White Paper

First-in-Human

Reach milestones sooner with a technology-driven approach to early-stage biologic development

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Biopharma start-up leaders feel a strong sense of urgency. They're driven not only by mission, but by pressure to prove their therapeutic modality will work for the intended indication. Success hinges on respect for the process while also finding ways to move forward, faster.

Early milestones such as successful toxicology (tox) studies, Investigational New Drug (IND) application clearance and the initiation of first-in-human (FIH) clinical trials are crucial inflection points that directly determine a biotech company's ability to secure its next round of funding. These achievements de-risk the program for investors by providing key evidence of safety and potential efficacy, thereby unlocking substantial later-stage capital.

Traditional process development delays these milestones by stretching the timeline between preclinical research and Phase I. Trial-and-error approaches to vector design and manual cell line development and process optimization raise the risk of exhausting funding before a biopharma company can produce important data.

Innovations such as AI-driven vector design, transposase-based cell line development and high throughput technologies enable biopharma companies to move through early-phase development faster while also ensuring quality and reliability. In addition to shortening timelines, a focus on platform processes, platform analytical methods, templated pre-prepared documentation and off-the-shelf raw materials have led to more efficient and robust process development.

"Even with accelerated timelines, biopharma companies want assurance that the processes we develop are robust and can be replicated at large scale," said Palak Patel, Scientific and Technical Affairs Manager for Patheon Pharma Services Thermo Fisher's global CDMO. "That's where our platform process comes in. It helps accelerate timelines, and the components are widely accepted by regulatory agencies."

This white paper explores how Patheon's next-generation capabilities propel biologics forward, faster. It focuses on the core elements of Patheon's Path to IND platform, which uses a suite of advanced tools and methodologies to deliver the following:

- Titer levels of up to ~8 g/L* with advanced transposase-based technology and high-throughput automation
- Scale up recombinant antibodies from DNA to first-in-human (FIH) trials in as few as 9 to 14 months*
- Integrated drug substance and drug product development
- Parallel preparation of IND/IMPD regulatory support

Reinventing upstream processes for speed and flexibility

To deliver on customers' need for speed and flexibility while developing complex molecules, many CDMOs have either adopted or are considering adopting advanced technologies to streamline processes and reduce costs. For example, a 2024 survey found 43% of CMO respondents planned to evaluate

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manufacturing platforms and technology to optimize production.[1] Meanwhile, upstream processing has evolved to include higher yield fed-batch processes using more robust cell lines and better cell culture media.

As CMOs and CDMOs work to improve efficiency and control costs, they're scrutinizing existing upstream processes. Industry-standard batch processing, trial-and-error vector design and other traditional approaches introduce risk, variability and inefficiency. Automation and high-throughput technologies have changed this trajectory; however, pressure to produce the highest quality at the lowest cost warrants additional innovation.

Advantages of a next-generation approach to CMC development

Patheon is one of the few global CDMOs to implement a full ecosystem of advanced technologies. Each innovation serves an isolated function while working to accelerate or strengthen an element of early biologic development.

Called Path to IND, this approach leverages a platform process and method approach, pre-templated documentation, and parallel development activities for unmatched efficiency. Use of the CHO-K1cell line, AI/machine learning-driven vector construction and high-throughput technology increase productivity by allowing for higher product titers (up to 8 g/L of molecule) and more material per batch.

While the platform delivers outcomes in as few as nine months in most cases,* the program doesn't lose sight of the bigger picture. "We spend the time in development to make sure the process can be replicated at large scale," said Patel. "For complex molecules, we still do resin screenings. Other CDMOs may promise a shorter timeline, but they may only be able to tackle a few specific molecules. We focus on more molecules in a larger biochemical space."

AI/ML-driven vector construction

Traditional vector design methods rely on iterative lab experiments, manual research and trial-and-error screening to identify constructs with acceptable expression or functional profiles. These approaches are time- and labor-intensive and often require multiple rounds of redesign, which can extend development timelines from several weeks to months.

AI/ML-enabled systems use data-driven models to score, generate, and prioritize vector designs, reducing reliance on handcrafted mechanistic models and manual screening. Machine learning accelerates experimentation by focusing resources on more promising candidates and can facilitate the design of nov-

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el vector configurations that could be difficult to conceive otherwise.[2] By enabling earlier prediction of high performing variants and continuously improving with experimental feedback, AI/ML based vector construction shortens cell line development timelines while maintaining robustness.

Transposase-based cell line development

Transposase-based systems operate at a different stage in the cell culture workflow than vector design, but together they accelerate the path to a stable, high-performing cell line. The platform used by Patheon generates productive stable pools with pool product quality predictive of final clonal cell line product quality.*

"Leveraging transposase technology is one reason we're able to achieve higher productivity with our cell lines," said Patrick Bennett, Scientist III, Cell Culture Development for Patheon. "The technology also allows us to get similar product quality across the development lifecycle so we can employ studies that require a final design earlier in our timeline."

Afycosylated cell line

Afucosylation enhances the therapeutic potency of many antibody-based biologics, particularly those whose mechanism of action relies on antibody-dependent cellular cytotoxicity (ADCC). Removing fucose from the Fc region increases the antibody's binding affinity to FcγRIIIa receptors on immune effector cells, resulting in significantly stronger cell-killing activity. This increased potency can translate into lower clinical doses, reduced batch size requirements and improved overall manufacturability.[3]

To support programs that require this mechanism, Patheon has licensed an afucosylated CHO cell line that enables consistent, stable production of afucosylated antibodies without the need for complex downstream engineering. Because of this, biopharma companies have access to an established platform that helps to accelerate development and ensure consistent product quality.

High-throughput automation

In addition to the innovations already mentioned, Patheon has invested in high-throughput technologies, including the Beacon® Optofluidic Platform and Ambr® 250 microbioreactor, to accelerate cell line development timelines.[4] The Beacon automates single-cell isolation and provides real-time image-based screening, earlier identification of high-performing clones and faster confirmation of monoclonality. These capabilities save weeks of manual work compared to limiting dilution and significantly reduce the risk of advancing suboptimal clones.

Three-chain Bispecific antibody achieves cloning efficiency of 93% with Beacon® platform

What we did:

We performed cell line development on the Beacon platform for two complex bispecific antibody formats (3-chain and 4-chain) and conducted comprehensive analytical comparison between stable pool and clonal cell lines to evaluate product quality attributes.

How we did it:

Using Beacon's optofluidic platform, we loaded more than 1,200 pens per chip for high-throughput single-cell cloning with automated monoclonality verification. We then performed detailed analytical characterization using Size Exclusion Chromatography (SEC) and Multi-Attribute Method (MAM) to compare stable pools against selected clones, evaluating aggregation, molecular integrity and post-translational modifications.

What we achieved:

For the 3-chain bispecific, we achieved 93% cloning efficiency with 100% monoclonality and an 18% titer increase while maintaining >98% monomeric purity. For the 4-chain bispecific, clone selection dramatically reduced aggregation from 18.5% to 11.4%, improved oxidative stability and enhanced sialylation—demonstrating that clonal isolation delivers tighter control over product consistency and quality critical for clinical-grade bispecific manufacturing.[5]

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“The beauty of the Beacon is its screening power,” said Bennett. “The ability to screen up to 7,032 clones in one go is a significant time saver during development. The machine also includes a number of internal assays, which provide a preliminary read on how cells perform from a growth, productivity and product quality standpoint once they are isolated. It also gives us proof of monoclonality, which is important for regulatory to ensure the cell lines we generate come from one single cell.”

Intensified fed-batch processes

Patheon’s Path to IND platform includes the option for an intensified fed-batch processes which provide higher viable cell densities and higher titers than traditional fed-batch, without requiring new equipment, adding training requirements or extending timelines. To meet the demand for higher product yields, Patheon recently developed a process intensification workstream aimed at increasing the titer of CHO processes by 20 to 50% while maintaining quality and timeline parameters.

By optimizing media composition, feed strategies and N-1 seed-train conditions, Patheon found that the intensified workflow generated four times more cells for inoculation and increased titers by 20% to 100% while maintaining comparable product quality attributes across molecules such as Rituximab and Herceptin.[6]

The result: a more streamlined development path that delivered more material from smaller-scale runs, accelerated process development and avoided the cost and complexity traditionally associated with perfusion-based intensification.

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PALAK PATEL
Scientific and Technical Affairs Manager
Patheon Pharma Services
Thermo Fisher’s global CDMO

Real-world impact: Driving higher titers in IgG 1 and IgG 4 antibodies through intensified upstream strategies

What we did:

We ran an Ambr 250 intensification experiment comparing two molecules (Rituximab and Herceptin) to evaluate how basal media enrichment, feeding strategy and temperature-shift timing influence growth and productivity.

How we did it:

Building on prior Ambr 250 and 10 L proof-of-concept data, we generated a Design of Experiment (DOE) study to test multiple starting feed rates, tapered feed amounts and early vs. late temperature shifts. This allowed us to pinpoint combinations that maintained viable growth while enhancing productivity.

What we achieved:

For both molecules, the optimized combination of **feed tapering and temperature shift** produced meaningful gains—reaching **5.6 g/L for Rituximab and 11.0 g/L for Herceptin**, representing **~60% titer improvement** compared to baseline conditions. These results demonstrate the consistency and impact of applying targeted optimization within Patheon’s intensification framework.[5]

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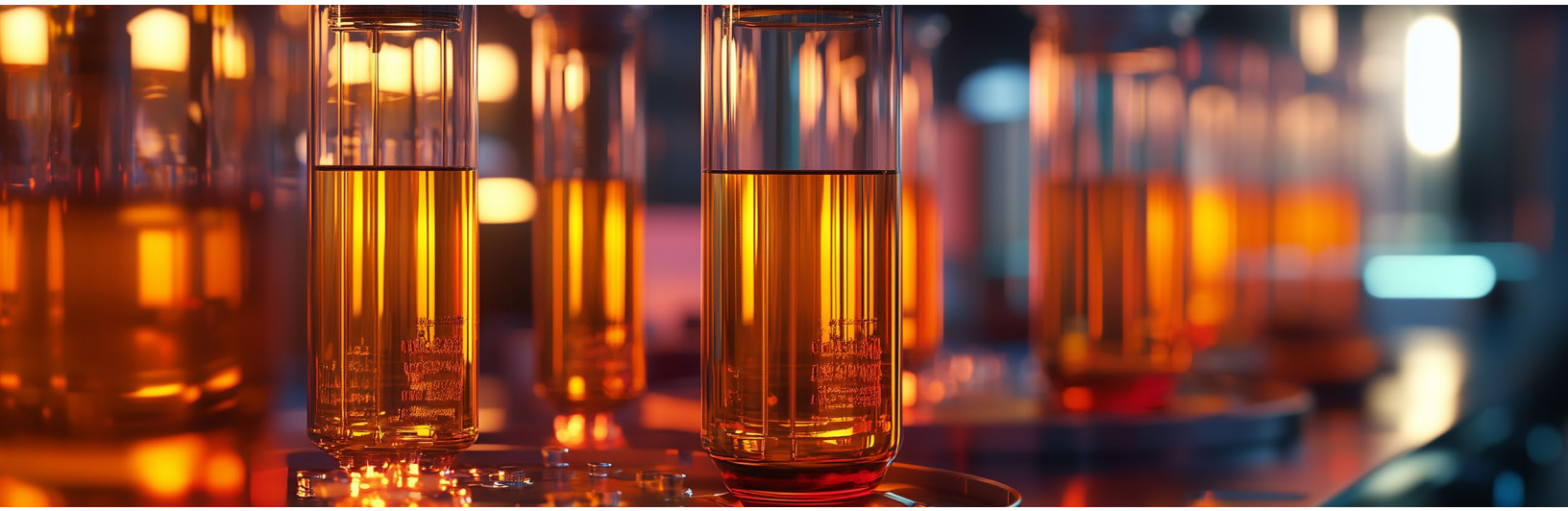

High-concentration formulation

As the demand grows for subcutaneous and ocular administration of monoclonal antibodies (mAb) and other protein-based therapeutics, developers increasingly require high-concentration formulations. These formulations often exceed 100–150 mg/mL and in some cases approach 200 mg/mL.7 High-concentration formulations can improve patient convenience by enabling lower-volume dosing, but they also present stability, viscosity and solubility challenges.

Patheon has developed a tailored process capable of producing concentration ranges of up to > 200 mg/mL. To address viscosity and solubility issues, scientists use viscosity-versus-concentration profiles to assess developability and identify strategies to mitigate non-ideal viscosity behavior.[5]

Scientists perform high-throughput stability characterization using tools such as PrometheusTMPantaTM, which provides thermal unfolding, aggregation and purity data from a single sample. This approach supports IgG1, IgG4, bispecifics, and Fc-fusion proteins, integrates seamlessly into existing downstream platforms and enables an optimized version for commercial scale.[5]

Conclusion

Early-phase development is a race against both biology and time. For emerging biopharma companies, the ability to generate compelling IND-enabling data quickly—without compromising quality—can determine whether a molecule advances or stalls.

By integrating AI-enabled vector design, transposase and afucosylation technologies, high-throughput clone selection, intensified fed-batch processes and high-concentration formulation expertise, a platform approach reduces risk, shortens timelines and strengthens manufacturability from the start. Its focus on efficiency and speed enables biopharma companies to potentially conserve critical funding while preparing the data to move toward the next milestone.

A combination of innovation and experience instills confidence that processes remain robust, scalable and aligned with regulatory expectations. As molecules grow more complex and speed becomes even more essential, streamlined, end-to-end approaches like Path to IND will play a critical role in helping biopharma companies bring transformative therapies to patients sooner.

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*Titer levels provided are estimates based on third party results and may vary depending on molecule type or other factors. Timeline from DNA to drug product and start of clinical trials for all path to IND for biologics options may vary depending on molecule type or other factors and are estimates to be finalized after third party cell line development dates are available and confirmed. 9-month timeline will incur additional risk.

ABOUT PATHEON

As a subsidiary of Thermo Fisher Scientific, Patheon strives to provide industry-leading pharma services solutions for drug development, clinical trial logistics and commercial manufacturing to customers through our Patheon brand. With more than 55 locations around the world, we provide integrated, end-to-end capabilities across all phases of development, including API, biologics, viral vectors, cGMP plasmids, formulation, clinical trials solutions, logistics services and commercial manufacturing and packaging. We give pharma and biotech companies of all sizes instant access to a global network of facilities and technical experts across the Americas, Europe, Asia and Australia. Our global leadership is built on a reputation for scientific and technical excellence. As a leading pharma services provider, we aim to deliver unrivaled quality, reliability and compliance. Together with our customers, we're rapidly turning pharmaceutical possibilities into realities.

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