Increasingly Vertically Integrated CDMOs: The Right Business Model For The Current Pharma Landscape

QUADRIGA PARTNERS

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Preface

Transformation in the healthcare industry is everywhere, driven by regulatory changes, healthcare reforms, technological advances, new entrants from outside the industry, and changing consumer expectations. The old ways of doing anything, such as R&D, clinical trials, and drug manufacturing, are no longer in effect, and companies must adjust to the new reality. It's an inevitable evolutionary process, and healthcare companies face a choice: transform to be part of the future or risk being left behind. The pharmaceutical services industry is no outlier in experiencing a fair amount of that transformation. In recent years, organizations across the value chain, from drug development to drug manufacturing and distribution, have had to adapt to a rapidly changing environment, with many being forced to reevaluate their business model and, more importantly, create a greater reliance on outsourcing services to help support their needs.

Pharmaceutical companies have long recognized the benefits of outsourcing certain operations, such as manufacturing, to contract and manufacturing organizations (CMOs). However, a new trend has emerged in which companies are shifting from the traditional CMO model to the contract development and manufacturing organization (CDMO) model. This shift is driven by the desire to create a one-stop-shop solution that covers all areas of the pharmaceutical business, from drug discovery to manufacturing and distribution, emphasizing the importance of CDMOs.

About Quadriga Partners

Quadriga Partners is a premier healthcare investment bank, providing merger and acquisition advisory and growth and debt capital raising services exclusively for healthcare companies. Quadriga has a particular emphasis on several key sectors, including outsourced pharmaceutical services, and is among the most active advisors for clinical research focused transactions. Quadriga begins by obtaining an intimate understanding of their client's short and long-term objectives.

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The shift towards CDMOs is also driven by the changing landscape of the pharmaceutical industry. With the development of personalized medicine and increasing demand for biologics solutions, companies are recognizing the importance of working with experienced CDMOs who have the complex manufacturing capabilities and regulatory expertise necessary to support these new therapeutics. The emergence of biopharma companies and the impact of COVID-19 has also increased the demand for CDMOs, as companies look for partners that can help them navigate the rapidly changing industry landscape.

A CDMO is a contract development and manufacturing organization that assists the pharma industry by providing various services, from drug development to manufacturing, covering a significant portion of the drug's development life cycle. It is a viable alternative to the in-house development and manufacturing of pharmaceutical products. These services enable pharma companies to reduce their R&D costs, shorten development and production timelines, and control capital investments while benefitting from the most advanced technologies. As a third-party provider, they can work with multiple clients (pharma and biopharma), allowing them to gain valuable knowledge and expertise to become an even more essential part of the system. As such, CDMOs usually hold the experience and knowledge needed to offer their clients a significant level of confidence. The same expertise is translated into their ability to offer services only they could.

Benefits of Working With a CDMO

Initial Risks and Costs – bringing a new drug to market always comes with huge risks. Oftentimes, companies need to invest in specialized infrastructure, equipment and recruit the right personnel upfront, all while having no guarantees that the drug will gain approval. CDMOs can mitigate that risk by owning the specialized equipment with the manufacturing space needed and employing the experienced staff required to perform complex manufacturing operations.

Time-to-Market – getting a new drug from the clinical trial stage through manufacturing is a long and risky journey. Sudden changes to production volume, requests for products that don't exist yet, adding new, sometimes untraditional, modifications, and jobs that fade out during a clinical trial or take off and become

Figure 1

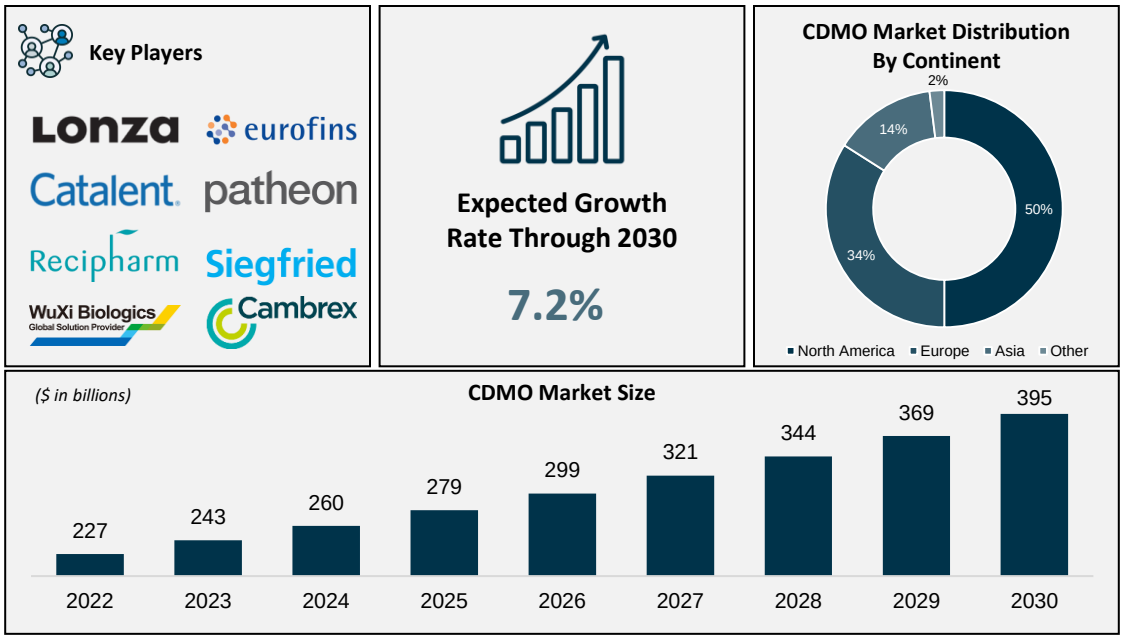


Figure 2

Opportunities and Risks in The Current CDMO Market

Opportunities	Risks
• Increasing pharma outsourcing • Technological advancement • Higher profitability in a more consolidated market • Favorable growth projections • Increased capital spending • Growth in segments such as precision medicine, gene therapy, and novel delivery modalities	• Lack of skilled labor • Increase in the number of drugs of low volume and higher complexity • Increasing regulatory hurdles • Price and cost pressure • Entry of new small players into the market • Restrictions of global imports and exports

blockbusters, are all common issues that a CDMO experiences. CDMOs have to be innovative and creative enough to meet that challenge. They have the operational flexibility to modify production without compromising on quality and efficiency yet meet cost goals. Although the challenges are many, having an end-to-end operation allows the 'lock-in' of supply contracts at an early stage in the product life cycle, making it a progressively more important part of the commercial strategy of many CDMOs.

Compliance and Regulatory Requirements – developing strong compliance practices and staying up to date with the ever-changing regulation takes significant resources and are time-consuming. It is also expensive if a process goes wrong and needs to restart. Partnering with a CDMO provides a logical strategic option, allowing companies to bypass the costly investment of having an in-house compliance team and can mean the difference between being first to market and being late with expensive consequences. CDMOs have regulatory experts and adequate facilities to meet stringent regulatory requirements.

Supply Chain Risks – at the onset of the pandemic, manufacturers were immediately hit as supply chain issues started to arise, with key suppliers, especially those from Asia, unable to produce and ship for months. CDMOs were quick to adjust their operations as they are used to dealing with a level of unpredictability, adapting their business practice to operate with constant uncertainty emanating from their operations, relationships with sponsors, or the general market, both in good and bad economic environments. CDMOs continuously assess supply scenarios, comparing them with market demands to understand how various events could impact their network. This assessment helps in the understanding of potential manufacturing capacity/delivery issues and how to be proactive in resolving those issues.

Pharma and biopharma companies prefer end-to-end service providers for offering a multitude of services to customers, who benefit from the convenience, time savings, and cost efficiency of dealing with a single provider. They also provide ease of manufacturing, shorter timelines, and reduced supply chain risks. Thereby, CDMOs have quickly adapted to the new market dynamics of demanding end-to-end providers by embracing the one-stop-shop model of bringing new drugs from the pre-clinical stage to post-manufacturing. However, as many have discovered, finding a well-rounded service provider can be challenging, with some providers being excellent in one area but lacking in others.

CDMO Market Overview: Key Drivers, Trends and Challenges

The CDMO industry has seen many trends in recent years caused by fundamental changes in market dynamics, forcing manufacturing organizations to modify their business model quickly. The pandemic, in turn, has accelerated many of those changes and pushed CDMOs out of their comfort zone.

Greater Focus on Targeted Therapies – Historically, the pharma industry was primarily focused on traditional drugs, producing small-molecule, chemically based drug solutions for the "average patient." It was developed to treat common conditions with a one size fits all approach to reach the largest patient population possible. Often aiming for a blockbuster drug, they focused on the philosophy of "one drug for all," trying to be profitable by maximizing volume and economies of scale. The pharma services industry, led by CMOs (before their expansion to becoming CDMOs), followed suit by adapting operations across traditional drug development, production, and distribution.

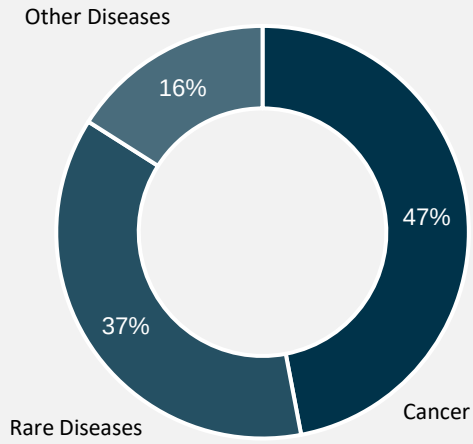
However, over the last decade, the industry has experienced a significant shift from the "one drug for all" to individualized, precision medicine (otherwise called personalized medicine), with more than 25% of FDA approvals going there in the last seven years. Those are treatments tailored to the specific characteristics of individuals, including genetic makeup, environment, and lifestyle, to target "the right treatments to the right patients at the right time."

Leveraging their vast experience and operational know-how, CDMOs are at the forefront of leading that shift within the pharma services industry. By making operational adjustments, CDMOs can expand their solutions to meet the new customized needs of precision medicine. The biggest challenge they are facing, since it's targeted to a small segment of the population, is the level of return on investment achievable compared to other drugs, which undermines pharma's ability to recoup its R&D investments and even make a profit.

Change in Customer Profile – As the CDMO industry evolves, a change in their customer profile has been taking place, causing a slow shift in the type of products requested. Over a decade ago, pharmaceutical companies began shifting their focus back to the core business of R&D while simultaneously increasing the outsourcing of all other elements in the supply chain, including drug development and manufacturing, to third-party providers, offering CDMOs with significant growth opportunities. In addition, the emergence and rapid expansion of the biopharma industry, which focuses on the R&D side of the business and rarely has the in-house manufacturing capabilities and technical know-how, and as the cost of building these is expensive and limiting for a company with little to no revenue stream, allowed CDMOs to develop new streams of revenue and new service capabilities at all stages, from drug discovery to commercialization.

Figure 3

Approved Personalized Medicines by Type



CDMOs understand that the drive to outsource is different in all parts of the pharmaceutical industry. Biopharma companies, for example, often rely more on CDMO services as they move products through the pipeline. Additionally, CDMOs now play an integral role in the biopharma overall business strategy and are essential to the future of their manufacturing. They are positioned to supplement deficiencies, enhance R&D efforts, streamline processes, produce high-quality data, organize and simplify regulatory compliance, and build global partnerships. They have proven to be increasingly successful and necessary to meet the demand for new therapies. Alongside adding R&D and manufacturing abilities, outsourcing those services provides biopharma with the technological know-how, including machine learning, AI, and digitization offered by CDMOs, to accelerate established processes and produce better results.

Figure 4

($ in billions)

Personalized Medicines as Percentage of total FDA Therapeutic Products Approved

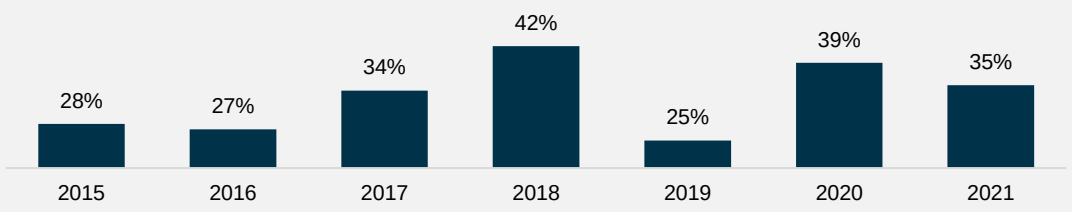
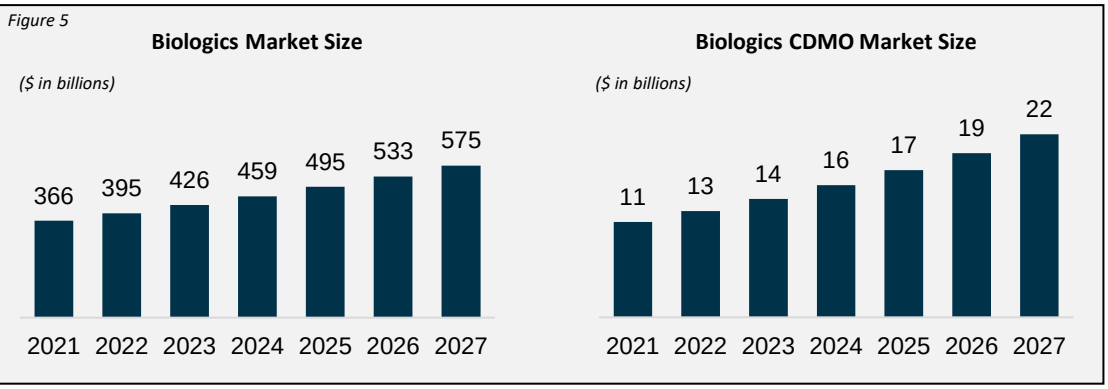


Figure 5



It has become vital for CDMOs to invest in their technological abilities and data-driven manufacturing, using advanced technology such as sensors, robotics, and automation to increase supply chain productivity, enhance the quality of drugs, and compete effectively.

In 2022, the White House unveiled a $2B initiative for the growth of the U.S. biotechnology and biomanufacturing sectors named "National Biotechnology and Biomanufacturing Initiative." The initiative will drive advances in biomanufacturing that substitute fragile supply chains abroad with strong supply chains at home, anchored by well-paying jobs in communities across the US.

The Biologics Boom – Pharma companies were historically focused on small molecules that drove their top-line revenue for decades. However, with the rate of innovation slowing in that space, companies have shifted their focus to large molecules, or biologics, and the biopharma and biotech industry has grown as a result. Biologics treatments are therapies made using living, biological materials to treat disease. Biologics has been the fastest-growing market segment in the pharmaceutical industry, with a market size of approximately $366 billion in 2021 and expected to reach $720 billion in 2030, producing a 7.8% CAGR. This trend has been driven by pharmaceutical and biopharmaceutical companies for years.

Although they've achieved incredible levels of growth, biologics still pose a different challenge to small molecules, as they are much more technologically complex, and have a lot less price sensitivity. These companies face significant hurdles in bringing their breakthroughs to market. As developing and manufacturing biologics is a complex task, many companies don't have the resources to do that, making handling the process in-house unfeasible for many but the largest pharmaceutical companies. This is where biologics CDMOs come into play, offering services such as formulation, dosage, stability, R&D, and manufacturing.

With approximately $11.3 billion in 2021, the biologics CDMO market size is expected to reach $21.7 billion in 2027, producing an 11.5% CAGR.

Although the sub-sector is growing strongly, and the focus on biologics manufacturing is higher than ever, both from capital investment and M&A strategy, biologics will remain a relatively minor part of the CDMO sector, with small molecule delivering most of the absolute growth over the next five years, representing over 50% of the commercial CDMO market.

Figure 6

New Drug Approvals by The FDA (2020-2022)

Molecule	2020	2021	2022
Small Molecule	40	36	22
% of Total Approvals	75.5%	72.0%	59.5%
Biologics	13	14	15
% of Total Approvals	24.5%	28.0%	40.5%
Total Approved Drugs	53	50	37

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Expanded Services – Moving Up and Down The Value Chain - In response to increasing demand from sponsors for R&D and the need to manufacture new types of drugs, a gradual shift in the pharma services has been underway, highlighting the need for operational integration between manufacturing and clinical trials. CDMOs, in turn, have been forced to seek ways of expanding their operations and product offering up and down the value chain. This has led to the shift from the traditional CMOs to the more inclusive CDMOs, covering all areas of the pharma business, starting from drug discovery to manufacturing and distribution, with the purpose of locking in drug partnerships at the early-stage clinical level. We've seen an increasing number of companies now expanding their service capabilities to include preclinical discovery, development, manufacturing, testing, and clinical and regulatory support. Hence, creating a lucrative, vertically integrated, one-stop-shop model. That model is particularly attractive for small to medium size biopharma companies with limited manufacturing capabilities, as a single outsourcing CDMO will take care of much of their development and scale-up work, reducing pipeline risk and increasing operating flexibility.

Using M&A to Broaden Product Offerings – Private equity firms are aggressively targeting the CDMO industry, seeing these particular pharmaceutical outsourcing companies as a prime opportunity to deploy their capital and reap substantial returns. They are drawn to the industry due to the robust market conditions, high-profit margins, and tremendous growth potential. Additionally, they perceive CDMOs as relatively recession-proof, making them an attractive long-term investment. The goals of private equity firms in this space can range from achieving larger scale through acquisitions, honing in on specific areas of expertise, or gaining a technological edge over competitors. They are not shying away from this opportunity and are actively seeking to acquire and grow these companies, with the ultimate goal of exiting with substantial returns.

Concluding Remarks – CDMOs are cost efficient outsourcing providers that offer a range of services to the pharmaceutical and biopharmaceutical industries. They provide access to manufacturing capabilities and technologies, allowing customers to reduce supply chain costs, provide end-to-end services and offer compliance and regulatory services. CDMOs help companies manage industry challenges such as increasing pricing pressures, manufacturing capacity, technological capabilities, regulatory changes, and development hurdles. **In short, they help reduce the reliance on fixed costs, allowing customers to focus on core competencies while outsourcing non-core activities.**

Our observations suggest that the CDMO industry is expected to continue to perform strongly, with high single-digit growth

Our observations suggest that the CDMO industry is expected to continue to perform strongly, with high single-digit growth based on solid underlying market fundamentals. The market's biologics and gene therapy sub-sectors are predicted to perform particularly well, driven by increased innovation and capital investment.

To respond to the evolving market changes and capitalize on growth opportunities, CDMOs are increasingly investing in capital projects to drive organic growth and M&A to accelerate expansion. The strategic direction of many CDMOs is to acquire differentiated capabilities to generate additional value and eventually achieve the desired one-stop-shop model. With a highly constructive M&A environment, growing capital investment, and ongoing innovation, our outlook for the CDMO sector is very bullish. In our conversation with private equity groups, continued investment in CDMOs is a recurring theme leading to more acquisitions as the outlook for the sector continues to be bright.

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Select CDMO Transactions

(in millions)

Target	Buyer	Price	Date	Target Description
aldevron	DANAHER	9,600	Jun-21	Developer of biological products, including plasmid DNA, nucleic acids, proteins, antibodies, and other related products used in the field of cell and gene therapy
Cognate BioServices, Inc.	charles river	875	Feb-21	Provider of cell and gene therapy CDMO services
Pierre Fabre	FAREVA	NA	July-20	A portfolio of pharma manufacturing units based in France. The portfolio consists of **2 pharma manufacturing units** that manufacture injectable drugs, mainly in oncology
Piramal Pharma Solutions	The Carlyle Group – Global Alternative Asset Management	2,450*	Jun-20	Provider of CDMO services, selling generic drugs and formulation. **A Piramal Enterprises subsidiary**
DALTON Pharma Services	SEIKAGAKU CORPORATION	30	Feb-20	Provider of CDMO services, formulation & drugs development, and analytical testing
ALLIANCE CONTRACT PHARMA	Audax Group	NA	Feb-20	Provider of contract manufacturing of liquid and powder filled capsules
MaSTherCell – Manufacturing Synergies for Therapeutic Cells	Catalent	315	Feb-20	Operator of CDMO intended to deliver optimized process industrialization capacities to cell therapy organizations
Kindeva DRUG DELIVERY	ALTARIS	650	Dec-19	Provider of formulation and product development and commercial manufacturing. Expert in developing inhalation, transdermal and microneedle drug delivery technologies. **A 3M Company**
Consort Medical	Recipharm	650	Nov-19	Leading manufacturers in the field of drug delivery devices, along with APIs and finished dose formulations
Cambrex	PERMIRA	2,319	Aug-19	Provider of drug substance, drug product and analytical services intended to serve the pharma industry
PARAGON BIOSERVICES	Catalent	1,192	Apr-19	Operator of CDMO services focusing on the development and manufacturing of biopharmaceuticals, providing research services, process development, and cGMP

* 20% Minority Investment

Select CDMO Transactions

(in millions)

Target	Buyer	Price	Date	Target Description
Biogen	FUJIFILM Diosynth biotechnologies	890	Mar-19	Manufacturer of biotechnology products for the treatment of diseases with a focus on neurological disorders. **Target acquired: manufacturing facility in Denmark**
brammer bio	ThermoFisher SCIENTIFIC	1,670	Mar-19	Manufacturer of viral vectors for in vivo gene therapy and ex vivo gene-modified cell therapy. Provider of clinical and commercial development
AVISTA PHARMA	Cambrex	252	Nov-18	Provider of CDMO services and testing services of newly created medicinal drugs. Also provides early-stage discovery, API and cGMP
HALO PHARMA	Cambrex	425	Jul-18	Provider of CDMO services offering fully integrated capabilities in a variety of dosage forms, including tablets, capsules, powders, liquids, creams, sterile and nonsterile ointments
AMPAC FINE CHEMICALS	SK holdings	455	Jul-18	Operates as a custom manufacturer of APIs and registered intermediates for the pharmaceutical industry
COOK MEDICAL	Catalent	950	Sep-17	Offering drug substance manufacturing, process development, clinical/commercial cGMP mammalian cell culture manufacturing, and formulation development
Amatsigroup	eurofins	150	Aug-17	Provider of preclinical and clinical phase services for the development of human and veterinary drugs
amri Complex Science. Expert Solutions.	GTCR / The Carlyle Group GLOBAL ALTERNATIVE ASSET MANAGEMENT	1,913	Jun-17	Provider of drug discovery solutions, drug development solutions, analytical services and manufacturing solutions to pharmaceutical and biotechnology industries
Patheon	ThermoFisher SCIENTIFIC	7,200	May-17	Operator of CDMO spanning the life cycle of a pharma molecule from early development through commercial manufacturing
Capsugel	Lonza	5,461	Dec-16	Developer and manufacturer of drug delivery systems
UNITHER PHARMACEUTICALS	IK Partners / GIC / KEENSIGHT CAPITAL / ARDIAN / parquest	717	Nov-16	Provider of sterile unit doses, non-sterile liquids and solid and semi-solid medications