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WHITEPAPER

Strategic CDMO partnerships: Leveraging infrastructure investments and innovation to accelerate biologics development

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Abstract

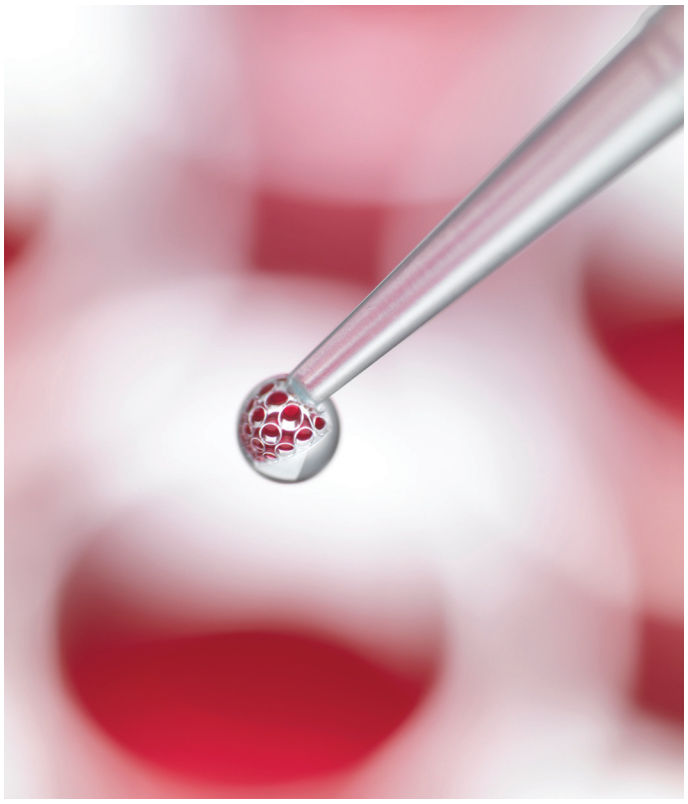
Rising to the challenges of biologics development in this period of disruptive change requires an appreciation for the science, technology, and market forces driving the transformation and a willingness to adopt strategies that align with these changes. For most pharmaceutical and biotech companies, this means identifying trusted partners who can provide access to innovative technologies and methodologies, sufficient manufacturing capacity for growing biologics demand, deep expertise in navigating regulatory channels, and the operational efficiencies needed to accelerate speed to market. This report provides a roadmap for assessing and selecting the right partner to get promising biological therapies to patients quickly.

Executive summary

The R&D pipeline for new drugs has changed dramatically over the past decade. Once dominated by big pharma and small molecules, today's pipeline is increasingly populated with small and emerging companies developing large molecules, or biologics, which now make up nearly 40% of the active R&D pipeline globally.

Big and small pharma companies are increasingly reliant on trusted partners who can provide state-of-the-art technologies, methodologies, and infrastructure to move complex biological molecules from chemistry to commercial-scale production.

In addition to this shift, the growing structural complexity of the molecules in development, the increasing percentage of drugs receiving orphan designation, the competitive pressure to get drugs to market faster, and the rising number of emerging biotech companies retaining control of their drugs into late-phase R&D have heightened the need for specialized technology and expertise to move biologics through clinical and commercial stage manufacturing. To rise to this challenge, drug sponsors are increasingly aligning with trusted partners who can provide access to state-of-the-science technologies and methodologies, sufficient manufacturing capacity for growing biologics demand, deep expertise in navigating regulatory channels, and the operational efficiencies needed to accelerate speed to market.



This white paper provides critical insights for leveraging these strategic partnerships, focusing specifically on the innovations and resources that create value across the drug development continuum, including the following:

- High-throughput screening technologies to speed up cell line and process development
- Integrated programs to expedite discovery-to clinic-timelines
- Strategies for meeting scale-up challenges that can be adapted as necessary to address unpredictable nature of volumetric demand forecasting

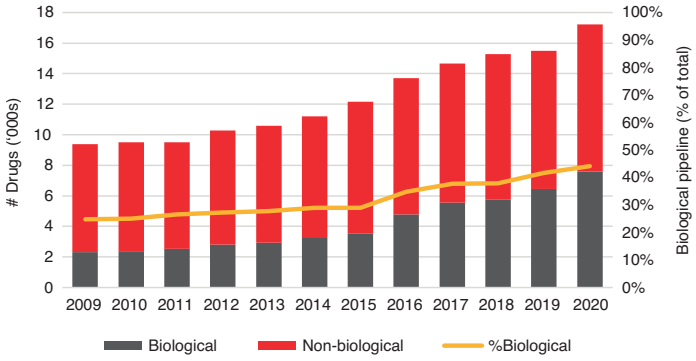
Keeping pace with the market dynamics that are transforming the biologics space requires a laser focus on innovation and access to the integrated resources needed to support it. For most drug sponsors, this access is provided by development and manufacturing partners who have made deep investments in the technologies and infrastructure needed to move molecules from chemistry to commercial-scale production.

Introduction

As one of the fastest growing classes of therapeutic compounds, biologics make up nearly 40% of the active research and development pipeline globally (Figure 1). Over the past decade, growth in biologics has outpaced small-molecule drugs (CAGR 11.4% vs. 2.9%, respectively).

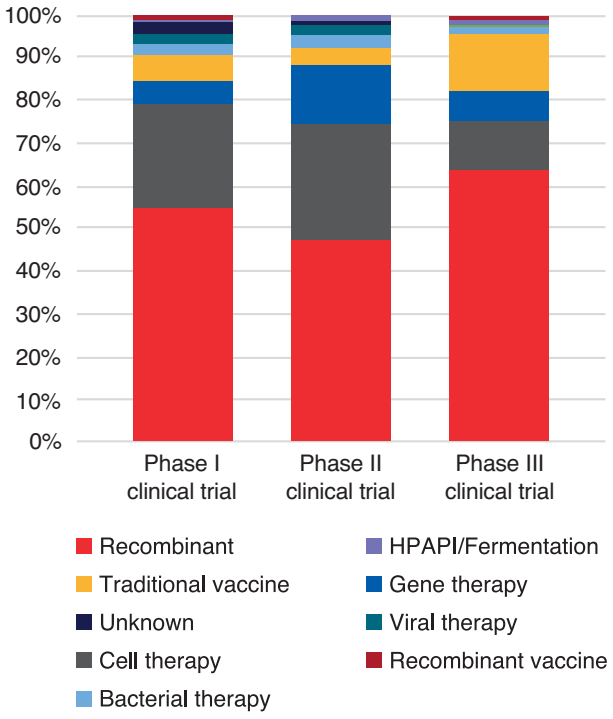
The implications of this growth are far-reaching in that biologics are more complex and difficult to manufacture than small molecules and they cost more to bring to market. This is true for the manufacture of more traditional recombinant proteins and monoclonal antibodies (mAbs), which make up nearly half of the biologics pipeline and have high volumetric requirements, and for highly potent and targeted therapies, including cell and gene therapies, which represent a growing proportion of biologics in development (Figure 2) and require specialized facility design, equipment, operation, and process safety considerations.

Figure 1. Worldwide Active R&D Pipeline, 2009-2020; Biological vs. non-biological drugs*



*Active pipeline is defined as Preclinical, Phase I, Phase II, Phase III, Pre-registration, Launched but still in development for additional markets/diseases. Data as of March of each year, 2009-2012; 2013-2018 figures are from January of each year. 2019 is from month of August. 2020 is from month of December.

Figure 2. Biological development opportunities by product type and phase (2020)



Biologics market growth: Small and emerging companies leading the charge

The growth in the biologics space is being driven largely by small and emerging biopharma and biotech companies. In 2019, these companies patented almost two-thirds of new active substances and registered 47% of them, whereas large pharma companies patented only about 25% of them.[1]

No longer viewed as transactional service providers, CDMOs are an integral part of the pharmaceutical supply chain and their collaboration is foundational to drug sponsors' success.

The competitive dynamics are also being influenced by the fact that more small and emerging companies are holding onto their compounds rather than selling them to big pharma during clinical development.

Because these small and emerging companies often lack the expertise, specialized capabilities, and state-of-the-art manufacturing technologies needed to advance their programs through each stage of development, they rely on CDMOs to fill the gap, in some instances collaborating across the entire project lifecycle, from process and formulation development to regulatory review and approval and commercialization. At the same time, big pharma is looking to CDMOs to fill their clinical and commercial supply needs and to develop cost-effective solutions for manufacturing smaller volumes of highly specialized orphan drugs.

These trends have contributed to a paradigm shift in outsourcing relationships. No longer viewed as transactional service providers, CDMOs are an integral part of the pharmaceutical supply chain and their collaboration is foundational to the drug sponsors' success. For both large and small pharma, the "best" CDMO partner is the one that understands the drug sponsor's commercial strategy and has the resources, expertise, capacity, and agility to see it through to fruition along a guaranteed timeline.

Leveraging CDMO investments in innovation and infrastructure

To compete meaningfully in the race to get novel and life-saving biological therapies to patients quickly and cost effectively, pharmaceutical companies are increasingly building CDMO relationships into their development and production blueprints to provide or augment internal capabilities. In many cases, the future success of their programs rests on the strength and reliability of the outsourced services.

For this reason, biologics sponsors are best served by building relationships with CDMOs that have deep and broad industry reach and consistently make strategic capital investments in innovative technologies, infrastructure, facilities that can accelerate drug development, streamline scale-up, respond to capacity changes, and navigate regulatory and other complexities. This is as true for small and emerging companies without dedicated innovation and manufacturing facilities as it is for large companies seeking to expand their inhouse capacities.

Following is a roundup of some of the technology, infrastructure, and process innovations with the highest potential for moving biologics to market more quickly.

Assisted high-throughput cloning

Selecting high-value clones is essential for optimized cell line development, which in turn is essential for developing high-quality biologics. Traditional cloning methods are hampered by lengthy protocols and low yields, both of which are incompatible with the competitive demands of biologics development. Technologies that automate and expedite cloning, expression, and screening can streamline workflows by an order of magnitude. In particular, instruments based on microfluidic and nanofluidic technologies can screen thousands of clones in parallel to select the best cells. For example, Thermo Fisher has integrated the Berkeley Lights Beacon® platform into its development workflows to shorten cell line development from weeks to days[2]. This method takes a starting population through up to four parallel workflows. The equipment can automatically screen a larger number of clones to identify those that have the potential to be the highest producers and move those into first-in-human (FIH) production as quickly as possible.

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Generating richer product quality data with innovative technologies

The complexity of large molecule drugs introduces analytical challenges throughout the development pipeline. Typically, product characterization, process development, and quality control of therapeutic proteins requires utilizing multiple methods, which is time consuming and costly.

Innovations in analytical workflows can expedite the timeline and improve cost efficiency substantially. For example, Thermo Fisher utilizes a multi-attribute method (MAM) workflow to streamline the identification and quantification of product quality attributes (PQAs).[3] A single analytical method, MAM combines high-resolution, high-mass accuracy mass spectrometric data with automation software and technology to simultaneously detect, identify, quantify, and monitor product quality attributes.

When implemented at the start of new developmental projects, MAM-based PQA identification and monitoring of various sample streams can guide process development, structure-function studies, control strategy and specification setting.

Integrated programs streamline start-to-finish workflows

Pharma companies are increasingly being asked to do more in less time. The pressure to file an investigative new drug (IND) application makes accelerated phase I safety testing a priority. This has been particularly apparent in the race for COVID-19 treatment, but is a common goal of nearly all drug developers today.

Integrating technical, quality, and customer engagement teams has the potential to move a molecule from lab to first-in-human trials up to 25% faster than nonintegrated approaches.

Programs that integrate technical, quality, and customer engagement teams to support drug development and meet accelerated timelines can facilitate getting a molecule from lab to first-in-human (FIH) trials up to 25% faster than nonintegrated programs. Some large pharmaceutical companies have established Centers of Excellence to facilitate this type of collaboration, while small and emerging pharma companies often do not have the breadth of expertise to thoughtfully assess or achieve this level of stakeholder integration across the drug development process. For these organizations, partnering with a CDMO that is able to provide support across the full development lifecycle can be a game changer. A truly integrated program enables more efficient production scheduling, better communications, and supply assurance. These attributes can accelerate the development timeline, streamline the supply chain, and better manage risk.

For example, the Quick to Clinic program from Thermo Fisher is an integrated early development service that can take biological molecules from transfection to IND in as few as 13 months.[4] The program offers a platform process that utilizes a royalty free, scalable high-yield expression system and includes critical activities such as cell line development, process fit, analytical development and qualification. Some of the key capabilities that compress time to phase I clinical trials include high-throughput automation with MAM, concurrent co-qualification of analytical methods, and the use of pre-qualified vials, contact parts. The ability to conduct certain operations in parallel, such as drug substance and drug product work, also accelerates development timelines.

In addition to these technology and production considerations, transparency and communication are critical characteristics of an effective CDMO partnership. The CDMO should set timeline expectations from the outset and consistently communicate issues that may affect the timeline or the ability to reach milestones. This is another area where a single vendor approach adds value. When timeline issues arise, the vendor has an overarching view of all of the connected activities and has more flexibility to make adjustments as needed.

	2020	2021	2022
Steriles	Steriles Development Expansion (Variosys fully robotic line for vials, syringes), Monza, Italy Steriles Commercial Expansion (PFS/ PFC filling line), Greenville, NC	Steriles Commercial Expansion, Ferentino, Italy Steriles Commercial Expansion, Monza, Italy Steriles Commercial Expansion, Greenville, NC Steriles Expansion, Swindon, UK	Steriles Commercial Expansion, Greenville, NC Live Virus Filling (BARDA), Greenville, NC Live Virus Filling, Singapore Steriles Fill/Finish, Hangzhou, China
Biologics	Bioprocessing Collaboration Center, St. Louis, MO Phase II Capacity Expansion Engineering, St. Louis, MO Strategic Partnership with CSL Ltd.	New Process and Analytical Development Facility, St. Louis, MO Phase II Capacity Expansion Construction, St. Louis, MO	Biologics Development & Mfg., Hangzhou, China Large Volume Stainless Steel (SS) Manufacturing, Lengnau, Switzerland
Cell and gene therapy	Viral Vector Services Expanded Capacity, Alachua, FL; Cambridge, MA; Lexington, MA Cell Therapy Facility & Collaboration Center, Princeton, NJ Cryocenter for Cell & Gene-Based Therapies, Weil am Rhein, Germany	Viral Vector Services Capacity, Plainville, MA Seneffe and Gosselies, Belgium Plasmid Manufacturing Capacity Carlsbad, CA; Watertown, MA Commercial Packaging & Distribution Frederick, MD; Weil am Rhein, German	
API	Commercial Spray Drying, Florence, SC		
Solid dose	Continuous Manufacturing, Greenville, NC Early Development Capabilities, Milton Park UK; Bend, OR	Continuous Manufacturing, Greenville, NC	
Clinical trials	Clinical Supply Chain Network Expansion, Rheinfelden, Germany		

Table 1.

Innovations in single-use bioreactor technology: flexibility and scalability reduce costs

The biologics pipeline is growing, as is the need for increased volumetric capacity overall. In 2018, annual volumetric requirements were just over 2,500 kL for all product types produced using mammalian-cell systems. That value is projected to increase to over 4,200 kL by 2023, representing a five-year growth rate of 11%[5].

While there is a large increase in the total number of therapeutics being manufactured, there are new developments that decrease total volumetric requirements per molecule due to higher titers, higher potency and smaller patient populations. There also has been a strong shift in the distribution of manufacturing capabilities required to produce those therapeutics, with a much larger percentage of drugs now being manufactured at volumes less than 5,000 liters. A considerable portion of molecules can even be manufactured at the 2,000-liter scale. Understanding these volume demands clearly impacts the conventional wisdom around single use manufacturing and the capability to achieve commercial volumes at these scales.

Single-use (SU) biotechnology opens new avenues and strategies for biologics manufacturing, enabling a new paradigm particularly for medium-scale volumetric demands and providing resolute support for modern cell culture processes. Having a 5kL SU bioreactor[6] will address most of the molecules' clinical and commercial manufacturing requirements and will enable sponsors to remain entirely on a single-use technology pathway without having to switch over to stainless steel bioreactors for later phase manufacturing needs. Single-use tech-nologies can significantly improve operational efficiency and flexibility while at the same time reducing cost[7]. Innovations and investments in SUB technology are another way that CDMOs can offer increased value in terms of efficiency, flexibility, and cost savings to their partners.

Integrated global networks extend manufacturing capabilities

CDMOs with an integrated global network of development and manufacturing facilities have the advantage of being able to access complex, state-of-the-art manufacturing capabilities in different locations while still providing service locally to drug sponsors, minimizing risks associated with working with multiple vendors in various locations. It also provides more the necessary flexibility to support niche, in-demand capabilities that may not be available through a single site. For example, Thermo Fisher's drug substance manufacturing network comprises multiple sites globally that support drug substance manufacturing, including viral vector manufacturing, and supply chain support from clinical trial distribution to cold chain storage (Table 1).

Conclusion

Choosing the right partner for biologics drug development is a critically important decision for pharmaceutical companies trying to get promising therapies to patients quickly. Identifying a CDMO that has the technological capabilities, manufacturing capacity, and depth of scientific and regulatory knowledge to manage the complexities of large molecule development is a strategic imperative.

To smooth and speed the road to commercialization, small and large pharmaceutical companies should consider the following questions when evaluating CDMO partners.

1. Do they offer a breadth of service from the discovery phase through commercial supply?
2. Have they made the deep investments in infrastructure and technology needed to drive innovation?
3. Do they provide support across all phases of clinical development, including regulatory and logistics?
4. Do they understand the unique needs of each project and the capabilities and capacity needed to meet them?
5. Can they facilitate production continuity from clinical trials to commercial scale?
6. Can they offer supply chain assurance?

An answer of "yes" to all of the below will help get life-changing biotherapeutic drugs to patients more quickly, while also managing risk and reducing developing and manufacturing costs.

Learn more about transformative investments and innovation that are helping to get life changing therapies to patients around the globe.

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About us

Thermo Fisher Scientific provides industry-leading pharma services solutions for drug development, clinical trial logistics and commercial manufacturing to customers through our Patheon brand. With more than 65 locations around the world, we provide integrated, end-to-end capabilities across all phases of development, including API, biologics, viral vectors, cGMP plasmids, cell therapy manufacturing, 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. We offer integrated drug development and clinical services tailored to fit your drug development journey through our Quick to Care™ program. Our Quick to Clinic solution is designed to accelerate the journey from DNA to INA/IMPD and may help biopharma companies reach Phase I/First-in-Human trials and file for Investigational New Drug (IND) review in as little as 13 months from transfection. As a leading pharma services provider, we deliver unrivaled quality, reliability and compliance. Together with our customers, we're rapidly turning pharmaceutical possibilities into realities.

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In this role, he oversees a global Biologics Drug Substance manufacturing and development network. Paul has held multiple leadership roles in process development, technology transfer and operations. In his career, he has developed, transferred or manufactured more than 75 biotherapeutic proteins at various clinical phases, including multiple commercial products. His experience includes business strategy development, operations management, technology transfer, process development, process characterization and process validation.

Prior to joining Thermo Fisher, Paul worked for Bristol Myers Squibb and GE Plastics (now SABIC). Paul holds a B.S. in Chemical Engineering and Management from Purdue University, West Lafayette, IN and a Masters in Chemical Engineering from Cornell University, Ithaca, NY.

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