Bora Biologics

Redefining scalability: Strategies for enhancing early drug development to future-proof later stages

Meeting the rising demand for biologics

Biologics have revolutionized the medical landscape with their targeted mechanisms of action and potential for treating a wide array of indications. As the global population grapples with an increasing burden of disease, including cancer and chronic conditions, the demand for effective biologics has surged, propelling the biopharmaceutical industry into an era of unprecedented growth and opportunity.

At the forefront of the biologic revolution are monoclonal antibodies (mAbs), offering the ability to mimic the body's natural immune response to precisely target specific molecules or cells involved in disease processes. With their targeted approach and efficacy, mAbs have become indispensable tools in treating cancer, autoimmune disorders, infectious diseases and other conditions.

As mAb applications continue to expand, the global market is experiencing significant growth, reflecting the increasing recognition of their transformative potential in modern medicine. Valued at $105.79 billion in 2023, the market is forecast to grow at a compound annual growth rate (CAGR) of 11.07% from 2024 to 2033, reaching $144.36 billion by 2030[1].

Beyond traditional mAbs, the biologics landscape is evolving with the emergence of more complex therapies:

Bi- and Tri-specific Antibodies: These innovative therapies can simultaneously bind to multiple targets, offering enhanced specificity, improved efficacy and novel mechanisms of action. They hold immense potential in oncology and other therapeutic areas, with the global bi- and tri-specific market projected to grow at a CAGR of 24.1% from 2024 to 2033[2].

Bioconjugates: By combining the targeting capabilities of mAbs with the potent effects of small molecule drugs (typically cytotoxins), bioconjugates enable targeted delivery of therapeutic payloads directly to diseased cells. This approach enhances efficacy while minimizing damage to healthy tissues. The global antibody-drug conjugates market is estimated to grow at a CAGR of 9.2% from 2024 to 2030[3].

[1]https://www.biospace.com/article/releases/monoclonal-antibodies-industry-is-rising-rapidly/
[2]https://nationalhealthcouncil.org/blog/a-major-health-crisis-the-alarming-rise-of-autoimmune-disease/
[3]https://www.gminsights.com/industry-analysis/monoclonal-antibodies-market

This expanding landscape of next-generation biologics reflects the industry's relentless pursuit of innovative solutions to combat complex diseases. However, the rapid growth and increasing complexity of biologics present a unique challenge: scaling manufacturing processes to meet the escalating demand. This must be achieved while maintaining rigorous quality, safety and efficacy standards as well as ensuring cost efficiency. Finding a solution to this challenge is necessary to deliver these critical therapies to patients swiftly.

To address this challenge, a strategic approach to scaling is crucial. Developers must focus on early optimization of development processes, striving for high product titers and quality, to overcome productivity and scalability hurdles in later stages. By implementing robust and scalable manufacturing strategies, drug developers and manufacturers can ensure that these life-saving therapies reach patients efficiently and effectively.

Exploring the challenges in early development and scaling

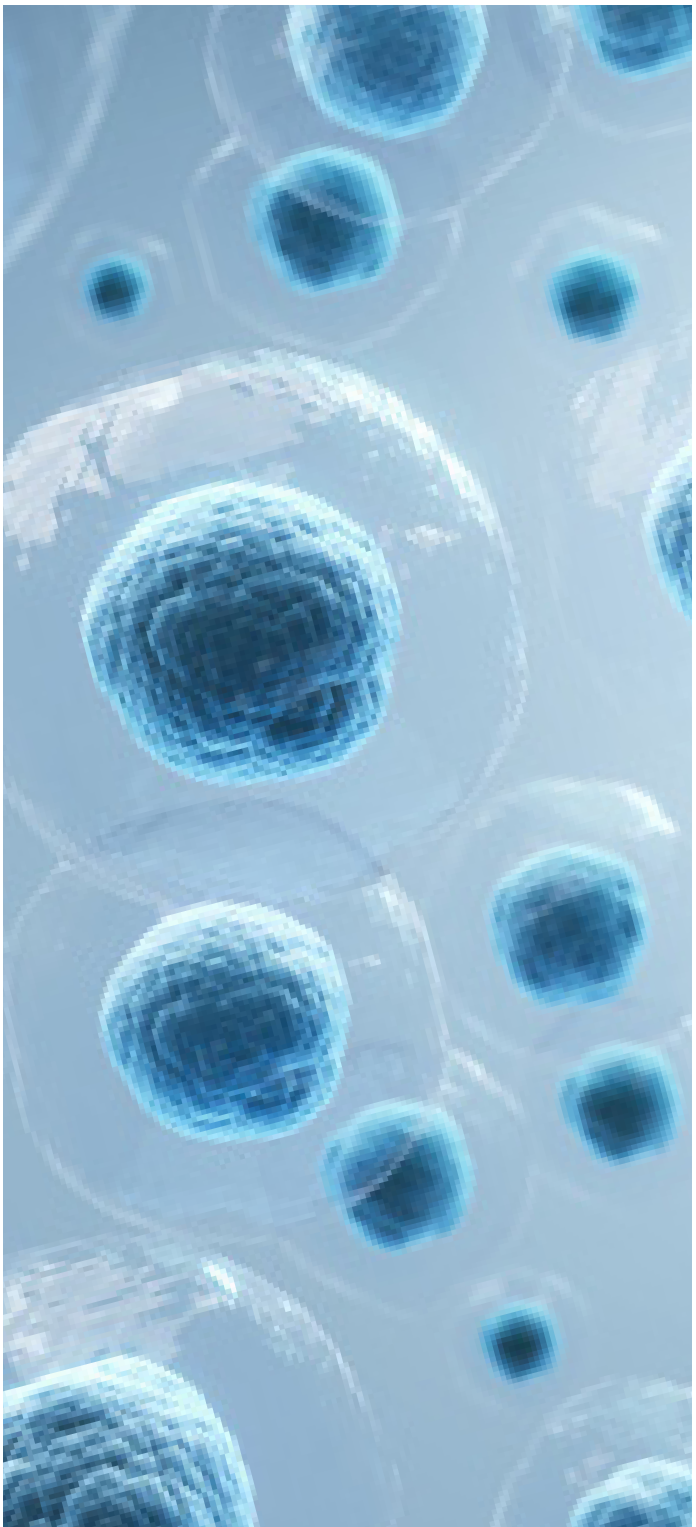
The path to developing and scaling a successful biologic is not simple, bringing challenges and risks, each with the potential to impact the journey from early development to large-scale manufacturing significantly. The intricate nature of these complex molecules, particularly emerging modalities like bi- and tri-specific antibodies and bioconjugates, presents a unique set of obstacles that must be navigated with precision and expertise.

1. Handling inherently complex biological systems

Biologics are inherently complex molecules. Their production involves intricate biological systems and processes, making them more susceptible to variability and difficult to characterize compared with small molecule drugs.

Variations can arise from post-translational modifications (PTMs) like glycosylation, phosphorylation and deamidation, which are influenced by the host cell line and culture conditions. Such modifications can affect the biologic's stability, efficacy and immunogenicity. As a result, having an in-depth understanding of the impact of these variations early in development, as well as carefully monitoring and controlling these processes throughout development and manufacturing, is critical for success.

The complexity of antibody-based therapeutics also makes them challenging to characterize thoroughly. Their complex structures and potential for aggregation require sophisticated analytical techniques to assess their purity, potency and stability, necessitating a deep understanding of their molecular intricacies and the biological processes involved in their production.



2. Low product quality

Product quality is paramount for patient safety. Impurities or inconsistencies in the final product can lead to adverse reactions and a compromised therapeutic benefit, underscoring the critical need for stringent quality control throughout the production process. Low product quality in antibody development and manufacturing can stem from several interconnected factors, with consequences seen throughout the entire process:

At the cellular level: The complex nature of protein folding can cause misfolded antibodies, affecting their stability, functionality and therapeutic efficacy.

Purification: As the process progresses to purification, challenges can arise in effectively removing impurities, such as host cell proteins and DNA, which can compromise product purity and safety.

Analytical characterization: The complex nature of antibodies also poses challenges in analytical characterization, requiring sophisticated techniques to assess critical quality attributes (CQAs) accurately.

The unique challenges of ensuring bi- and tri-specific antibody purity

Bi- and Tri-specific antibodies, while holding immense therapeutic promise, present unique challenges in development. One of the most significant hurdles is chain mispairing, where the heavy and light chains of the antibody components can incorrectly assemble, resulting in a reduced yield of the desired bispecific structure and the formation of undesired byproducts. These byproducts not only reduce overall production efficiency but also complicate downstream purification processes.

Additionally, the unconventional structures of bispecific antibodies (bsAbs) and tri-specific antibodies can lead to protein folding and stability issues. Improper folding can render the bsAb or tri-specific antibody inactive or unstable, impacting both the quantity and quality of the final product. These complexities underscore the need for specialized expertise and innovative approaches in the development and manufacturing of these next-generation biologics.

Formulation and stability: Particularly with high-concentration formulations, antibodies can aggregate or degrade over time, affecting their shelf life and therapeutic potential.

It is important to address low product quality issues at an early stage to avoid issues at later stages, which could require costly fixes and potentially cause timeline delays.

3. Poor efficiency and productivity

The production of biologics, especially complex modalities like bsAbs and tri-specific antibodies and bioconjugates, is inherently resource-intensive, demanding specialized equipment, highly skilled personnel and stringent quality control measures. When cell lines yield low product titers or manufacturing processes are not streamlined, achieving the desired output often necessitates larger-scale bioreactors, increased production cycles and additional purification steps, all of which significantly escalate costs.

In the later stages of drug development, where commercial-scale production is required, these challenges can become particularly pronounced, potentially hindering the ability to meet market demands efficiently.

Conversely, establishing a highly productive cell line through cell line development (CLD) and manufacturing process early in development can significantly alleviate these issues. A cell line with optimized productivity can yield up to 2-4 times more product compared with a less productive one. This allows for commercial production using smaller bioreactors, reducing capital investment and operational costs.

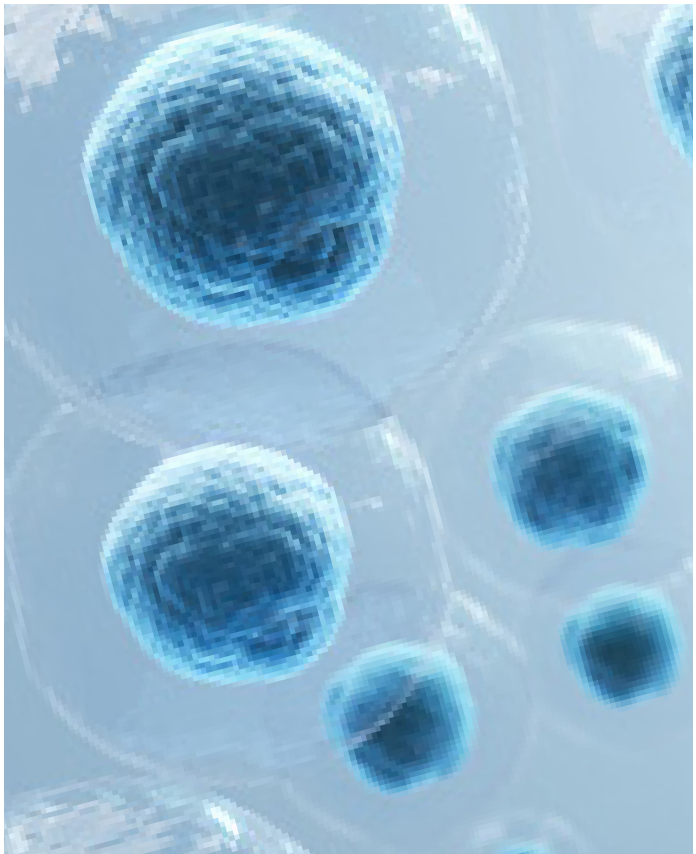
As a result, prioritizing early-stage optimization of cell line productivity and manufacturing processes is a crucial strategy for mitigating the challenges associated with poor efficiency and ensuring the economic viability of biologics production.

Optimized early development for manufacturing success

Strategic decisions made during the early stages of biologics development can significantly affect the success and efficiency of subsequent manufacturing processes as the project scales. By establishing a highly productive cell line and efficient process early on, production needs can be met at lower volumes, reducing the reliance on large-scale bioreactors and lowering capital investment. Moreover, high titers and robust processes translate into shorter production timelines and increased manufacturing flexibility, enabling a swift response to market demands.

Ensuring a smooth transition to commercial scale relies on prioritizing optimization and de-risking in early development; this is only made possible by leveraging:

Expertise in biologics CMC: A cohesive collaboration among cell line, process, analytical and formulation development teams is essential for optimizing drug production in the early stages. Experienced teams with a proven track record in biologics development can streamline the process, leveraging their expertise to create productive and scalable processes that lay the foundation for successful manufacturing. This collaborative approach ensures that all aspects of development are aligned, minimizing the risk of encountering unforeseen challenges in later stages.



Bora's proven expertise: A track record of success

Bora's expertise in biologics is evident in its impressive track record of successful projects and client collaborations, achieving milestones efficiently and delivering high-quality products:

- 30+ 500L GMP batches for Phase 1 & 3 clinical trials
- 70+ batches manufactured under cGMP for 25+ different products
- 45+ Clinical Trials Applications (CTA)/Investigational New Drug (IND) applications filed and successful audits by clients, EU Qualified Person (QP) and Taiwan FDA

Additionally, teams with extensive CLD expertise can develop high-expressing, stable cell lines tailored to the specific needs of a biologic, including complex antibody therapeutics. This reduces the risk of low productivity and inconsistent product quality.

By optimizing cell lines early in development, these experts can set the stage for efficient and cost-effective commercial production. Drug developers can reduce the reliance on large-scale bioreactors during commercial production by achieving high product titers early on, translating into lower capital expenditures for equipment and facility expansion. A highly productive cell line also requires fewer production cycles to achieve the desired output, leading to reduced consumables and labor costs.

Integrated platforms: Using integrated platforms can significantly accelerate the development timeline. These platforms offer a seamless workflow, from CLD and process optimization to analytical characterization and formulation. By consolidating these essential steps, integrated platforms reduce bottlenecks and enable rapid iteration, ultimately accelerating the path to clinical trials and commercialization.

An integrated platform also promotes close collaboration between different functional teams, including CLD, process development, analytical development and manufacturing. This streamlined communication facilitates rapid decision-making and problem-solving, accelerating development timelines and reducing time to market.

Streamlining development and accelerating timelines

Bora's integrated biologics platform streamlines development, accelerating timelines from DNA to drug substance release by leveraging:

Proprietary technologies: Proprietary host cell lines and high-expression vectors optimize product quality and yield.

Scalable platforms: Cell culture and purification platforms enable seamless scale-up from 3L to 1,000L (2x500L) for non-clinical, clinical and commercial production.

Advanced analytics: State-of-the-Art and comprehensive analytical capabilities (can develop, qualify, validate over 50 Assays in-house, including Bioassays) ensure detailed product characterization and quality control.

Experienced team: A dedicated team that has been together for over 10 years, with extensive experience in biologics development and manufacturing ensures efficient and consistent project execution and regulatory compliance.

In-house analytical capabilities: Analytical capabilities are essential for ensuring the safety, efficacy and regulatory compliance of biologics. Comprehensive characterization, utilizing a wide array of analytical techniques, enables a deep understanding of molecular intricacies, ensuring the final product is free from impurities or inconsistencies that could compromise patient safety.

Beyond quality control, analytics plays a pivotal role in accelerating project progression. By identifying potential issues early in development, biologics producers can proactively implement corrective measures, preventing costly delays in later stages. This proactive approach, combined with the comprehensive characterization of complex antibodies, ensures that these innovative therapies are developed and manufactured to the highest standards, ultimately benefiting patients and advancing biopharmaceutical innovation.

Access to specialized in-house analytical capabilities is crucial for optimizing early development, offering specialized analytical tools to assess CQAs, identify potential impurities and ensure product consistency.

Ensuring quality and accelerating development

Bora's advanced analytical capabilities are integral to its integrated biologics platform, ensuring product quality and accelerating development timelines.

Comprehensive characterization: In-depth analysis of drug substances (DS) and drug products (DP), including release and stability testing, ensures compliance with regulatory standards and supports data-driven decision-making.

Bioassay expertise: Development, validation and execution of cell-based bioassays under cGMP guidelines provide accurate assessment of biological activity and therapeutic efficacy.

Fingerprint analysis: A unique approach utilizing 40+ analytical methods for meticulous comparison of biosimilars to reference products, ensuring quality and consistency.

Stand-alone services: Comprehensive analytical support includes product interrogation, release testing and stability studies, offering a holistic view of product characteristics and enabling proactive risk mitigation.

Effectively navigating scale-up: Balancing quality, robustness and cost

Even after setting a strong foundation at early development, as projects scale, biologics producers can anticipate a series of interconnected challenges that demand a strategic and adaptable approach. Three critical areas where developers and manufacturers need to focus their expertise are:

Maintaining product quality at scale: As production volumes increase, subtle changes in the manufacturing environment, such as bioreactor size, media composition or process parameters, can affect product characteristics. To mitigate this, a comprehensive tech transfer process is essential, ensuring that critical process parameters and CQAs are faithfully reproduced at scale. Additionally, implementing robust quality control measures and utilizing advanced analytical techniques to monitor product attributes throughout the scale-up process can help quickly identify and address any deviations from the desired quality profile.

Ensuring process robustness for scalability: A scalable process can consistently produce the desired product quality and yield, even with variations in raw materials, equipment or operator performance. Achieving process robustness requires a deep understanding of the critical process parameters and their impact on product quality. By conducting thorough risk assessments and implementing effective control strategies, drug developers and manufacturers can proactively address potential vulnerabilities and ensure the process remains reliable and consistent as production volumes increase.

Managing the cost of goods and supply chains: Scaling up production often leads to increased costs associated with raw materials, consumables, personnel and facility expansion. To optimize cost-effectiveness, biologics manufacturers can leverage strategic sourcing of high-quality materials, negotiate favorable pricing agreements with suppliers and streamline logistics for efficient delivery. Additionally, implementing process improvements and automation can reduce labor costs and enhance operational efficiency.

Critical considerations when working with a CDMO

Contract development and manufacturing organizations (CDMOs) can help to significantly relieve the burden of scaling challenges for their customers, leveraging extensive experience and expertise in biologics development and manufacturing.

When selecting a CDMO partner to help ensure a seamless transition from CLD to commercial production, identify whether the potential partner adopts a client-centric approach. By fostering open communication and collaboration with clients, CDMOs can tailor the scale-up strategy to meet specific needs and preferences. Regular updates, transparent data sharing and proactive problem-solving enable a collaborative effort to address any challenges that may arise, ensuring a smooth and successful transition from development to commercial-scale manufacturing.

A specialist partner drives scale-up success

Choosing the right partner to navigate the transition from development to commercial-scale manufacturing can be a pivotal decision for the success of a biologic. A capable partner should not only possess the technical expertise and infrastructure to handle large-scale production but also offer a comprehensive understanding of regulatory requirements, quality assurance and supply chain management. Additionally, a collaborative and client-centric approach is crucial, ensuring that the partner aligns with the developer's specific needs and goals, providing transparent communication and proactive problem-solving throughout the scaling process.

Bora offers a proven track record of successful scale-up projects for a diverse range of biologics. With an integrated platform, encompassing CLD, process optimization and manufacturing, we can ensure a seamless transition from early development to commercial production. Our state-of-the-art analytical capabilities protect product quality and regulatory compliance, while our experienced and collaborative team provides tailored solutions to address specific challenges. With a strong commitment to innovation, quality and client satisfaction, Bora is well equipped to guide drug developers through the complexities of scaling biologics manufacturing, ultimately accelerating the delivery of life-saving therapies to patients in need.

Discover how we can support the scale-up of your next biologics project to make success more certain.