



Integrated Solutions for Efficient Process Scale-Up and Single-Use Facility Start-Up

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Pall Biotech

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Continuously Improving Bioprocesses

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Agenda

- Aligning Therapy Development to Facility Start-Up Project Execution
- Process Technologies and Platforms for Rapid Implementation and Production Start-up
- Streamlining Single-Use Flow Path Design, Standardization, and Management
- HakoBio Facility Design Tool for Optimal Process Flow Operation
- Scale-up and Optimization Services for Rapid Process Industrialization
- Leveraging Partnerships for Process Improvement and Speed to Production
- Efficient Single-Point Project Management for Integrated Solutions
- Summary of Integrated Solutions Approach



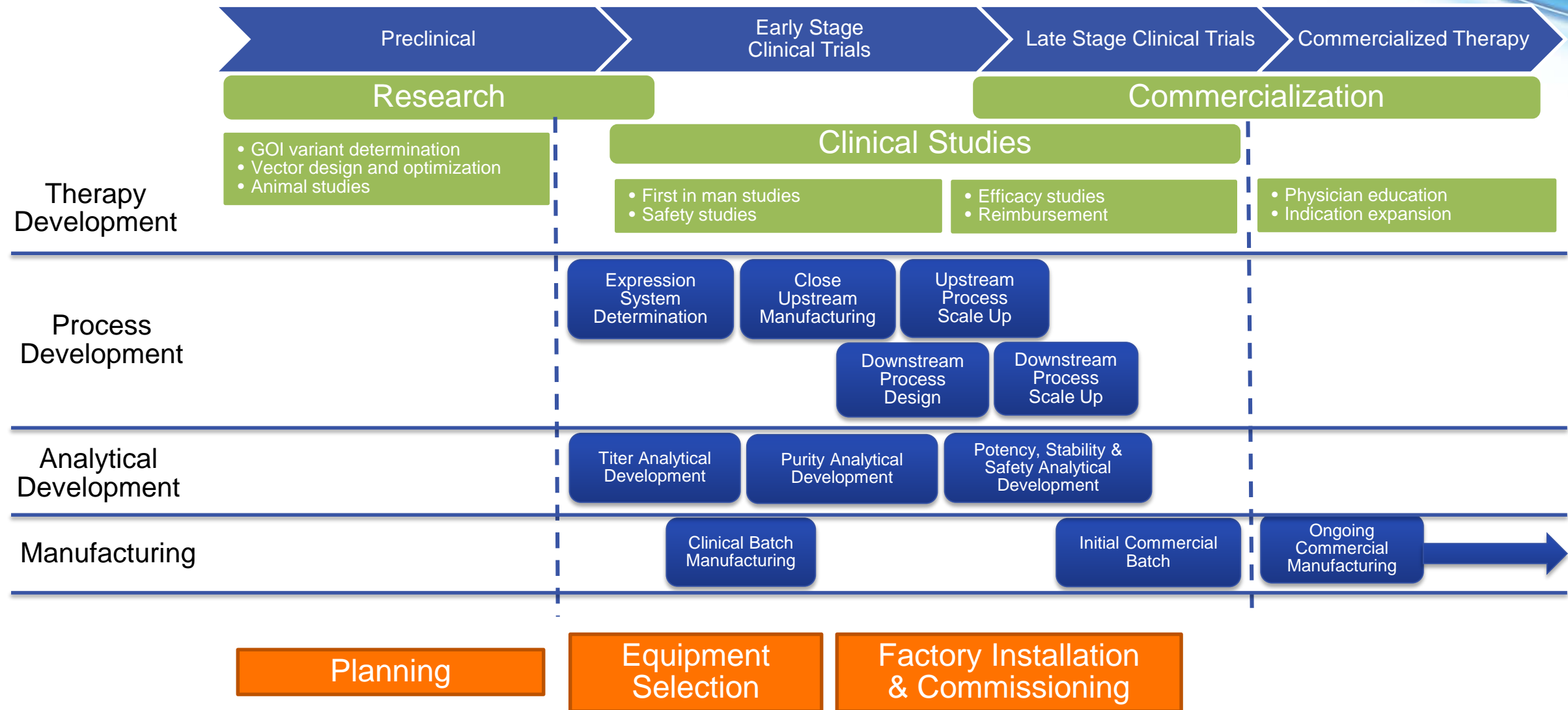
Aligning Therapy Development to Facility Start-Up Project Execution

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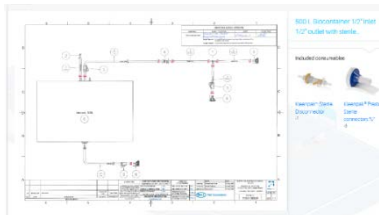
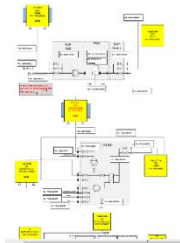
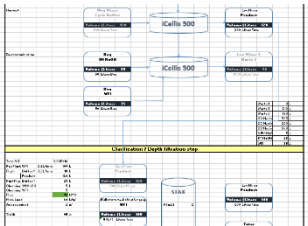
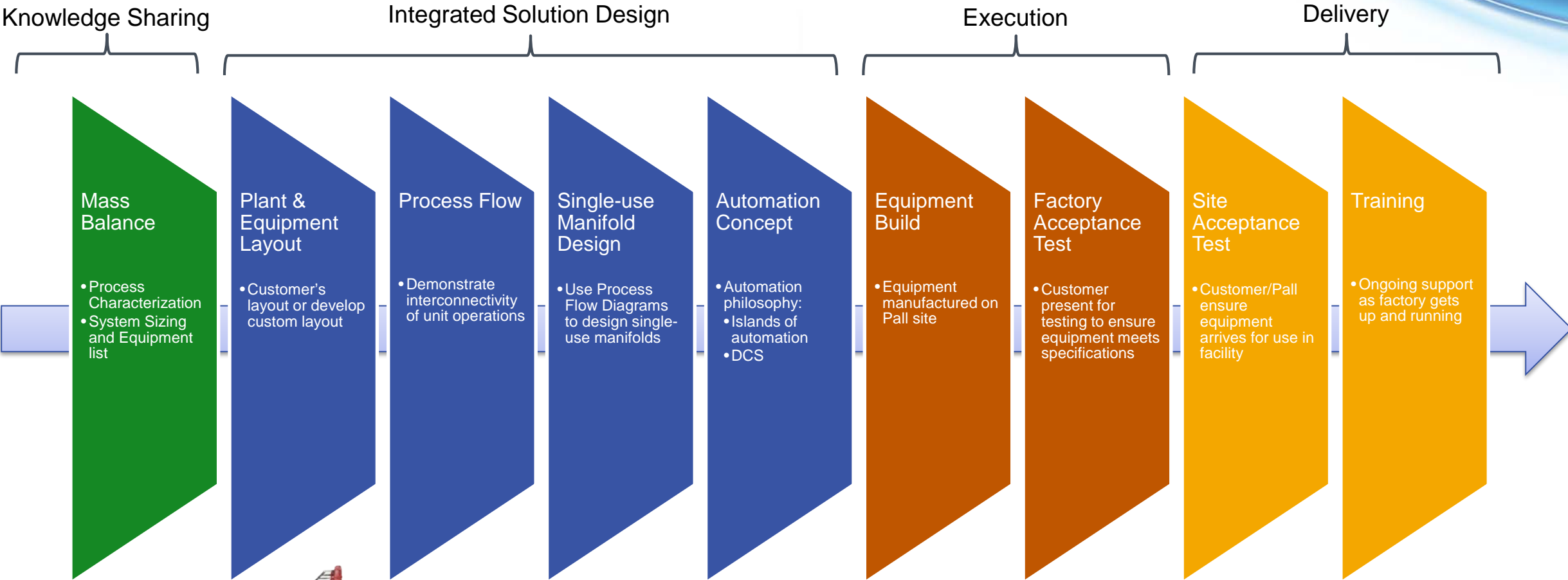
Therapy Development

Speed to mfg and new technologies shrink timelines for new facilities



Pall's Approach To Integrated Solutions Project Execution

Speed, project management, and process expertise are paramount for success...





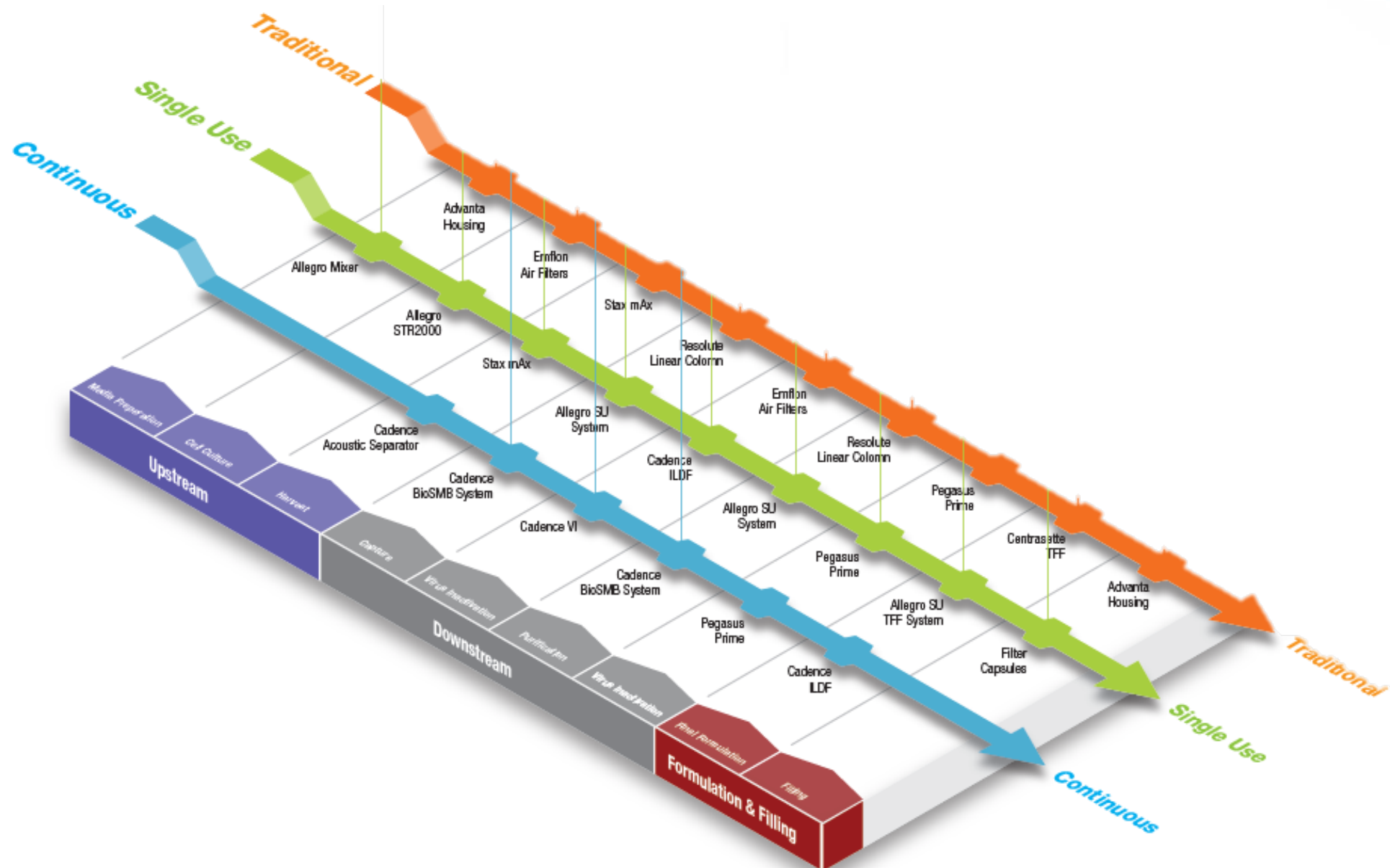
Process Technologies and Platforms for Rapid Implementation and Production Start-up

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Pall Biotech Integrated Solutions

Selecting the right approach for your biotech journey...



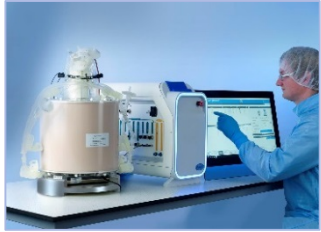
Pall Biotech Integrated Solutions

Serving the complete single-use value stream



Pall Biotech Integrated Solutions

Standardized single-use systems facilitate platforms



Adherent seed train:
Xpansion® multiplate
bioreactor



Adherent bioreactor:
iCELLis 500+ bioreactor



Suspension seed train and bioreactor:
Allegro™ XRS 25 bioreactor & Allegro STR
50, 200, 1000, 2000 L bioreactors



Clarification:
Stax™ depth filter systems



Purification:
Allegro single-use chromatography system



Concentration:
Allegro single-use tangential
flow filtration systems



Media/Buffer Prep:
Allegro mixers



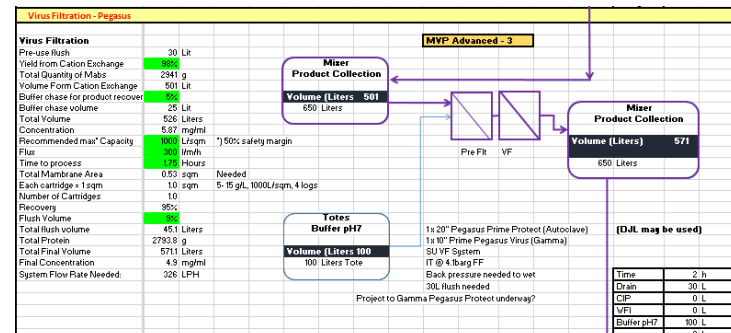
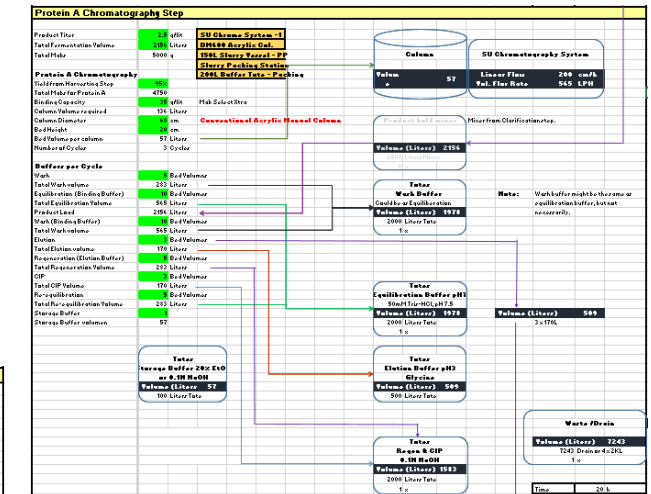
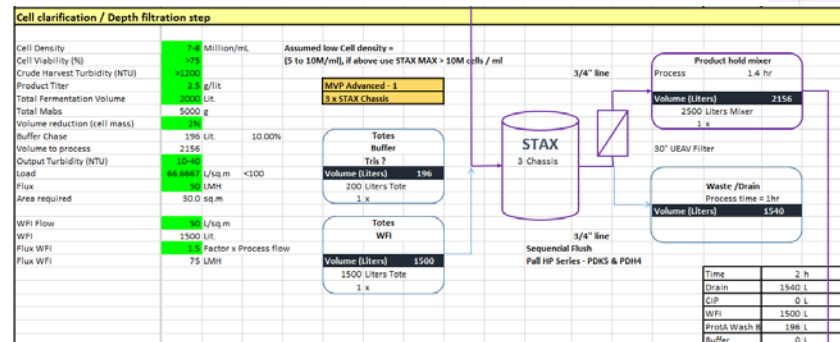
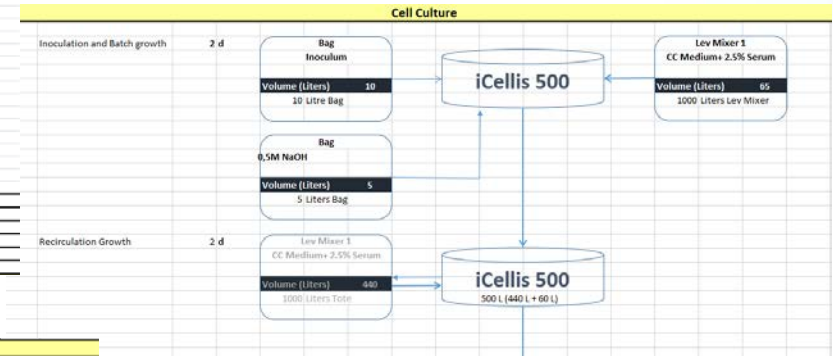
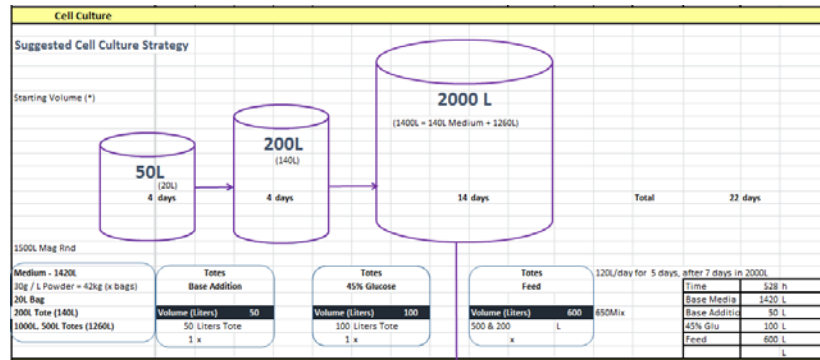
Media/Buffer Storage/Handling:
Allegro plastic/stainless steel totes



Sterile filtration:
Allegro MVP single-use system

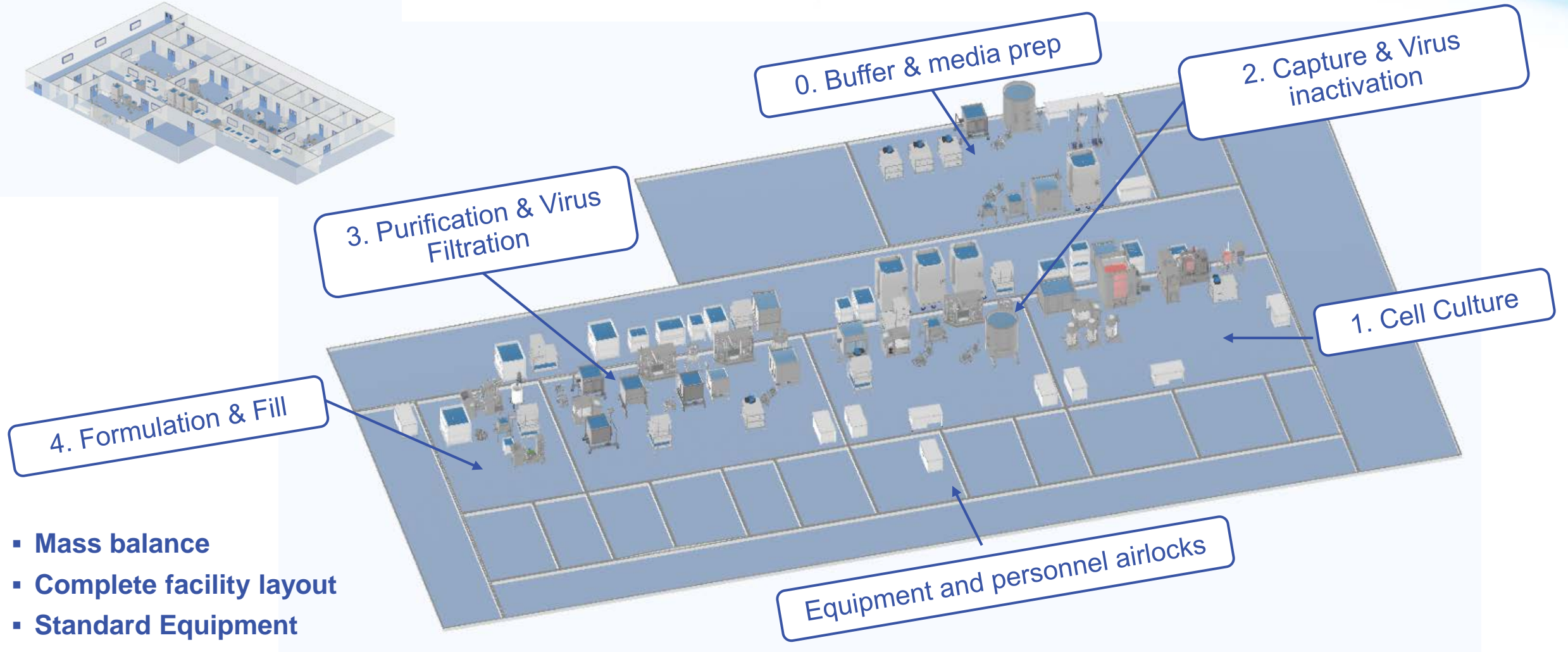
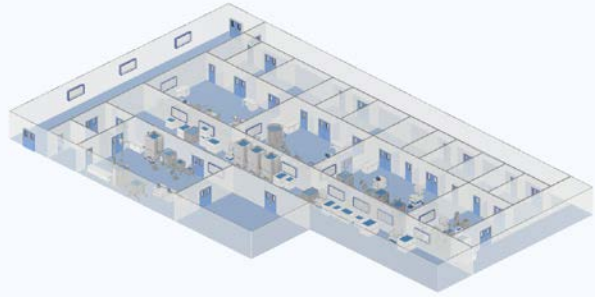
Platforms Established from Mass Balance

- Map all inputs and outputs from each unit operation
- Allows equipment sizing, specifications and equipment list generation
- Understanding of interconnectivity between unit operations
- Ensures the process is completely characterized



Pall Integrated Solution Platforms

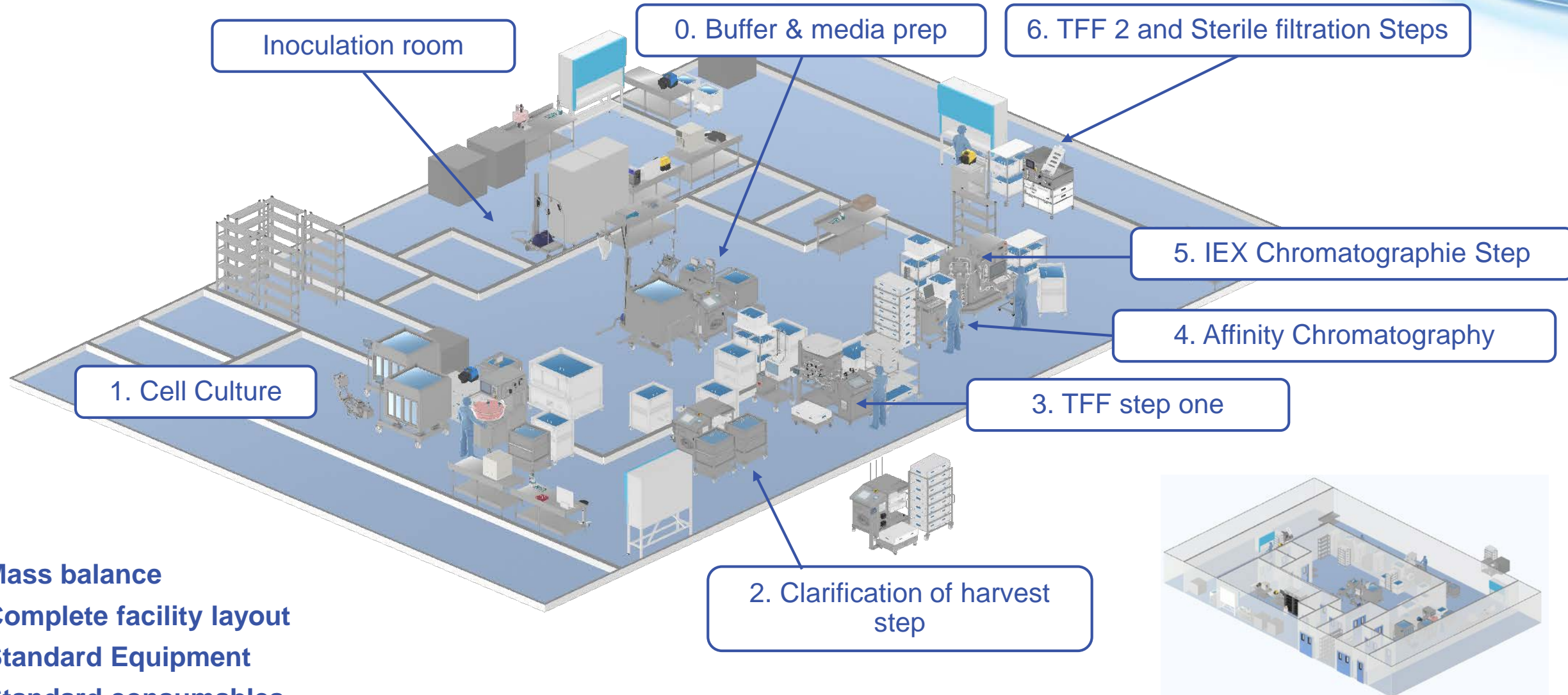
2000L mAb Fed Batch Platform CHO 2,5g/L



- Mass balance
- Complete facility layout
- Standard Equipment
- Standard consumables package for complete flow path

Pall Integrated Solution Platforms

AAV Viral Vector Production Platform; $3e^{16}$ vg



- Mass balance
- Complete facility layout
- Standard Equipment
- Standard consumables package for complete flow path

Pall Integrated Solution Platforms

Viral Vector Production

Cell Culture options for adherent or challenging suspension processes

Xpansion & iCELLis 500 scalable bioreactors versus flatware or suspension STR for high k_La / low shear requirements

Cell & Debris Removal

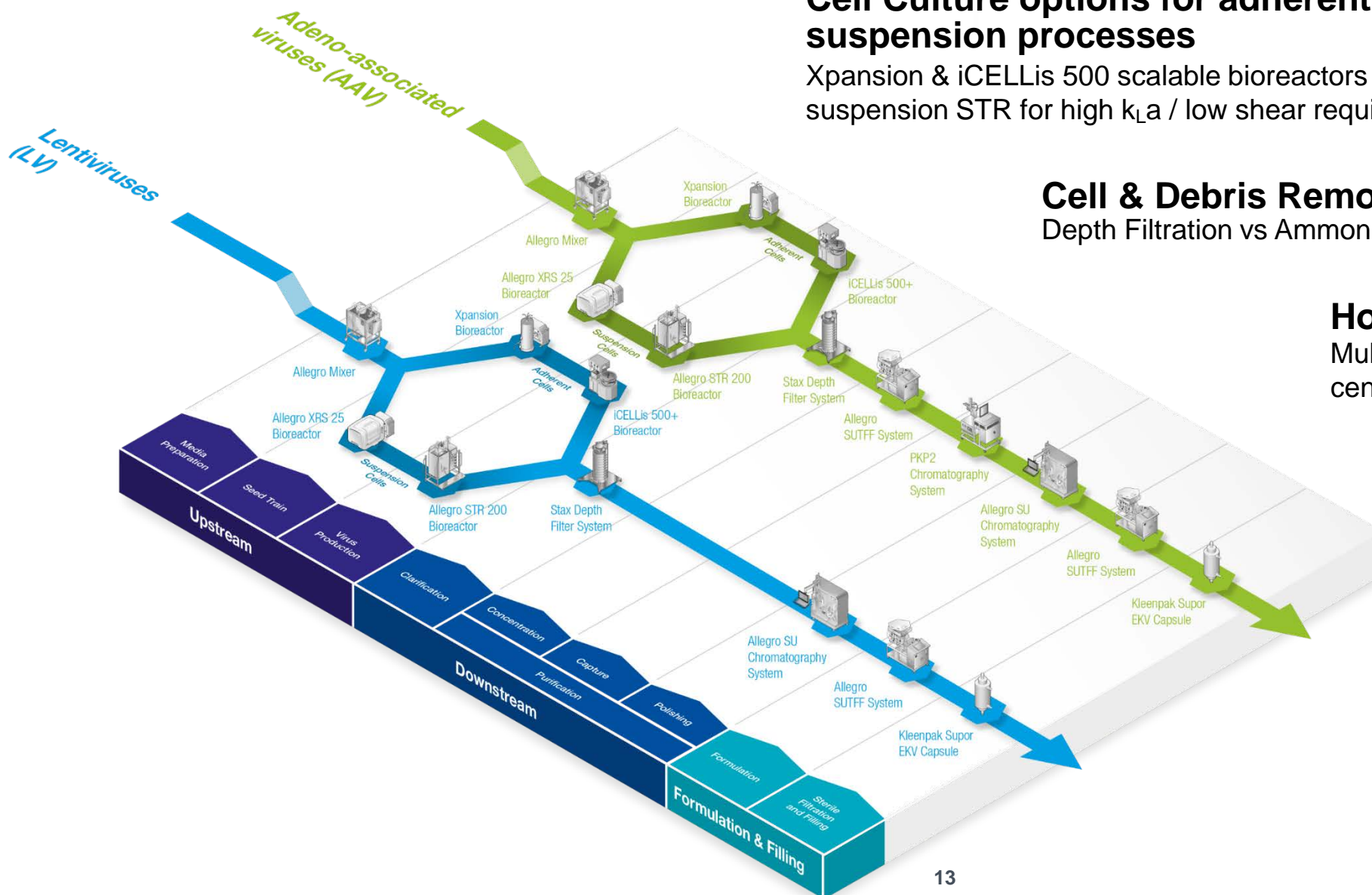
Depth Filtration vs Ammonium sulfate precipitation

Host cell DNA/protein removal

Multiple modes of chromatography vs centrifugation

Host cell DNA/protein removal

Tangential Flow Filtration vs Dialyzation





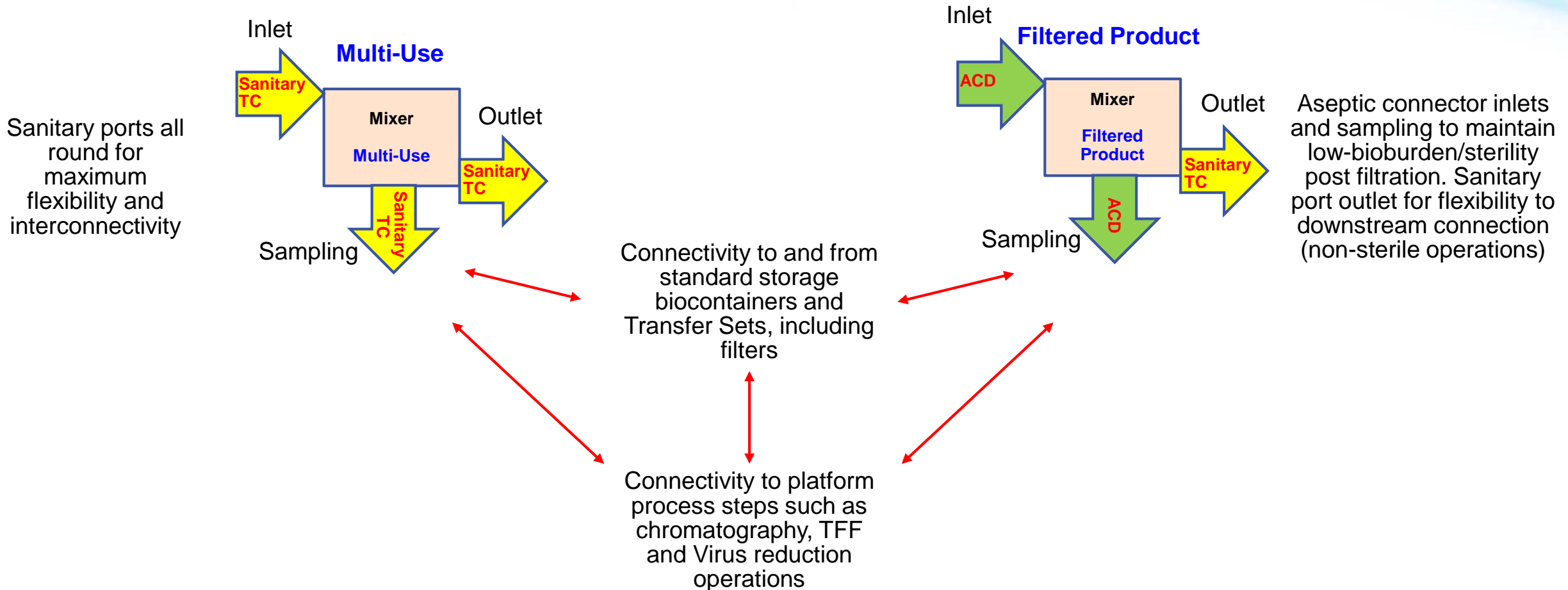
Streamlining Single-Use Flow Path Design, Standardization, and Management

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Integrated Single-Use Platform Solutions

Standard consumables designed for maximum flexibility



Optimized and flexible interconnectivity

Integrated Single-Use Platform Solutions

Standardized consumables for the full process

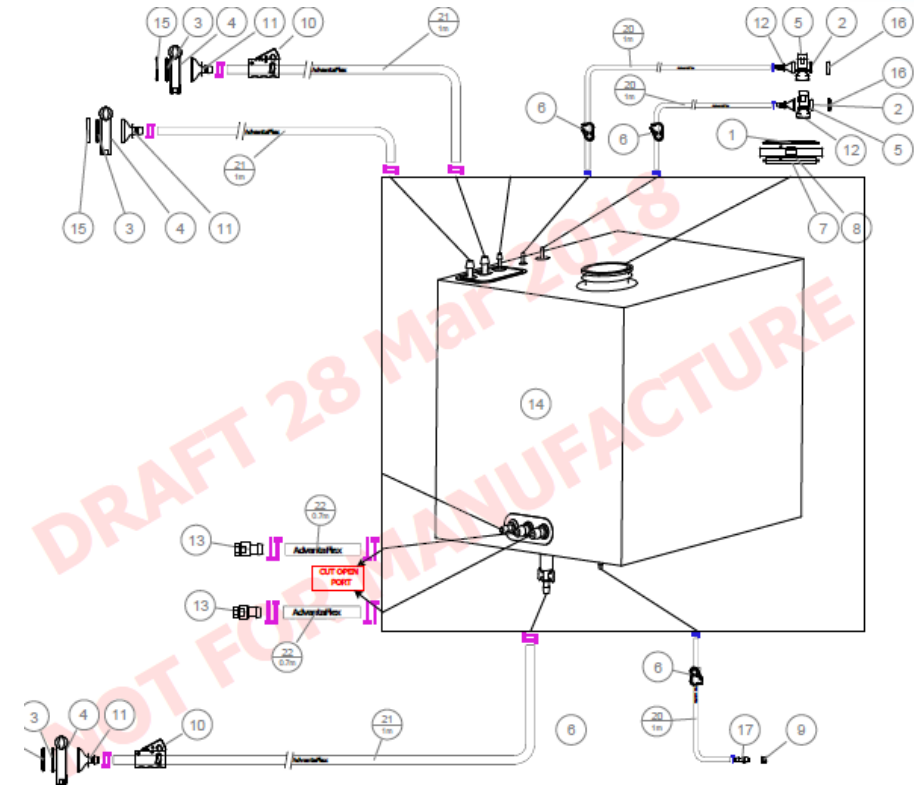
Benefits

- ~ 30% reduction in part codes
- Save warehouse space
- Maximize flexibility
- Increase batch size modular designs



78 consumable part codes used in the 2,000L mAb process

Conventional design	Modular design
112 articles	78 articles

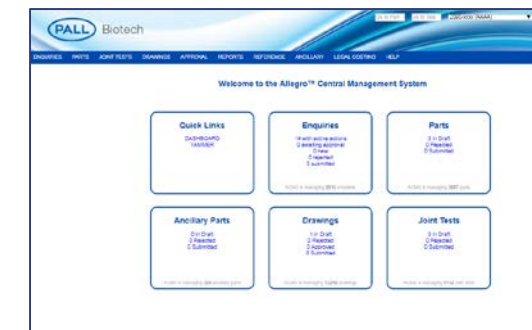
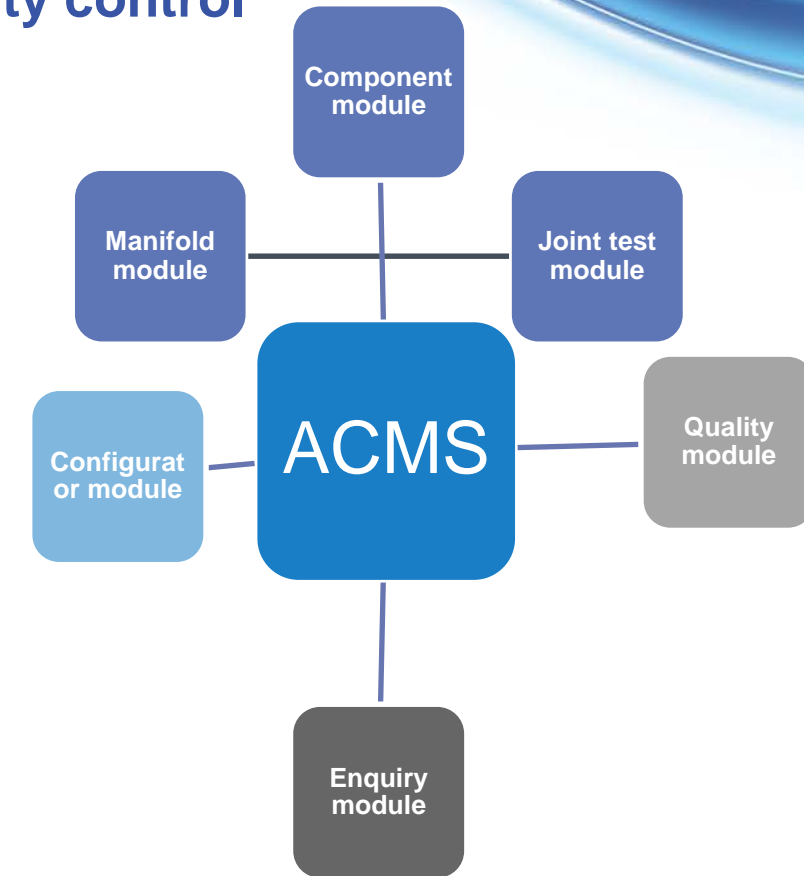
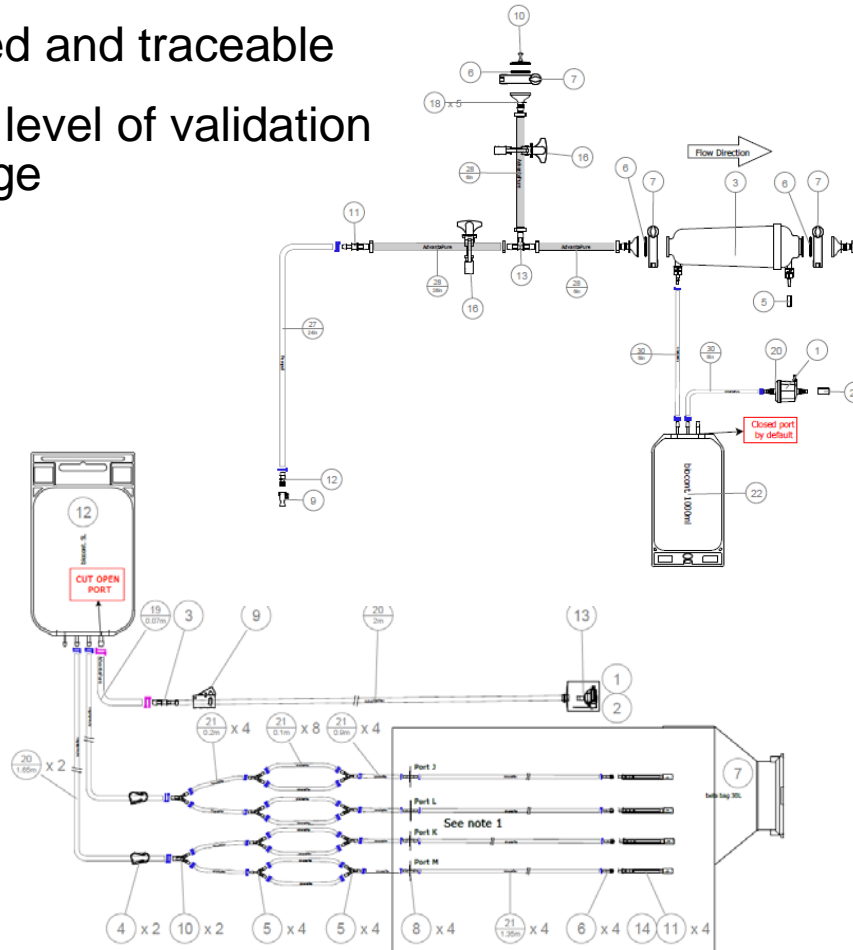


Integrated Single-Use Platform Solutions

Allegro Component Management System for consumables quality control

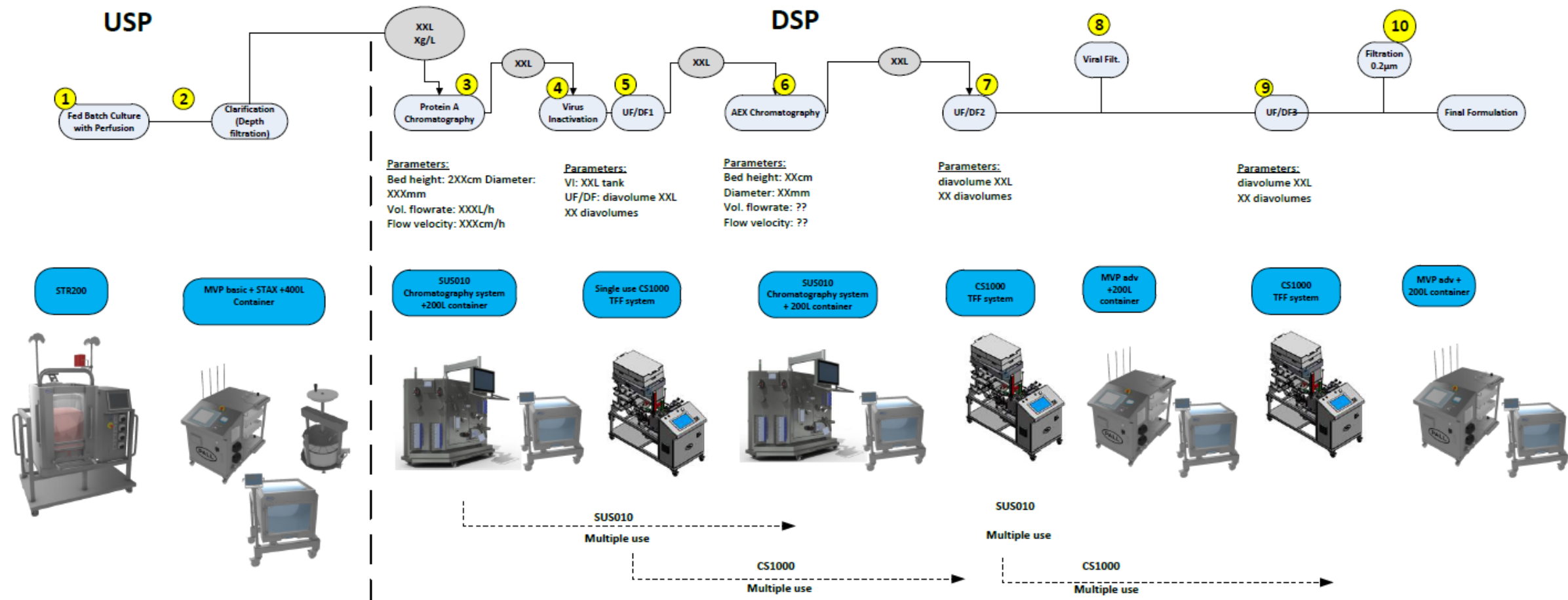
ACMS : Quality By Design for Allegro Systems

- A single database which is a repository of all our design information
- All information is fully controlled and traceable
- Guide our engineer to highest level of validation and preferred component usage
- For all Allegro systems
 - Supplier/ component fully approved
 - Joints fully validated
 - Suited to application → full review
- On line system
 - Information always up-to-date
 - No duplication



Integrated Single-Use Platform Solutions

Client-specific process flow and standard consumable selections



Integrated Single-Use Platform Solutions

Standard and flexible design works for all customers

Allegro film

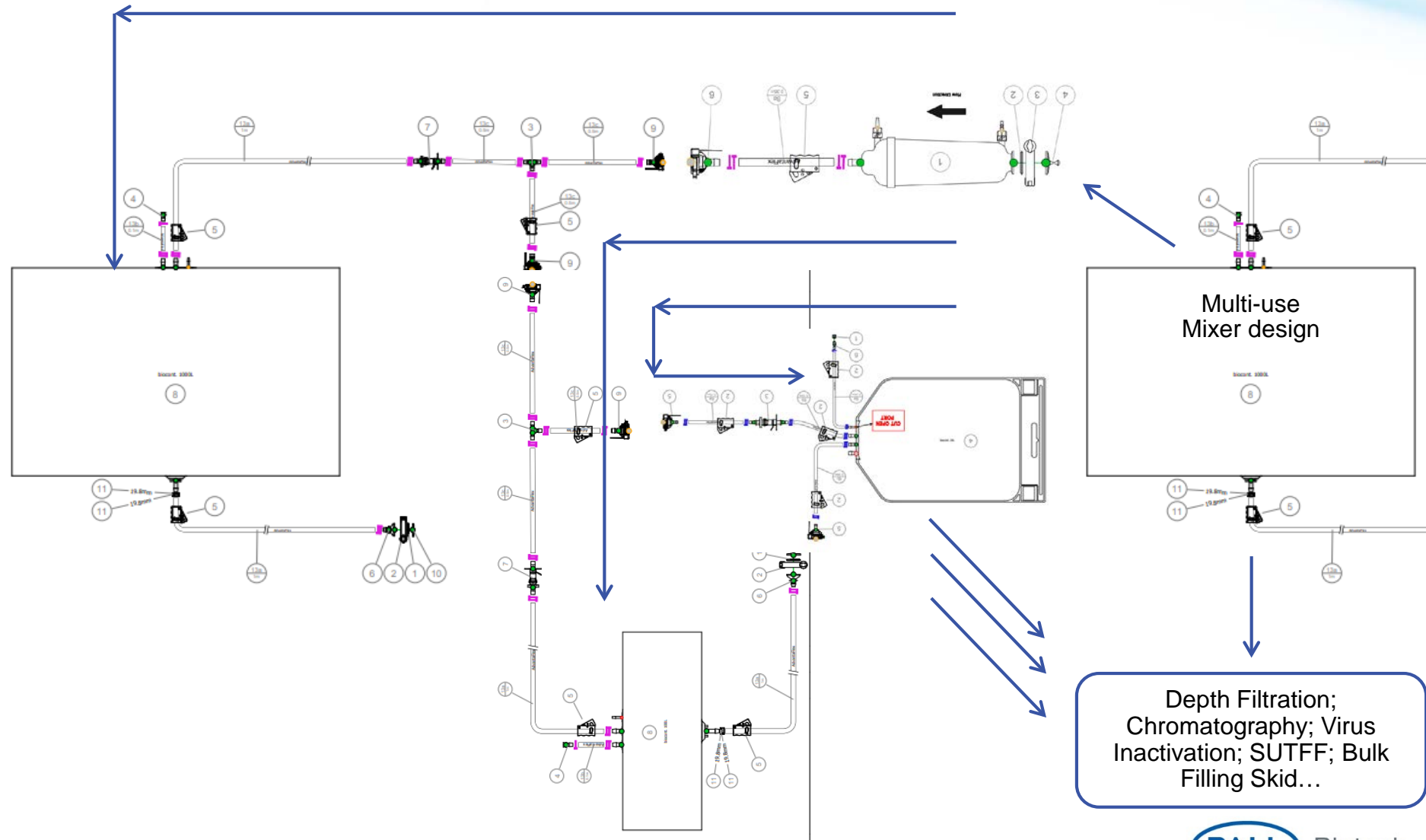
- One Film (Storage, Mixing, BioRx)

Preferred components

- 4 week delivery
- Component quality info

Presto sterile connectors

- Modular design
- Maximize filter usage





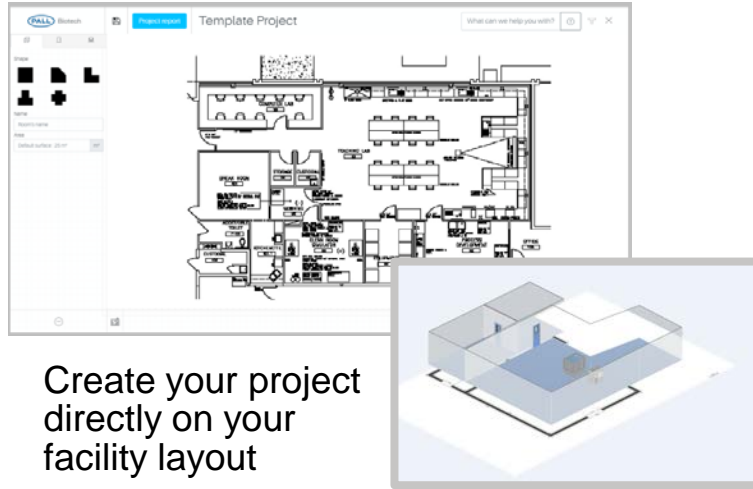
HakoBio Facility Design Tool for Optimal Process Flow Operation

Continuously Improving Bioprocesses

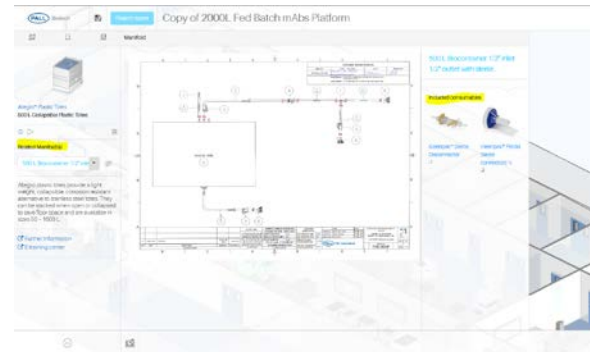
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HakoBio Facility Design Program

A powerful tool for optimizing your process layout



Select equipment, review specifications, and optimize location within the suite



Selection of standard consumables for disposable flow path

Reports

- Surface area
- Equipment List
- Dimensions
- Quantities
- Manifolds

HakoBio Facility Design Program

A powerful tool for optimizing your process layout



Play



Scale-up and Optimization Services for Rapid Process Industrialization

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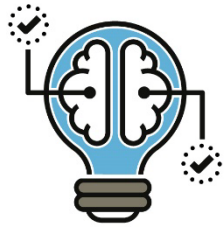
Accelerator Process Development Services

Process Development and Scale-Up Challenges



Process industrialization

Not everything that works at small scale can deliver what is needed at full scale



Limited resources & expertise

Not possible to be expert in everything



Developing a platform

Repeated developments for similar therapeutics are not efficient



Bottlenecks

Platform versatility
Communication breakdown
Technology transfer



Implications and costs

Re-creating a process
Expensive equipment
Delayed clinical trials

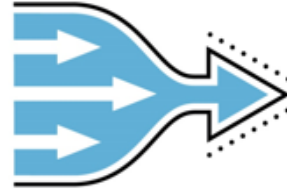
Accelerator Process Development Services

Co-Developing Your Journey



Industrialization

Develop integrated and industrial scale platform



Simplicity and robustness

Incorporating simplicity and robustness into the manufacturing process



Technology transfer

Successfully translating the process back to you



Increased Speed

Reduce time to market



Decreased Cost

Through simplicity and footprint reduction



Decrease Risk

Leveraging our industry expertise and platforms

Accelerator Process Development Services

Project Phases

1 Tech Transfer and
Proof of Concept

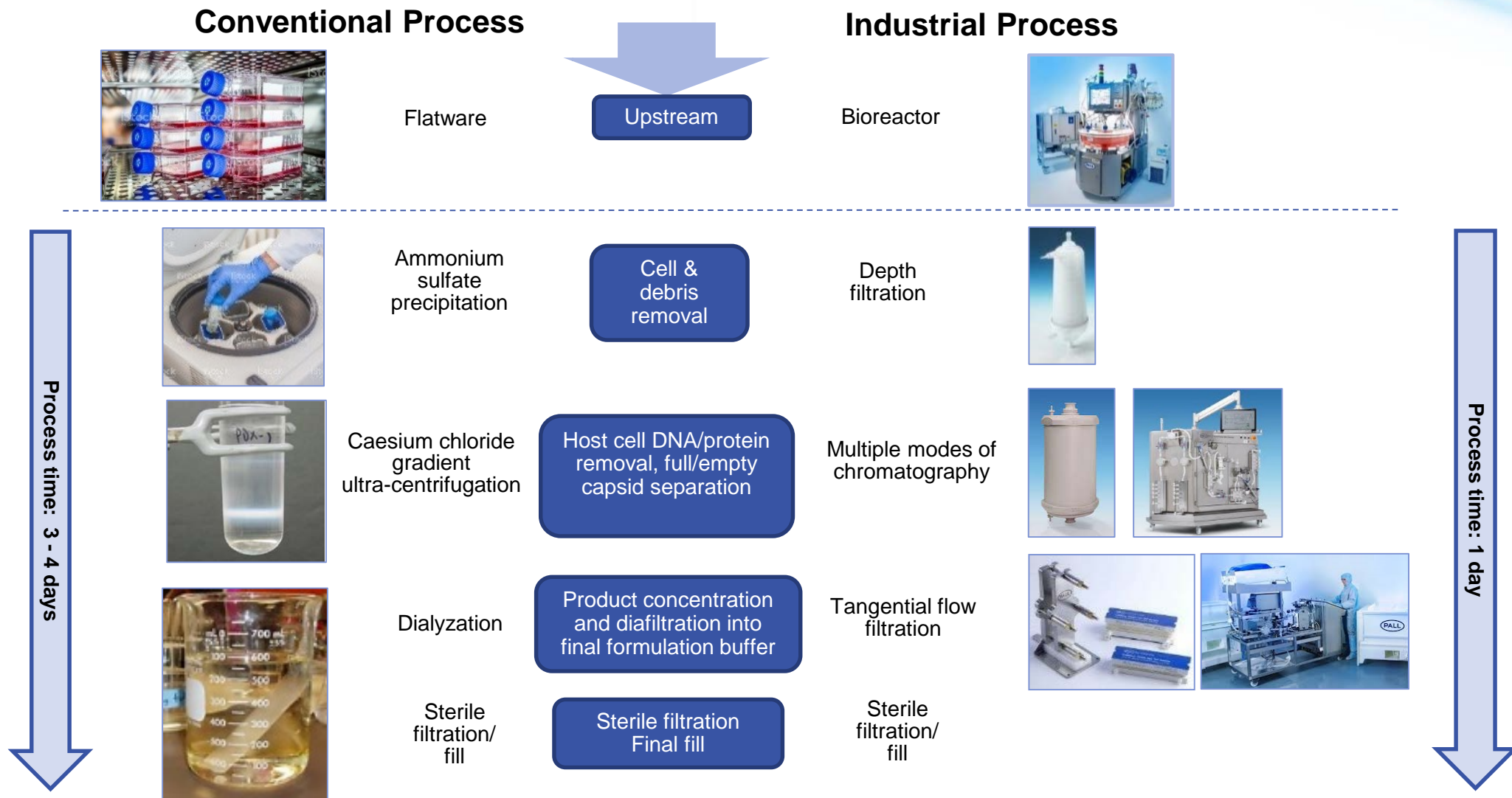
2 Process Development

3 Scale-Up and
Technology Transfer



Accelerator Process Development Services

Industrializing Large Scale Viral Vector Production





Leveraging Partnerships for Process Improvement and Speed to Production

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Modular Facilities for Predictable Delivery and Start-Up

G-CON Partnership



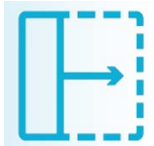
Turnkey Cleanroom

Prefabricated PODs - manufactured offsite –
IQ/OQ is standard – FAT & SAT – multiple
interior finishes



Definite Price

Prefabrication = set price leading to
delayed and lowered CAPEX investment



Containment

HVAC, fire suppression, PLCs are
standard.



Delivery

Definitive and set timelines



Pall Viral Vector Platform with G-CON PODs

Advantages of Standard Offering

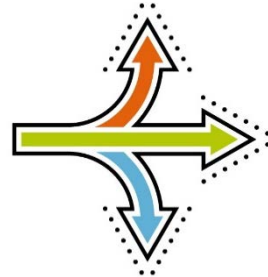
Integrated Solution

Complete end-to-end viral vector process that is well integrated and reproducible



Flexibility

Platform designed for multiple manufacturing scales. PODs can be moved, reconfigured, or repurposed



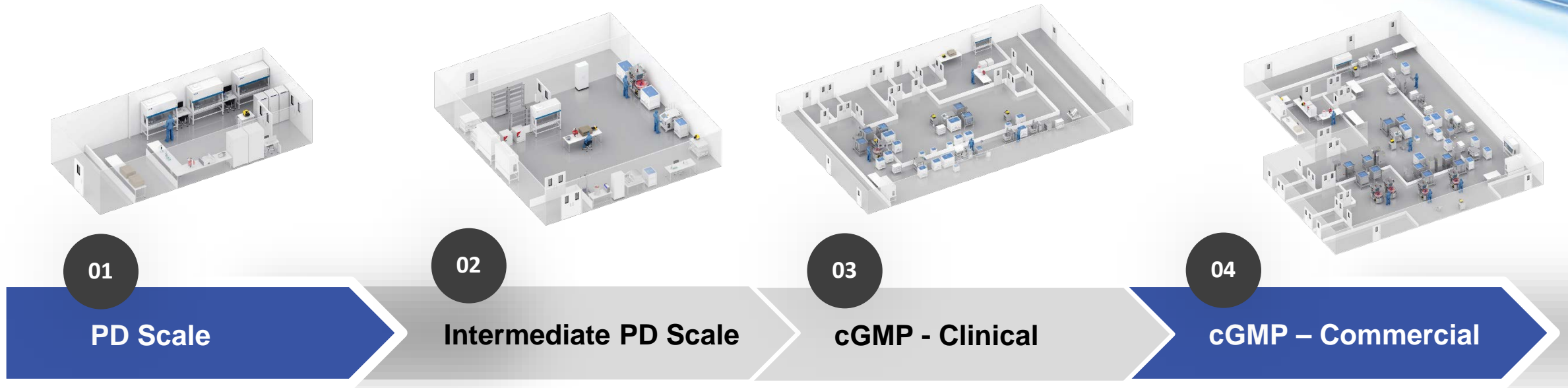
Speed

Ability to deploy full cGMP facility with process equipment within months.



Pall Viral Vector Platform with G-CON PODs

Scale-Out Approach



Proof of Concept

Intended for small scale process development work and proof of concept using the iCELLis nano

Process Development

Ideal for conducting process development work.

Clinical Manufacturing

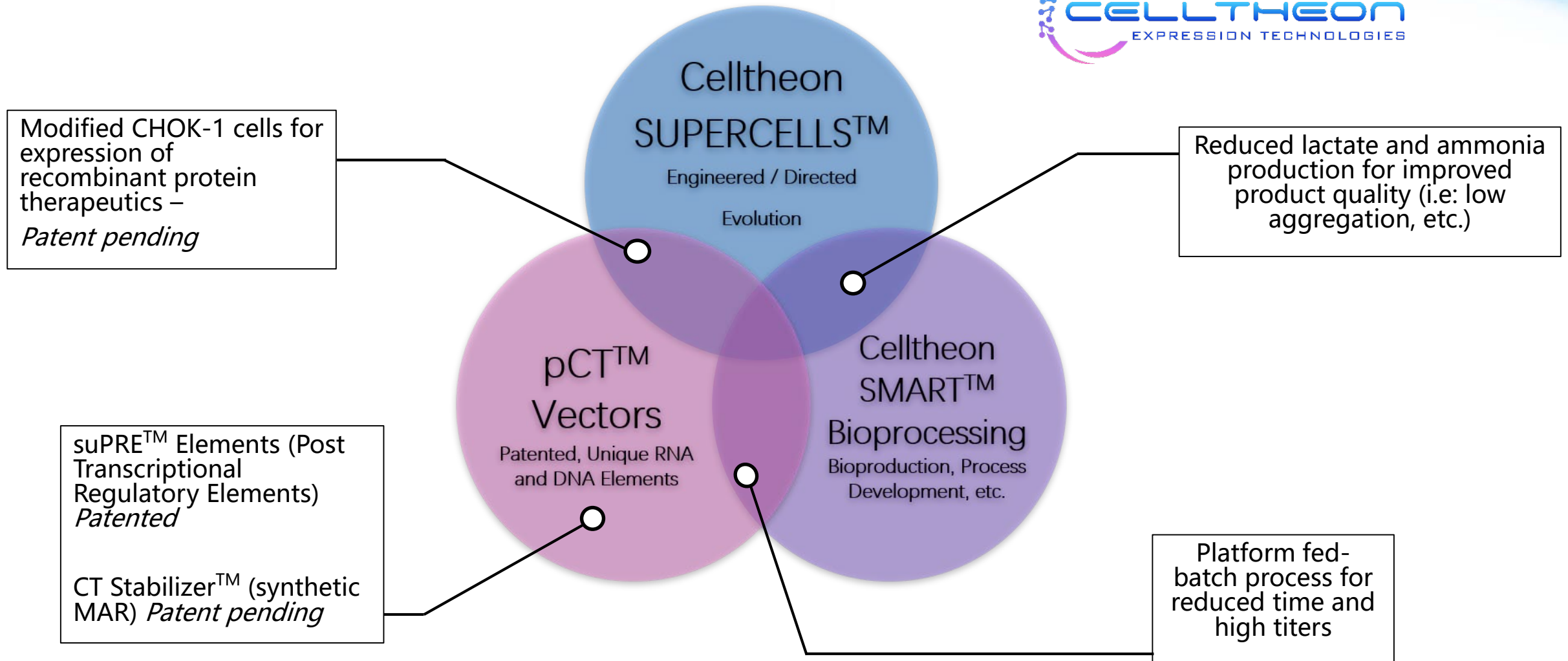
Designed with Pall's end-to-end viral vector platform ideal for clinical manufacturing

Commercial Manufacturing

With multiple iCellis 500 bioreactors, ideal for commercial manufacturing

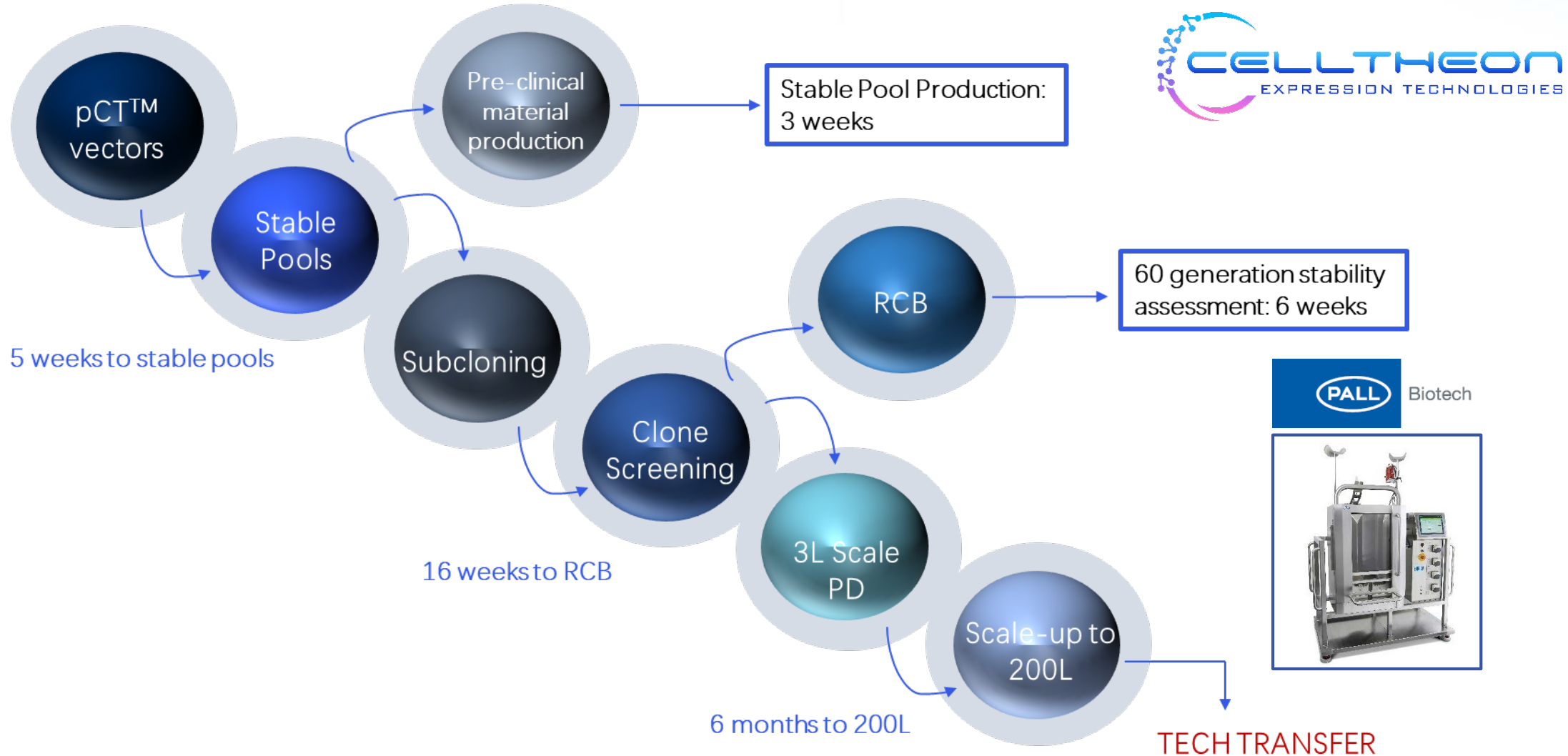
Cell Line Development and Scale-Up

Celltheon Smart™ Expression Platform Partnership



Cell Line Development and Scale-Up

Celltheon Smart™ Expression Platform Partnership

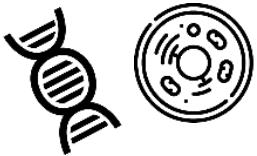


Pre-Clinical Biosimilar Molecule Development

Aetos Biologics Partnership



High Titer Clone Development



Cell Line Technology

Patented Novel DNA/RNA elements and engineered cell line \Rightarrow High Titer, High Quality By Design

Business Outcome

- High titers / High Quality
- ~70% reduced manufacturing cost

Upstream Process Development



AI PD Software

Artificial intelligence tools for titer enhancement and biosimilarity matching

Business Outcome

- Faster development with “dead on” biosimilarity
- Reduced risk in clinical performance

Downstream Process Development



Defined Platform

Pall technologies from harvest, chromatography and, the entire downstream process optimized

Business Outcome

- Predictable downstream processes \Rightarrow high quality
- High recovery > 75%

Large-scale Process Development



Defined Scalability

Scale up \Rightarrow Pall Allegro STR 200
Scale down models accelerate tech transfer to Mfg

Business Outcome

- Fewer large scale bioreactor runs to validate commercial scale \Rightarrow Reduced costs

Clinical program - licensee Risk reduction approach



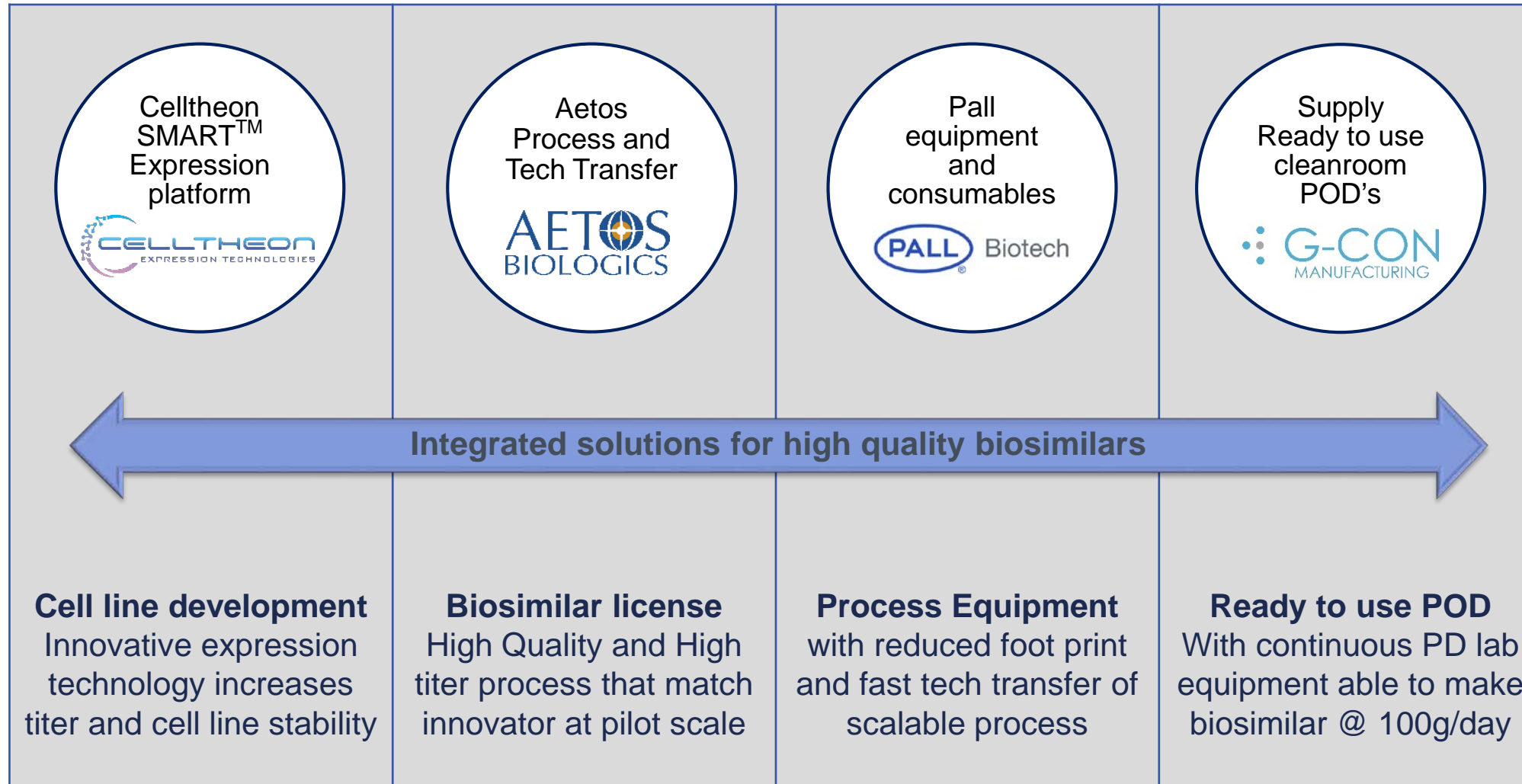
Biosimilar Platform

Biosimilar platform for High CQAs and High Productivity

Business Outcome

- High success clinical trials
- reduction in manufacturing cost

Biosimilars integrated solution through collaboration



Biosimilar
100g/day

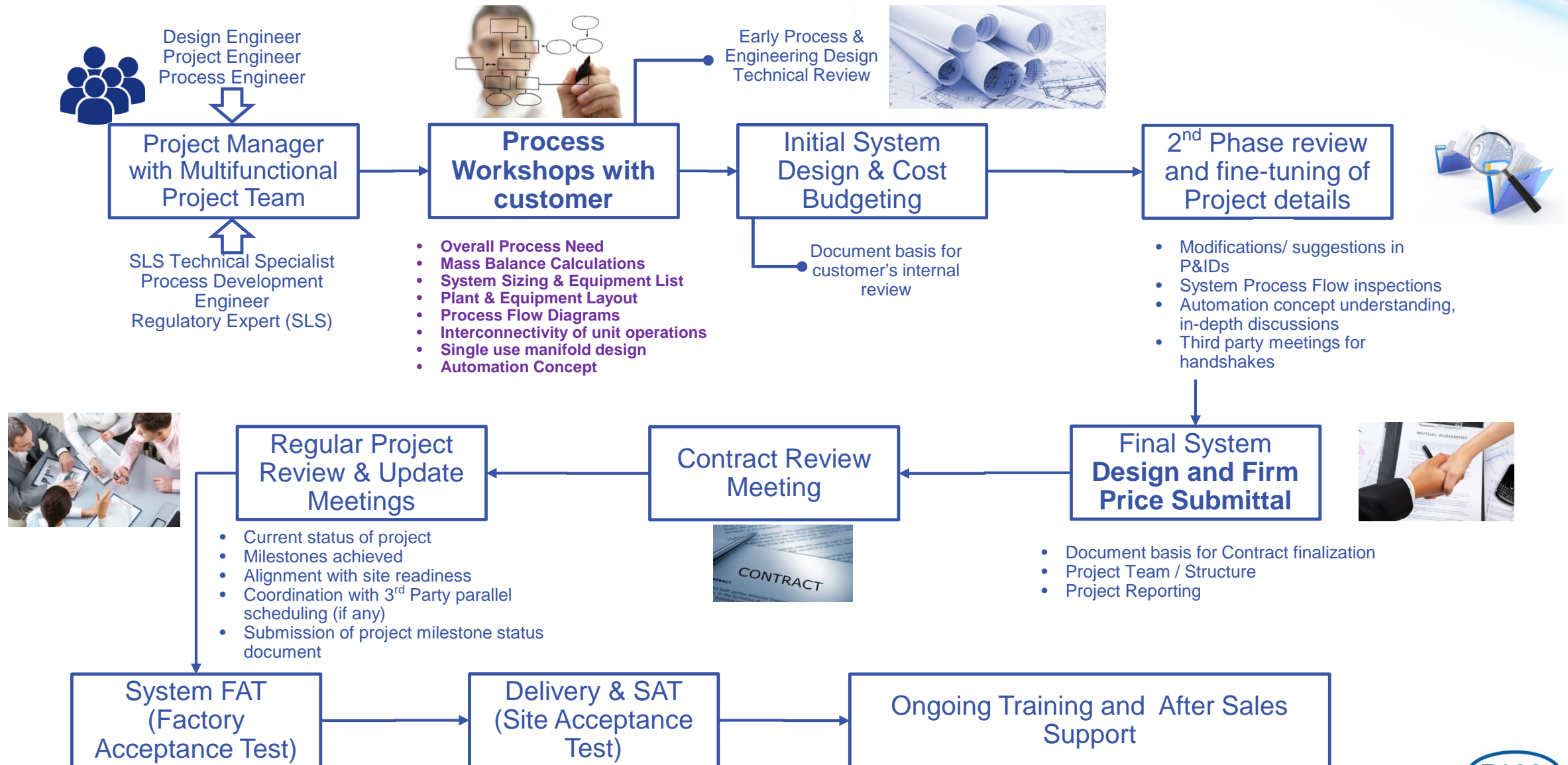


Efficient Single-Point Project Management for Integrated Solutions

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End-to-end Solutions Project Management



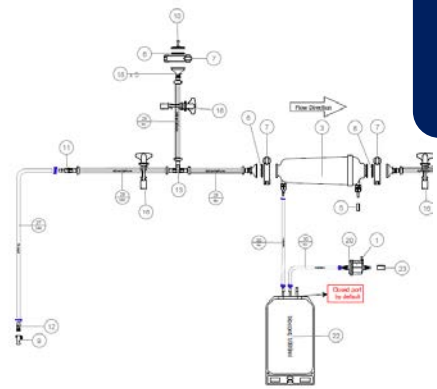
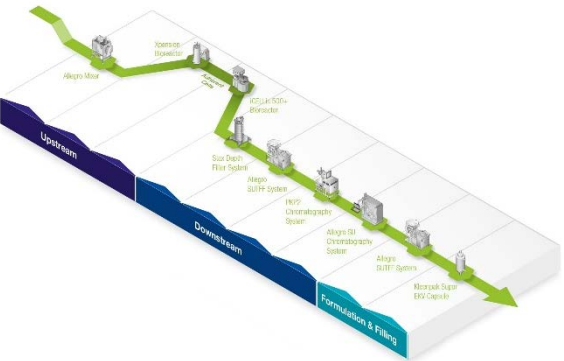
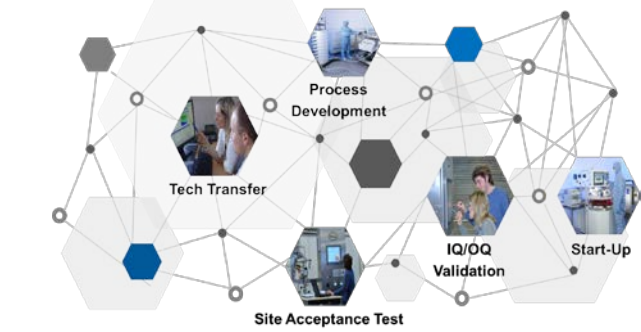


Summary of Integrated Solutions Approach

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Pall Biotech Integrated Solutions Summary



Facility Design and Optimal Operational Layout

Expert Commissioning & Start Up Support

Process Platforms for Rapid Implementation

Standardized Process Consumables

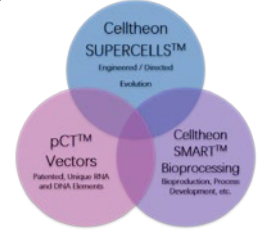
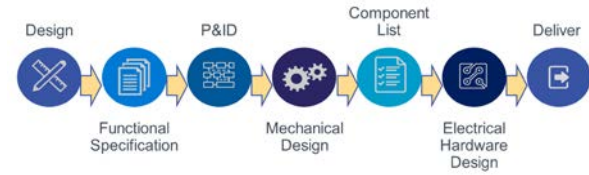
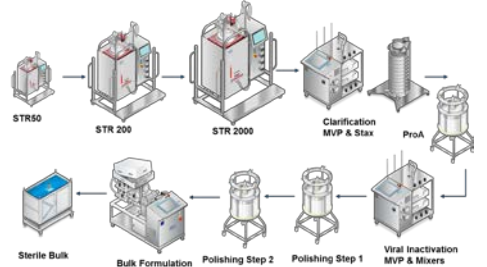
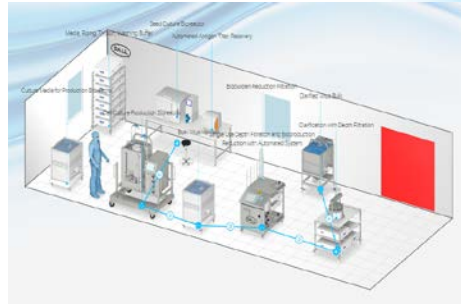


Broadest process technology portfolio

Experienced Project Engineering and Management

Process Development Services for Industrialization

High Titer Cell Line Development Partnership



Pall Biotech Integrated Solutions

Working hand in hand with innovator drug developers and manufacturers





Thank You

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