“Right-sized” Efficient Multi-product Manufacturing

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NASEM Workshop on Technical & Regulatory Barriers to Innovations in Pharmaceutical Manufacturing

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Our Goal: Enable more medicines for patients world-wide

Accessible global health innovation requires

- Supply of Phase-Appropriate Protein Supply for Discovery & Development
- Path to Clinical-Grade Lots on Time and Budget
- Line-of-Sight to Commercial Sourcing

to accelerate products and pipelines

WHO WE ARE
Public Benefit Corporation and a socially responsible CDMO partner for biopharma

VALUE WE PROVIDE
Access to high-quality proteins on accelerated timelines with an improved customer experience

OUR SOCIAL MISSION
Support global health initiatives with Sunflower's transformational manufacturing & services

Two Systems, One Process: Many Applications

Sunflower is developing "right-sized" automated manufacturing systems for protein production

Seamless process transfer between systems

DAISY™ System

~0.1 - 1 kg annual capacity
Lab scale production
Process development applications
Support early discovery research

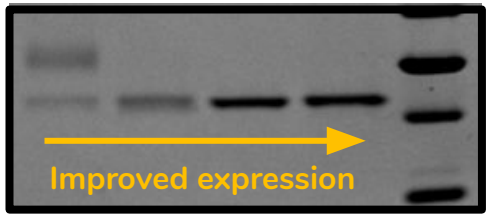
DAHLIA™ System

1 - 10 kg annual capacity
Pilot scale production
Support for clinical development
Line-of-sight to commercial use

Critical Enabling Technologies

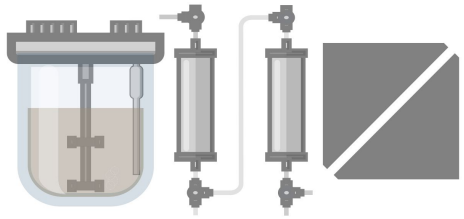
FAST & SAFE MICROBIAL HOST (*Pichia pastoris*)

GRAS organism used to make licensed products and global insulin supply
No known adventitious agents and few host-cell proteins simplify purification
Small haploid genome efficiently characterized by next-gen sequencing



BIOLOGY-DRIVEN EXPRESSION ENGINEERING

Molecular design to address quality & manufacturability
Strain engineering with genomic precision for production



INTEGRATED PROCESS DEVELOPMENT

End-to-end approach to process design and development
Data-driven acceleration of platform processes for related products

Sunflower's Platform Compatibility for Multiple Products

2020

CURRENT CAPABILITIES

Cytokines
Hormones
Enzymes (<80 kDa)
Single-domain antibodies
Bacterial toxins
Viral antigen subunits

2021+

DEVELOPING CLASSES

Glycosylated mAbs

Insulin-like products

2023+

FUTURE CLASSES

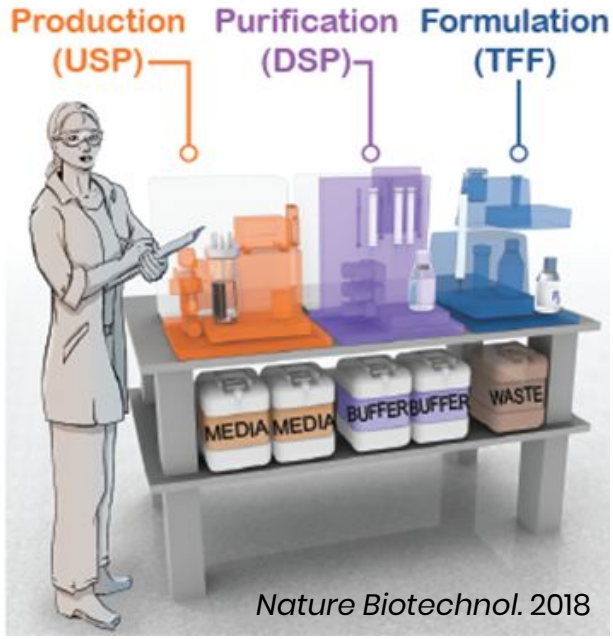
Antibody-fusion proteins

Thrombolytics

Enzymes (>80 kDa)

* Not pursuing: Blood products and enzymes with post-translational modifications beyond glycosylation

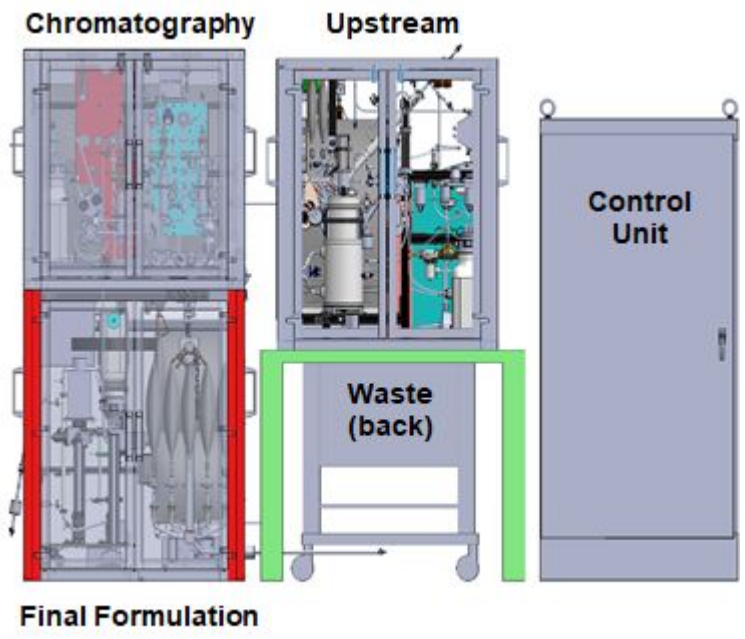
Proof-of-Concept Prototypes Built and Tested at MIT



InSCyT 2.0 System

~1 gram annual capacity

Routine production of G-CSF, hGH, IFN-α2b, Nanobodies, Vaccine Components



InSCyT 4.0 System

~1 kg annual capacity

Developed as pre-cGMP model

Demonstrated production of G-CSF

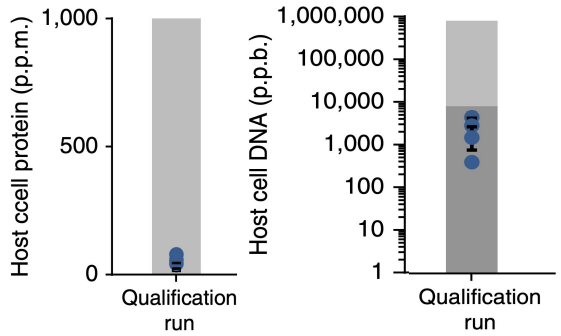
Consistent Quality with 3 Systems (MIT InSCyT)

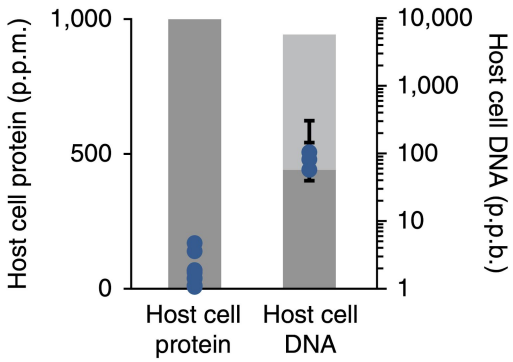
IFN-α2b

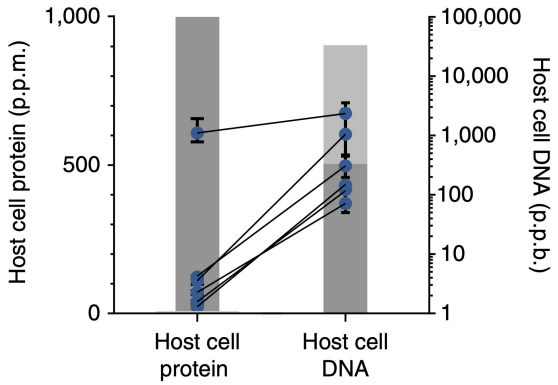
hGH

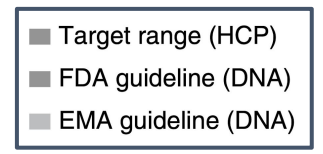
G-CSF

Process-related variants

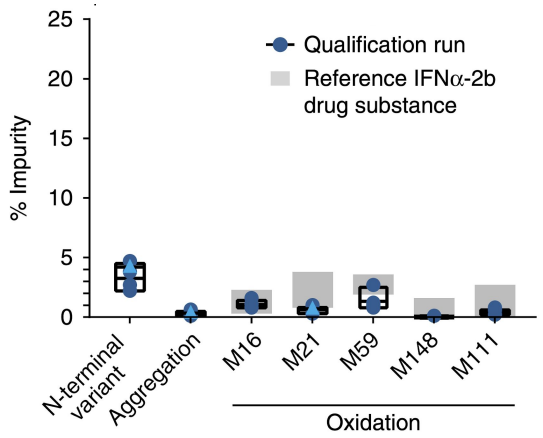


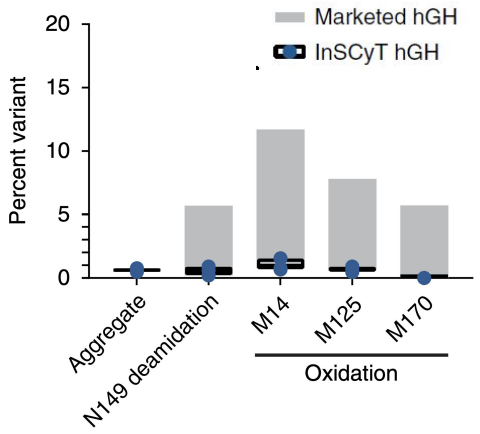


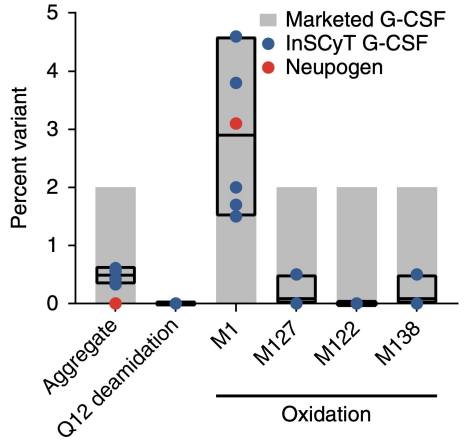




Product-related variants







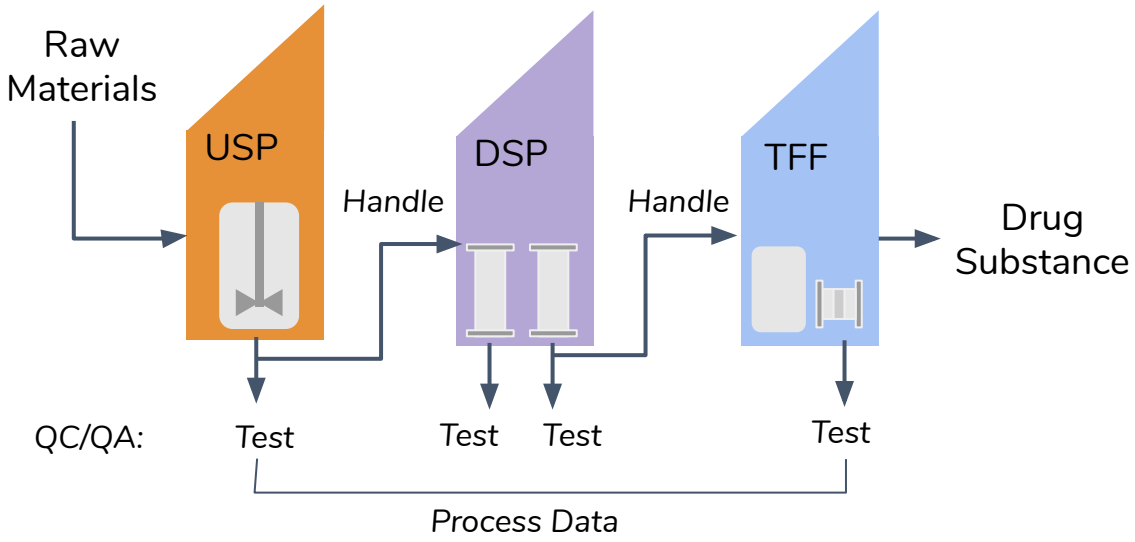
Adapted from *Nature Biotechnol.* 2018

Sunflower integrates technologies for manufacturing

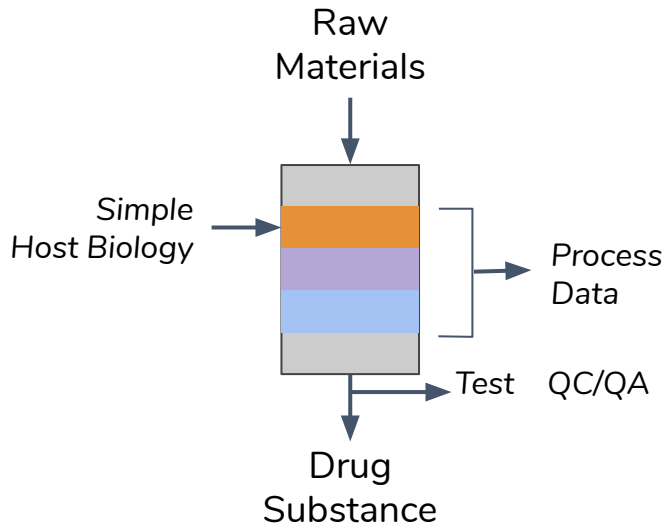
	Industry Precedent?	Technical Risk	Patient Safety Risk
YEAST AS A HOST	Yes	Low	Low
ASEPTIC SINGLE-USE COMPONENTS	Yes	Moderate	Low
FUNCTIONALLY CLOSED PROCESSING	Yes	Low	Low
PROCESS AUTOMATION	Yes	Low	Very Low
CONTINUOUS OPERATIONS	Yes	Low	Very Low
DRUG SUBSTANCE RELEASE TESTING	Yes	Low	Low

Predictive Performance by Holistic Design for Reduced Testing

CONVENTIONAL



SUNFLOWER

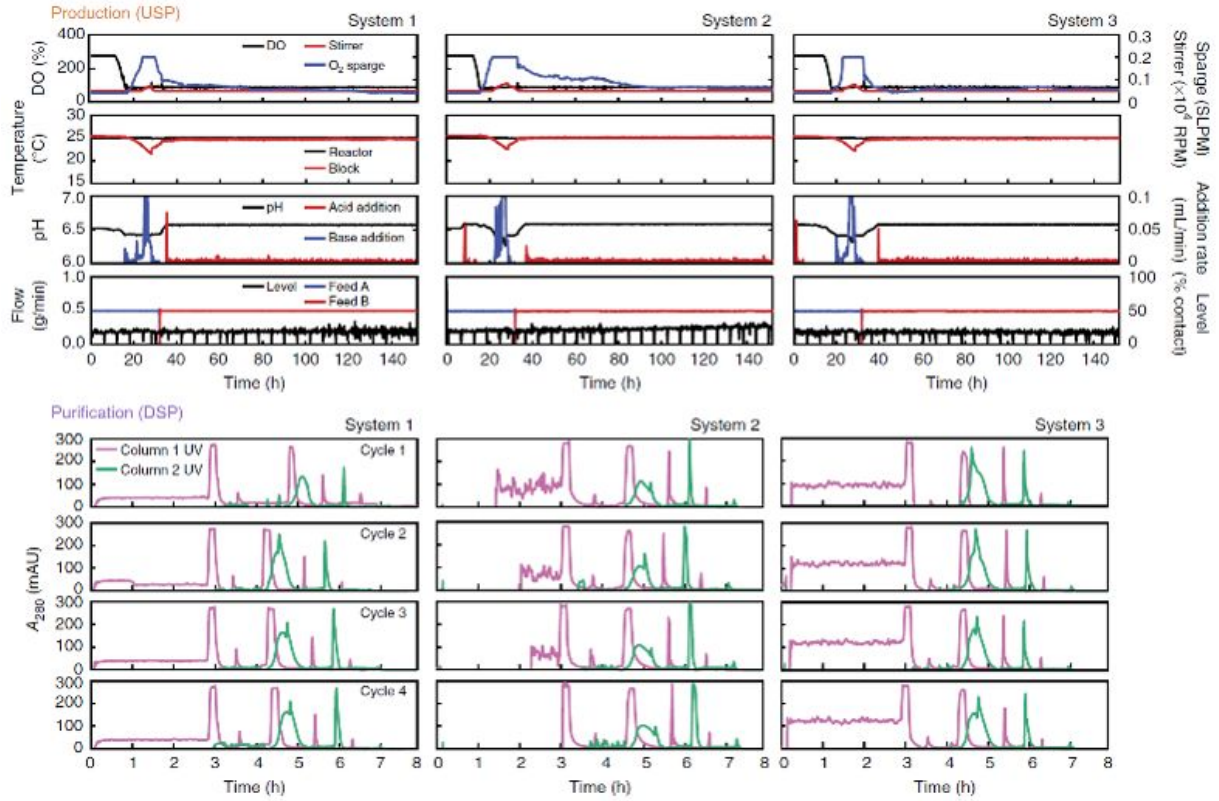


KEY INNOVATIONS FOR IMPROVING PREDICTABLE PERFORMANCE

- Reduce interfaces and handling
- Reduce biological variance with simple 'engineering-ready' hosts
- Employ holistic strategies to achieve quality (Molecule + Host + Process)

Standardized Systems Provide Opportunity for Accumulating Significant Process Performance Data

REPRODUCIBLE SYSTEM OPERATIONS



Nature Biotechnology, Oct 1 2018

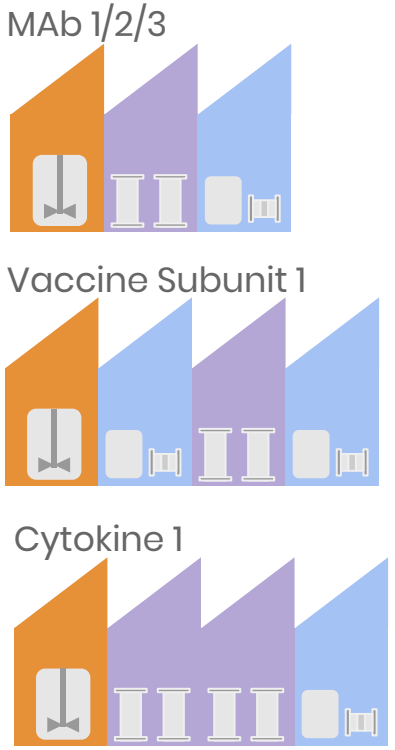
3 ➡ **60**

SYSTEMS — DATA SETS PER YEAR

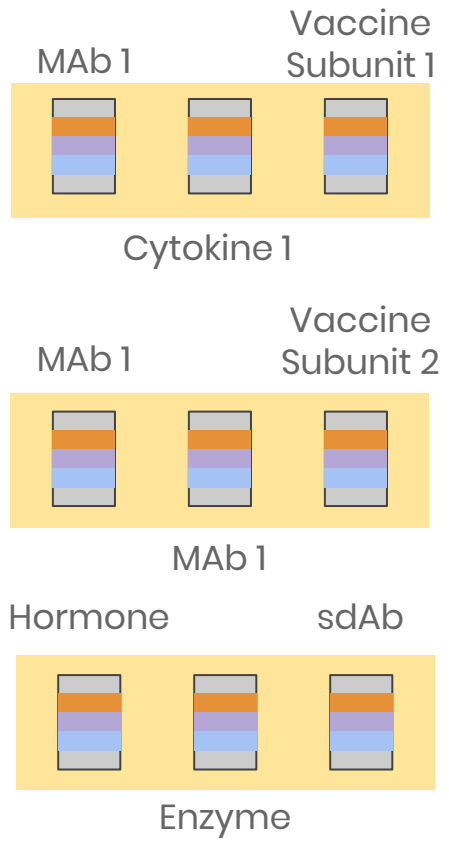
10 ➡ **200**

SYSTEMS — DATA SETS PER YEAR

Standardized Systems Support Flexible Capacity

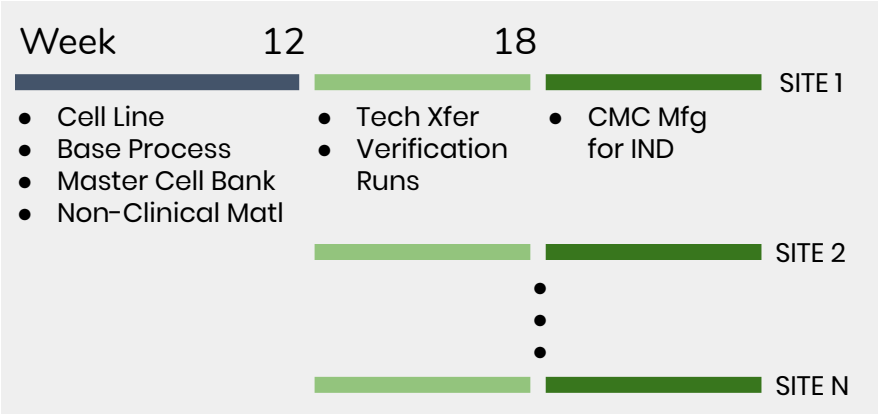


CONVENTIONAL		SUNFLOWER
Variable	BUILD COST	Consistent
Variable	PROCESS EQUIPMENT	Fixed
Variable	VALIDATION	Consistent
Low	RE-FIT POTENTIAL	High
Sometimes	MULTI-PRODUCT	By Design



Standardized Systems are Agile and Distributable

POTENTIAL TIMELINE FOR CLINICAL SUPPLY

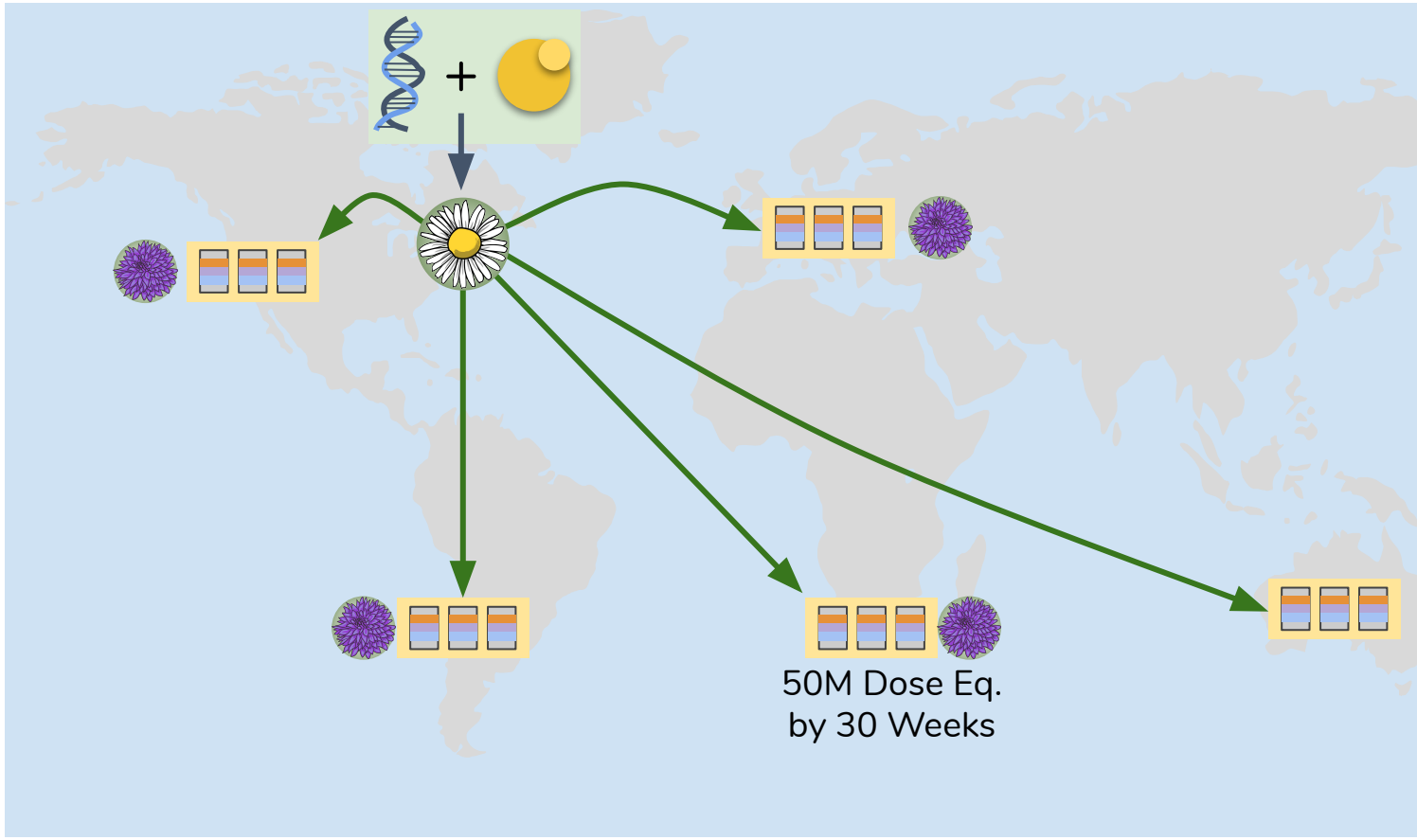


10 FACILITIES = ~ 500M DOSE EQUIVALENTS OF A SUBUNIT VACCINE IN 30 WEEKS

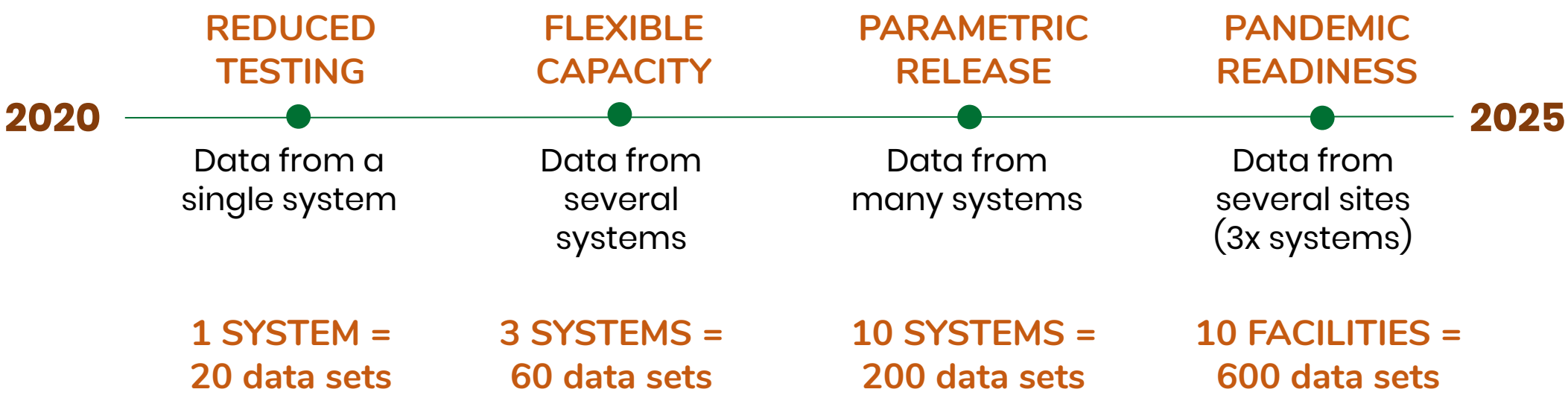
STOCKPILES BUILD DURING CLINICAL EVALUATION OF VACCINE

IMPLICATIONS BEYOND PANDEMICS

Ability to reach new markets quickly
Regional products for regional markets



Projecting A Future State for Global Manufacturing



HOW COULD WE GO EVEN FASTER? COLLECT MORE DATA USING MORE SYSTEMS IN PARALLEL

Sunflower's Team

KERRY R. LOVE, PHD
CEO & PRESIDENT
FOUNDER

J. CHRISTOPHER LOVE
FOUNDER

KATHRYN GOLDEN
FOUNDER
12+ Yrs CMC Mfg

ALEX BONNYMAN
TECHNICAL PROGRAM MANAGER
Trained at MIT

ASHLEY PARKER
PROGRAM MANAGER
Contract specialist

MARY KATE TRACEY
PROCESS DEVELOPMENT ENG.
Trained at MIT

Sunflower is a women-owned small business

Key Advisors

LARRY WEINER
GLOBAL SUPPLY & CMC MANUFACTURING
30+ years Biopharmaceutical Experience
Prior engagements with FDA on CMC Mfg

MIKE NASH
SERIAL ENTREPRENEUR & CEO
30+ years venture & management experience
Successful exits on multiple start-ups

CHRISTINA WHITING
DATA SECURITY EXPERT
15+ years computer systems & data security
Information technology innovation

REGULATORY EXPERT
20+ years Regulatory Compliance experience for GMP-compliant CMC, many engagements with FDA on IND filings

PROCESS DEVELOPMENT EXPERT
10+ years Biopharmaceutical Experience with CRO/CMOs for product development


Sunflower
THERAPEUTICS