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CPHI Online Trend Report

Uplifting Biologics from Billion-Dollar Drugs to Billions of Patients

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Key takeaways

Key takeaways 1/2

Scaling biologics technology is in a Fourth Wave of innovation

The fourth revolutionary wave of biologics manufacturing marks a transformative chapter in the industry's development, with companies charging towards ultra-large-scale production that will ultimately benefit patients worldwide through improved access to biological therapies at reduced manufacturing costs.

Biosimilars are increasing the demand for innovative and at-scale biologics manufacturing

Biosimilars are significantly influencing the biologics manufacturing landscape through a complex dynamic of both competition and complementary growth. As patents for major biologics continue to expire, manufacturers are adapting by enhancing their production capabilities to serve both markets, ultimately driving innovation and expansion in biologics manufacturing infrastructure despite the competitive pressure biosimilars place on original biologics pricing.

Key takeaways 2/2

Driving biologics manufacturing isn't just about technology, but also about people

As biologics continue to represent an increasing share of breakthrough therapies and the global pharmaceutical market, addressing workforce development challenges has become a critical strategic priority for companies seeking to maintain innovation, quality, and operational excellence in this highly specialised field.

Patient accessibility starts with the industry

As the biologics landscape continues evolving, industry stakeholders are increasingly aligning incentives, streamlining workflows, partnering with industry players, and providing targeted education to unlock the full potential of biologics and biosimilars in improving patient access to these transformative therapies.

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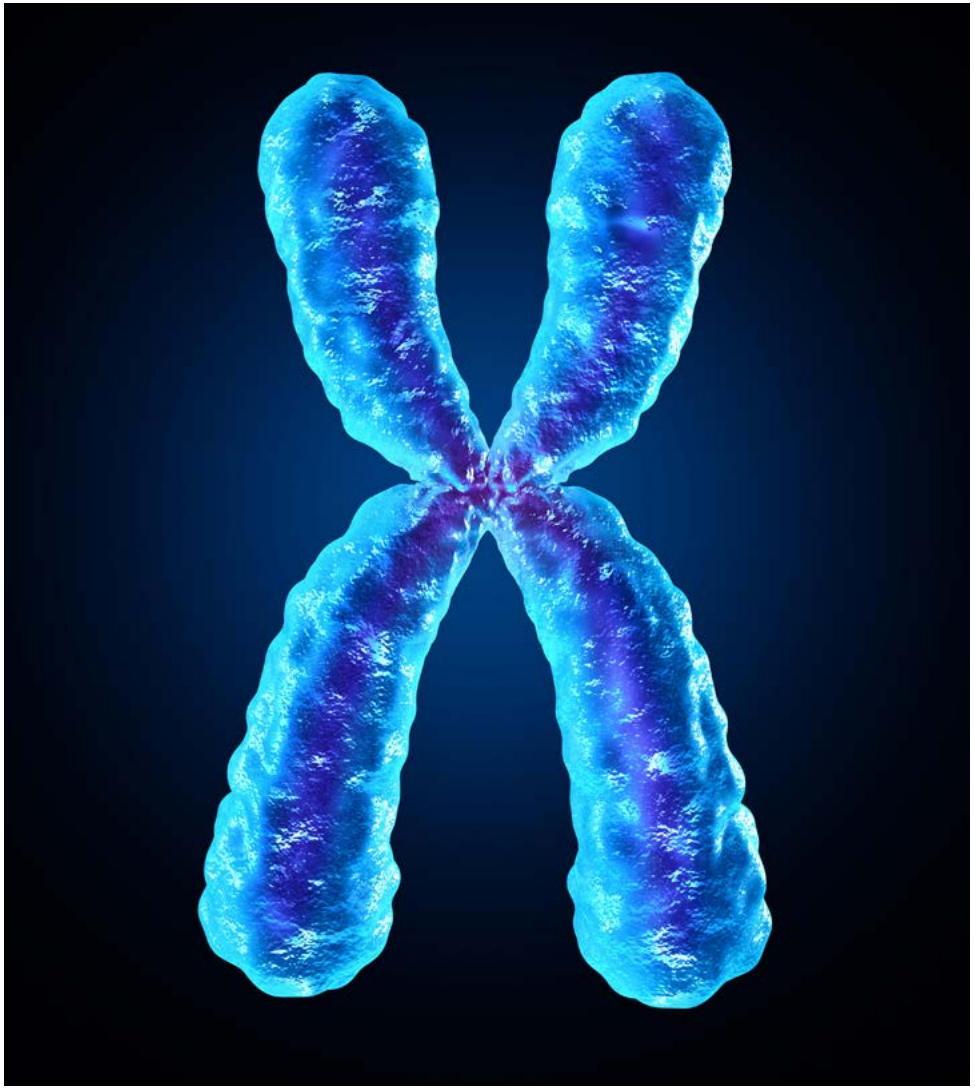
Biologics, biosimilars, and biomanufacturing: an introduction

Biologics, biosimilars, and biomanufacturing: an introduction



In recent years, biological products or 'biologics', have taken the healthcare and pharmaceutical industries to new levels of innovation – sales of biologics are predicted to overtake innovative small molecule drugs by as much as US$120 billion by 2027 [1].

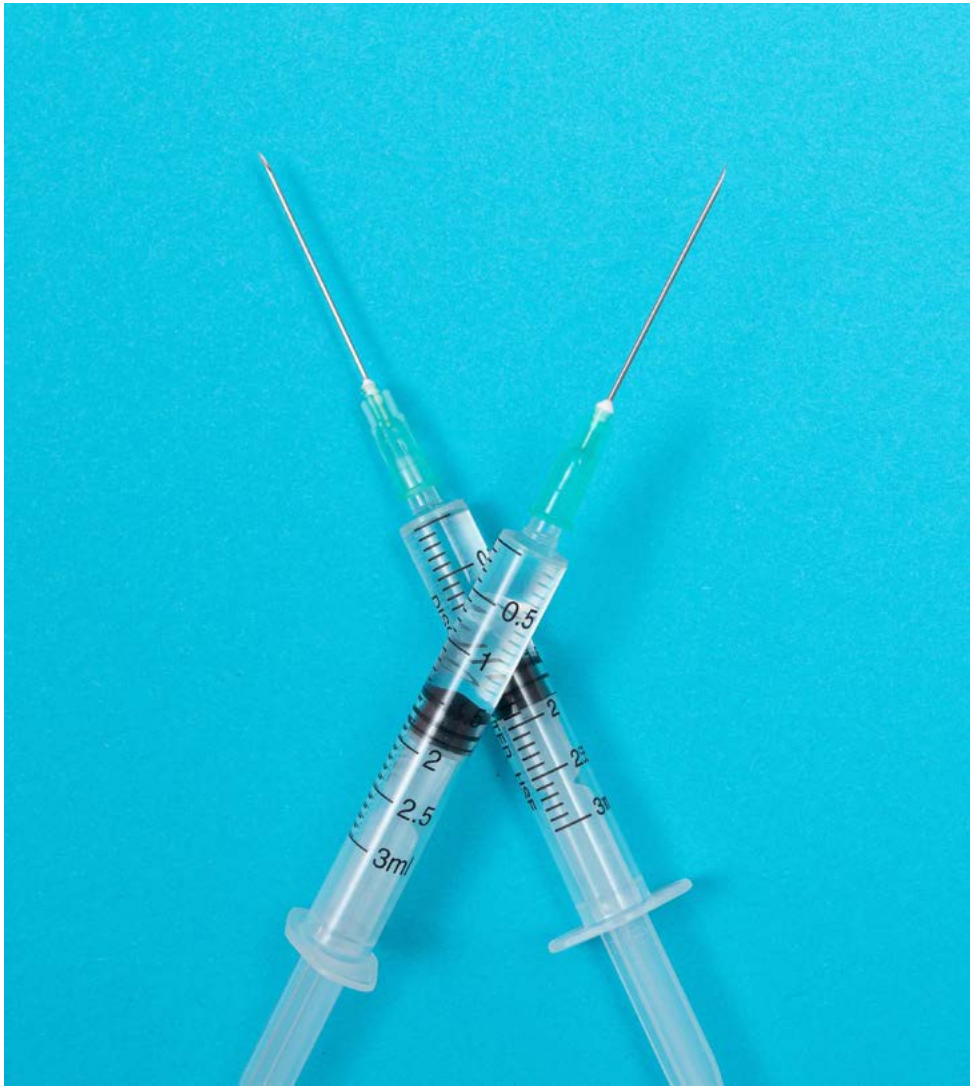
This represents nearly 55% of all innovative drug sales, and with experts valuing the current global biologics market between US$410 billion [2] and US$487 billion [3] in 2025, it is little wonder why pharmaceutical players are revving up innovations to meet the demand for this promising portfolio of therapeutics.

Breaking through the biologics and biosimilars barriers

In 2024, the US FDA saw the approval of 50 new therapeutics, 32% of which were biologics (16 biologic products) [4]. While this number is only slightly under the numbers seen in 2018 and 2023 (17 biologic approvals each), these approvals indicate an increasingly fertile market for biomanufacturing and biosimilar innovation [4]. On top of this, the expiry of various biologic patents are spurring biosimilar development and manufacturing across the globe, allowing wider access to potentially life-saving treatments [5]. Personalised medicines with cell and gene therapy (CGT) technologies as well as antibody drug conjugates (ADCs) are also witnessing a level of research, development, and commercialisation like never before – with over 2000 affiliations ranging from start-ups to academic institutions to global pharmaceutical developers and manufacturers, experts anticipate the approval of 10-15 new biologic approvals every year [5]. As of the publication of this report, the first patient in the UK has received CSL Behring's gene therapy Hemgenix to treat haemophilia B [6]. Hemgenix reportedly cost GBP£2.6 million per dose, representing the level of investment from pharmaceutical companies in such innovative therapeutics, with doctors calling it a "testament to the advancement of cell and gene therapies in the UK – these are exciting times." [6].

Since the 1970s, the growth of the biologics market can be attributed to several key developments in clinical and manufacturing innovation [1]. Regulatory changes in the last decade – the first since 1977 – have completely overhauled general biologic standards such as "duties of inspector" requirements, giving the FDA more efficient risk-based approaches when assessing manufacturing facilities for biologic products [1]. Other regulations concerning standard preparations, storage, and potency limits have also been redesigned to allow for faster time-to-market while reducing development costs for biologics [1].

The complexity of biologics manufacturing and innovations in this sector have also driven the growth of the market. Advances such as continuous manufacturing over batch manufacturing, Bioprocessing



and Manufacturing 4.0 advances, and integration of machine learning, artificial intelligence, and automation technologies are bringing biologics manufacturing to a new level of efficiency, safety, and precision [1].

This excitement around biologics, and particularly biosimilars, however, are not without their complications. Bringing biologic drugs to the market can be a lengthy and costly process, and accessibility remains a major concern [7]. While biosimilars can offer greater access to lifesaving treatments for a wider population, the pharmaceutical industry faces a minefield of complexities and barriers [7]. "The production process for biologic drugs is complex, and the regulatory requirement to conduct clinical trials, combined with intricate patent landscapes, makes the barrier to entry for biosimilars relatively high," comments **Dr Peng Jiao, Founder and CEO of BiBo Pharma.** "Particularly in the early stages of biosimilar development, due to the limited number of existing reference biologics available and the impact of patent protection for new drugs, this has resulted in a limited number of biosimilar players in the market. Since the US FDA approved its first biosimilar in March 2015, a total of 70 biosimilars have been approved by April

2025. These approvals utilise 19 reference products and are held by 21 Marketing Authorization Holders (MAHs). For pharmaceutical companies, the biosimilar market is an attractive opportunity. On one hand, by targeting commercialised biologics drugs with demonstrated market success, biosimilar players inherently bypass two major risks associated with novel drug development: the high failure rate of novel drug candidates and the market uncertainties. On the other hand, biosimilars represent a relatively high-end segment of the generic drug market. However, due to the significantly higher costs associated with developing and manufacturing biologics compared to small-molecule drugs, the price of biosimilars remains a substantial burden for payers, even when lower than that of reference products."

Factors impacting drug pricing also have consequences for the biosimilar and biologics markets – with executive administrations increasing efforts to control the price at which drugs are set and expand access to lifesaving treatments, some policies such as the Inflation Reduction Act under the Biden administration are subjecting biologics that have not seen generic or biosimilar competition to pricing negotiations [7]. This could be a great opportunity for biosimilar development: "With patents expiring for a number of biologics, the rise of biosimilars shall fundamentally impact the biologics industry," Jiao explains. "Between 1995 and 2015, an average of 50-60 new biologics were approved every 5 years. However, during the period between 2015 and 2020, over 250 new biologics gained approval. It is projected that the number of newly approved biologics will further

increase in the most recent 5-year period. Concurrently, it is evident that the cumulative stock of approved drugs will surpass the number of new drugs approved annually. Furthermore, it is anticipated that by 2027, the number of drugs losing patent protection each year will exceed the number of newly approved biologics. Therefore, 2027 can be regarded as a landmark year for biosimilars. Beyond this point, in terms of product variety, biosimilars will outnumber newly approved biologics, and the gap between these two categories is expected to widen progressively thereafter. Consequently, the biologics market will gradually transition into one dominated by biosimilars. Based on this, it can be anticipated that, in the near future, the biologics field will inevitably transition toward a landscape dominated by biosimilars – just as the small molecule drug sector did. Biologics companies, especially large multinational corporations, must confront this trend."

Renato Azevedo, Sr Director, Global Product Management – Bioprocessing at Ecolab Life Sciences, adds that "The biosimilars market stands at a pivotal crossroads driven by two primary catalysts: the imminent 'patent cliff' with over 100 biologics losing protection in the next decade, and the growing demand for cost-effective treatments in healthcare systems under budgetary constraints. While not every biologic will see biosimilar development—what we call the 'biosimilar void'—due to market size limitations or manufacturing complexity, these alternatives represent a critical opportunity to improve patient access to life-saving therapies for cancer, diabetes, and autoimmune diseases."

Whether the demand be for innovative biologics or biosimilar development for better patient access, the market for lifesaving treatments with these complex drug products is only set to grow in the coming years.

Transforming treatments: top therapy areas for biologics

Patent filings and journal publications can say a lot about what kinds of therapeutics are currently under investigation and working towards market and commercialisation [1]. Early biologics include monoclonal antibodies (mAbs) such as infliximab to treat inflammation from autoimmune diseases [8]. Since then, continued advancements in biomanufacturing

and biotechnology have led to over 600,000 journal articles published between 1987 and 2021 detailing biologics ranging from cell and gene therapies, vaccines, antibodies, and fusion proteins [1].

CTO of BiBo Pharma Dr Roy Lin comments on some of the top therapy areas and biologic types transforming the pharmaceutical landscape:

"- Antibody drug conjugates (ADCs) offer a combined chemotherapy and targeted therapy for cancer treatment, offering increased tumour specificity and selectivity, resulting in reduced side effects;

- CGTs offer potential disruption treatment of blood cancers via CAR-T therapy, as well as rare diseases such as spinal muscular atrophy and haemophilia via AAV viral vectors;

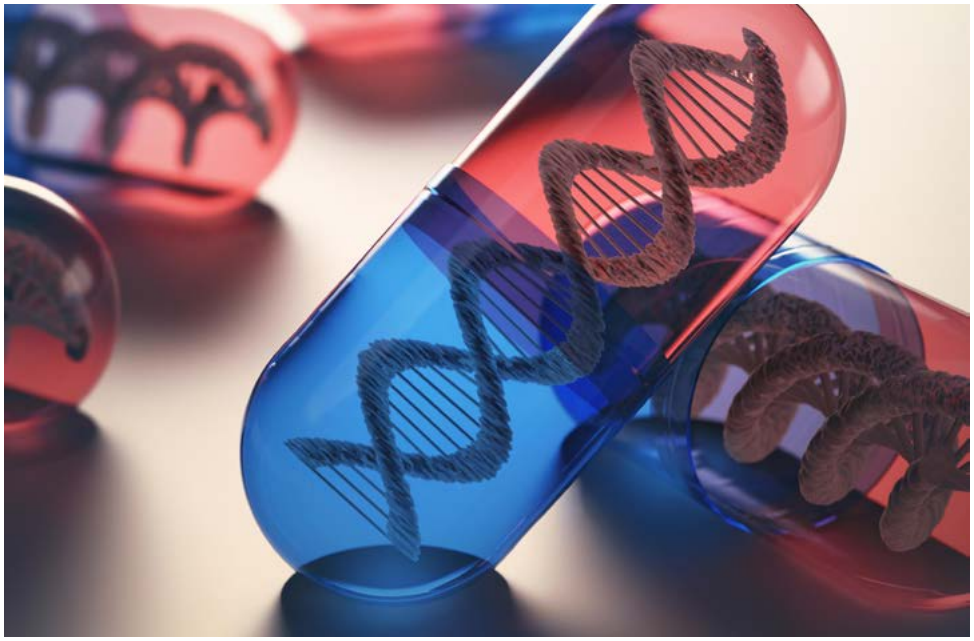
- GLP-1 agonists for metabolic disorders such as obesity and Type 2 diabetes;

- Innovative biologics for autoimmune and inflammatory diseases such as systemic lupus erythematosus (SLE) and systemic sclerosis, and are also used for neurodegenerative diseases such as Alzheimer's and Parkinson's disease;

- RNA-based therapeutics, as we've seen with the COVID-19 pandemic, for respiratory syncytial virus, SARS-CoV-2, and influenza;

- Biosimilars are gaining traction due to cost reductions, increased affordability, and patient access to expensive biologic therapies;

- Radiopharmaceuticals for targeted radiation treatment of cancer cells."



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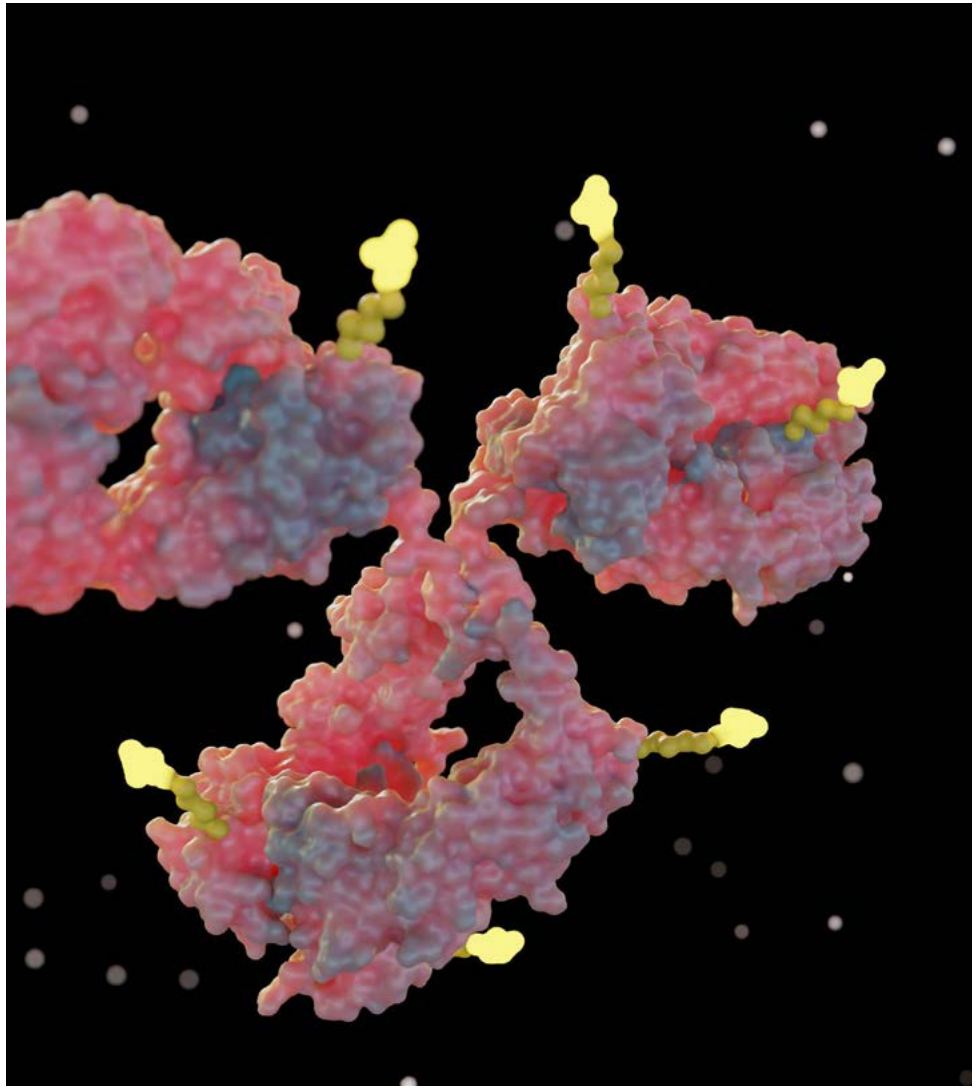
Strategic considerations for biomanufacturing

Strategic considerations for biomanufacturing

The excitement around biologics has the pharmaceutical industry and supply chain revving up investment on all fronts – from discovery and development to clinical research to manufacturing and commercialisation, we are currently witnessing what experts deem the Fourth Wave of biologics manufacturing [9].



> **The complexity of these products are demanding more than ever before from the pharmaceutical industry and their service providers, with factors from all aspects of the manufacturing process to consider and redevelop.**

Complex products, complex manufacturing processes

Due to their complexity, there are a great number of considerations to be accounted for when manufacturing and scaling production of biologics [9]. "The development of biologics manufacturing processes involves many complex stages," explains Lin. "Starting with cell line development and upstream processing, followed by downstream purification, formulation development, and fill and finish, it is crucial for analytical and quality support to be provided throughout to ensure consistent process performance and a safe and effective product quality that meets regulatory requirements."

For many manufacturers, the final mode of delivery also influences the manufacturing processes of biologics. "The mode of delivery directly affects biologics formulation and fill and finish operations," continues Lin. "Injectable formulations (e.g. IV, subcutaneous etc.) are most common for protein therapeutics as proteins are prone to denaturation when exposed to harsh GI environments. Oral doses often involve protective coatings or encapsulations to protect proteins from low pH GI tract and digestive enzymes."

Further considerations from drug delivery perspectives involve drug payload and potency. "The nature of the primary container for the formulation is key to support the stability of the biologics over the shelf life of the product," adds **Chris Hurlstone, Director of Drug Delivery, and Kella Kapnisi, Head of Cell and Gene Therapy at Team Consulting.** "For example, delivery of biologics as an aerosol to the lungs will challenge formulators on whether an aqueous formulation is most appropriate vs a dry powder. The answer may depend on the drug payload required and the therapeutic regime e.g. how often a dose is taken etc. If the drug payload is large and the potency is low, then it may be that only a nebuliser can deliver the required volume per dose. Alternatively, if the payload is lower, then other devices like soft mist inhalers may be considered, provided they are able to meet the shelf life requirements of the biologic and not damage the delicate molecules at the point of delivery (e.g. high shear forces)."

"Right now, there's lots of talk about bioavailability and stability that affect mode of delivery and subsequently biologics manufacturing," says **Andrew Mears, CEO and Co-Founder of Lead Candidate.**

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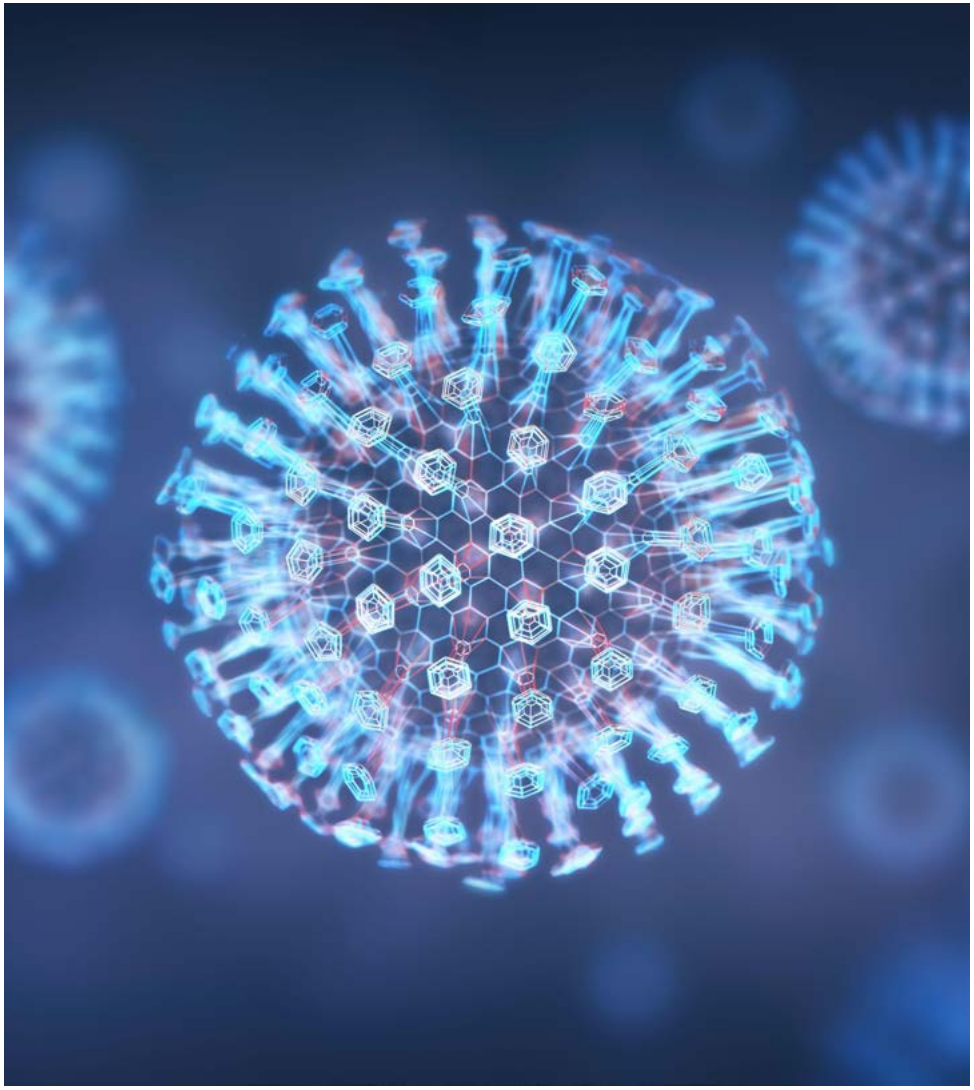
“Oral biologics are emerging as a preferred option due to their potential for fewer side effects compared to injectable biologics”

Andrew Mears

CEO and Co-Founder of Lead Candidate



However, this delivery method presents significant manufacturing challenges, including stringent potency requirements and complex aseptic manufacturing processes to ensure sterility. We're observing considerable industry activity in this area, particularly among our customers in the CDMO (Contract Development and Manufacturing Organization) space. For example, one of our customers recently made a significant announcement about acquiring a major spray drying facility in the UK. This company, Particle Dynamics, is experiencing substantial growth in their spray drying technologies, which are specifically designed to enhance stability and bioavailability of specialised biologic formulations. This acquisition demonstrates the industry's growing focus on innovative delivery methods and manufacturing processes for biologics. We've definitely identified growth opportunities in both the delivery mechanisms and manufacturing techniques for these complex biological products."

One key aspect surrounding biologics manufacturing is the development, characterisation, and validation of bioprocessing steps – from start to finish [10]. Raw materials, procurement, and transportation become

increasingly complex with biologics manufacturing, as Mears describes: "There are strict control elements that have to be implemented around cell culture purification processes and then the formulation process to ensure product quality, safety, and efficacy levels. When you're thinking about biologics manufacturing, it's not just what happens at your site – it is also all the raw materials and the sourcing of everything that flows into the manufacturing site. Then, as the drug product develops, it becomes about process scalability and how it impacts regulatory compliance. These are all critical factors that are really feeding into manufacturing processes right now."

The development and validation is equally as important to ensuring good manufacturing practices (GMPs) for biologics [10]. "For biologics development, drug developers should establish a Quality Target Product Profile (QTPP) by following the regulatory' agency's Quality by Design (QbD) guidance," Lin explains. "The QTPP summarises the desired quality characteristics of a drug product, including its intended use, route of administration, dosage form, and critical quality attributes (CQAs). It outlines the product's ideal attributes to ensure quality, safety, and efficacy – the QTPP serves as a foundation for product and process design. An early-phase development of manufacturing processes will involve the following activities: cell line development (to establish a stable cell line with desired product tier and quality attributes), upstream and downstream development, optimisation and scale-up to establish a manufacturing process capable of delivering the required product quality and quantity, analytical method development, and formulation and fill & finish processes." Questions related to measuring CQAs for different biologics, defining raw materials (especially chemically raw materials) and understanding impurity risks, and an appropriate and reliable model for scaling operations later down the line become critical components of early process development [10].

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“Biologic molecules are typically delicate and vulnerable to enzymatic and other modes of degradation on exposure to the environment”

Chris Hurlstone

Director of Drug Delivery,
Team Consulting

Kella Kapnisi

Head of Cell and Gene Therapy,
Team Consulting

"It is essential for these molecules to be protected from manufacture and processing all the way up to delivery to the patient. At manufacture, this will place a burden on achieving and maintaining sterile manufacturing conditions, along with other environmental controls such as temperature and humidity.

Similarly, the processing of the molecules needs to be tightly controlled to not impart undue stresses to these delicate molecules e.g., high local shear forces or temperatures."

Once a process is defined from start to finish, scaling such operations to that of a commercial manufacturing site has its own considerations [10]. "For late-phase process development, typical activities include further process optimisation (to ensure required product quality and cost of goods targets are achieved), process characterisation (to establish the process design space and identify critical process parameters (CPPs) and corresponding control strategies), and lastly process performance qualification (PPQ) as well as other validation activities such as QC method validation, cleaning validation, viral clearance validation, resin reuse validation etc.," adds Lin.

Batch vs continuous: processing excellence for your product

Once a process has been developed and designed, the next big bottleneck faced by pharmaceutical sponsors

and the manufacturers they work with is scaling production [11].

In the biologics industry, as with other commercial manufacturing sectors, continuous manufacturing has emerged as an alternative to fed-batch production. "Batch processing and continuous manufacturing are different production approaches with distinct pros and cons," explains Lin. "Batch processing is the most established biomanufacturing platform with several decades of successful track records from preclinical to commercialisation that regulatory agencies are most familiar with. It offers greater flexibility for a multi-product facility and, should there be any critical deviations or failure with a relatively smaller production batch size, there are fewer financial and timeline impacts.

However, batch processing facilities typically experience greater batch-to-batch variability and lower volumetric productivity. Continuous manufacturing, in contrast, delivers a significantly higher volumetric throughput and efficiency in a smaller facility footprint when compared to batch processing. Continuous manufacturing can provide better product quality and consistency, especially when the product is inherently unstable with a short shelf-life during upstream production. It may also provide a potential real-time batch release when continuous monitoring of product CQAs via appropriate PAT are established. However, due to inherent technical complexity and scale-up challenges, which require deep process knowledge with advanced control systems, plus a lack of successful regulatory agency track records, the adoption of continuous manufacturing is relatively slow in the bio-industry."

Mears also comments on the current adoption of continuous manufacturing, expanding on what the industry has termed 'modular' laboratories: "We've seen quite a bit in the last few years the advancement and development of new systems with movable and flexible lab operations that can be effectively selected or acquired as a module and easily installed or repurposed and sent elsewhere. Rather than building a physical brick and mortar business, we are now seeing more flexible and agile solutions that can be developed and used. The entire continuous manufacturing and process analytics – using smart data to make informed decisions around cost and time reduction, efficiency etc. - are clearly a trend right now in pharma."

Deciding which production process to use depends on several factors:

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“The selection typically depends on each company’s legacy manufacturing platform, production process complexity and in-house expertise, quality, and regulatory risk consideration, supply chain, cost (including facility infrastructure and flexibility assessment), and timeline to market factors”

Dr Roy Lin

CTO, BiBo Pharma

Such manufacturing considerations ring true whether a drugmaker chooses to manufacture in-house or to rely on a network of partners and suppliers.

Finally, the transportation of biologics must be met with the same scrutiny. “Transportation will need to meet the same criteria as manufacturing and storage up to the point of use – protect delicate molecules,” Hurlstone and Kapnisi state. “Transport may be of a bulk product or product packaged into primary containers outside of the delivery device. Assuming the primary container is fit for purpose, transportation will, at a minimum, need to include tight control of environmental conditions such as temperature and mechanical stressors e.g., vibration and shock.”

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Smart factories, smarter molecules: Bioproduction technologies

Smart factories, smarter molecules: Bioproduction technologies

Innovation in manufacturing tools and technology are also informing the growth of biologics and biosimilar manufacturing [12].

> **With many disruptive technologies becoming more accessible, understanding the advantages and drawbacks of each can help manufacturers determine what is best for their production.**

AI and automation for biologics production

Artificial intelligence and innovative translational models are poised to transform pharmaceutical research and development in the coming years. AI offers significant advantages through rapid data analysis, compound screening, and drug candidate design capabilities, potentially reducing preclinical discovery timelines by 30-50% and costs by 25-50% [12]. Early results show promising Phase 1 success rates, with some exceeding 85% in particular cases [12]. Despite these benefits, traditional pharmaceutical companies have been slow to adopt AI technologies, with over 40% of companies yet to meaningfully incorporate them into discovery processes. However, for pharmaceutical manufacturers, AI and automation represent an innovative and flexible approach to manufacturing and regulatory compliance in biologics production [5].

“The integration of AI and automation is making a significant impact on large-scale biomanufacturing, leading to unprecedented improvement in manufacturing efficiency, quality, and cost reduction ” states Lin.

"Key impacts include:

- Accelerated process development, optimisation, and scale-up through smart process design with predictive analytics, data integration, and decision support
- Manufacturing optimisation and control through digital twins predictive modelling and real-time monitoring and error detection, leading to increased success rates, productivity, and lower costs of goods
- Enhanced quality control and compliance with reduced deviations, improved production consistency and product quality
- Data integration and decision-making
- Predictive maintenance to improve equipment reliability and reduced downtime
- Supply chain optimisation to improve demand vs supply forecasting and logistics efficiency and reliability"

For manufacturers, many of these technologies become exceptionally useful when scaling production – complex steps during both upstream and downstream biomanufacturing can be optimised with automated

and fully digitised process analytics technologies (PAT), as well as machine learning. However, this slow adoption among pharmaceutical sponsors has delayed the advancement of the industry, according to experts like Mears: "It surprises me how the pharmaceutical industry is actually a bit behind other industry such as the automotive industry, where things like lean manufacturing, continuous improvement etc. were implemented years ago. To some degree, pharmaceutical companies are wary of these principles because there are complexities that prevent their adoption. But now, I think businesses, particularly biologics manufacturing, which is arguable the most complex part of the pharmaceutical chain, are catching onto lean manufacturing, continuous process manufacturing, total productive maintenance (TPM), and such methodologies. It is a huge source of profitability and speeding up time-to-market and patient, and optimising return on investment – it's a huge opportunity within manufacturing processes for these technologies to drive efficiencies and impact profitability that can reinvested back into the industry."

Despite this, there still remain certain challenges regarding the implementation of AI and automation in biologics production lines. "Developing and implementing an AI-based manufacturing process in the highly regulated, complex, and rapidly evolving biologics field can face many hurdles," comments Lin. "These include:

- Data quality, availability, consistency, and representativeness
- Technological challenges with model robustness, integration with legacy systems, scalability, cybersecurity, and data privacy
- Regulatory compliance challenges with model explainability and validation, change control and lifecycle management, and regulatory uncertainty with evolving guidance
- Organisational and human factor challenges such as costly computational infrastructure and equipment investment, workforce training and talent acquisition, and reducing roles, responsibility, and accountability."

In an increasingly saturated market, it will be imperative for biopharmaceutical contract organisations to find their competitive edge – and for drug sponsors to find a partner with the capability to bring their projects forward. For pharmaceutical manufacturers looking to remain competitive, Jiao comments "In terms of technology, biologics are diverse, with complex and unstable protein structures, making process development and upstream-downstream coordination highly challenging. Many pharmaceutical companies and biotech start-ups lack the capability for production process development... As a biopharmaceutical CDMO enterprise, only by consistently maintaining technological advancement, production efficiency, and service timelines can it remain invincible in continuous competition."

Translating laboratory success to production scale: bioreactor boom

The upstream process in biopharmaceutical manufacturing relies on various components including raw materials, excipients, equipment, consumables, and integrated production lines [9]. Among the critical equipment in these facilities - which include solution conditioning systems, chromatography systems, membrane filtration systems, and packaging equipment - bioreactors stand as particularly essential components [9].

Despite their advantages for large batch production, such as excelling in standardised large-batch production with advanced automation and intelligence, stainless steel systems require significant initial investment, involve lengthy manufacturing cycles, and demand complex cleaning validation procedures [9]. For up-and-coming drugmakers, these initial investments may prove a challenge to overcome.

Single-use bioreactors, conversely, feature disposable incubation bags typically constructed from materials like polyethylene, ethylene vinyl acetate, and polycarbonate [9]. These systems offer lower initial costs, faster commissioning times, and eliminate cleaning validation requirements. However, their application in large-scale production faces limitations related to material constraints, as the bags must simultaneously demonstrate high robustness, wear resistance, biocompatibility, and low endotoxin levels while withstanding strict sterilization protocols. Additionally, single-use systems necessitate reliable and sustainable supply chains.

"A common challenge in the pharmaceutical industry is achieving global supply at lower production costs without compromising quality," Jiao comments. "Certain advances have been made to address the challenges related to scaling bioproduction – BiBo Pharma has pioneered the world's first 30,000-litre ultra-large-scale stainless steel production line. Combined with the PanFlex® engineering system, it enables rapid deployment of production capacities ranging from 50-30,000 litres, ultimately achieving low-cost production at US$10 per gram. This provides optimal production solutions for global partners."

During commercialisation, pharmaceutical companies will need to strategically prioritise process stability and cost efficiency, making stainless steel bioreactors the preferred choice for large-scale commercial production due to their superior efficiency and economic benefits at scale [9].

The human element: talent acquisition challenges

One element Mears adds to this discussion is the need for skilled talent within biologics manufacturing. Unlike traditional pharmaceutical manufacturing, biologics production requires specialised expertise with complex living systems, advanced bioprocess techniques, and stringent regulatory compliance, which could spell difficulties for organisations identifying candidates with the right combination of scientific and technical proficiency as well as manufacturing experience with sophisticated operations.

"There have been a lot of moves by companies like Lonza and Samsung Biologics really focusing on biologics and increasing their capacity for manufacturing but with all that complexity comes a need for new skill types and experiences," Mears states. "Those skills aren't readily available right now and so there is a scarcity of skill associated with an increasing demand for talent. While we tend to think of challenges with biologics to relate to technologies and systems, there really is a human element to it, acutely related to the availability of skill and talent that's needed to ensure that biologics manufacturing can be done to the level that is needed." When questioned on what is driving the scarcity of talent in biologics manufacturing, Mears says "One piece of the equation is the demand – there is such increased growth and expansion in the sector that the skill supply simply cannot keep pace in an evolving market. The other piece of the equation is that, in the last couple of years, STEM subjects have become far less interesting to younger demographics coming through education. There's been a real drop off globally in people selecting STEM subjects at school. At the same time, you have an aging population of the workforce retiring, who are not necessarily being replaced by people coming in. The pharmaceutical industry, in my view, has a responsibility to modernise how it presents itself to the world in terms of what an incredible industry it can be to work within, the projects and real-life successes that can be achieved, and the benefit of the work they do for society."

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A Fourth Revolution of bioproduction: Collaborative innovation

A Fourth Revolution of bioproduction: Collaborative innovation

As with any process in the pharmaceutical industry, collaboration can become a key component for success in the development, production, and large-scale commercialisation of a biologic product [9]. Leading CDMOs such as Lonza, Samsung Biologics, and Fujifilm Diosynth have already announced ambitious plans to expand upon existing bioreactors that exceed 10,000 litres, with an estimated investment of US$12.6 billion announced since 2021 [9]. CDMOs thus are pivotal players in large-scale biologics production, with industry analysis from Bioprocess indicating that the share of mammalian cell-based biologics manufacturing capacity provided by external contractors and hybrid manufacturing

partners have risen from 27% in 2002 to 33% in 2022, with projections estimating 44% of capacity to be provided by third-party collaborators [9].

"Biopharmaceutical services innovation is advancing rapidly, with emerging technologies such as ADCs, peptide drugs, bispecific antibodies, multi-specific antibodies, and XDCs," Jiao adds. "However, the demand for CDMO service timeliness remains unchanged and ever present. BiBo operates R&D centres in both China and the US, keeping pace with the latest global technological advancements and continuously improving its own technology platforms. Upholding the principle of customer-first, it delivers the fastest response times to serve global clients."

Bridging scientific borders amid geopolitical storms

With ever-changing policies around the globe creating uncertainty around where supply chain risks and challenges are, the pharmaceutical contract organisation sector is uniquely contending with where they sit in the pharmaceutical food chain [13]. While many experts state it is still too volatile to make any definitive decisions on where to manufacture, it is nevertheless on everyone's minds [13].

"In recent years, geopolitical risks have shown a fluctuating upward trend," Jiao says. "The implementation of a series of 'America First' policies by US President Trump, such as the American Priority Investment Policy memorandum and reciprocal tariffs, has exerted sustained pressure on global supply chains, including those for biopharmaceuticals – in the short term. From a long-term perspective, there is no need for excessive concern about the global supply chain for biopharmaceuticals.

Mears adds his own thoughts on the importance of industry collaboration, stating that "I think there are significant geopolitical elements influencing the biologics market, particularly around trade agreements and tariff structures. When engaging with our colleagues in the investment community and advisors to businesses in this sector, we're seeing a definite trend of companies seeking collaborations with partners in more favourably viewed regions as a means to access markets they can't approach directly due to geopolitical dynamics or tariff barriers.

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“Biopharmaceutical services innovation is advancing rapidly, with emerging technologies such as ADCs, peptide drugs, bispecific antibodies, multi-specific antibodies, and XDCs.”

Dr Peng Jiao

Founder and CEO, BiBo Pharma

While this market instability is driving partnerships, I don't necessarily think it's a sustainable long-term approach. Looking at the Asia Pacific region, particularly India, there's undoubtedly huge demand for biologics manufacturing. We've witnessed substantial investment in infrastructure, technology, and regulatory frameworks to support this growth. These opportunities and volume are clearly present in these markets. Beyond partnerships, companies are making strategic decisions about their corporate structure and deliberately diversifying their suppliers and supply chains to balance and mitigate risks while navigating an increasingly complicated global landscape."

As alluded to by Mears, certain regional markets may be seeing an increase in demand for biologics manufacturing in the coming years. "The global biopharmaceutical market continues to exhibit strong growth and is projected to maintain a compound annual growth rate (CAGR) of over 7.5% in the next 5 years," Jiao states. "According to IQVIA forecasts, global biopharmaceutical spending is expected to reach US892 billion by 2028, accounting for approximately 39% of total global drug expenditures. Currently, the primary markets for biopharmaceuticals remain traditionally developed regions such as the US, Europe, and Japan. In the top ten high-income countries, including the US, UK, and Germany, biopharmaceuticals already represent 50% of drug spending, a figure expected to rise to 55% by 2028. In contrast, this proportion stands at only 13% in emerging markets. With the declining prices of biopharmaceuticals

– particularly due to the increasing availability and adoption of biosimilars – emerging markets in the APAC region and South America are poised for rapid expansion, with biopharmaceutical spending expected to rise significantly in the coming years. It is conceivable that if a growing number of biopharmaceuticals can achieve low-cost production, such as US$10 per gram, the vast consumer market of billions in emerging economies could be quickly activated, unlocking even greater growth potential for the biopharmaceutical industry."

In a panel hosted at the Biotechnology Innovation Organization (BIO) International Convention in Boston, held June 16-19, 2025, Bartłomiej Czubek, Director of Business Development at Mabion, emphasised the kinds of partnerships developing in the biopharmaceutical space [14]. On the panel, Czubek stated "What really works is a mix of good planning, strong technology, and open communication with clients. At the same time, building an integrated process from cell line to final product helps save time and avoid delays. Another key point is flexibility. Every project is different, so having modular equipment, skilled teams, and the ability to adjust timelines or batch sizes makes a big difference. It's also very important to build strong relations with trusted suppliers for raw materials and reagents or services that a CDMO doesn't have in-house."

Azevedo summarises with ""In the evolving landscape of biosimilar development, strategic partnerships are the cornerstone of improving global access. The Asia Pacific region - particularly China and India - is emerging as a powerhouse with their manufacturing capabilities and government incentives. Success in this space demands three critical elements: in-region expertise to solve complex problems, robust supply chains ensuring consistent product availability, and external collaboration to overcome unexpected challenges. No single organisation possesses complete expertise across all processes; we must solve complex problems together with our customers, patients, regulatory authorities, and the broader community to successfully navigate the path to market."

Regulating biologics and patient access: the ultimate balancing act

The intersection of patient access and manufacturing economics remains one of the most significant

challenges facing the biologics sector. While these products have revolutionised how we treat diseases previously thought 'incurable' - cancers, autoimmune disorders, and rare diseases – the complex production requirements involving living cell cultures, precise environmental controls, and rigorous testing and analytics add to manufacturing costs that can present huge costs to the final patient. Biologic medicines can go through up to 20x the quality checks as that of small molecule drugs, and their non-interchangeability leads to fewer options for treatment substitutions [15]. This tension between accessibility and economic sustainability has sparked innovation across the biopharmaceutical value chain, from novel manufacturing technologies and biosimilar development to creative pricing models and patient assistance programs. These are all aimed at broadening access without compromising the economic viability that drives continued therapeutic advancement.

"Enhancing accessibility through cost reduction is a shared goal of pharmaceutical companies worldwide," Jiao comments. "Since the advent of biologics, global biologics production has undergone three major waves of evolution. In terms of production equipment, there

have been three leaps in innovation – from hundred-litre reactors to thousand-litre reactors, and now to ten-thousand-litre reactors. In terms of production organisation, the industry has transitioned from primarily in-house production by pharmaceutical companies to a model dominated by CDMOs. In terms of scale, single production sites have also achieved breakthroughs,

expanding from tens of thousands of litres to hundreds of thousands of litres."

"Patient inequality is a real issue – people are unable to access genuinely life-changing therapies simply because of the price point, and that sits uncomfortably for most people," Mears adds. "From my experience in the automotive industry, that sector has genuinely adopted a partnership approach to their suppliers – they wanted to know about our cultural values, our human capital strategies, and they were very involved in the entire partnership. I don't necessarily see that within the pharmaceutical industry yet – but there's a piece to be said around the industry partnering better with their vendors in a reciprocal approach. There's enough margins and costs in this industry that can be shared in a way that benefits the patient. The real focus should be on continuous processing, continuous improvement, and using technology to improve and advance stability and product yields. This in turn drives efficiency and quality, driving better profitability. I also think perhaps rather than profitability just going to shareholders, perhaps that profitability can be used in a way that benefits access to therapies from a patient perspective. There are definitely things that the value chain can do to partner in a slightly different way that will benefit the whole value chain, and in turn ultimately benefit accessibility of these treatments to patients."

"In 2023, BiBo Pharma became the first in the world to deliver a next-generation ultra-large-scale 30,000-litre production platform, with a main bioreactor working volume of 30,000 litres and a total volume exceeding 40,000 litres – this milestone marks the biologics manufacturing industry's entry into a new era," Jiao adds. "Amid the dual challenges of global biologics capacity shortages and the need to reduce production costs, the Fourth Wave of biomanufacturing innovation has arrived. Production facilities are now advancing toward the million-litre scale to further achieve capacity consolidation. BiBo's vision is to 'make medicines accessible, affordable, and high quality for all.' As more products achieve a production cost of US$10 per gram on its 30,000-litre ultra-large-scale platform, the global accessibility of biologics will be further enhanced."

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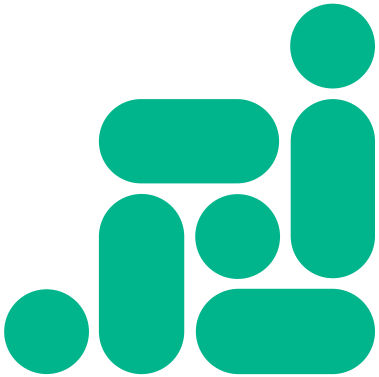
On the precipice of innovation for all: Concluding thoughts

On the precipice of innovation for all: Concluding thoughts

The biologics landscape stands at a pivotal crossroads, with unprecedented opportunities for growth amid significant challenges. As biologics transition from billion-dollar drugs to treatments accessible to billions of patients worldwide, the industry must continue embracing the Fourth Wave of biomanufacturing innovation.

From ultra-large-scale production platforms, AI integration, continuous processing, and reciprocal sponsor-vendor partnerships, these represent a transformative approach to addressing the dual challenges of capacity constraints and production costs, as well as achieving the ultimate goal of patient accessibility to lifesaving treatments.

With biosimilars projected to dominate the market after 2027, pharmaceutical companies must adapt their strategies accordingly. By balancing regulatory requirements with manufacturing economics, leveraging strategic partnerships across geopolitical boundaries, and focusing on patient-centric accessibility, the biologics sector can fulfill its promise of delivering life-changing therapies to patients globally. Ultimately, the industry's success will be measured not just by scientific breakthroughs and profit margins, but by its ability to make these revolutionary treatments truly accessible and affordable for all who need them.



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