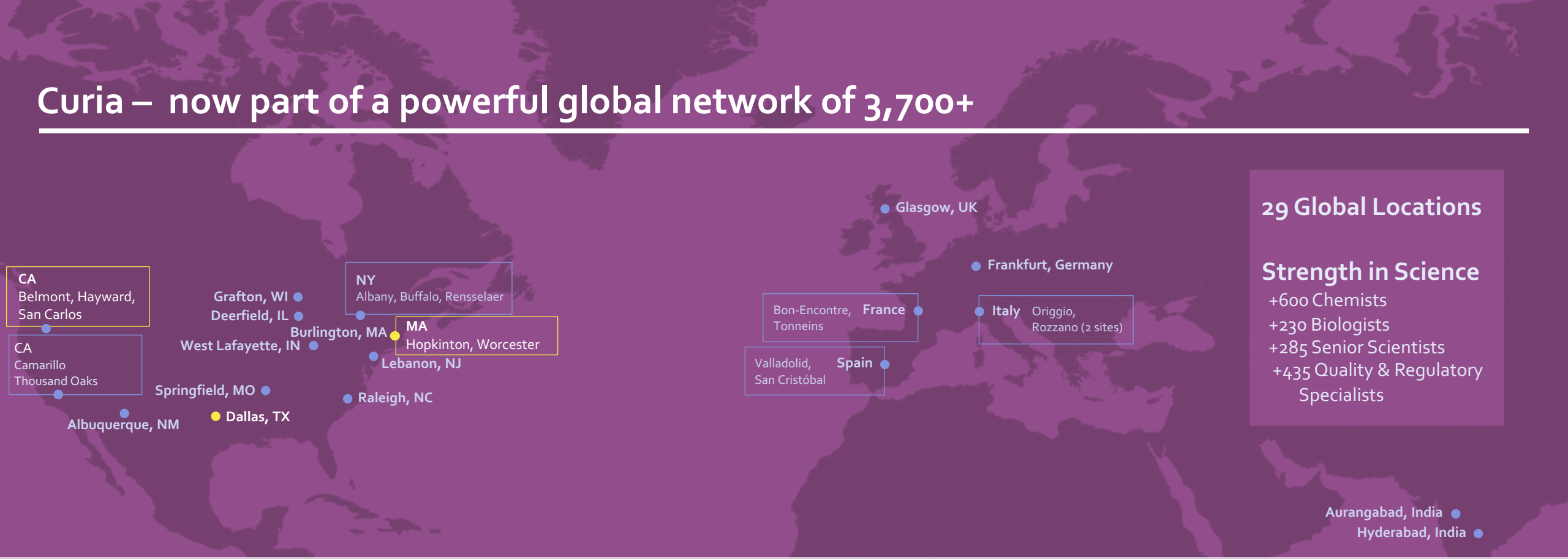
curia

Biologics Discovery Development & Manufacturing

5/2022

Curia – now part of a powerful global network of 3,700+



29 Global Locations

Strength in Science

+600 Chemists
+230 Biologists
+285 Senior Scientists
+435 Quality & Regulatory Specialists

DISCOVERY

Albany, NY
Buffalo, NY
Hyderabad, India
San Carlos, CA
Belmont, CA
Worcester, MA

DEVELOPMENT

Albany, NY
Hopkinton, MA
Worcester, MA
Grafton, WI
Frankfurt, Germany
San Cristóbal, Spain
Belmont, CA

Hayward, CA
San Carlos, CA
Hyderabad, India

LAB TESTING SERVICES

Albany, NY
West Lafayette, IN
Lebanon, NJ
San Carlos, CA
Hayward, CA
Valladolid, Spain
Hyderabad, India

API MANUFACTURING

Springfield, MO
Grafton, WI
Rensselaer, NY
Bon-Encontre, France
Tonneins, France
Frankfurt, Germany
Aurangabad, India
Origgio, Italy
Rozzano, Italy
Valladolid, Spain

DRUG PRODUCT

Camarillo, CA
Thousand Oaks, CA
Burlington, MA
Albuquerque, NM
Glasgow, UK

Integrated Solutions Approach for Biological Therapeutics

*Our integrated solutions and capabilities **bridge discovery, engineering, development, and manufacturing across sites***

Technical Sites with Project/Scientific Management

San Carlos, CA

Belmont, CA

Worcester, MA

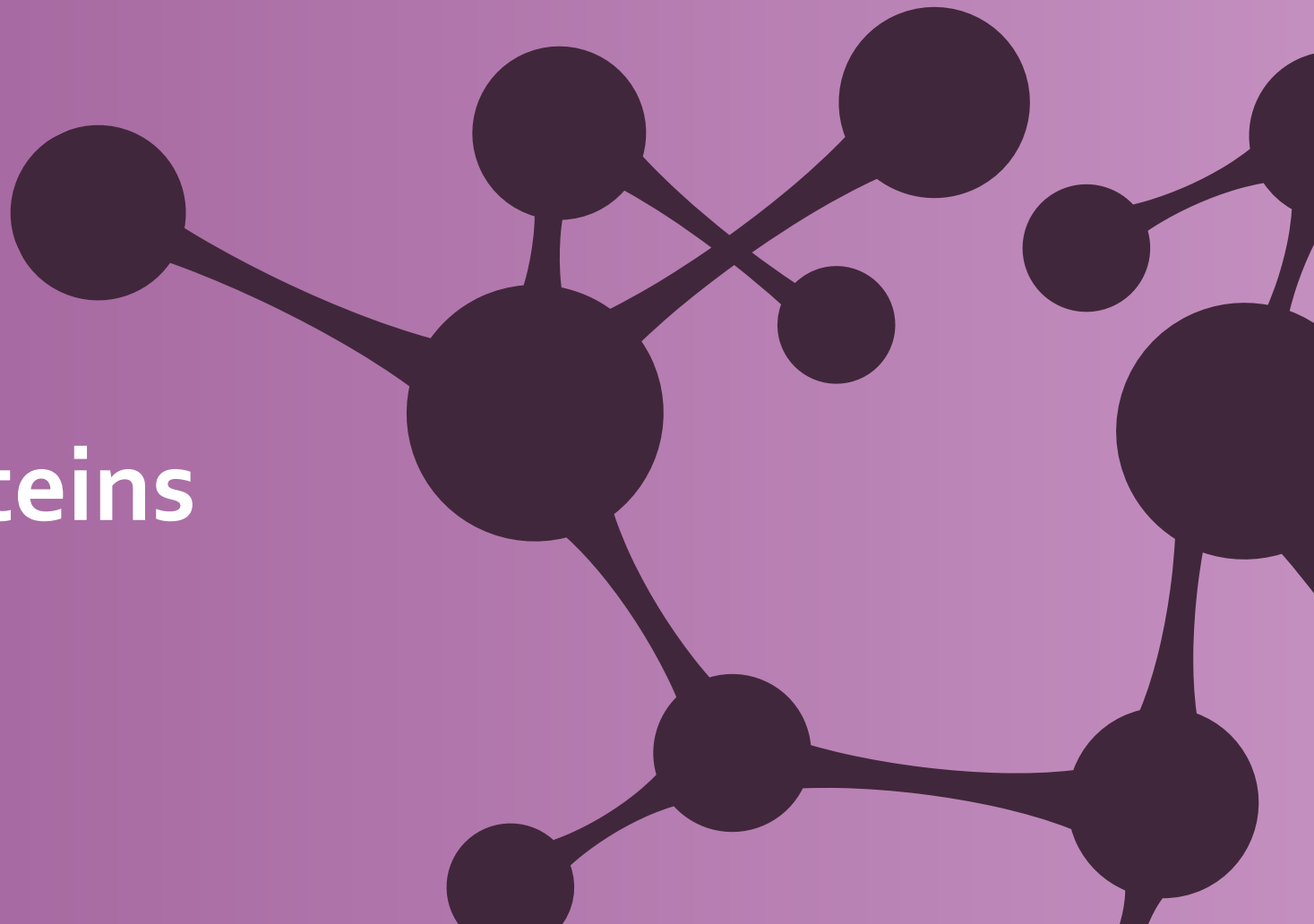
Hayward, CA

GMP manufacturing for diagnostic reagents only

Hopkinton, MA

Thousand Oaks, Camarillo , CA

Drug Substance: Antibodies and Proteins



Antibody and Protein Therapeutic Discovery Development and Manufacturing

- Antibody discovery and engineering services
- Engineered CHO cell lines
- Free of animal-derived raw materials
- Tech transfer projects accepted
- Full development services

- ISO 13485:2016 certified
- Manufacturing to support clinical development
- 200-2000 L SUBs
- Full analytics on-site for in-process testing and batch release

Antibody Discovery and Engineering

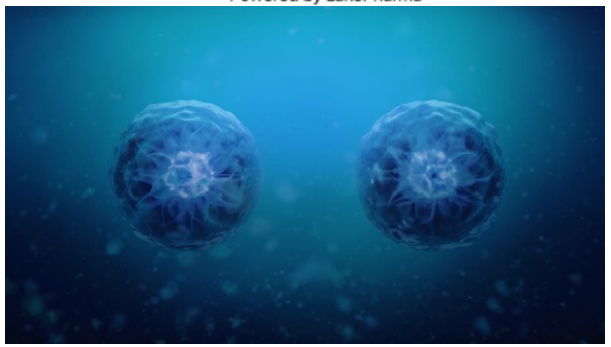
Culture facilities

- BSL2 level facilities
- Dedicated AAALAC accredited vivarium for rodent immunizations
- Comprehensive projects with consultation and upfront due diligence, followed by immunization, hybridoma generation, selection, cloning and screening validated leads as deliverables. Purified mAbs are provided for Client testing.
- IgG, scFv, Fab, VHH, and other formats

Key Features and Proprietary Technologies

- Multiple Discovery Platforms: Hybridoma, Phage Display, Yeast Display, Single B Cell
- In-line HTP Affinity Analysis and Ab Production
- PentaMice®
- Rapid immunization protocols
- XOMA human scFv and Fab libraries

HYBRIDOMA.COM
Powered by LakePharma



PentaMice

PROUDLY, AN aaalac INTERNATIONAL ACCREDITED PROGRAM

Single B Cell Antibody Discovery at Curia Using Berkeley Lights Beacon® System

Superior Mouse System

PentaMice

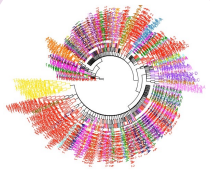
- Industry leading immunological diversity
- Optimized Immunizations and proven high titers
- Royalty-free

AI-Enabled B Cell Selection

- High throughput; screen 50,000+ B cells in days
- On chip hit ID & cDNA generation
- V_H/V_L paired sequence recovery; mAb diversity & developability assessments

Fast Gene-to-Development Candidate

- Gene to mgs Protein in <8 weeks
- HT epitope binning & affinity determination: Carterra® system, BLI



- Humanization (or humanized mouse starting point)
- *In vitro* efficacy & safety assessments: ADCC, ADA, ADC/CS.

17-42 Days → **14 Days** → **90+ Days**

Hit-to-candidate in 120 days • First-to-Human-enabling technology

Antibody & Protein Therapeutic Development and cGMP Manufacturing

GMP Overview

- Single use equipment
- 200, 500, and 2000 liter SUBs
- ISO7 post-viral and fill/finish suite
- Onsite analytics for in-process testing and batch release

*Timelines are subject to change depending on the manufacturability of the candidates

Stages

Cell Line Development	Master Cell Bank	Upstream Process Development	Downstream Process Development	Engineering and Manufacturing Batches
CHO cell line engineering, cloning, and RCB	Master Cell Bank generation and characterization	Optimize culture conditions in Ambr® and scale up to 2L through 50L SUBs Batch record creation	Develop purification process Batch record creation	Engineering run in suite and cGMP manufacturing of bulk drug substance

Total timeline 12-16 months from CLD to phase I drug substance*

Cell Line Development - Curia CHO-GSN℠ Technology

Highlights

- Royalty-free, no commercial milestone payments
- CHO-K1 GS knockout with stronger GS selection, high titers
- Generational stability >80 generations demonstrated
- Established track record; multi-programs in clinical stages

Proprietary Stable Expression Vectors

- High expression stable expression vectors
- Bicistronic vectors for antibodies
- Monocistronic vectors for proteins
- Vectors for 3+ chain molecules available

+

CHO-GSN Parental Cells

- CHO-K1 GS knockout
- Suspension adapted
- Animal product-free culturing
- Path to commercialization

+

Proprietary Stable Cell Line Generation Know-how

- Stable pool and single clone selection
- Experience in stability and scalability
- Upstream process development
- Downstream process development

CHO-GSN Stable Cell Line Generation

Stable Vector Construction

Proprietary Stable Expression Vectors

- Custom designed for CHO-GSN platform
- Non-CMV promoters
- Thorough QC & sequence confirmation

2-3 weeks

Stable Pool Generation

CHO-GSN Platform

- CHO-K1 derived
- MaxCyte Electroporation
- MSX as high selection pressure
- 50 mL production runs to assess titer

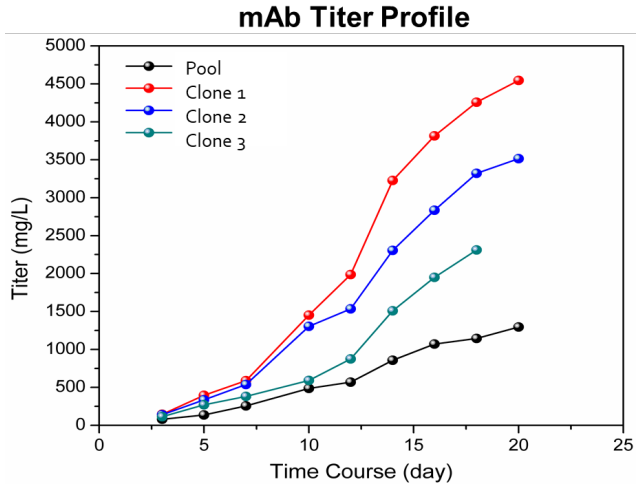
6-7 weeks

Stable Clone Generation

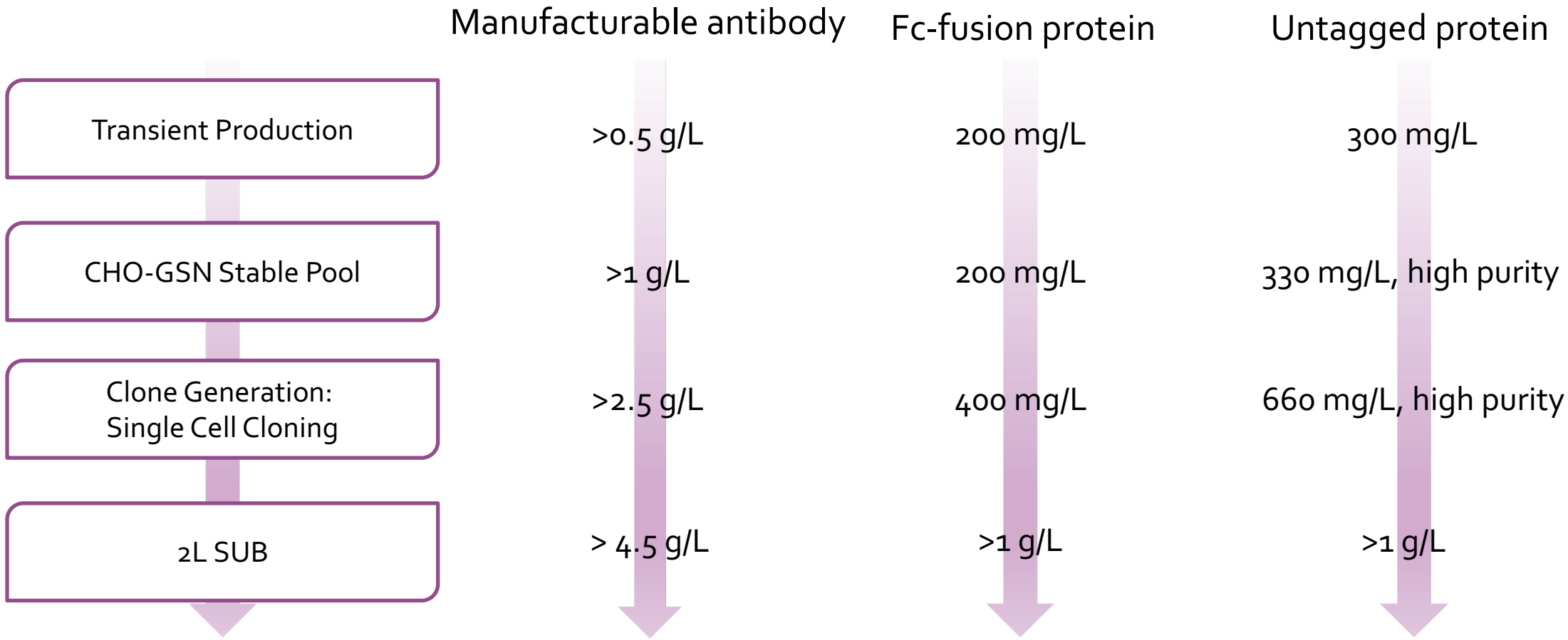
CHO-GSN High Titer Clone and Monoclonal Cell Line

- Solentim™ VIPS for single cell cloning
- Solentim™ Cell Metric for confirmation of monoclonality
- 50 mL production runs to assess titer
- Generational stability test

11-12 weeks



Successful Progression from Transient to RCB



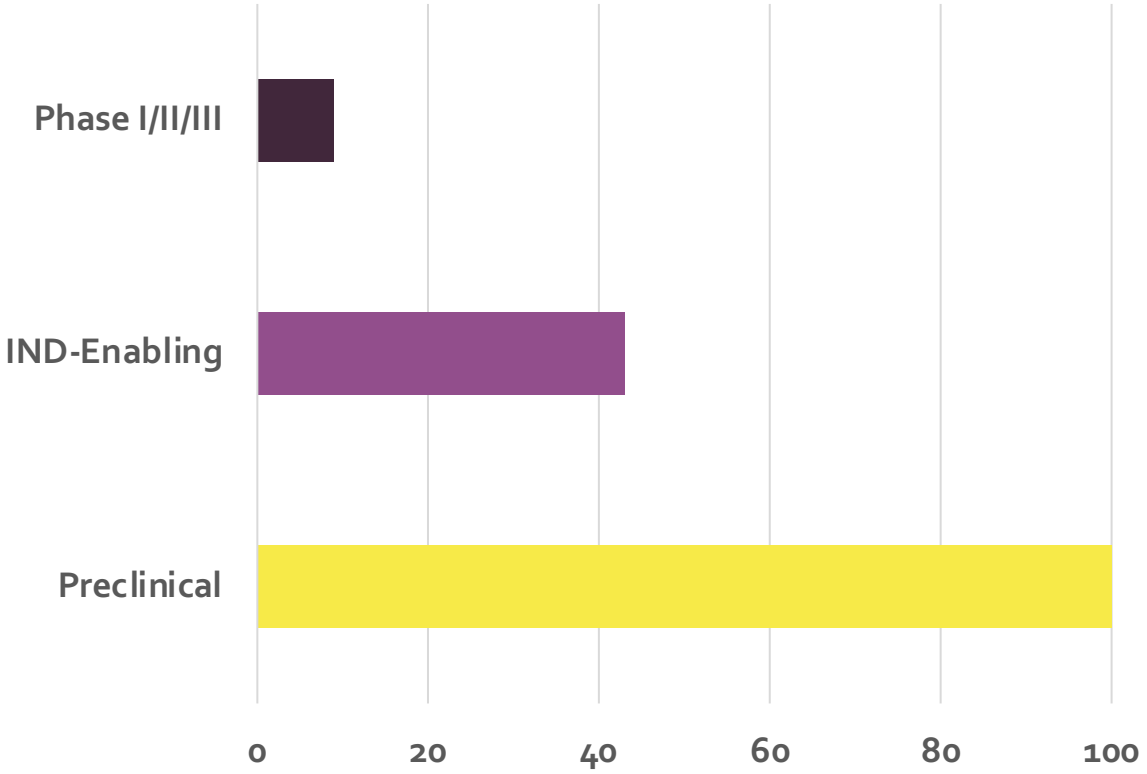
CHO-GSN Research Cell Bank Characterization and Process Development

Final Research Cell Bank

- High titer clones selected
- Monoclonality ensured
- Tolerance to shear force & other bioreactor conditions tested

RCB Characterization & Testing	Stability Studies	Process Development	Scale-up Productions
• Sterility • Mycoplasma • Gene Copy Number Determination	• Cryopreservation and stability study over 80 generations • Scalability in small scale bioreactors • Generate sufficient stability data to support shelf-life of clinical material	• Process optimization • Scale Down/Up Models • Formulation Development • Analytical Assay Development • Perfusion Method Development (proof of concept showed GSN cells can grow to $80x10^6$ cells/mL)	• WAVE bag production • Medium to large scale bioreactor (up to 2000 L) • Produce and support GMP grade Drug Substance and Drug Product

CHO-GSN Cell Lines in Preclinical and Clinical stages



Upstream Therapeutic Antibody/Protein Process Development

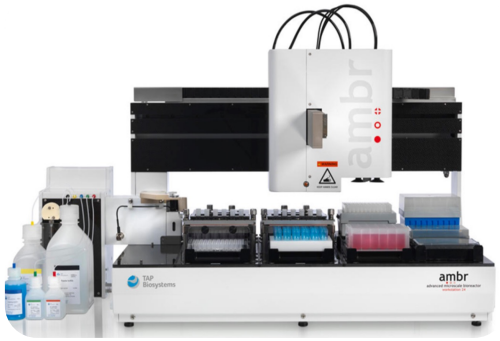
Preliminary Upstream Media and feed screening

Evaluate production in flasks
DoE for media and feed screening

Sartorius Ambr® 15 Microbioreactor Clone & Parameter Screening

Evaluate key parameters in Microbioreactors using Ambr® 15 system :

- Clone selection
- Evaluate select culture parameters
- Early –stage process optimization



2L SUB Confirmation Run

Evaluate cell line scalability

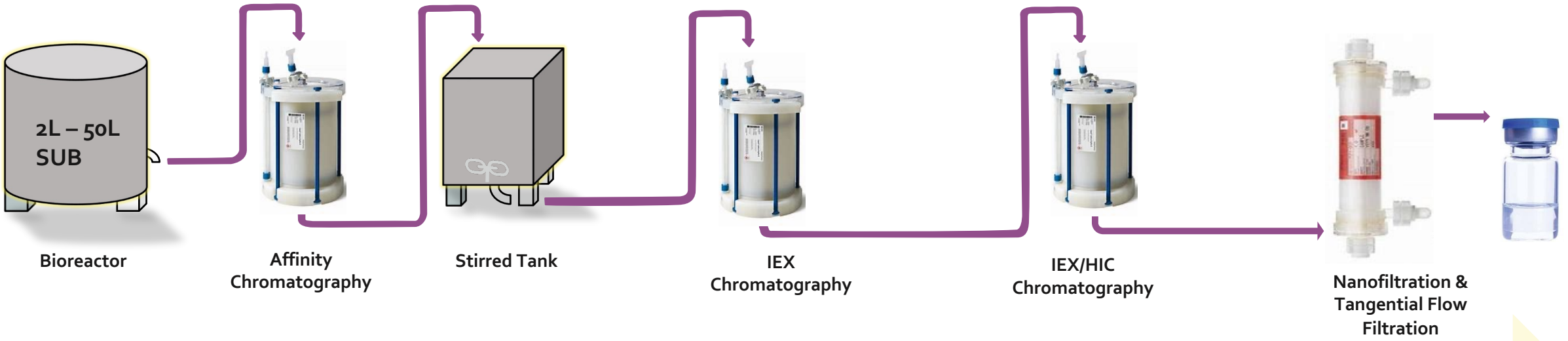
50L SUB Scale Up

Confirm cell culture parameters in scale up production

Downstream Therapeutic Antibody Process Development

Downstream Process Development Stages

Capture Step	Viral Inactivation	Polishing Step #1	Polishing Step# 2	Nanofiltration/UF/DF
Capture produced material	Inactivates any potential enveloped viruses	Remove Aggregates or product related impurities	Remove Process Related impurities (HCP, DNA, leachate)	Remove potential viruses Buffer exchange

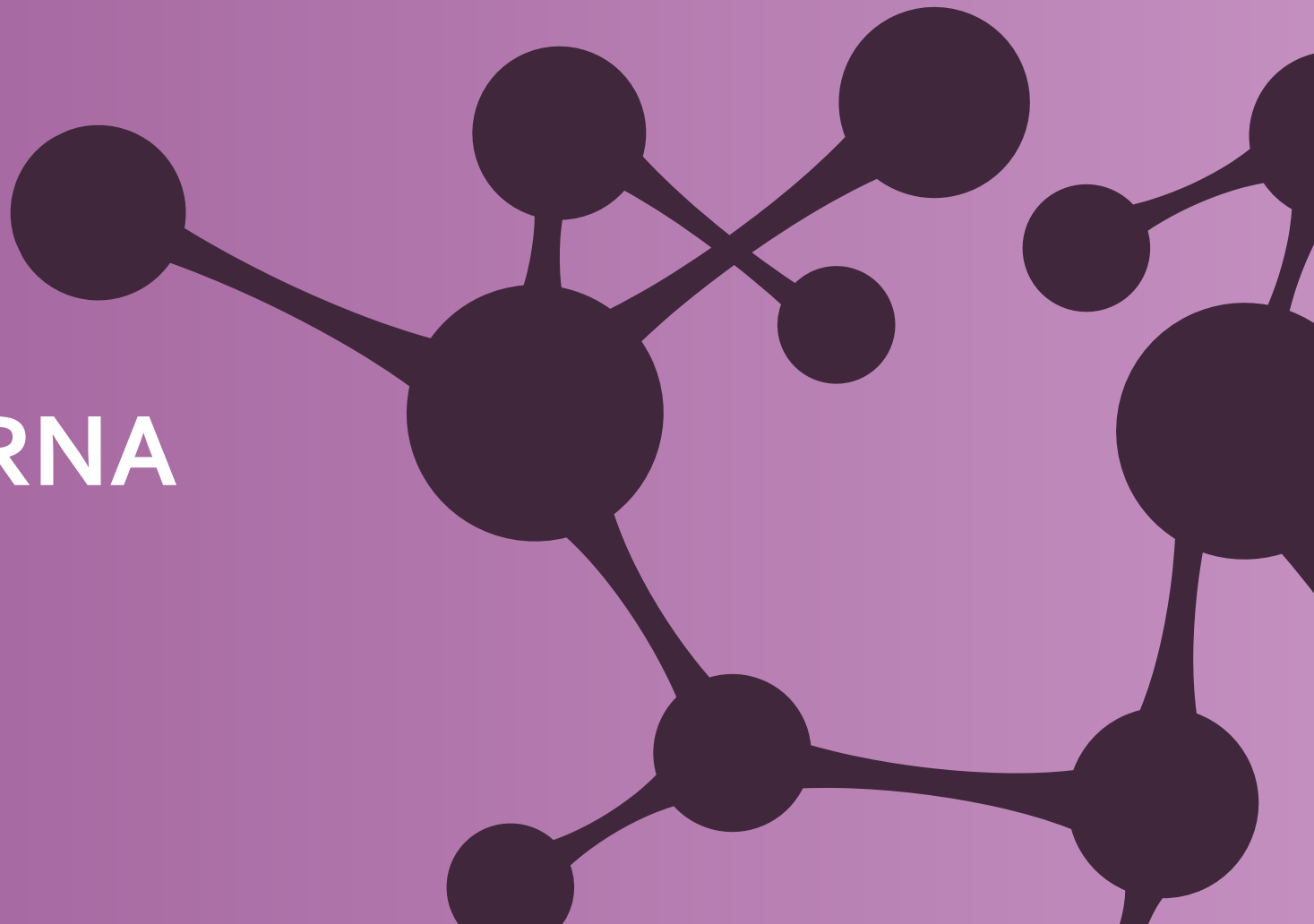


Conditioned Medium — **Purify** — **Final Product**

Antibody/Protein Assays and Analytics

Test	Purpose	Assay	Reference
Appearance	Safety, Quality	Visual Inspection	USP<790>
Bacterial Endotoxin	Safety, Quality	Chromogenic LAL	USP<85>
Bioburden	Safety/quality		USP<61>
Sterility (w/ BnF)	Safety, Quality	1 mL x 2 Direct Inoculation	USP<71>
pH	Safety, Quality	pH Test	USP<791>
Osmolality	Safety, Quality	Osmolality Test	USP<785>
Protein Concentration	Strength	Spectrophotometry	USP<1057>
Residual Host Cell Protein	Purity	ELISA	
Residual Protein A	Safety, quality	ELISA	
Residual Host Cell DNA	Purity	qPCR	
Charge by IEF	Purity/Identity	Capillary Electorphoresis	
% Monomer by SEC	Purity	HPLC	
RP, AEX, & IEX HPLC	Identity/Purity	HPLC	
CE-SDS	Purity	Capillary Electrophoresis	
Endotoxin by colorimetric LAL	Safety/quality	Spectrophotometry	
Subvisible Particles	Safety	Subvisible particle analysis, various equipment	
Stability	Various	Various assays	
Activity	Potency	Octet or cellular assay	

Drug Substance: mRNA



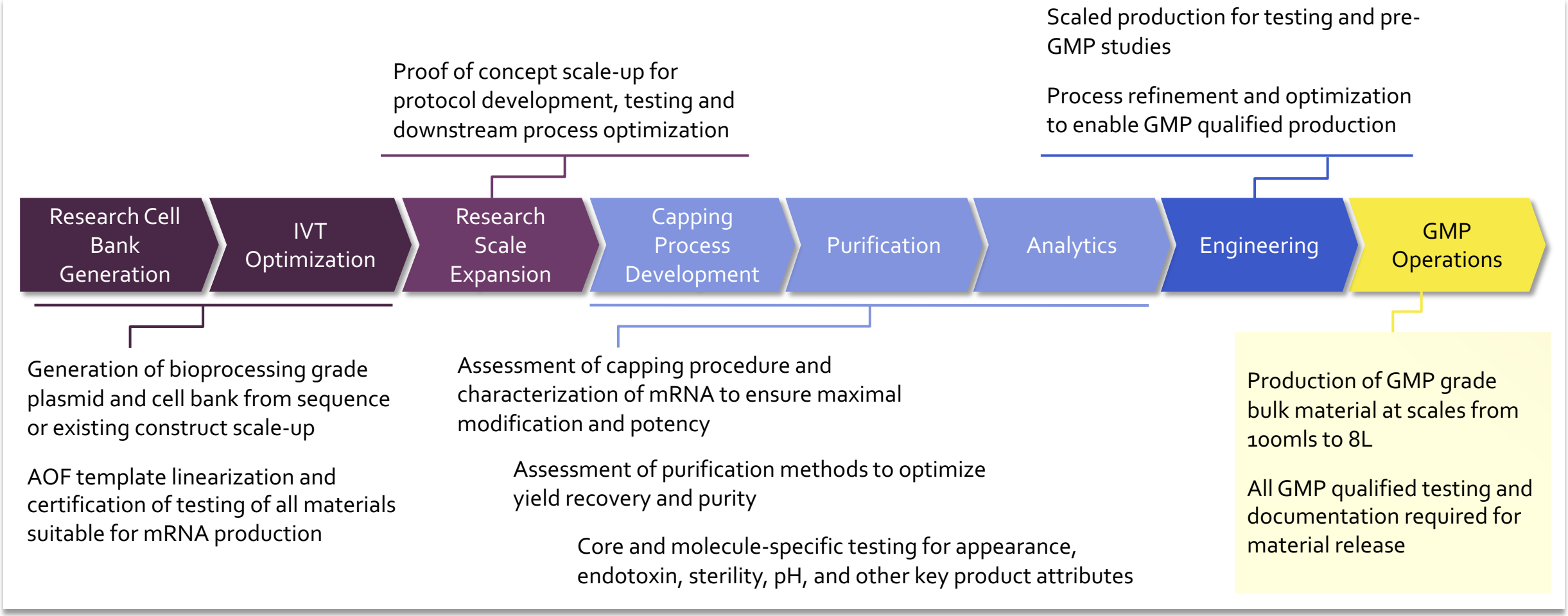
Features of mRNA Development and Manufacturing Services

- DNA template engineering
- Cell-free, enzymatic synthesis
- Relatively short manufacturing timelines relative to traditional biologics
- Free of animal-derived raw materials
- Short and long RNAs
  - Self-amplifying RNA (saRNA): typically 9-16 kb
  - Non amplifying RNA: typically 3-6 kb

- ISO 13485:2016 certified
- ISO 7 RNA suite
- Manufacturing to support clinical development
- 0.1 to 8 L scale (current)
- Expanding capacity to 100 L in 2022
- Full analytics on-site for in-process testing and batch release

Curia supports mRNA Platform Development from Research to Clinic

mRNA Research and Manufacturing Services



mRNA Analytics

Test	Purpose	Assay	Reference
Appearance	Safety, Quality	Visual Inspection	USP<790>
Bacterial Endotoxin	Safety, Quality	Chromogenic LAL	USP<85>
Bioburden (w/ BnF)	Safety, Quality	1 mL x 2 Direct Inoculation	USP<61>
pH	Safety, Quality	pH	USP<791>
Osmolality	Safety, Quality	Osmolality	USP<785>
RNA Concentration	Strength	UV A260	USP<1126>
RNA Identity	Identity	CE-Based (Size Confirmation)	
Identity (as RNA)	Identity	Enzyme Degradation and CE	
Residual protein	Purity	PAGE (silver stain) or Fluorescent	
Residual DNA	Purity	qPCR (Thermo "kan" reagent)	
Residual DS RNA	Purity	Dot Blot	Report
RNA Integrity	Quality	CE-Based	
Functional Assay	Strength	OPTIONAL	
% Cap [Optional]	Strength	R&D available; GMP in development	

Curia Bulk Drug Substance mRNA Manufacturing Capabilities

- GMP compliant, single use equipment
- Cell-free mRNA manufacturing
- Large scale production up to 8-80 grams/batch
- ISO7 suite
- Expertise in self-amplifying mRNA production
- Onsite analytics for in-process testing and batch release

Stages and Timeline

RCB Generation, DNA Production and Linearization

mRNA IVT Scouting → Pilot Program Production → Process Development → Production Run

8-10 weeks

Plasmid DNA template

1 -2 weeks

Small scale optimization and production level proof-of-concept

1 -2 weeks

Target small scale deliverable / purification optimization

2-4 weeks

Target client specific quantity for GMP run

Scale-up process for analysis and downstream development

GMP compliant batch record creation

1-2 weeks

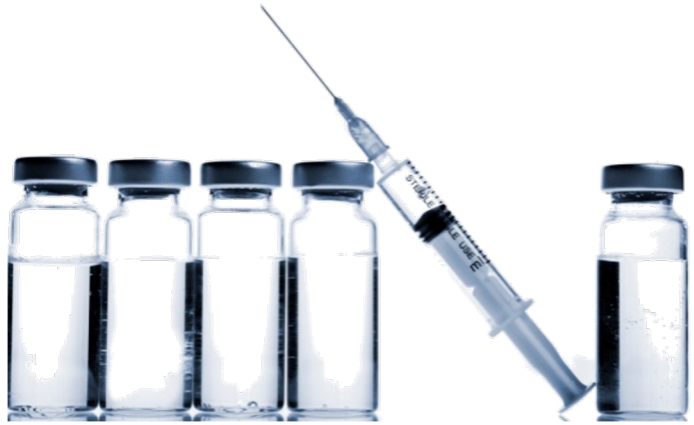
Repeat of engineering run conditions in GMP suite

Execution of process as developed in engineering run and deliverable of GMP grade bulk material

Drug Product: Antibodies, Proteins, and mRNA-LNP

Formulation Development

- Based on the most relevant ICH stability guidelines
- Upon the foundation of the most critical parameters:
  - Stress factors
  - Degradation products
  - Stability indicating assays
  - Formulation sweet-spot(s)
- Targeting for the most competitive presentations:
  - Liquid, lyophilized, or multidose formulations
  - Ideal container/closure systems
  - Convenient routes of administration



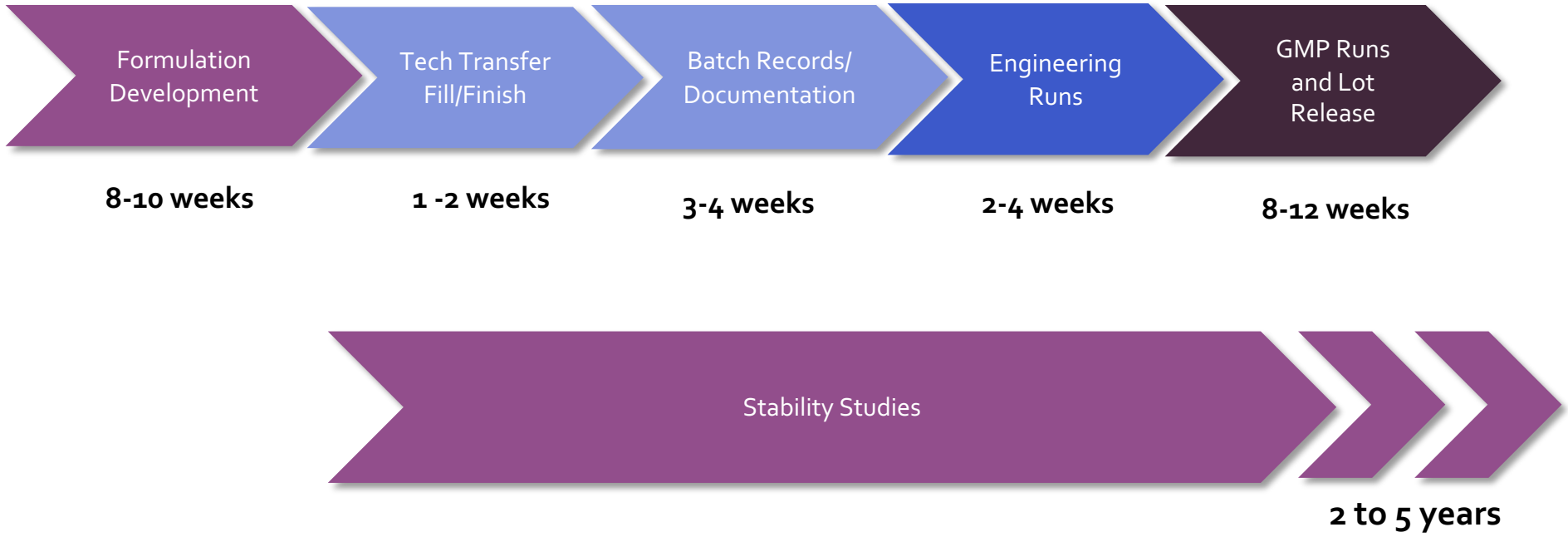
Process Development

- Formulation, Fill Finish, Lyophilization Process Development (disposable product contact manufacturing train available)
  - Antibodies, proteins, peptides, mRNA-LNPs
- Specializing in First In Human manufacturing support
- Tech Transfer
- Engineering runs
- Validation
- Novel processes

Drug Product Formulation Development and Manufacturing

- EU Grade A Environment
- Vial size: 2-30cc
- Fill Volume: 0.2-32 mL
- Max batch size:
  - Liquid: 20,000 units
  - Lyophilized: 1200-5,000 (2 cc to 20 cc)
- Onsite analytics for in-process testing and batch release

Stages and Timeline



Biomanufacturing at Curia

GMP manufacturing of biologics: single use, and flexible

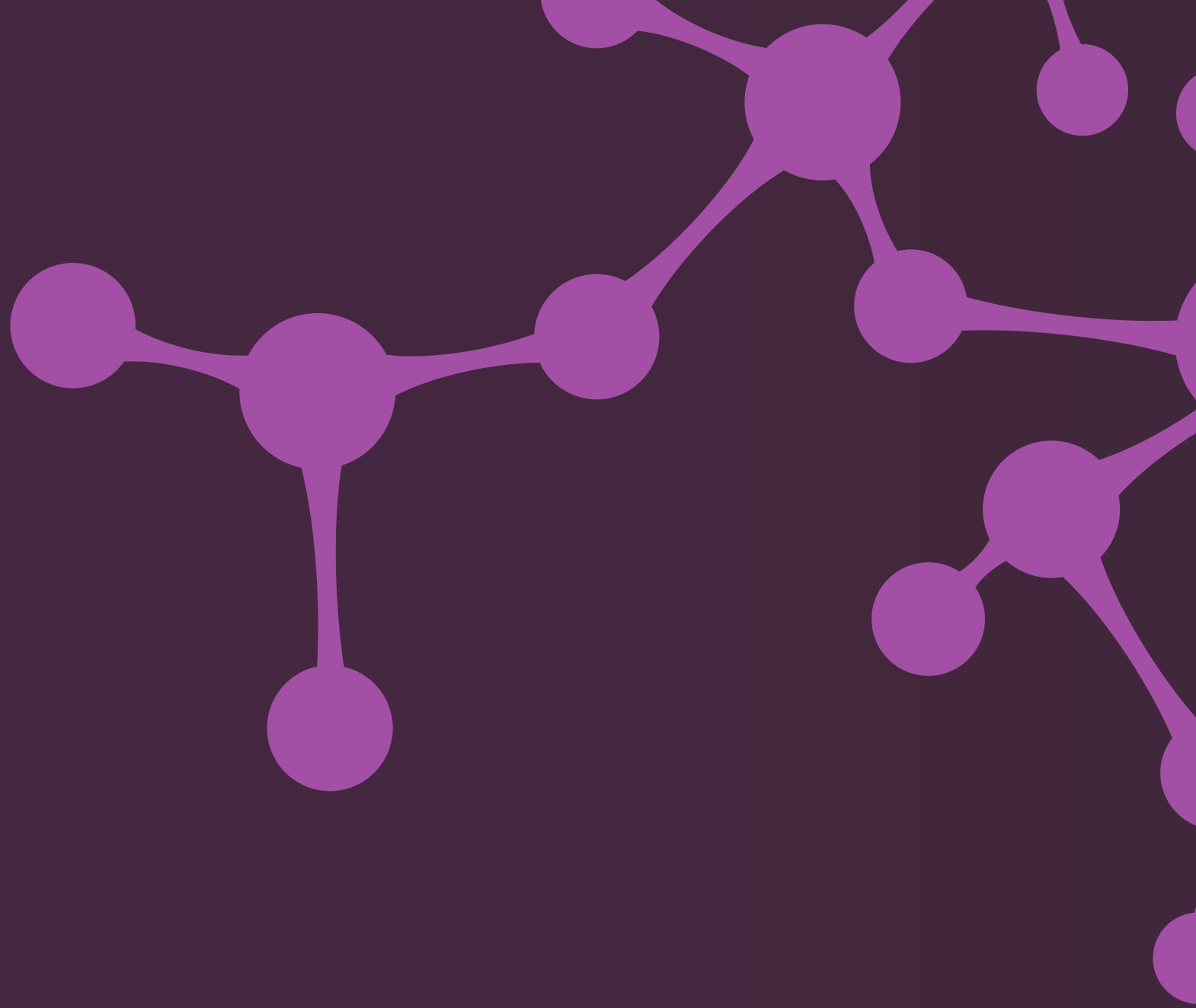
- First in human manufacturing that bridges the gap between development and late-stage manufacturing
- ISO 13485:2016 certified

Integrated Solution approach for biologics development

- On-site assays and analytics for in-process testing and batch release
- Rapid advancement from process development to clinical supply
- Thought partnership and close collaboration with clients

Advantages

- **Comprehensive platforms for development, manufacturing, and analytics**
- **Close collaboration and open communication**
- **On-site analytics for rapid turn-around**



Thank You

Contact us for more information