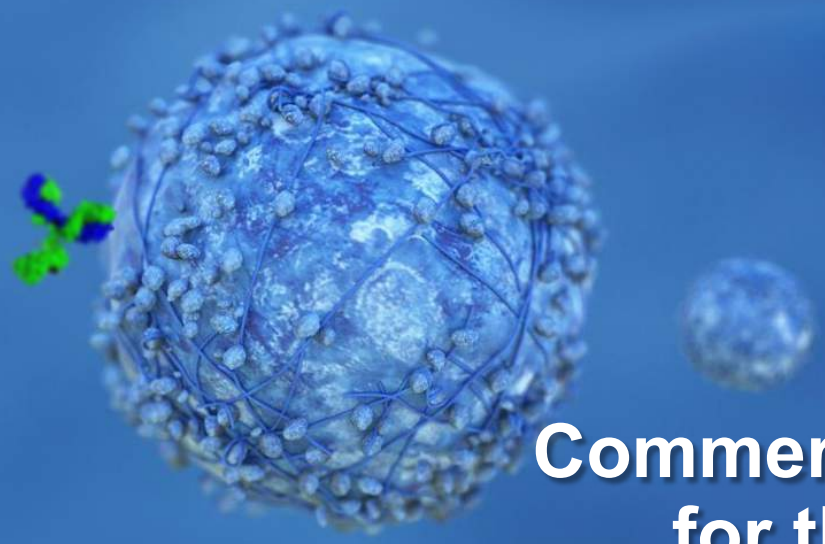


Commercialization of Cell-Free Protein Synthesis for the manufacture of Antibody/Protein Drug Conjugates

World ADC Conference
September 2020

Shabbir Anik
Chief Technical Operations Officer

SUTRO BIOPHARMA

Cell-Free Manufacturing of Therapeutic Proteins

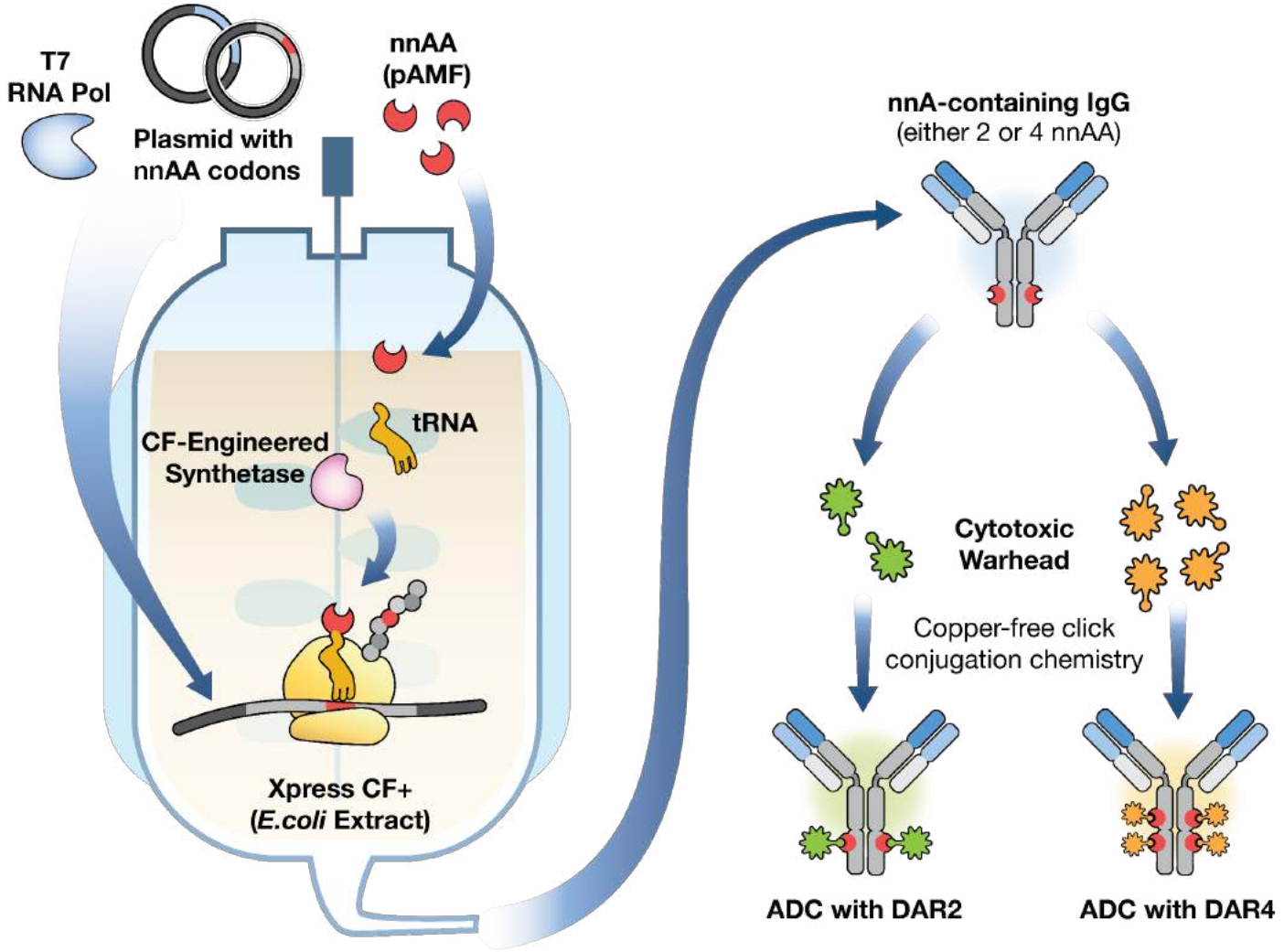
Prof. Jim Swartz, Stanford University, initiated work in the late 90's to answer the question:

Is it possible to harvest the internal machinery of *E. coli* and use it in a biochemical reaction, free of living cells, to cost- effectively manufacture therapeutic proteins?

Sutro founded in 2003 to develop and explore applications of the cell-free system.

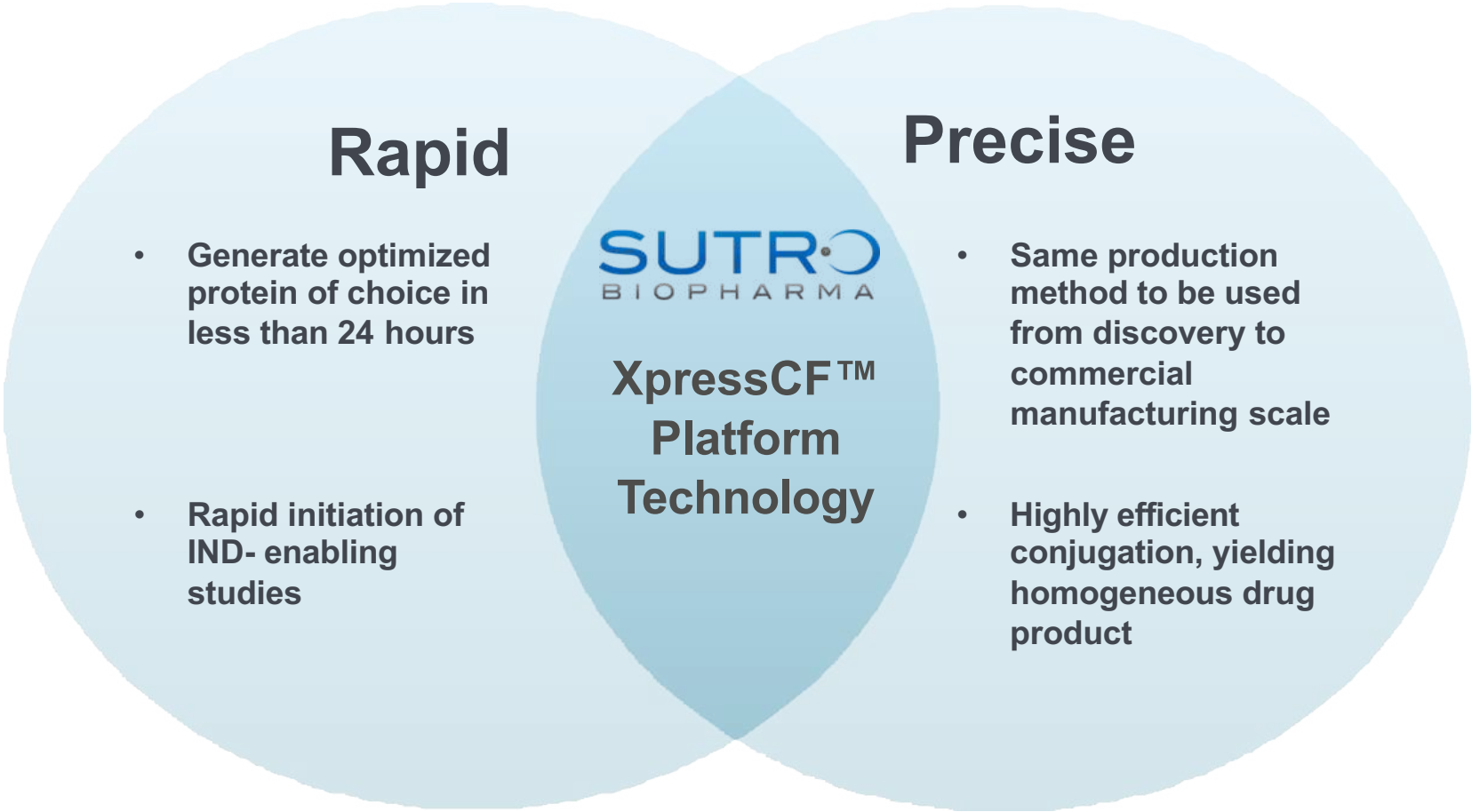
Sutro Technology: XpressCF+™

Manufacturing Proteins and Antibodies with Site Specific incorporation of Non-natural Amino Acids



Sutro's XpressCF™ Platform Advantage:

XpressCF™ enables a rapid and precise drug discovery process

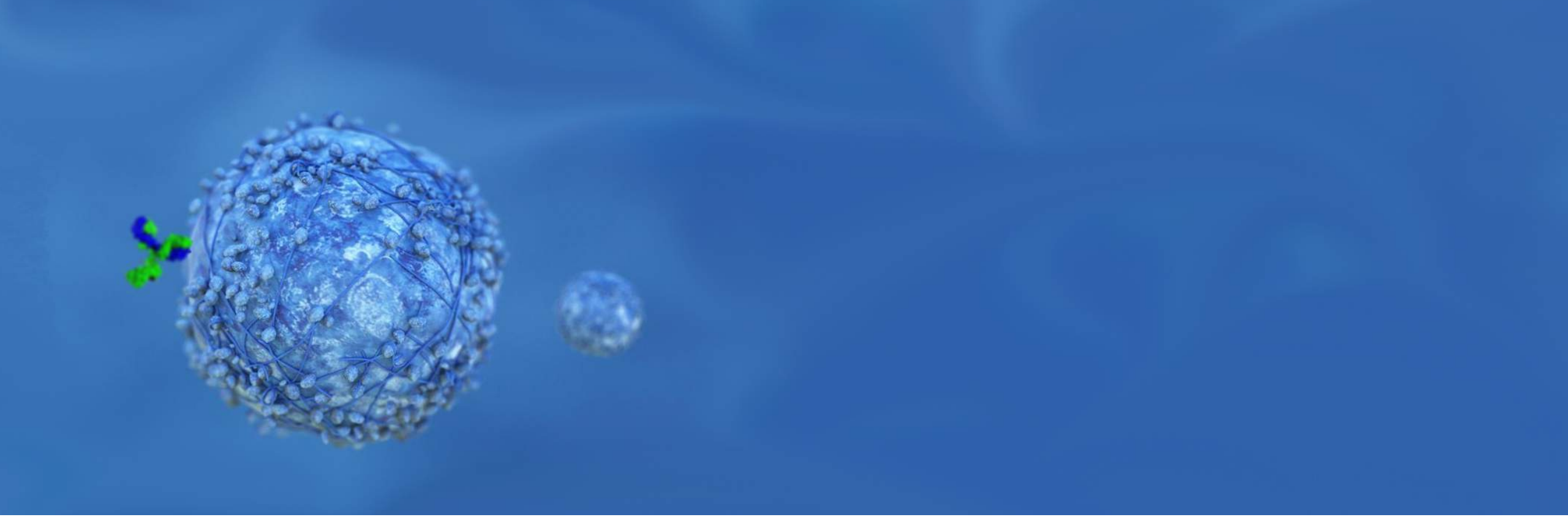


Sutro Clinical Pipeline

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				Clinical Data Presented Sep 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 Human Projected 1Q21	EMD Serono (B)
Cytokine Derivatives	Oncology & Autoimmune					MERCK
	Oncology					

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

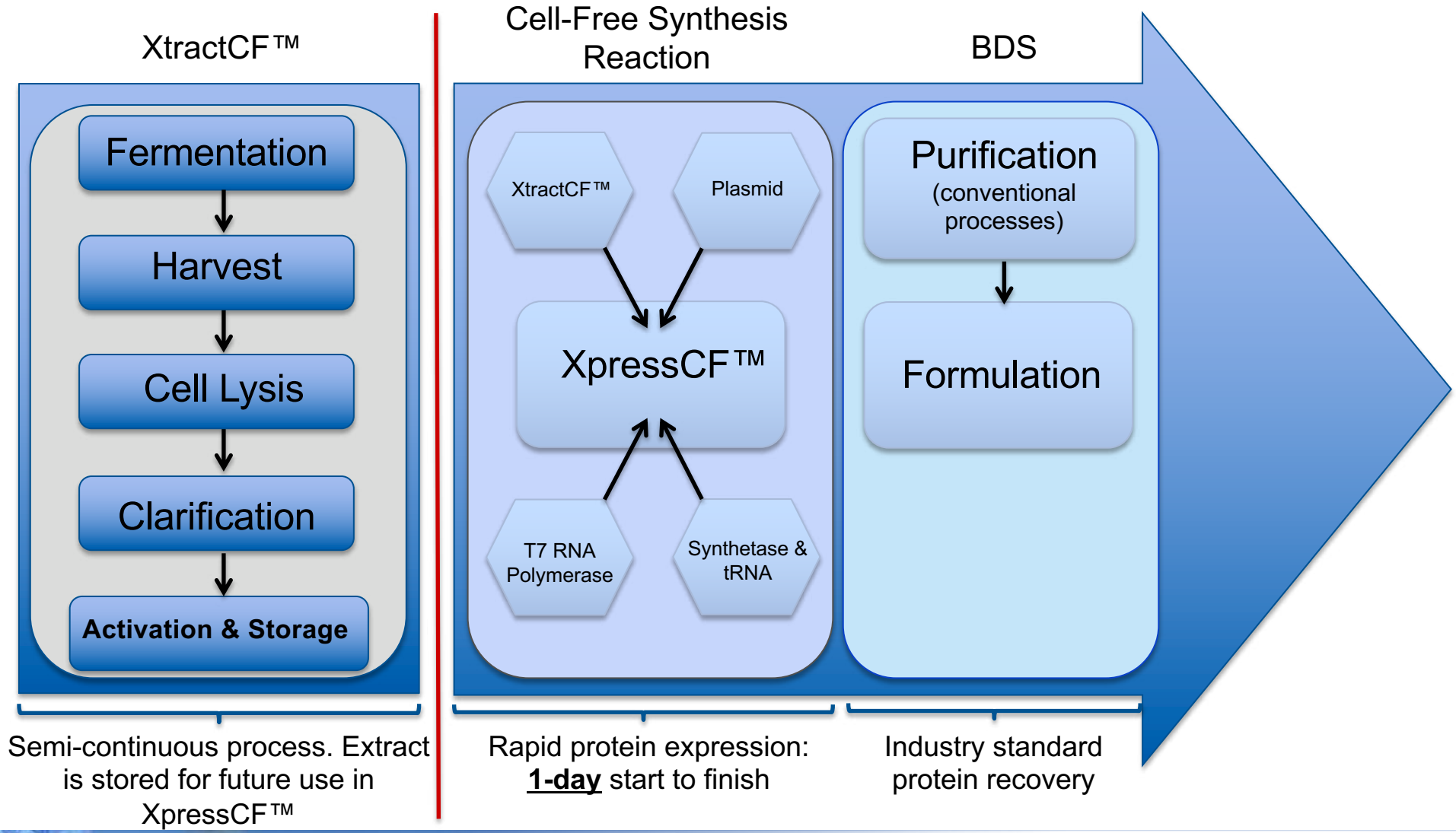


Scalability and Commercialization of Sutro's Cell-Free System (XpressCF™) for the manufacture of antibody/protein drug conjugates

SUTRO BIOPHARMA

Sutro's Protein Expression Platform

1. Cell lysate (XtractCF™) is manufactured from a proprietary *E. coli* strain
2. XtractCF™ is used in a cell-free reaction (XpressCF™) to manufacture the protein of interest
3. Bulk drug substance is purified using conventional chromatography & filtration techniques



World's Only cGMP Cell-Free Synthesis Manufacturing Facility
San Carlos, CA

Continuous culture (chemostat) bioreactor for the cell-free extract (XtractCF™) production

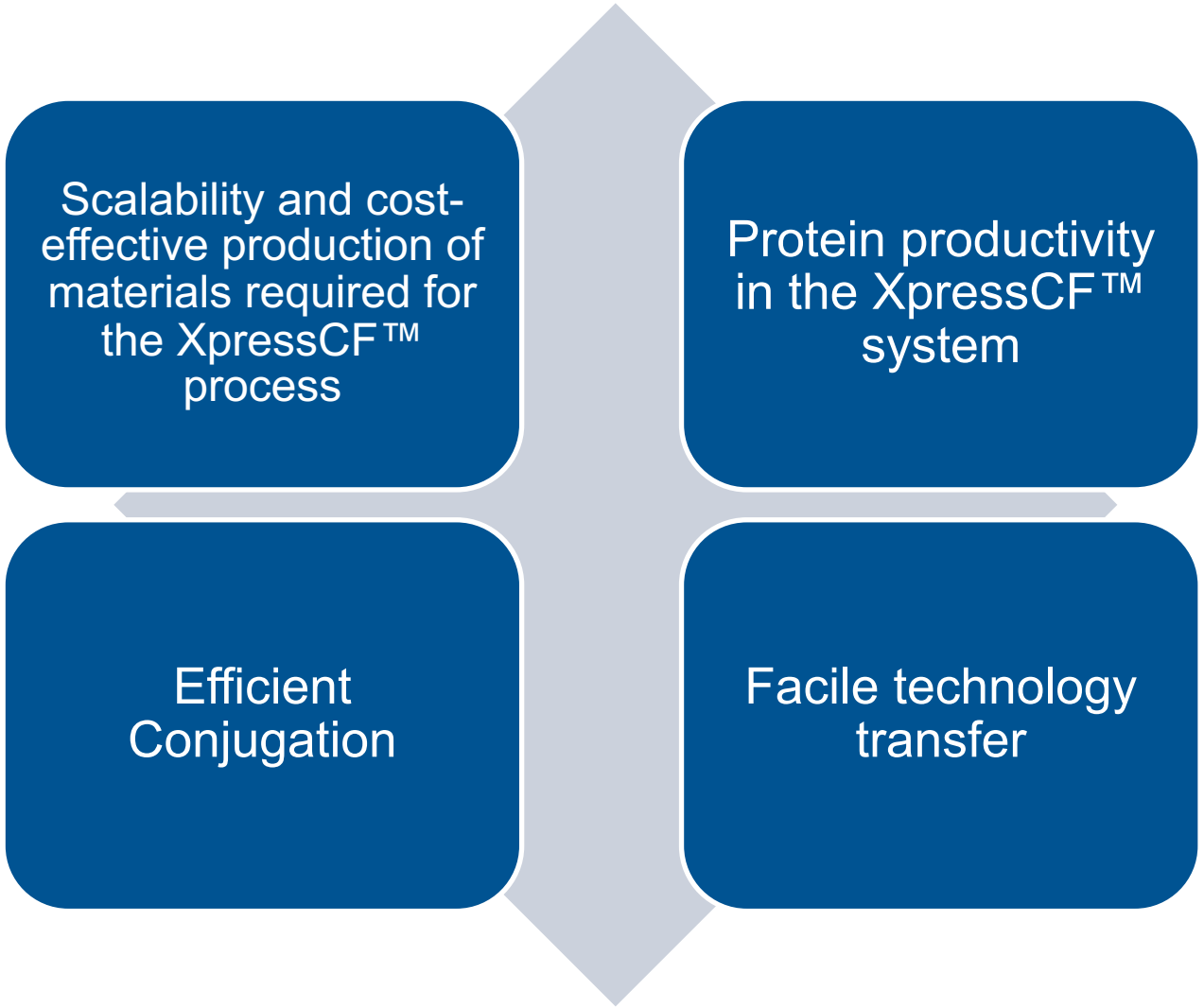
Example: GMP Antibody Production Batch

Step Yield and Purity for an Ab GMP Lot (800 L reaction)

Step	Protein (g)	Step Yield	Purity (% monomer, HMW, LMW)
CF Reaction	233	-	ND
Clarified Harvest	222.5	96%	ND
Protein A Pool	200.9	90%	93.2, 0.3, 6.5
Chrom 2 Pool	180.7	90%	99.7, 0.3, 0.0
Chrom 3 Pool	146.8	81%	99.8, 0.2, 0.0
TFF Pool	146.4	100%	ND
Overall Yield		63%	

The Ab production process takes 7 process days from start of CF reaction to filtered bulk.

Commercialization Considerations



Inputs to the XpressCF™ Cell Free system

Sutro Technology and Manufacturing Processes

- **XtractCF™** – 35% of XpressCF™ process volume
- **Lysates** (multiple) – <1% of XpressCF™ process volume

Commercial Sources

- **Plasmid**: approx. 6g per Kg Ab
- **nnAA** (para-methyl azido phenylalanine, pAMF): approx. 2kgs per Kg Ab
- **Payload**: approx. 4-8% per kg Ab; efficient conjugation to Ab through click-chemistry >85% yield

XtractCF™ – Commercialization Plan

E.coli (Sutro proprietary strain) - Continuous fermentation process in industry standard equipment affords ease of scalability, efficient utilization of manufacturing suites and cost-effective manufacture.

Process developed to spray dry extract to produce a dry powder form for ease of storage, transportation and use.

Current Strategy – High Volume production at CMO

1250L bioreactor working volume and matching spray dryer will produce approx. 7000L (900kgs dry powder) per week (equivalent to 8-10kgs of Ab at 0.5g/L yield in the XpressCF™ process)

Lysates – Commercialization Plan

Sutro Proprietary E. coli strains

Batch Fermentation and recovery process in industry Standard equipment affords ease of scalability and cost-effective manufacture

Usage requirements per XpressCF™ batch are small. Frozen storage.

<u>Current Strategy for large scale production at CMO</u>

Bioreactor working volume 1000L will produce >500L/batch (equivalent to 25kgs of Ab at 0.5g/L yield in the XpressCF™ process)

XpressCF™ – Commercialization Plan

- **Increase in Protein Productivity through process improvements**
  - Current target >0.5g/L sufficient for commercial requirements given 24hr cycle time and no need for viral clearance.
- **Existing scalability data at 1000L suggests 5000-10,000L XpressCF™ batch process achievable**
- **Industry standard equipment allows for rapid tech transfer for multi-plant global operations**

Sutro – Commercializing Cell-Free Manufacturing

Manufacturing

- Large Scale production of Extract and Lysates on timeline to commercialization
- Scalability of the XpressCF+™ process established

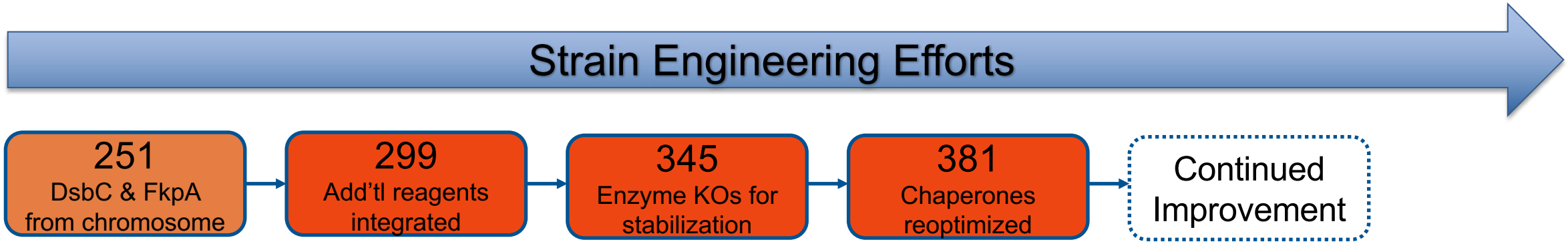
Regulatory Strategy in place

- 4 DMF's filed for Extract and Reagents
- 3 products in clinical trials (2 Sutro,1 partner)

Technology Platform

- Scalable/Transferable: Extract and Reagents from Sutro/CMO facility can be shipped globally for the manufacture of proteins/antibodies
- Broad Applications: ADCs, bioconjugates, bsAbs, cytokines, Vaxcyte - Pneumococcal conjugate vaccine

Continuing to Refine and Optimize The XpressCF™ Process



The progression of the XpressCF™ platform over the last 10 years went from enabling basic protein expression to refining expression with nnAAs in antibodies, to addressing scalability, and ultimately optimization.

Improving protein productivity through strain engineering and process optimization

Cell Free Manufacturing – Better, Faster, Cheaper?

XpressCF™ - Production of best-in-class complex biotherapeutic molecules:

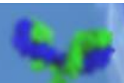
- Site-specific, homogeneous ADCs and protein conjugates
- Conjugate vaccines
- Bispecific antibodies

Technology Platform

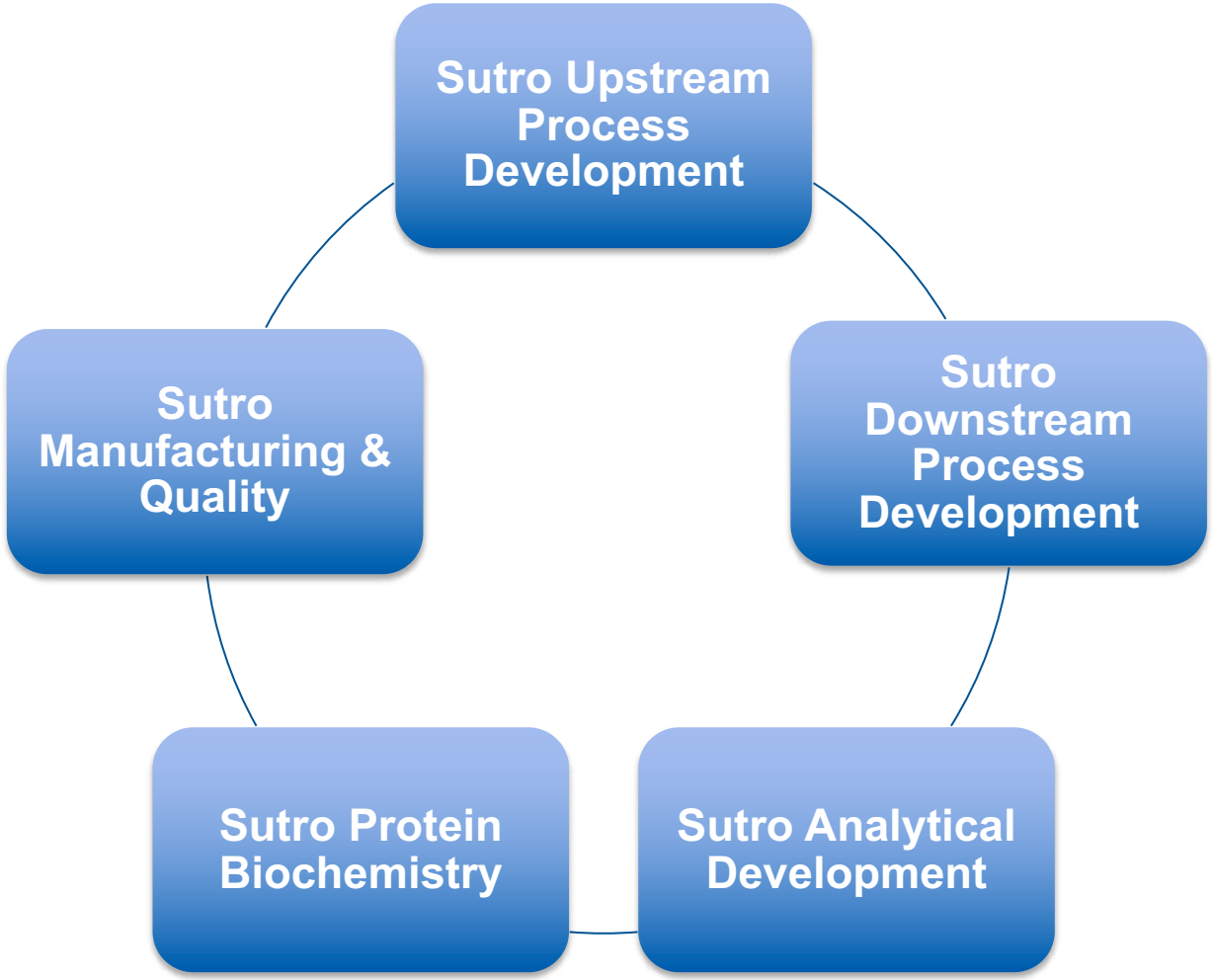
- Scalable/Transferable: Extract and Reagents from Sutro facility can be shipped globally for the manufacture of proteins/antibodies

Extract in inventory provides manufacturing flexibility and reduces cycle times (<24hr) allowing for efficient plant design, capital utilization and capacity planning.

No Viral testing a plus!



Acknowledgements



Questions?

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