor.
• Optimized cytotoxin positioning and consistent drug-antibody ratio (DAR = 4)	• Many designs tested to identify STRO-002, the candidate with potential for best potency and safety
• Potent and Sutro proprietary hemiasterlin-derivative warhead	• Efficacious, potent killing of tumor cells
• Cleavable linker warhead designed for optimized pharmacology	• Rapid clearance of toxic catabolite **after** release & cell killing in tumor; potential for improved safety

No ocular toxicity observed in NHP study

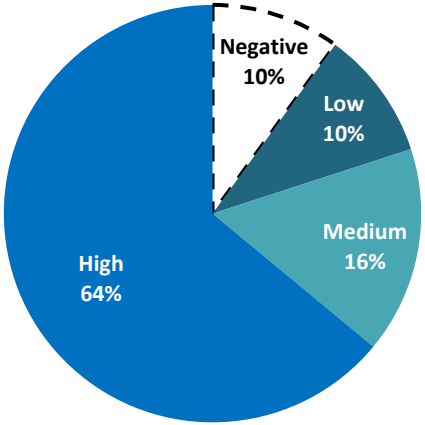
STRO-002: Targeting FolRα in Ovarian and Endometrial Cancers

FolRα

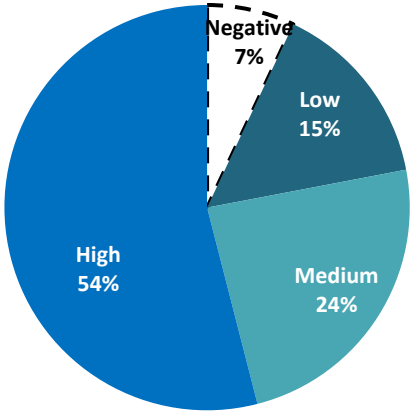
- ✓ Clinically validated target + site directed conjugation resulting in homogeneous ADC
- ✓ Expressed on a variety of tumor types
- ✓ Limited expression in normal tissue

FolRα expressed in more than 90% of evaluated ovarian and endometrial cancer tissue samples[(a)]

Ovarian



Endometrial

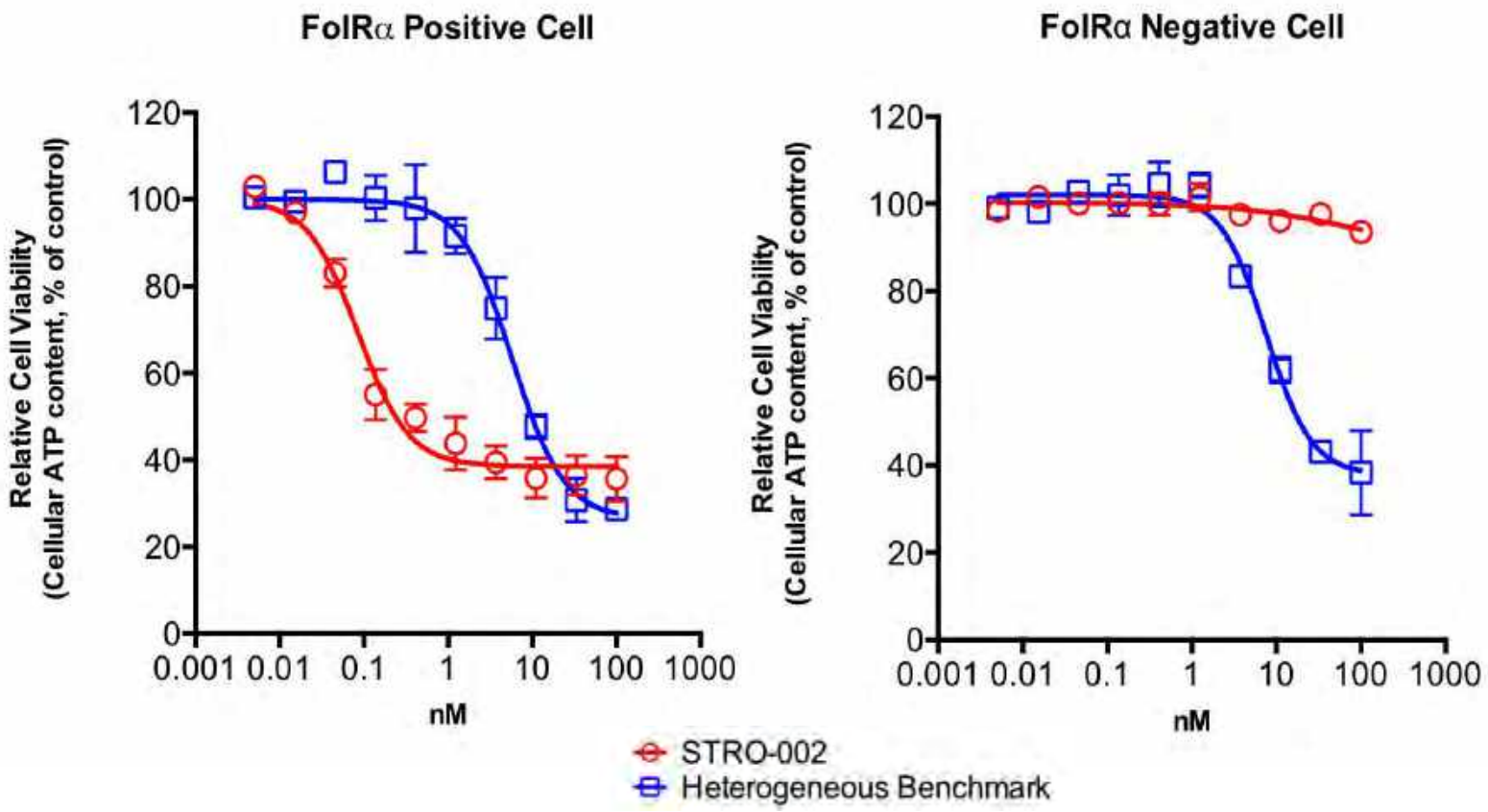


FolRα Expression Appears to Correlate with Disease Progression in Ovarian Cancer

(a) Source: Sutro Biopharma report, Expression Of Folate Receptor Alpha In Ovarian And Endometrial Cancer Samples, TR-TPPD-0039-V1.0, dated March 12, 2018.

STRO-002 in Ovarian Cancer

Design features facilitate improved potency and specificity



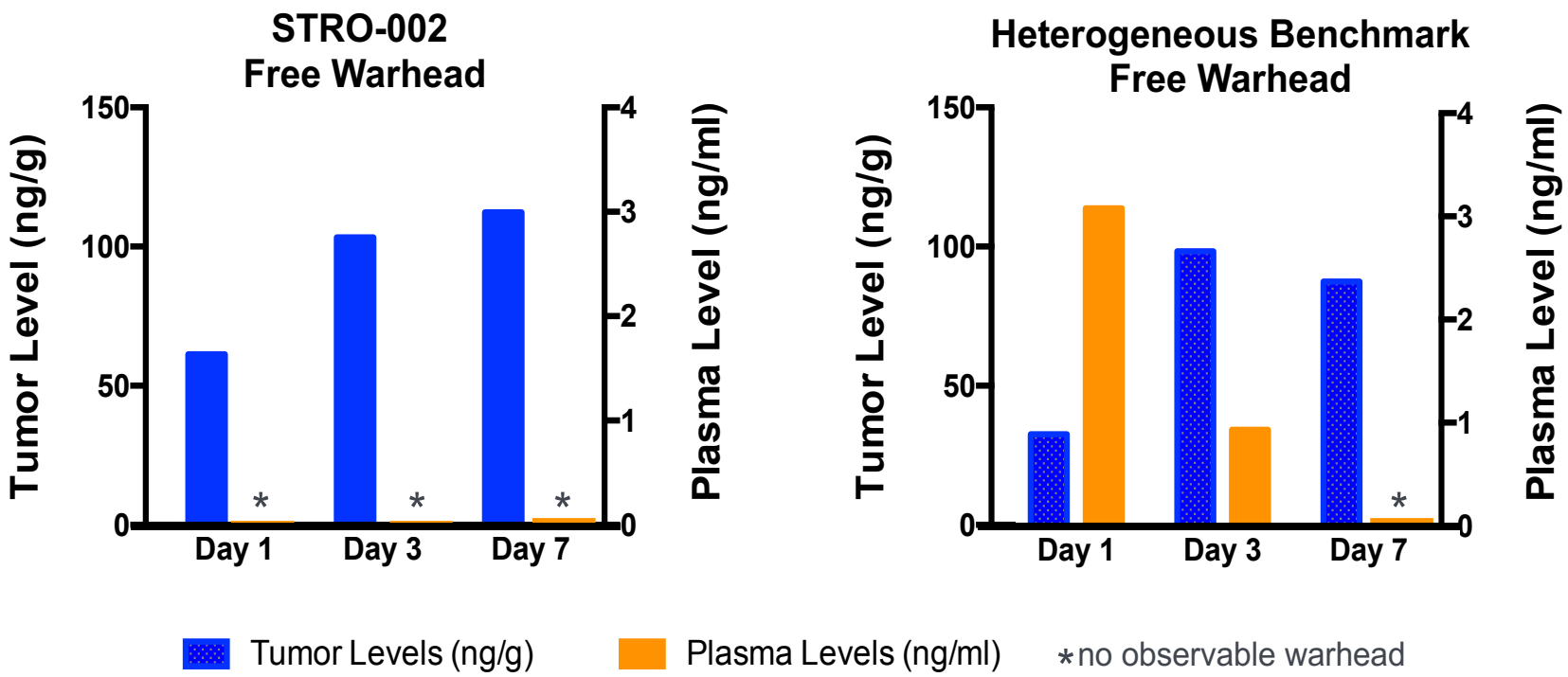
STRO-002 Demonstrates More Potent Cell Killing Compared to the Benchmark and Has Minimal Off-Target Activity

Source: Sutro Biopharma report, STRO-002 Cell Killing Compared to SP8435, TR-TPPD-0021-V1.0, dated May 18, 2018.

STRO-002: A Potentially Superior FolRα ADC

Improved stability can widen therapeutic index

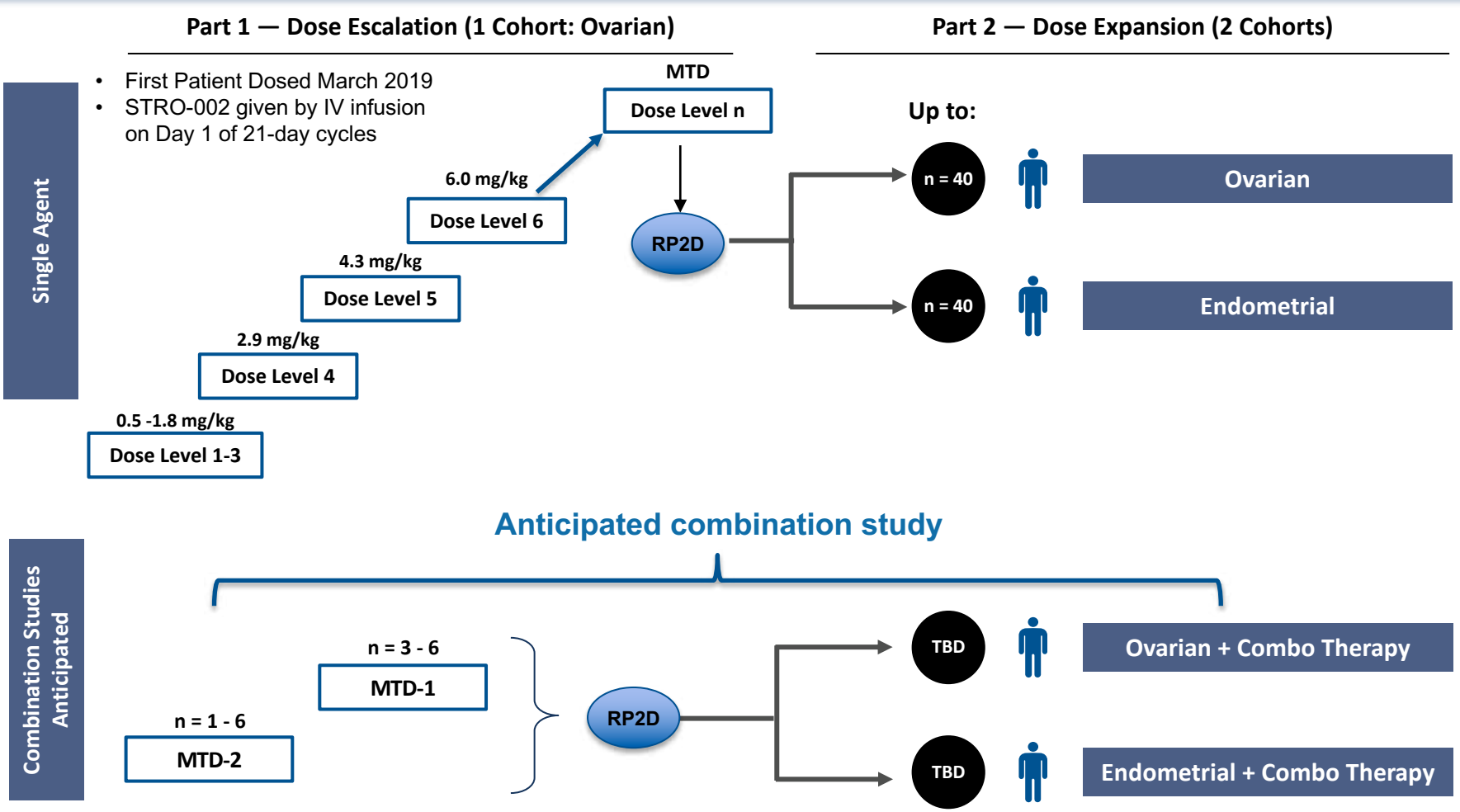
Mouse Tumor Model – Free Warhead in Tumor vs. Blood After Dosing



No Evidence of STRO-002 Free Warhead Circulating in the Blood Post Dosing
No evidence of Free Warhead Accumulation in FolRα Negative Tumors

Source: Sutro Biopharma report, In Vivo Catabolite Profiling for SP8193 and SP8435 in Tumor and Plasma, TR-PHRM-0036-V1.1, dated January 8, 2018.

STRO-002 Phase 1 Clinical Trial Design



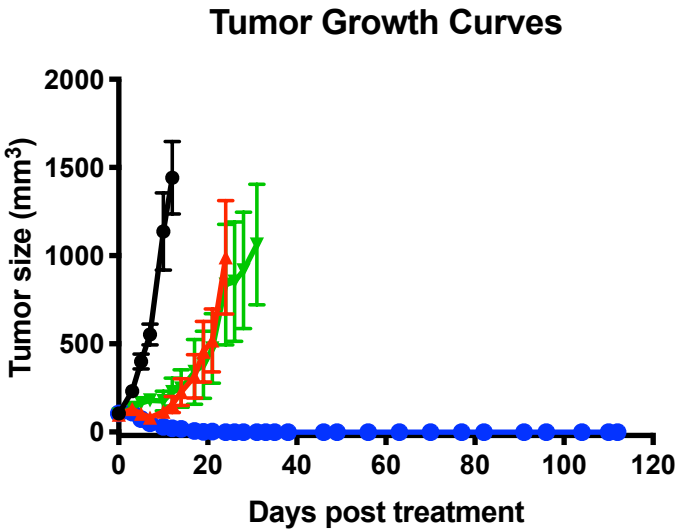
FPD in 1Q19

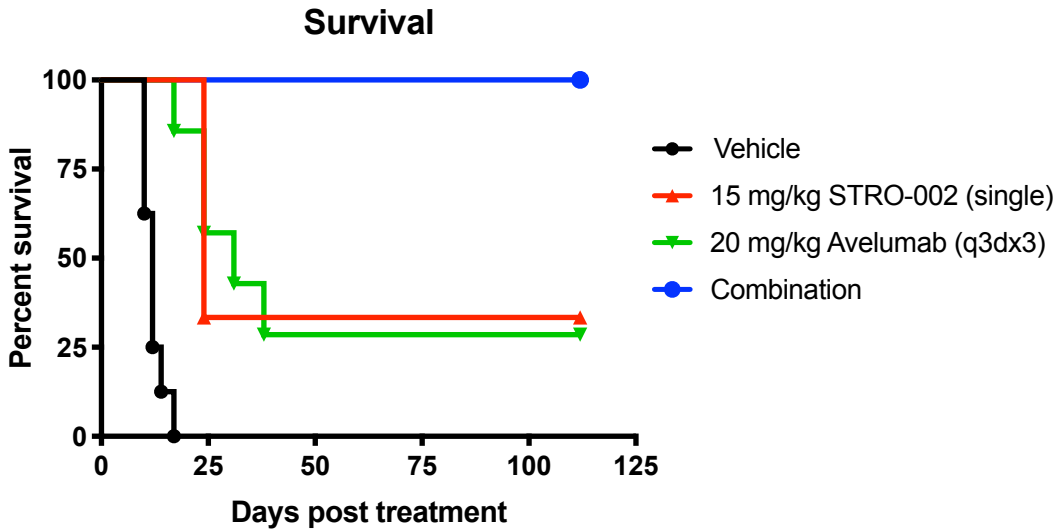
STRO-002 Phase 1 Emerging Clinical Data in Ovarian Cancer (All Comers)

- **STRO-002 has been well tolerated**
  - No DLTs or infusion reactions have been observed
  - No ocular toxicity observed; No prophylactic corticosteroid eye drops being utilized
- **MTD not yet determined**
  - Dose escalation continuing at 6.0 mg/kg
- **Preliminary evidence of clinical benefit and anti-tumor activity**
  - One confirmed PR by RECIST 1.1 (Cycle 5) with a confirmed CA-125 response
  - Five patients have stable disease per RECIST 1.1 (confirmed & unconfirmed) in first 13 patients

Data as of Oct 15, 2019
Presented at AACR-NCI-EORTC 2019

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

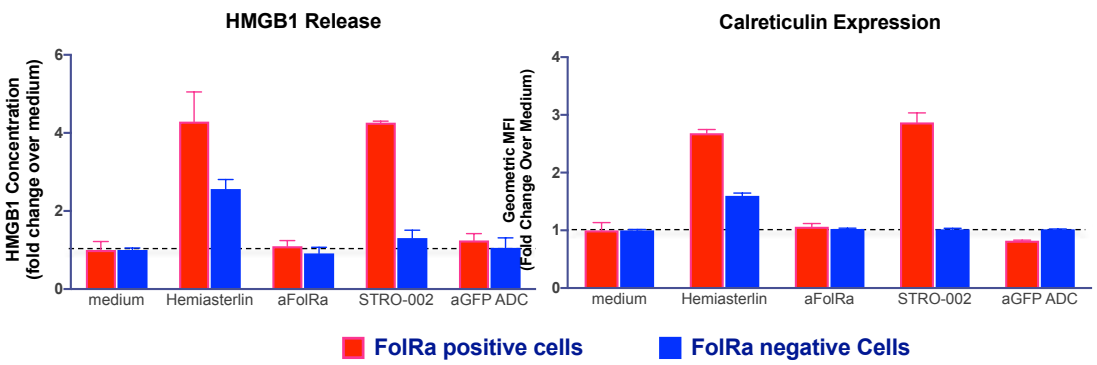




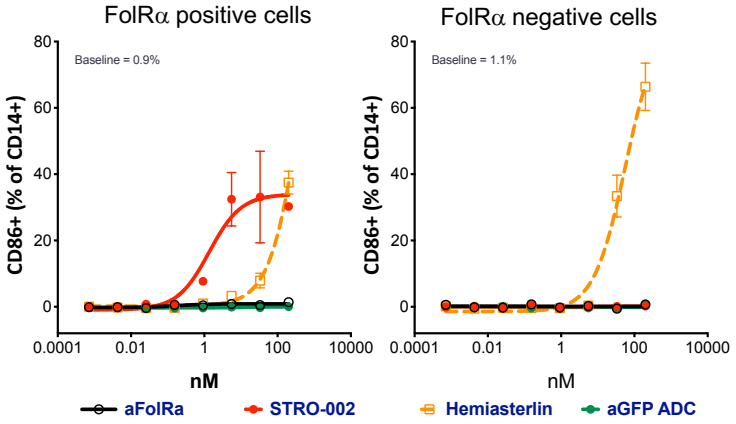
- Markedly enhanced anti-tumor activity observed with combination treatments compared to either single agent alone
- Combination treatment extended median survival compared to single agent therapy
- Combination treatment significantly increased infiltration of CD8+ T Cells into tumor; T cell infiltration 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

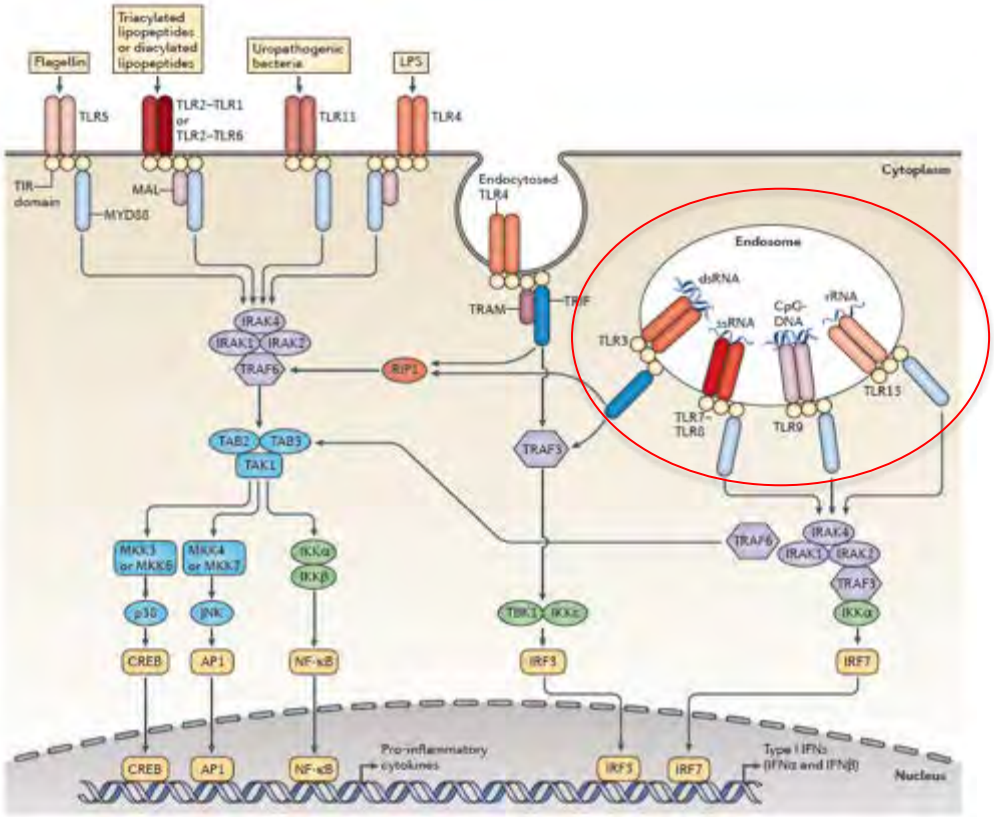


- Tumor targeted immunogenic cell death (ICD) induces activation of monocytes in the tumor microenvironment
- Calreticulin and HMGB1 are markers of ICD and can enhance APC activation, recruitment and tumor antigen uptake
- Tumor ICD promotes innate immune activation and synergy with PD1 checkpoints

STRO-002 Induces ICD Markers only in FolRα Positive Cells

Intratumoral (IT) dosing of synthetic Toll-like Receptor agonists (TLRs) under evaluation as potential new cancer therapies

Immune cell

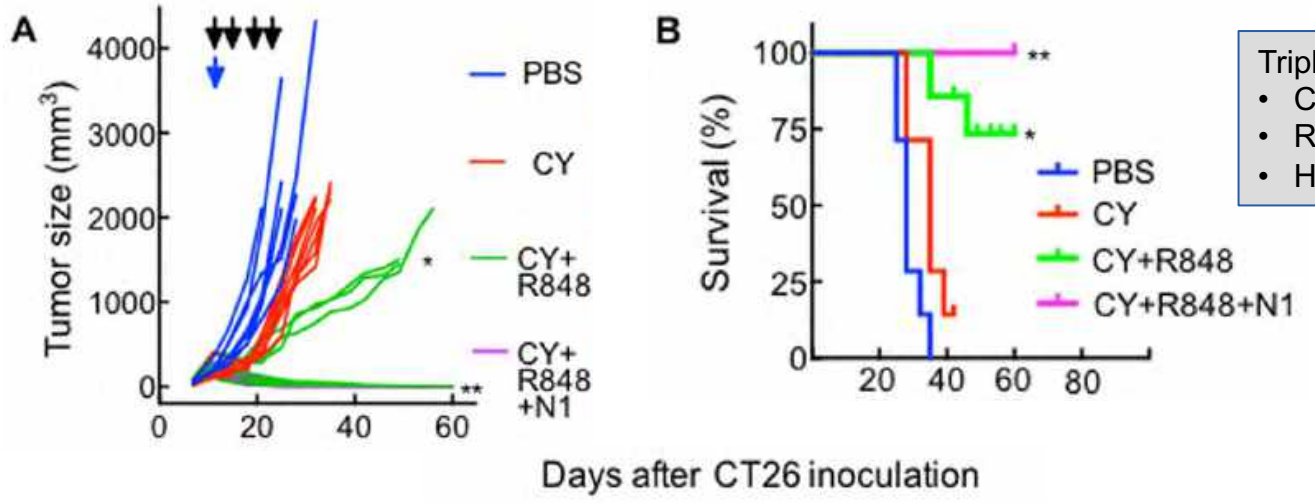


Several Clinical trials with TLR agonists have shown promise with tumor regression and abscopal effects; however limited by I.T. administration

- **Challenges:**
  - Despite localized (IT) injection, cytokine storm is a dose limiting toxicity.
  - IT administration is limited to external or cutaneous tumor indications.

TLR4 and TLR7/8 Agonists Synergistically Activate Dendritic Cells

Further enhancement seen with CPIs or ICD Inducers



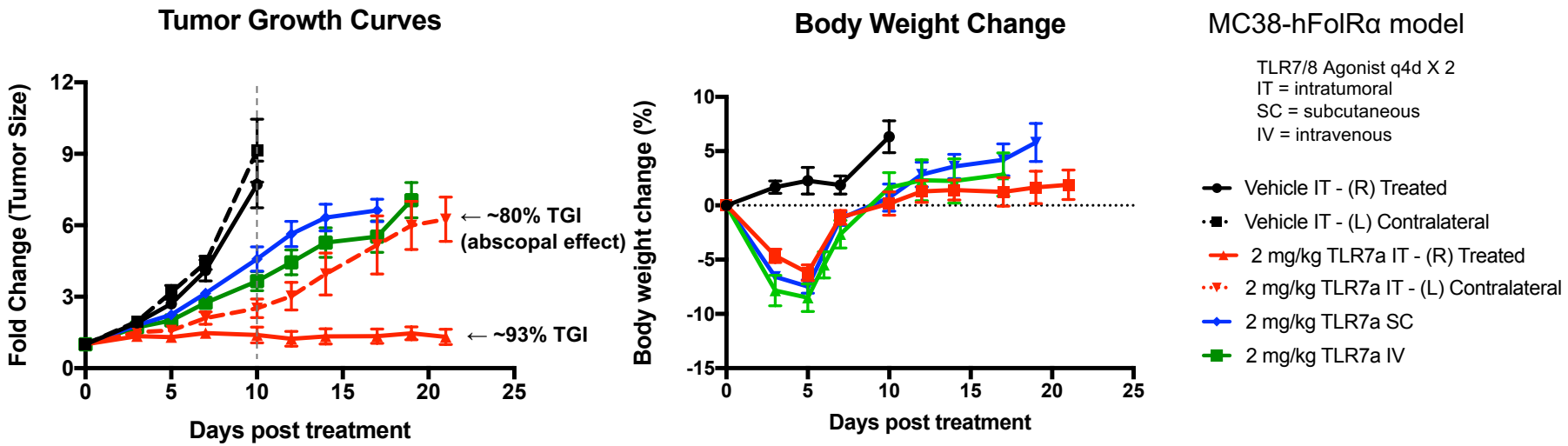
Triplet of Cytoxan, R848 and HMGN1
- Cy: Cytoxan
- R848: TLR7/8 agonist
- HMGN1: TLR4 agonist

- Cytoxan (cyclophosphamide) induces ICD which promotes DC proliferation.
- HMGN1 and R848 synergistically activate DCs through TLR4 and TLR7/8, respectively
- Triplet treatment enhanced tumor infiltrating DC activation and increased infiltration of CD4+ and CD8+ T cells.
- Tumor-free mice treated were resistant to subsequent challenge with CT26, indicating protective immunity

Nie et al (2017)

Would a Dual Conjugate of A Tumor Targeting Antibody and TLR4 and TLR7/8 Agonists Act As an *In Situ Vaccine*?

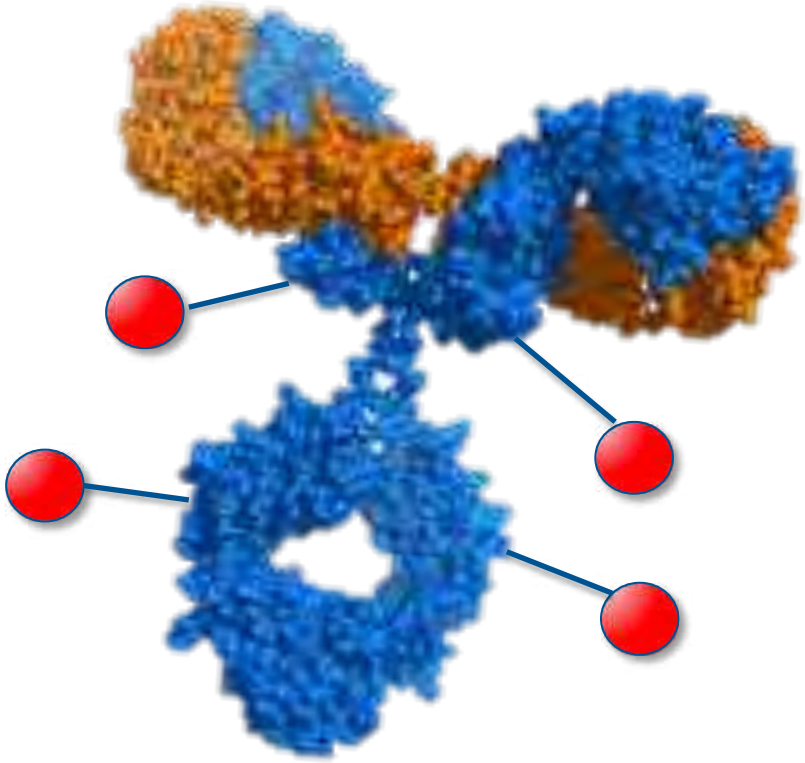
Systemic Administration of TLR7/8-agonist Resulted in Tumor Growth Inhibition but with Transient BW loss



- 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.

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



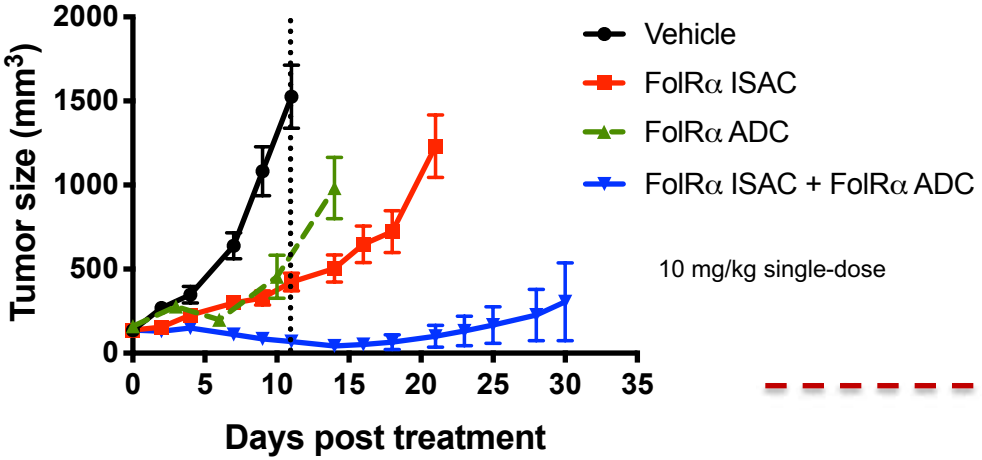
FolRα ISAC
(Immune Stimulator Antibody Conjugate)

FolRα Ab conjugated to TLR7/8 agonist via cleavable linker

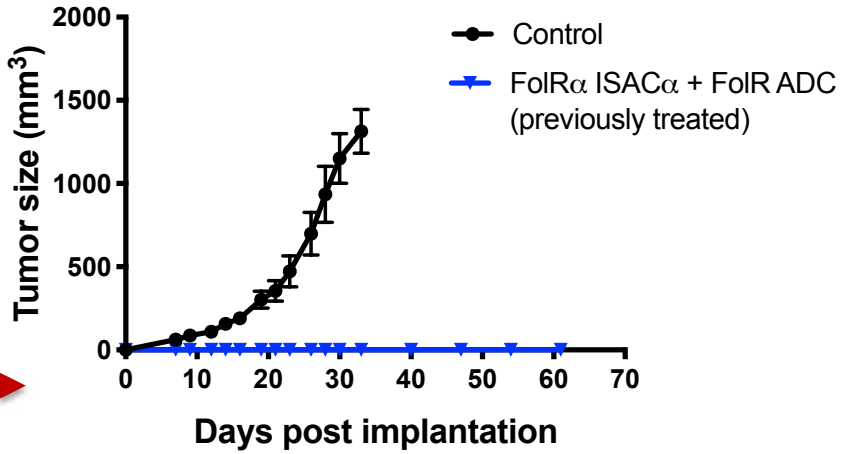
Site-Specific Conjugation Technology Allows For Optimization of Pharmacological Properties

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

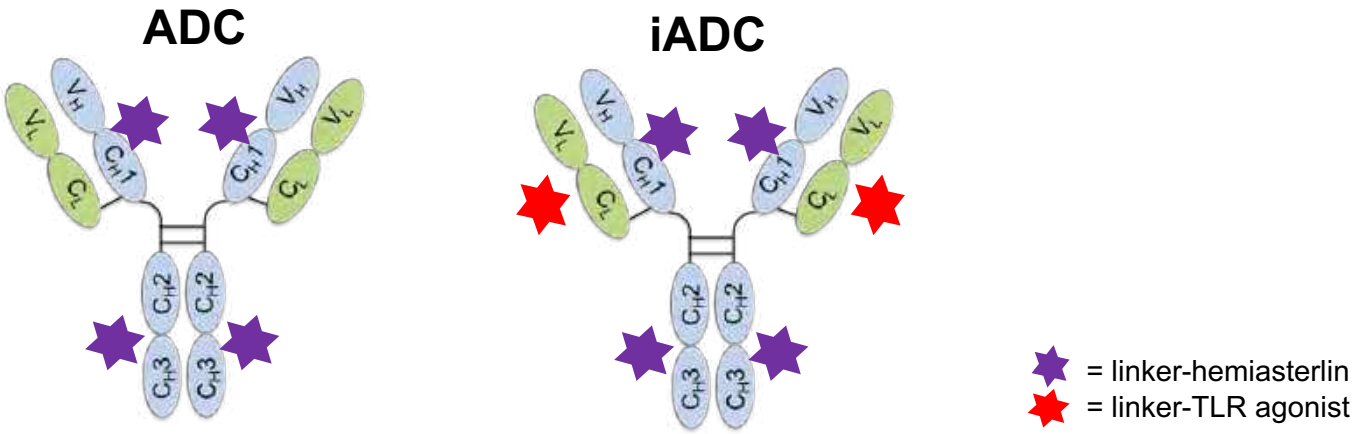


Part 2: Tumor re-challenge in ISAC/ADC tumor-free mice (no additional treatment administered)



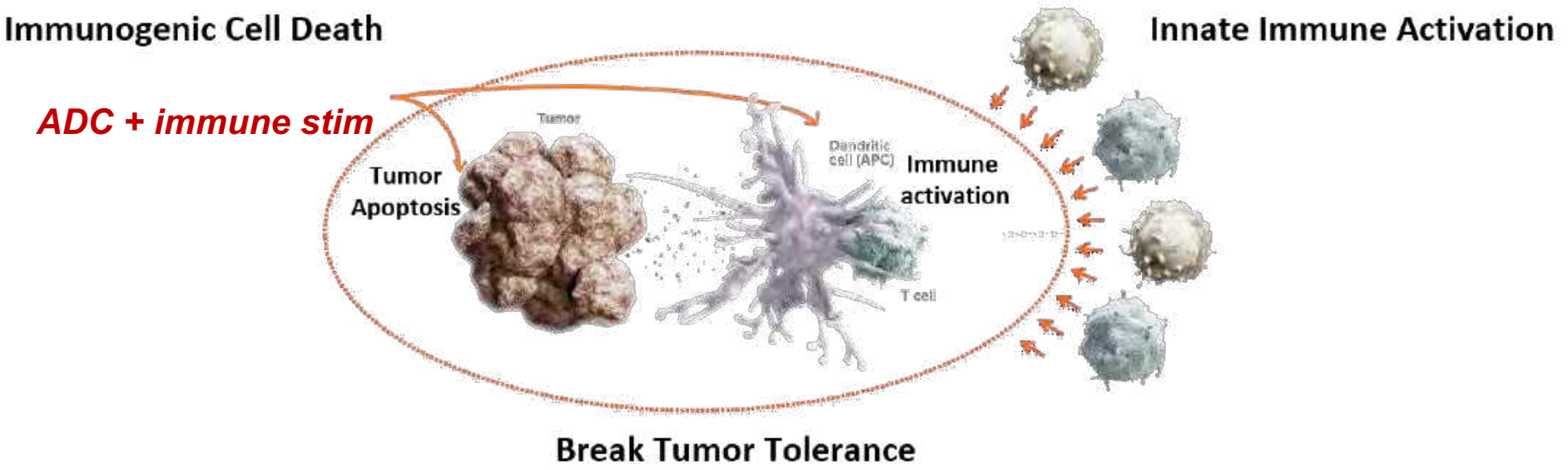
- FolRα ISAC (immune stimulator antibody conjugate) product concept supported by impressive *in vivo* anti-tumor activity and good tolerability with 1/40th dose of free TLR agonist
- Combination of ADC and ISAC gave greater anti-tumor response with evidence of regressions.
- No tumor re-growth in survivors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

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

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

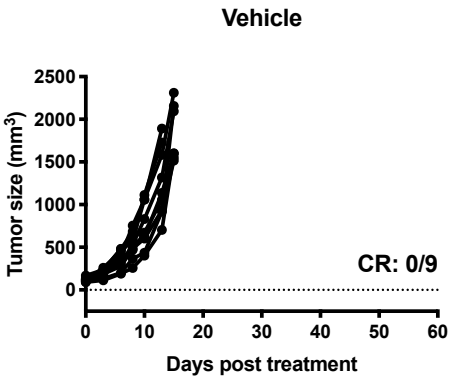


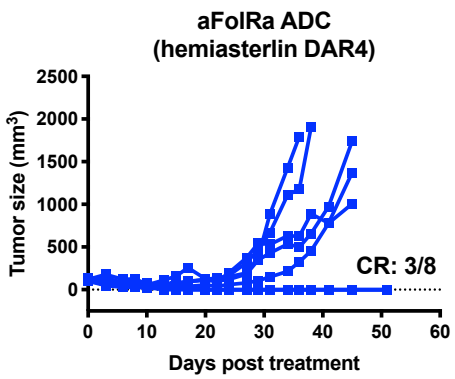
iADC approach can elicit protective tumor immunity by two mechanisms:

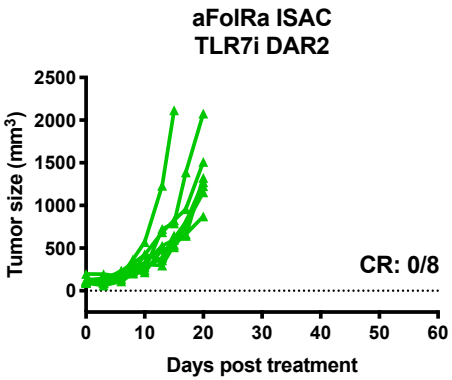
1. Tumor targeted ***immunogenic cell death***
   - Induce tumor killing that alerts immune response
2. Directly ***activate immune cells*** (i.e. dendritic cells)
   - Demonstrates tumor immunity in vivo

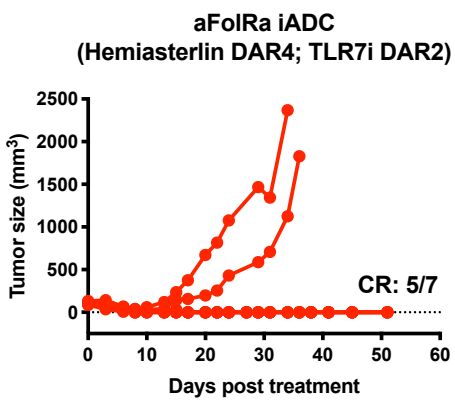
Some patients will require multiple therapies to enable cancer immunity, an iADC combines multiple MOAs into a single tumor targeted therapy

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

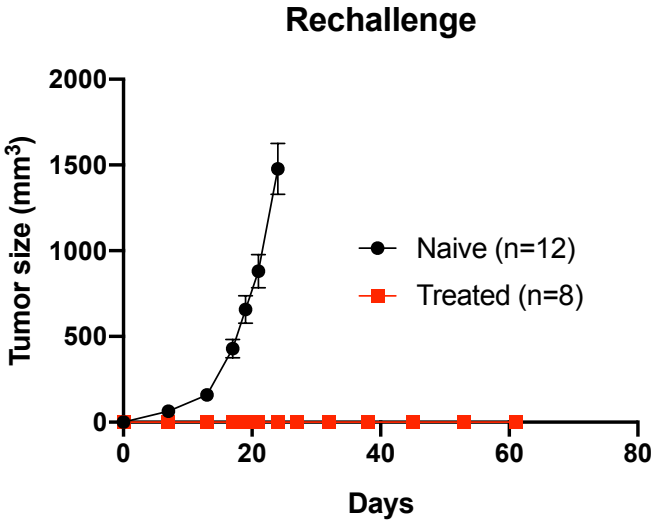








All treated animals that achieved CR were re-challenged with MC38-hFolRα cells



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

A new precedent

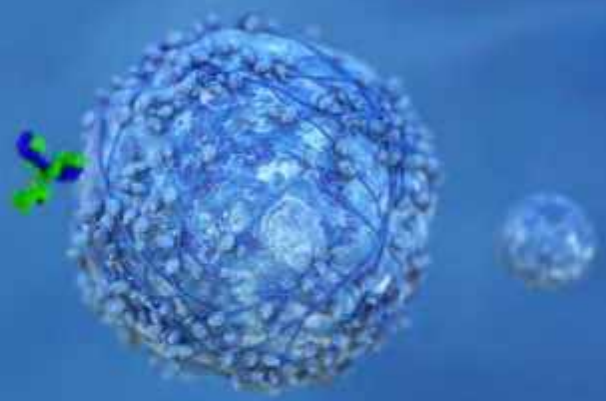
Turning a tumour into a vaccine *in situ*…..

- This program is one of a number of approaches at Sutro exploring whether systemically administered TME-targeting of conjugated combination payloads can set up a sustained and robust anti-tumor immune response

- In our illustrated case a targeted cytotoxin, our proprietary hemiasterlin, that stimulates immunogenic cell death, provides a synergistic stimulation of memory responses when paired together with TLR agonists.

- This systemically delivered trigger for the immune system induces an adaptive and protective response

  …….”an immunization triggered *in situ* ”



Thanks!

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