curia

Biologics Development & Manufacturing

3/2022

LakePharma & Integrity Bio – 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

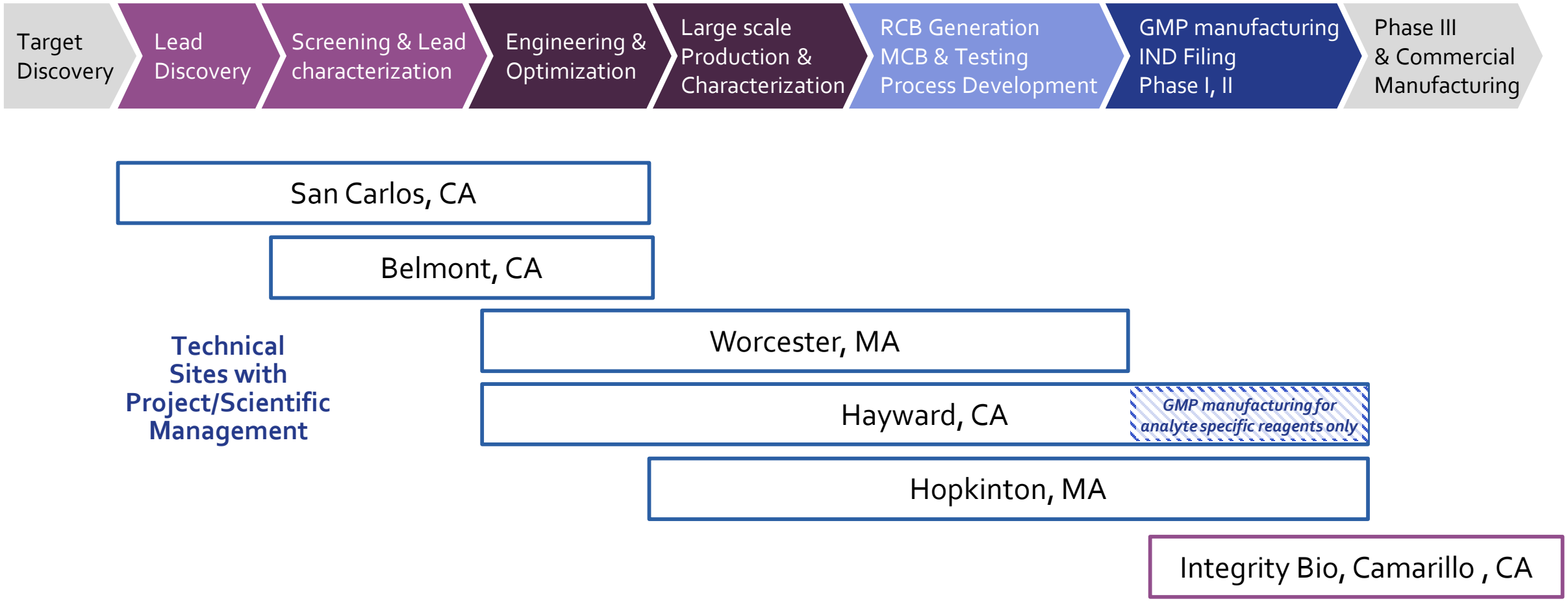
Springfield, MO
Grafton, WI
Rensselaer, NY
Bon-Encontre, France
Tonneins, France
Frankfurt, Germany
Aurangabad, India
Origgio, Italy
Rozzano, Italy
Valladolid, Spain

DRUG PRODUCT

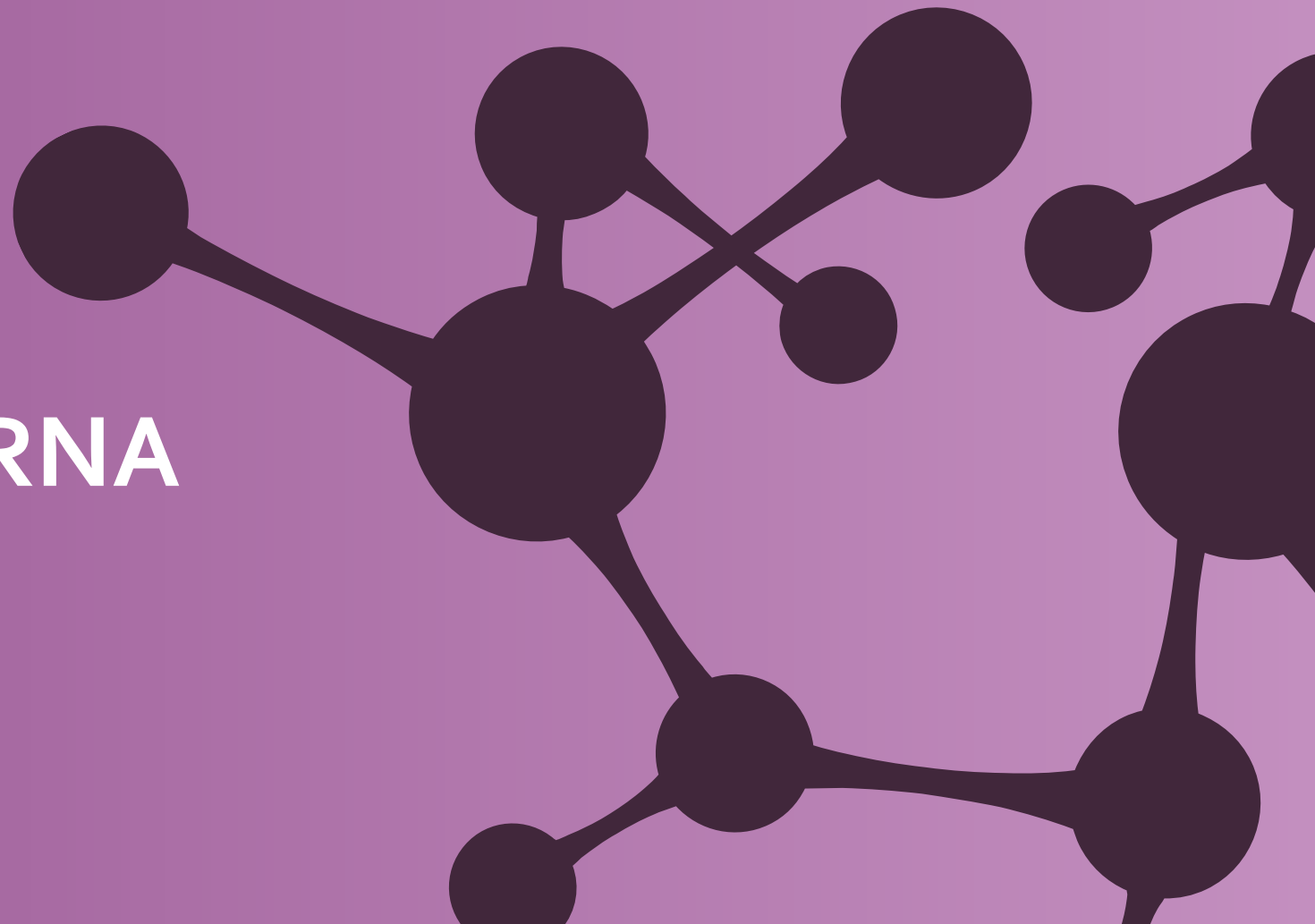
Camarillo, CA
Thousand Oaks, CA
Burlington, MA
Albuquerque, NM
Glasgow, UK

Integrated Solutions Approach for Biological Therapeutics

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



Drug Substance: mRNA



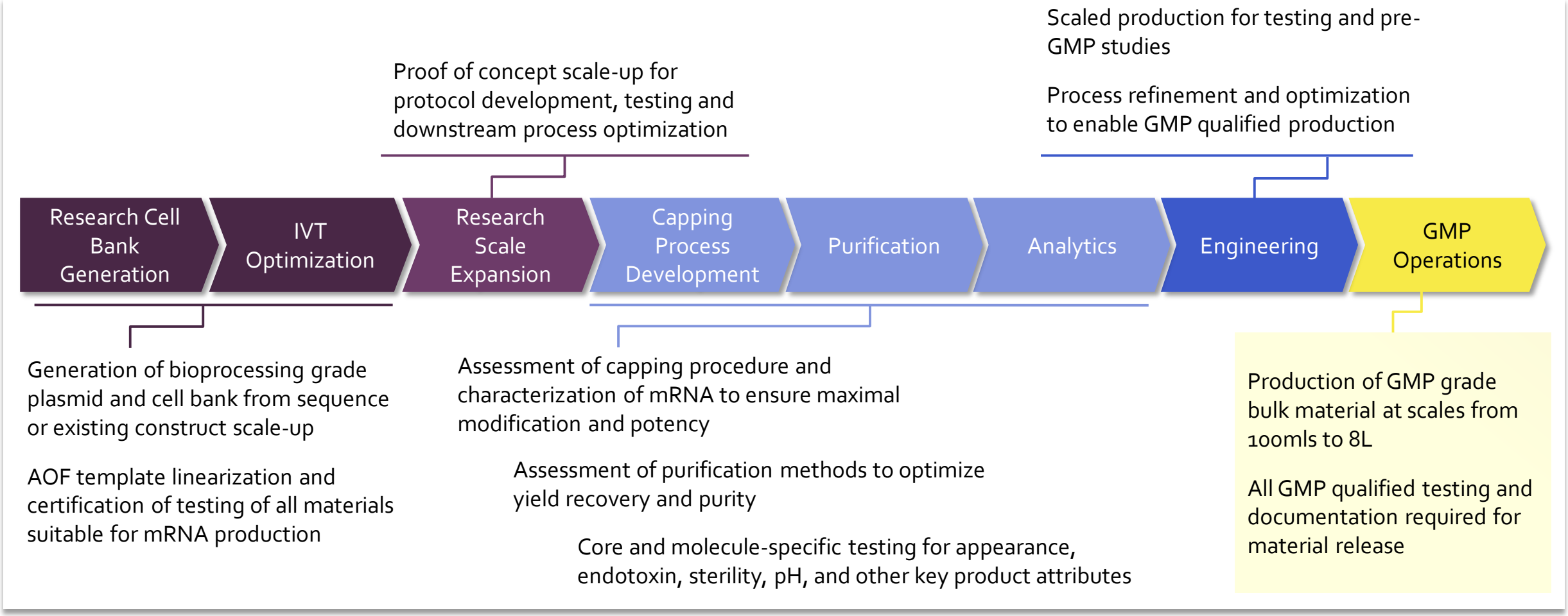
Features of mRNA Development and Manufacturing Services

- 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 13485:2006 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



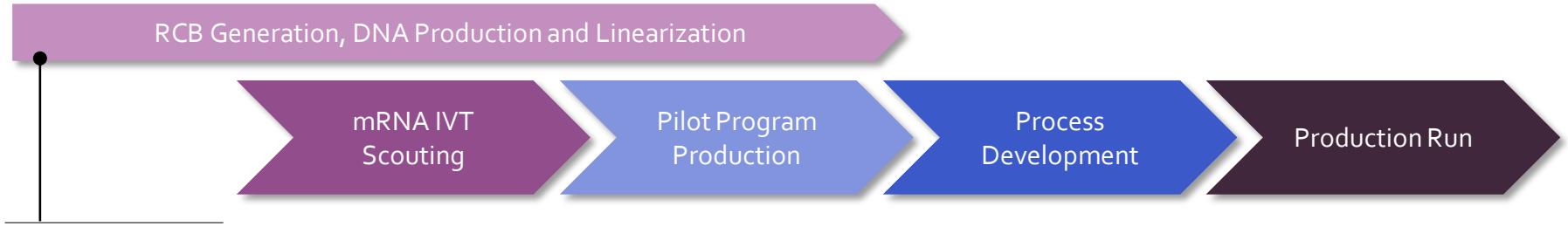
mRNA Analytics

Test	Purpose	Assay
Appearance	Safety, Quality	Visual Inspection
Bacterial Endotoxin	Safety, Quality	Chromogenic LAL
Sterility (w/ BnF)	Safety, Quality	1 mL x 2 Direct Inoculation
pH	Safety, Quality	
Osmolality	Safety, Quality	
RNA Concentration	Strength	UV A260
RNA Identity	Identity	CE-Based
Identity (as RNA)	Identity	Enzyme Degradation and CE
Identity (RNA sequence)	Identity	NGS
Residual protein	Purity	PAGE (silver stain) or Fluorescent
Residual DNA	Purity	qPCR (Thermo "kan" reagent)
Residual DS RNA	Purity	ELISA
Residual DNA:RNA Hybrids	Purity	ELISA
RNA Integrity	Quality	Capillary Electrophoresis
% Cap [Optional]	Strength	In Development
Functional Assay	Strength	OPTIONAL

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



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

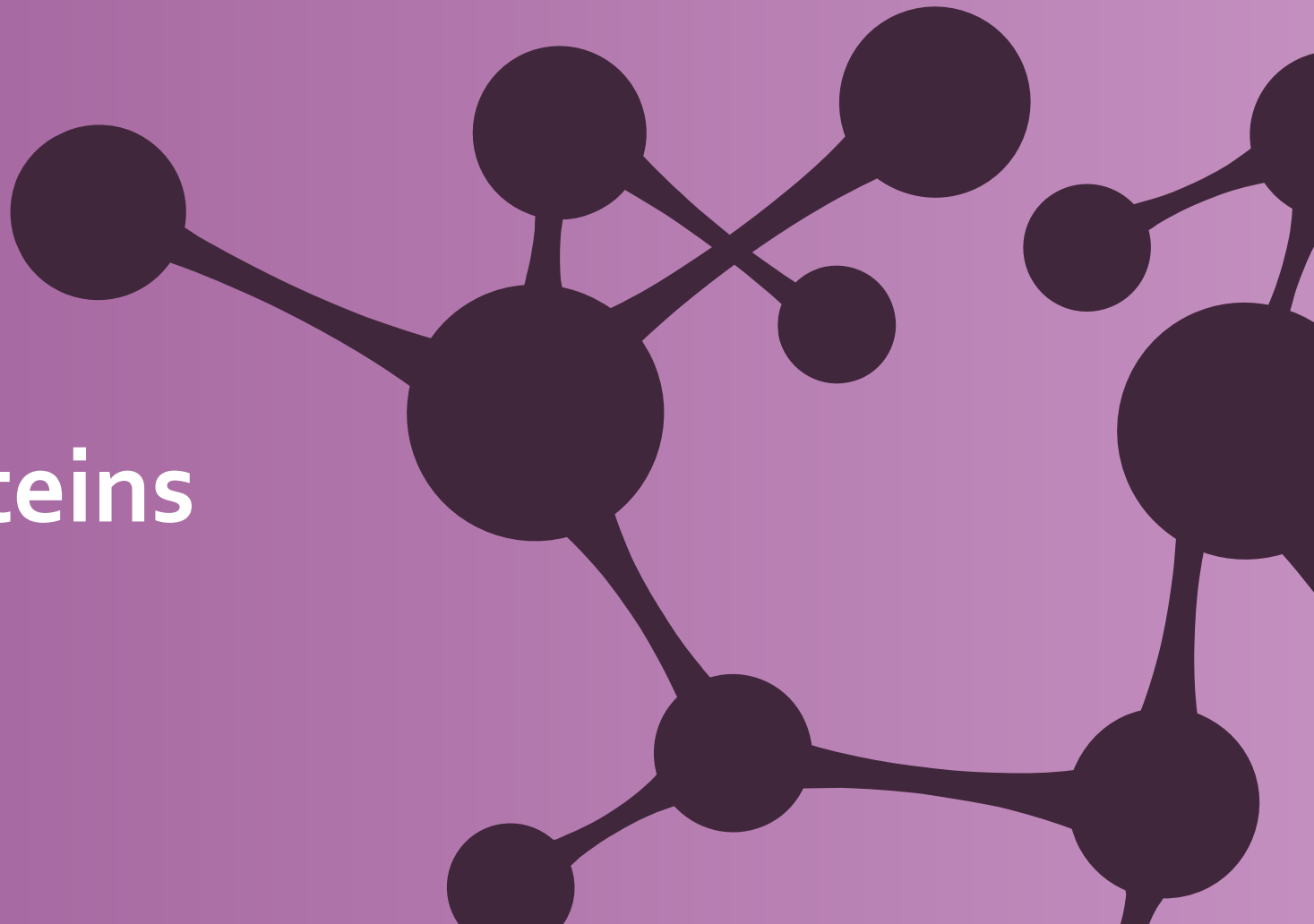
GMP compliant batch record creation

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 Substance: Antibodies and Proteins



Antibody and Protein Therapeutics Development and Manufacturing Services

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

- ISO 13485:2006 certified
- Manufacturing to support clinical development
- 200-2000 L SUBs
- Full analytics on-site for in-process testing and batch release

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
- Total timeline ~18 months for phrase I drug substance

Stages and Timeline

16-24 weeks

CHO cell line engineering, cloning, and RCB

6-8 weeks

Master Cell Bank generation and characterization

~12 weeks

Optimize culture conditions in Ambr® and scale up to 2L through 50L SUBs

Batch record creation

~12 weeks

Develop purification process

Batch record creation

4-6 weeks Engineering

10-12 weeks GMP Mfg & batch release

Engineering run in suite and cGMP manufacturing of bulk drug substance

Upstream Therapeutic Antibody/Protein Process Development

Preliminary Upstream Media and feed screening

Evaluate production in flasks

Sartorius Ambr® 15 Microbioreactor Clone & Parameter Screening

Evaluate key parameters in Microbioreactors:

- Clone selection
- media and feed development
- Early –stage process optimization

2L SUB Confirmation Run

Evaluate select culture parameters identified using Ambr® 15 system

50L SUB Scale Up

Confirm cell culture parameters in scale up production

Downstream Therapeutic Antibody Process Development

Downstream Process Development Stages

Capture Step

Capture 100% of produced material

Polishing Step #1

Remove Aggregates or product related impurities

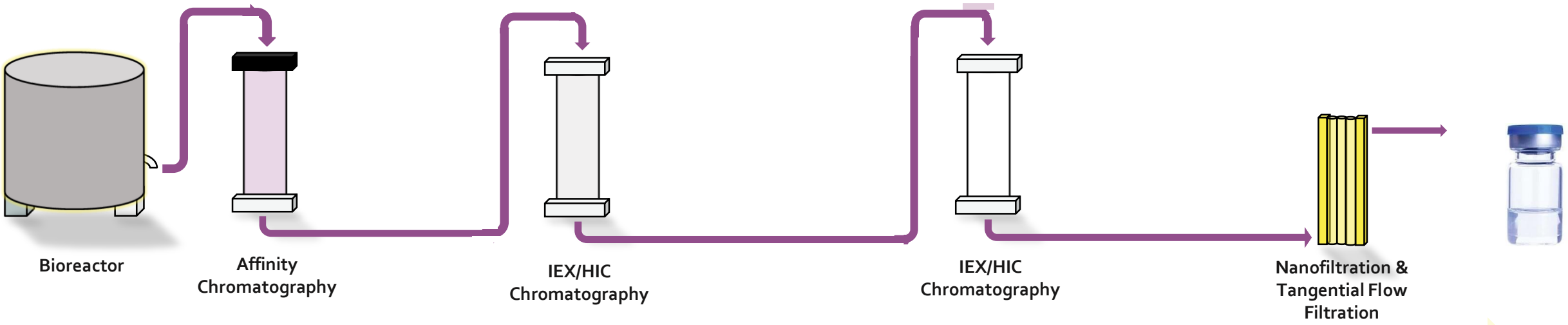
Polishing Step# 2

Remove Process Related impurities (HCP, DNA, leachate)

Nanofiltration/UF/DF

Remove Viruses

Buffer Exchange



Conditioned Medium — **Purity** — **Final Product**

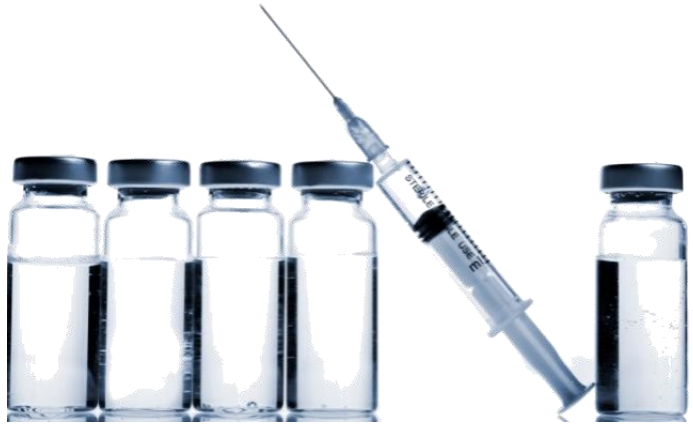
Antibody/Protein Assays and Analytics

Test	Purpose	Assay
Appearance	Safety, Quality	Visual Inspection
Bacterial Endotoxin	Safety, Quality	Chromogenic LAL
Bioburden	Safety/quality	
Sterility (w/ BnF)	Safety, Quality	1 mL x 2 Direct Inoculation
pH	Safety, Quality	pH Test
Osmolality	Safety, Quality	Osmolality Test
Protein Concentration	Strength	Spectrophotometry
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 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



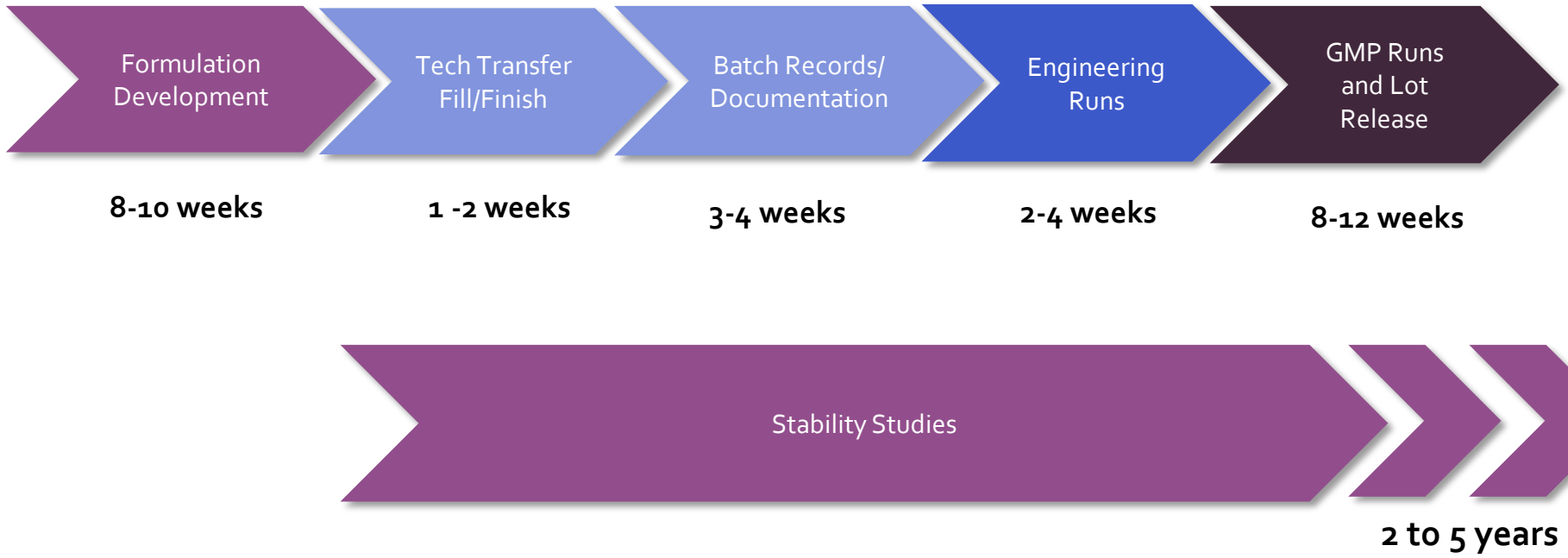
Process Development

- 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 13485:2006 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