SCORPIUS BIOMANUFACTURING

An Experienced CDMO Can Be a Differentiator in the Rapidly Growing Biologics Market

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The demand for biologic drugs continues to grow at a steady 12–14% annually. To keep up, biotech and biopharma developers are increasingly relying on outsourcing partners to meet both clinical and commercial research, development, and production needs. Contract research, development, and manufacturing organizations like Scorpius BioManufacturing (previously Scorpion Biological Services) that provide end-to-end services, including secure supply chains, can help biologics developers meet accelerated timelines and establish a real competitive advantage in today's competitive market.

Continued Strong Growth for the Biologics Market

The biologics market today comprises a wide range of modalities, including proteins, antibodies, antibody-based materials (e.g., antibody–drug conjugates, antibody fragments, multispecific antibodies), hormones, enzymes, peptides, nucleic acids, cell therapies, gene therapies, vaccines, and more. In addition to innovator molecules, the market now also includes biosimilars and biobetters.

Estimated values for the global biologics market vary widely, owing to the inclusion/exclusion of certain product classes in individual calculations. There is general agreement, however, that the market has grown steadily over the last decade and will continue to do so going forward. According to consulting firm BioPlan Associates, the biologics market has grown at a consistent 12–13% annually for the past decade, with even higher rates observed for some segments during the COVID-19 pandemic.[1] Going forward, the company anticipates continued growth at 12–14% per year for therapeutics and bioprocess supplies.

Demand for biologic drugs varies around the world. From a global perspective, small molecule drugs account for approximately 90% of sales.[2] In the United States and other wealthy nations that can afford biotherapeutics, biologics account for greater percentages of the market.

Monoclonal Antibodies Still Predominant

From January 2018 to June 2022, 180 distinct biopharmaceutical drug substances were approved in the United States and/or the European Union. At 97 (53.5%), monoclonal antibodies (mAbs) accounted for the greatest number of those products, by a large margin.[3] In addition, mAbs make up just over half (51%) of the genuinely new biologic drugs that received approval during this period. From a financial perspective, mAbs are even more dominant, accounting for 80% of total protein-based global biopharmaceutical sales in 2021. Total sales of mAb-based products, which included 15 of the top 20 products by sales generated, were valued at $217 billion that year.

All newly approved antibodies are engineered to enhance structural or functional features, including glycoengineering.[3] Next-generation antibodies have also received approvals, including bispecific mAbs, bivalent nanobodies, antibody fragments, and antibody–drug conjugates (ADCs).

With regard to products in development, nearly one-third (2,500+) in clinical trials are mAbs or mAb-derived drug substances, which represents the largest class of candidate compounds.[3] Many of these drug candidates are ADCs, bispecifics, or antibody fragments.

Biosimilars Finally Start Making a Splash

Biosimilars were slow to receive approvals – the U.S. FDA approved the first biosimilar, filgrastim-sndz (Zarxio; Sandoz/Novartis), in 2015 – and then slow to achieve widespread adoption by physicians and patients. That has changed, with biosimilar approvals rising dramatically around the world. In the United States alone, 39 biosimilar products have been approved, with 74% of them reaching the market in the period from January 2018 to September 2022.[3,4] In mid-June 2022, nearly 100 biosimilars intended for marketing in the United States were in clinical development.[3]

According to an Xcenda report, the sales price of reference products has declined on average by 45% since the introduction of biosimilar competitors.[5] Meanwhile, annualized savings from biosimilars reached $6.5 billion in 2020,[4] and IQVIA estimates that physician-administered biosimilars will generate $215 billion in savings through 2026.[6]

Mammalian Cell Culture is Preferred

Most (85%) novel biologic drug substances that have received approval in recent years have been produced via mammalian cell culture.[3] Chinese hamster ovary (CHO) cells remain the top expression system, with 89% of large molecule active pharmaceutical ingredients (APIs) produced in this manner. Fermentation is used when glycosylation is not required and for smaller biologic molecules. *Escherichia coli* was most widely used (for 36 approved products since 2018). Other systems employed for approved products include *Pichia pastoris, Saccharomyces cerevisiae,* and *Pseudomonas fluorescens.*

The growing adoption of single-use technologies at commercial scale further enhances efficiency and productivity, reducing facility costs and size and enabling faster changeovers for reduced overall processing times. It also affords greater flexibility, which is essential for modern multiproduct facilities that must have the capability to rapidly switch between processes and manufacture products over wide volume ranges.

Targeting Greater Efficiency and Productivity

One of the biggest challenges facing the biopharmaceutical industry is the shortage of trained and skilled staff with experience in producing high-quality biologics under GMP conditions.[1] One way to reduce the human resource need is to increase efficiency and productivity. Multiple strategies can be employed to achieve that goal.

Higher titers and yields mean that more material is obtained per batch, and both continue to increase due to process optimization efforts.[1] Increasing yields is but one way in which biologics manufacturers are seeking to achieve process intensification. Continuous bioprocessing is another.

Most biologics manufacturers are also automating some or all of their bioprocess operations, and equipment suppliers are facilitating this trend by building automation solutions into their products.[1] Automation leads to reduced need for operators, reduced risk of human error, and – typically – improved efficiency. McKinsey estimates that by 2030 up to 30% of manufacturing personnel in the biopharma industry could be displaced by automation.[7]

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In addition to implementing automation strategies, many pharma companies have embarked on digital transformation journeys with the goal of increasing efficiency and productivity across all activities, including drug discovery, development, and manufacturing. Artificial intelligence (AI), machine learning (ML), natural language processing, cloud and edge computing, the Internet of Things, and big data analytics are all being leveraged. Some companies are also exploring even newer digital solutions, such as quantum computing, digital twins, and augmented reality.[8]

AI finds the greatest use in drug discovery, with many pharma companies partnering with AI-focused developers to deploy new algorithms that can enable selection and then further development of candidates with the greatest likelihood of exhibiting high efficacy and commercializability. Nearly 270 companies have been identified as pursuing AI-driven drug discovery technologies, with more than half located in the United States.[9] Approximately 15% of them also have their own candidates in preclinical development.

AI has the greatest impact, however, when biopharma companies integrate AI technologies into day-to-day activities – managed by a dedicated team of experts in data science, engineering, software development, epidemiology, discovery sciences, clinical, and design.[9] Specific to biologics development, AI accelerates experimental biology research, dramatically reduces the time required to generate protein structures, facilitates drug repurposing, and aids in the identification of novel mechanisms of action. Computer-aided biology leveraging ML, meanwhile, allows for better design and modeling of biologic systems.[7]

Potential Capacity Concerns

In addition to workforce issues, biopharmaceutical manufacturers continue to face supply chain challenges and concerns about production capacity that can be attributed to the COVID-19 pandemic.[10] Expansion of both R&D and commercial production capacity is underway. This has some worried about an over-capacity crisis once shift in demand in the wake of the pandemic eases. In the meantime, increased outsourcing and reorganization of supply chains, including more second sourcing, can be expected.

The United States has the greatest number of bioprocessing facilities, while Europe, with larger plants, has the greatest capacity.[10] Asia is rapidly adding sites, but with lower capacities. The 100 largest facilities account for approximately two-thirds of global capacity, but the largest sites rely on legacy stainless-steel bioreactors of 10,000 L or more, and few of these facilities are being built today.

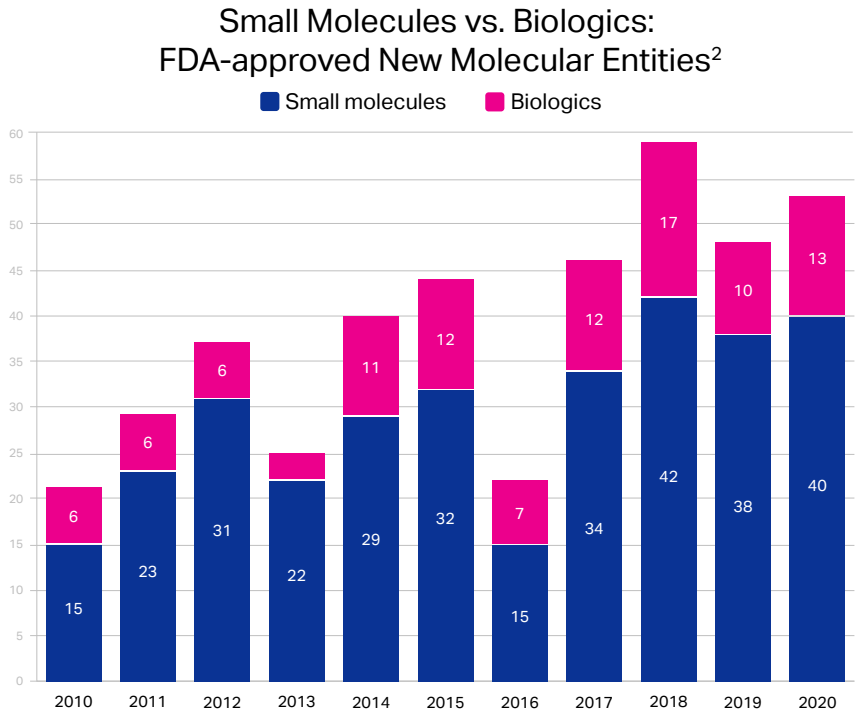
Biologics R&D Outsourcing Market Trends

The COVID-19 pandemic highlighted severe shortcomings within the biopharmaceutical supply chain. Building flexibility and agility has become a key focus for all biopharma companies. Outsourcing has become a bigger part of manufacturing strategies, particularly increased regionalization with greater levels of second sourcing.[7]

The global biologics discovery market is anticipated to expand from a value of approximately $17 billion in 2022 to reach approximately $22.5 billion in 2025.[11] From 2016 through 2025, lead optimization was the largest segment in dollar terms. Demand for lead identification and target identification services was similar, with each about one-third that for lead optimization. Hit generation/validation was the smallest segment of the market.

Combined estimates for the value of the market for biopharmaceutical contract manufacturing and contract research services in 2021 total $28.7 billion, with growth projected at a CAGR of 6.68% and the value reaching $51.36 billion by 2030.[12] A top driver of this growth is the strong pipeline of biology drug candidates for which outsourcing is extensively relied upon. The CRO segment is expected to experience the highest growth rate.

The global biologics contract development and manufacturing market, meanwhile, is expected to expand at a CAGR of 12.20%, adding $8.65 billion of additional revenue from 2021 to 2026.[13] North America will contribute 41%



of that market growth with a growth rate higher than that for the rest of the world.[14] Prioritization of in-country manufacturing by the largest CDMOs is a key reason for the rapid growth in North America, particularly after the COVID-19 pandemic underscored potential vulnerabilities in complex, global supply chains, leading North American biopharma companies to increasingly seek manufacturing partners in the region.[13]

It should be noted that Asia, including India, China, and South Korea, accounts for the largest percentage of the market, and demand for CDMO services is expanding rapidly there as well.[13] South America will also see significant growth in coming years.

With this fast growth, it is anticipated that, by 2025, nearly half of biopharma capacity (small molecule and biologics) will be performed by CDMOs.[13] The largest CDMOs – Samsung Biologics, Lonza, WuXi Biologics, and FUJIFILM Diosynth Biotechnologies – will account for half of that production capacity. Nearly 90% of respondents to a 2022 survey of executives at major biopharmaceutical firms indicated that their companies outsource at least some of their activities.[15]

Biologics Services from Scorpius BioManufacturing

One of the greatest challenges in biologic drug development today is to develop robust processes and analytical methods to support the production of preclinical, clinical, and hopefully commercial material for promising drug candidates. Emerging biotech and biopharma companies in particular, but also many medium and large firms as well, rely on outsourcing partners to develop reliable, efficient, and cost-effective production processes. They also require outsourcing partners that can help identify the necessary assays that must be performed to support early process development through product release and can then develop robust methods that can ultimately be qualified and validated.

Scorpius BioManufacturing (formerly known as Scorpion Biological Services) has a wealth of experience taking large molecule drugs to market. Our leadership team has extensive experience providing R&D, bioanalytics, manufacturing, and regulatory support. Integrated process and analytical development expertise enables the design of robust processes while reducing time to the clinic. We also have the deep know-how needed to overcome the biomanufacturing challenges that inevitably arise as candidates progress through the stages of drug development and marketing approval.

Our new purpose-built facility designed to meet current and future biomanufacturing needs can support clinical programs that involve mammalian cell culture and microbial fermentation with flexible, available capacity and state-of-the-art equipment. Our sourcing team has established extensive material stocks and relationship with suppliers, ensuring a resilient supply chain and the ability to meet aggressive client timelines.

A brand-new commercial-scale facility currently planned in Manhattan, Kansas, will support clinical customers as their projects progress to later stages and ultimately commercialization. The equipment to be installed in the commercial-scale facility will be of the same configuration as the equipment used at the San Antonio clinical site to facilitate effective and efficient scale-up. In addition, the largest process development bioreactors and fermenters used at the San Antonio site will also be installed at the Manhattan facility to streamline tech transfer from one site to the other.

As an accessible U.S.-based contract research, development, and manufacturing organization (CRDMO) offering end-to-end support to biologics developers combined with speed and supply chain security, Scorpius BioManufacturing is ready to welcome clients who wish to work with a customer-oriented outsourcing partner that emphasizes transparency, open communication, and true collaboration. ■

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Michael started his career working in bioprocessing for organizations like Genzyme and Baxter, then worked in business development for platforms supplying critical components of the biomanufacturing processes. For the past 15 years, he has expanded his expertise in the business development space for CRO/CDMO organizations, focusing on helping clients place their biologics programs into commercial manufacturing. He has an extensive understanding of client needs within mammalian cell culture, large scale commercial, and microbial production as well as other areas, supporting programs ranging in size from $1M to $300M. At Scorpius, Michael is focusing the western half of the United States for the CDMO capabilities and the analytical support services for their U.S.-based biomanufacturing.

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