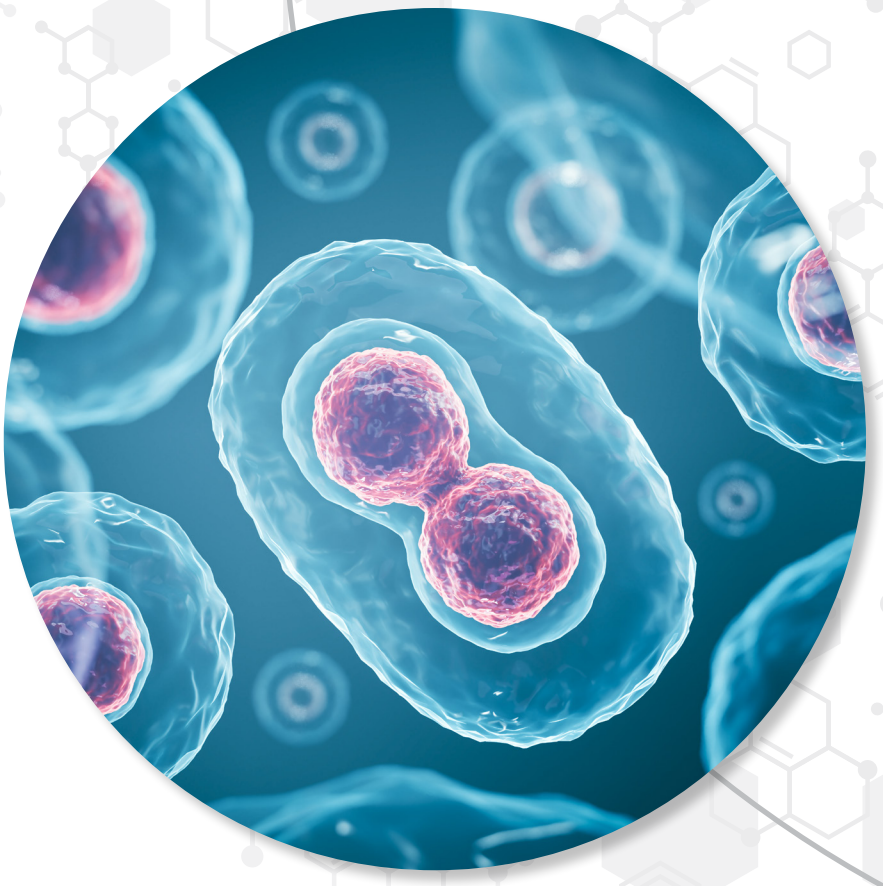


WHITE PAPER

Scalable Solutions Through kojoX™:

Building a Biomanufacturing Ecosystem for Supply Agility Starts as Early as Cell Line Development

Author: **Charles Heise, PhD**
Associate Director, Bioprocessing Strategy & Development
FUJIFILM Biotechnologies

FUJIFILM
Value from Innovation

The global demand for biopharmaceuticals has the potential to outpace existing capacity, and across the globe substantial investments are being directed towards expanding the biomanufacturing capacity of Contract Development and Manufacturing Organizations (CDMOs). FUJIFILM Biotechnologies recognizes that constructing new facilities is insufficient to address the complex supply challenges facing the industry. As such, our unprecedented capital investments of >$8bn to expand capacity are just one of the vital means we have in place to improve patient access. Going beyond expansions, we have deployed a holistic, globally harmonized operational ecosystem that we call kojoX. In an era where speed, cost efficiency, and market responsiveness are crucial, we offer our partners future-ready solutions for biopharmaceutical production through our innovative MaruX™ continuous bioprocessing system. This system seamlessly integrates our powerful ApolloX™ cell line development solutions with the award winning SymphonX™ purification system. Furthermore, our kojoX operational ecosystem provides access to modular, scalable manufacturing capacity, ensuring that production can effortlessly expand across our global network.

kojoX™

KojoX – An Operational Ecosystem that Delivers Biotherapeutics to the Market Faster and More Reliably than Seen Before

By integrating a modular, standardized operating system and aligning processes, equipment, and digital systems across our global network, kojoX delivers seamless technology transfer, de-risks supply chains and reduces regulatory burden [1] with the agility needed to deliver biotherapeutics to the market faster and more reliably than ever before. Through standardized equipment and procedures, kojoX ensures that processes can be efficiently transferred between facilities, regardless of scale or geographic location [2]. Standardized yet flexible, kojoX operates across modalities and scales from <100 L to 20,000 L (Figure 1).

Delivering Supply Agility Starts as Early as Cell Line Development

Achieving true biomanufacturing agility hinges on the advancement and optimization of core technologies supporting these processes. Our highly productive and adaptable mammalian expression system, ApolloX delivers high-quality biopharmaceuticals at scale and with speed.

Our experts created ApolloX to optimize cell growth and product yield, recognizing that product titer and process robustness are highly dependent on the upstream media and process parameters. The ApolloX system encompasses a comprehensive suite of tools and technologies that streamline biomanufacturing processes and provides a bedrock for flexible and robust manufacturing across our network. At its core, the platform features a proprietary expression vector and optimized cell line, enabling rapid cell line development, reaching a research cell bank in approximately 10 weeks and titers in the range of 5-7 g/L

for mAbs in fed-batch and 1.5-2 g/L in perfusion, supporting fast-paced advancement to clinical supply. Meanwhile the use of medias and feeds provided via FUJIFILM Irvine Scientific, affords our partners supply chain security and the efficiencies of scaling to 20,000 L.

ApolloX leverages a deep understanding of bioreactor operations, encompassing both fed-batch and perfusion processes, allowing for the development of scalable processes that are adaptable to both single-use and stainless-steel bioreactors. The significance of this integrated approach lies in its ability to address the critical demands of current biomanufacturing while preserving speed through rapid cell line development and scalable processes that:

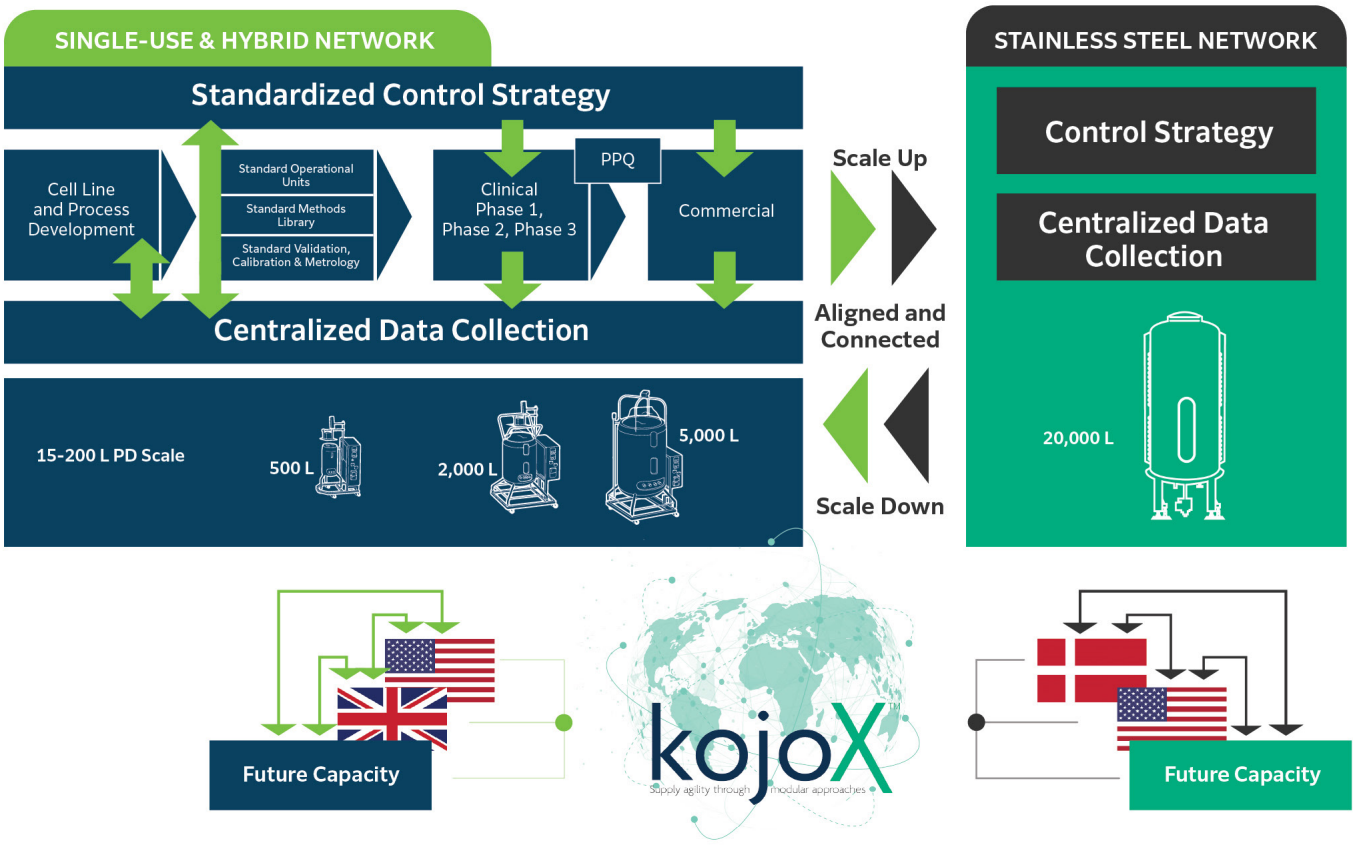
Ensure robustness and scalability through adaptability to various bioreactor configurations

Prioritize regulatory compliance and quality through a well characterized cell line and the flexibility to pivot from fed-batch to perfusion production methods, and vice versa from the same master cell bank

Provides process flexibility and efficiencies by enabling the use of the same master cell bank for both fed-batch and perfusion processes, eliminating the need to redesign the expression system when switching production methods

The extensive experience and knowledge embedded in ApolloX, coupled with its proven track record in GMP manufacturing, significantly mitigates risks associated

Figure 1: KojoX, an aligned and connected operational ecosystem that provides consistent bioproduction across geographical locations, scales and product phases.



with process development and optimization. As a result, ApolloX meets the demands of modern biopharmaceutical production, particularly in the antibody space, where the benefits outlined above are critical to the development of biotherapeutics amid uncertain market dynamics.

Complementing ApolloX, SymphonX™ is our unit operation-agnostic purification platform that can be used for all down-stream steps and is capable of integrated in-line buffer dilution or blending for both batch and continuous processing. SymphonX utilizes a robust disposable flow path and is deployed across our single-use facility network for downstream processing. With the same software and communication protocols, connecting SymphonX systems is both simple and highly synergistic, exemplifying the principles of our kojoX operational philosophy. Both batch and continuous processes can be performed with SymphonX, which further enhances the flexibility and efficiency of manufacturing to accommodate fluctuating therapeutic demands.

SymphonX – Our Commitment to Supply Agility Through a Standardized Purification Approach

Standardized, flexible equipment as part of a holistic biomanufacturing network is crucial in enabling streamlined development activities that lead into adaptable production processes. To support this level of integration, SymphonX (Figure 2), provides developers with the option to scale-up, scale-out, or adopt continuous processing (scale-on) (Figure 3). SymphonX was designed intentionally by FUJIFILM Biotechnologies for both continuous and batch bioreactor operation by integrating advanced buffer management at point-of-use, rendering both the control strategy and its validation nearly identical for both batch and continuous operations. A centralized data approach also enables the development of robust control strategies early in the development process, ensuring they are applicable across clinical and commercial phases. This is particularly important when scaling up to large production volumes, as it ensures that processes remain consistent and compliant throughout the product life cycle. The ability to standardize operational units and instructional frameworks further enhances the portability of processes across different scales and facilities, ensuring seamless transitions as market demands evolve.

Through standardizing equipment and processes across facilities, developers can design processes with differing end goals in mind, whether for smaller single-use bioreactors or 20,000 L stainless steel bioreactors. This standardization allows for the collection and utilization of data across the entire product life cycle, informing and derisking process design, process characterization and validation, and continuous improvement efforts.

Achieving Scalability Across Manufacturing Networks for a Range of CHO Derived Therapies

Whether a developer is targeting large-scale commercial production or smaller-scale clinical batches, the ApolloX system can be applied across our global kojoX network ensuring consistency and regulatory compliance across all phases of development. Its flexibility is particularly advantageous in the context of novel therapeutic molecules (for example Fc-fusions, bi-, tri- and multi-specifics and virus like particles), where dosage requirements and market penetration are often uncertain. Within our kojoX ecosystem, partners can pivot with ease between different production scales ranging from single-use bioreactors (e.g., 2,000 L to 5,000 L) to large-scale 20,000 L facilities. With our kojoX global network, we can respond dynamically to market demands as technology and scale are no longer barriers and our partners can be confident in responding to clinical trial outcomes and market dynamics without the need for time-consuming, costly process redesigns.

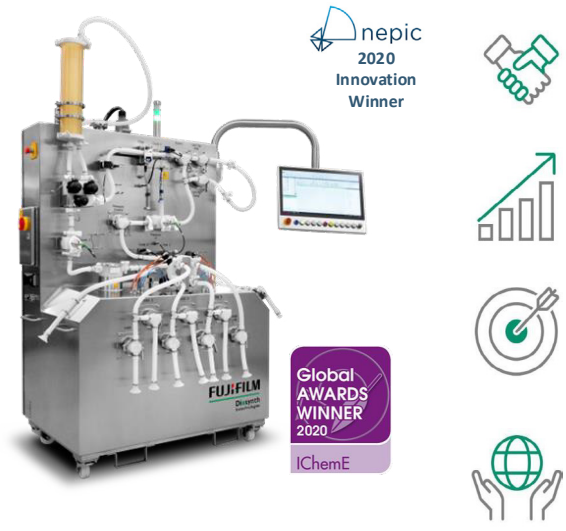
Risk Mitigation, Market Responsiveness, and End-to-End Network Capabilities

The flexibility of ApolloX to adapt to both fed-batch and perfusion cell culture provides our partners with the option to scale-up, scale-out, or adopt continuous processing. Within our end-to-end kojoX CDMO network, partners can respond to clinical trial outcomes and market dynamics without the need for costly and time-consuming process redesigns. This is particularly important in an industry where the success of a product can hinge on the ability to rapidly adjust production volumes and strategies to meet market demand.

Our single-use facility in the UK, equipped with up to five production lanes, to further enhance capacity and flexibility within our network is due on-line in 2026 for fed-batch and 2027 for continuous manufacturing. This facility, along with existing sites in Denmark and the US (Figure 4), ensures that manufacturers have access to the right geographical locations and production scales to meet market supply timelines.

Transformative innovations like ApolloX and SymphonX bring their own unique benefits, but when combined and unified by kojoX their true potential is maximized to result in next generation biopharmaceutical manufacturing that future proofs the portfolios of our partners. By combining flexibility, scalability, and regulatory compliance, FUJIFILM Biotechnologies can overcome key challenges facing the industry today and ensure that its partners can navigate the complexities of modern biopharmaceutical development with confidence and respond dynamically to market demands.

Figure 2. The SymphonX system by FUJIFILM Biotechnologies is a standardized yet flexible purification system designed to run all down-stream purification steps.



Supply Resilience

- Strong supply chain network with vendors providing standardised equipment and consumables
- Simplified tech transfer across one kojoX network – Europe and USA
- Provides rapid responsivity to changing demand fluctuations via an ability to adopt an alternative manufacturing strategy (scale-up, scale-out or continuous)

Speed to market

- Flexible purification system with platform downstream purification for batch or perfusion processes
- Continuous biomanufacturing ready and provides options to alter manufacturing campaign time to optimise clinical supply without additional scaling work

Regulatory simplification

- One purification system for all unit operations with a single operating strategy aligned for batch and connected operations
- Established single-use materials of construction with biocompatibility data for product contact parts
- Standard data format for all unit operations complying with latest data integrity expectations and requirements

Sustainability

- Robust disposable and re-usable flow path - single product campaign use minimising waste
- Reduction in facility size reduces energy requirements supporting 2030 sustainability targets
- Efficient use of raw materials and buffer concentrates results in fewer / smaller buffer bags

Figure 3. ApolloX is adaptable to perfusion and fed-batch, single-use or stainless bioreactors with all three production strategies and be purified with SymphonX.

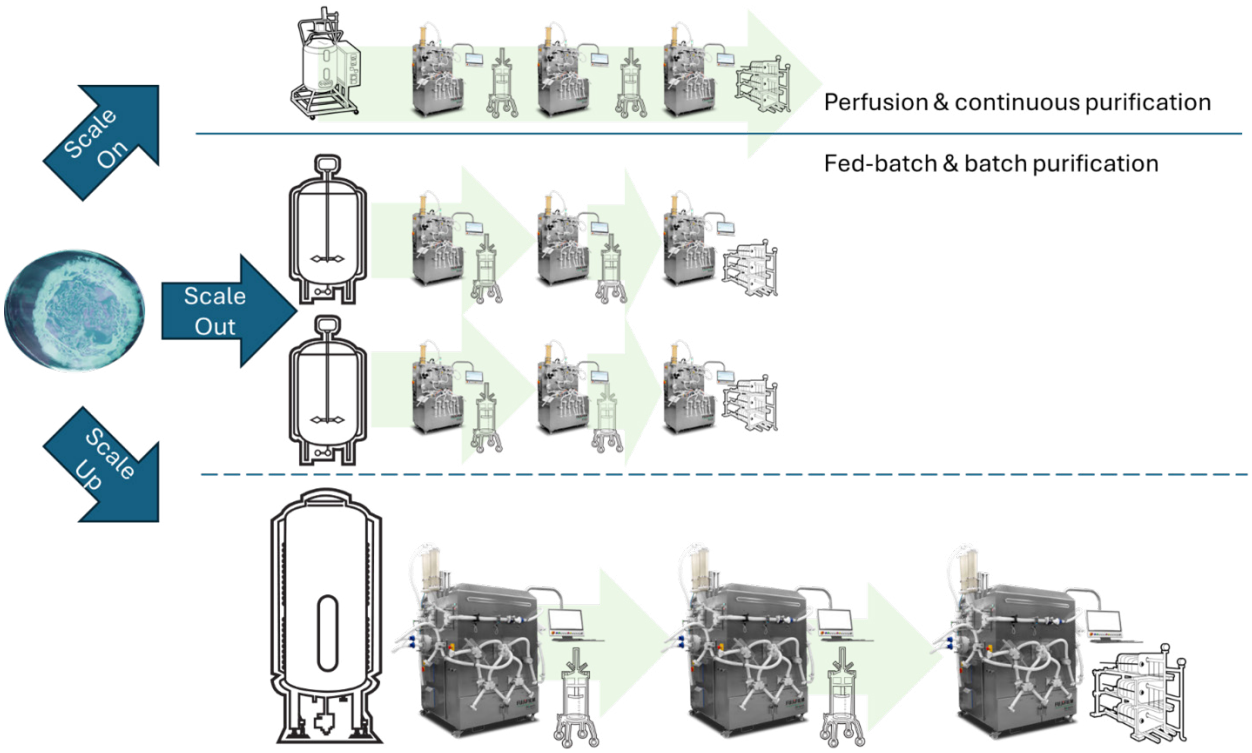
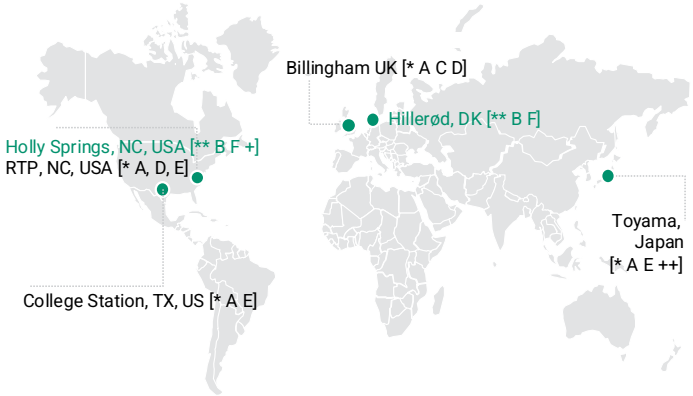


Figure 4. FUJIFILM Biotechnologies kojoX globally harmonized network - provides rapid and seamless support from development to commercialization



A- DS clinical and commercial manufacturing various scales 500 L to 5K L
B- DS clinical and commercial manufacturing at 20K L plus finished good capabilities
C - DS clinical and commercial continuous manufacturing
D - DP Process and formulation development
E - Clinical scale DP fill
F - Clinical -Commercial DP fill
* DS/DP process Development:: Features formulation, advanced analytics and process characterization centers of excellence
**MSAT - supporting 20K L manufacturing

+ Holly Springs, NC, USA site available Summer 2025

++Toyama, Japan online 2027 for Process Development (mAb and ADC)

Learn More

1. **kojoX™ in Action: Optimizing Regulatory Pathways**
2. **Unlocking Agility and Efficiency in Biomanufacturing**

About the Author

CHARLES HEISE
Associate Director, Bioprocessing Strategy & Development

Charles Heise is Associate Director in the Bioprocessing Strategy & Development group at FUJIFILM Biotechnologies working on developing connected, integrated processes. He has over 15 years of experience in the biologics industry leading the development of cGMP processes for clinical and commercial recombinant protein manufacture and academic research collaborations. He is a co-inventor of the award winning SymphonX purification system and the downstream technical lead for the continuous biomanufacturing platform, MaruX. Charles graduated in the UK from the University of Oxford and obtained his doctorate from the University of York.

Partners for *Life*

"Partners for Life" represents a transformative approach to development and manufacturing, emphasizing relationships founded on trust and transparency — founded in people-centric values, transformative science and innovation, and unprecedented delivery.

CDMO LEADERSHIP AWARDS2024

Contact us to discuss your science.

USA

College Station, Texas
3940 Fujifilm Way
College Station, TX 77845
+1 979 431 3500

Holly Springs, North Carolina
100 Biotechnology Avenue
Holly Springs, NC 27540

Research Triangle Park, North Carolina
101 J Morris Commons Lane
Morrisville, NC 27560
+1 919 337 4400

Thousand Oaks, California
2430 Conejo Spectrum Street
Thousand Oaks, CA 91320
+1 805 699 5579

DENMARK

Hillerød
Biotek Allé 1
3400 Hillerød
+45 7741 6000

UNITED KINGDOM

Teesside
Belasis Avenue
Billingham, TS23 1LH
+44 1642 363511

JAPAN

Tokyo
R7 Building, 7-12-2 Roppongi
Minato-ku, Tokyo 106-0032
+81 3 6871 7736

FUJIFILM Biotechnologies

fujifilmbiotechnologies.fujifilm.com

FSC

MKT0177-WP-Rev01