Placing drug strategies on a solid foundation for success

A review of the market dynamics and drug development trends driving strategic outsourcing decisions

Pfizer CentreOne

Demand for drugs and therapeutics of all kinds is growing with the globalization of pharmaceutical-based medicine. Manufacturing safe, effective and affordable medications and putting them into the hands of patients has always been the pharmaceutical industry's main objective. That hasn't changed; what has changed is how the industry is fulfilling its core mission.

According to the FDA, more than half of all the novel drugs approved in the last decade came from companies with fewer than 500 employees.[1] In addition, as pharma's focus on smaller patient groups continues to grow, so does the complexity and risk of developing effective drugs to treat them.

Getting new, more effective drugs to market faster, more economically and safely is prompting innovative development strategies and business models to support successful outcomes – for investors and patients.

To commercialize drugs efficiently, outsourcing has become an increasingly attractive business model for pharma, especially for small and medium companies. The demand for partners able to deliver comprehensive end- to-end drug substance and drug product development prompted contract manufacturing organizations (CMOs) to consolidate and expand, creating the more comprehensive contract development and manufacturing organization (CDMO). The CDMO model provides pharma with more sustainable, efficient commercialization paths and end-to-end integrated development, commercialization and manufacturing services.

In this white paper, we look at the broad set of trends influencing pharmaceutical development and manufacturing strategy today, and how these drivers are impacting traditional drug development strategies and relationships with outsourced drug development and manufacturing partners. From the extreme costs associated with biopharmaceutical drug development, to the push and pull of novel therapies in the pipeline, this whitepaper takes a close look at how the pharma industry can better leverage CDMO partners facilitate success from the start.

Offering distinct competitive advantages, this paper also seeks to highlight the inherent strategic value that comes with engaging high-performance commercial partners built on a foundation of experience and integrated capabilities that can assure programs will be successful from the very start.

Trends influencing pharmaceutical development and manufacturing strategy

Pipelines are filled with hard-to-make drugs. Within the legacy of pharmaceutical development, a deeper understanding of all the physical sciences has brought tremendous advancement. Innovation is coming from new areas of pharma, and primarily from small-to-mid size pharma companies and start-up biopharma drug developers with promising "investment grade" molecules.

Tufts CSDD attributed the acceleration of costs and lengthening development timelines to several factors stemming from both large and small molecule development, as researchers seek even more novel, effective and high performing therapeutics to treat and cure disease.[2]

Demand for drugs containing high-potency active pharmaceutical ingredients (APIs) and their potential to bring investors returns extends tremendous pull on the pharma supply chain and fuels the need to strategically outsource to specialist partners.

Currently, the high-potency API (HP API) market is experiencing significant growth driven by demand for compounds to treat cancer, organ rejection and conditions treated with hormone products. In 2017 this market segment was valued at $16 billion and is predicted to grow to $27 billion by 2023.[3]

This sector of pharma has tremendous energy and paired with specialized regulatory pathways for orphan drug and cures-based therapies, the drug pipeline continues to fill with therapeutics that rely on hard-to-make, hard-to-handle APIs.

First in class therapy nearing $3 billion

For everyone along the drug development and manufacturing continuum, taking a compound from lab to patient has become an incredibly complex and expensive journey. The costs associated with bringing novel therapeutics to market are well known and a primary driver of recent drug development and manufacturing trends.

Financing new drug development to the tune of billions is just one of the many challenges drug owners face bringing the potential of their intellectual property, science and innovation to market.

Tufts Center for the Study of Drug Development (CSDD) continues to study the cost of drug development. Its 2014 landmark study on drug development costs found developing a new prescription medicine and seeing it to market approval has become a 10-year, $2.6 billion effort.[2]

Roughly split between average out-of-pocket costs and time costs, Tufts explains that adding in the projected $312 million in post-approval R&D costs pushes this figure closer to $2.8 billion. Tufts also notes that since its 2003 cost study, the price of developing and marketing a new drug over the past 15 years has risen 145 percent at an 8.5 percent compound annual growth rate.

Oral solid dose forms will continue to dominate development

Contributing to the dynamics of drug development is the increasingly global nature of pharmaceutical-based healthcare and the commoditization of all drugs, especially oral solid dose (OSD) forms. The availability of generics and the rising consumption of over-the-counter (OTC) medications continue to drive this trend.

Regardless of how strong biopharma drug development is fuelling growth, the industry's pipeline remains dominated by small molecule API OSD forms. According to FDA statistics, in 2017, just under half of all approved new drug applications (NDAs) were for traditional OSD tablet forms. In 2018, 58 percent of the industry's drug approval pipeline was filled by small molecule formulations.[4]

Asia's ascending pharmaceutical demand

Although people around the world are consuming more drugs, North America and Western Europe still account for half of the global pharmaceuticals market.[5] That said, Asia-Pacific has overtaken Western Europe as the second largest region – led by a strong Japanese market and booming Indian and Chinese markets.[6] The latter market is now the second largest national market in the world behind the US.

Growth in the Asia-Pacific region is largely fuelled by the increased affordability of drugs resulting from the rise of low-priced generics. Physicians and caregivers of all kinds are dispensing the products of pharmaceutical science to more patients with increasing efficiency.

Due to a rise in per-capita GDP, growing government programs to support healthcare, rapid urbanization and other social and political forces shaping society, more people are gaining better access to all types of medications and therapeutic agents. Somebody has to meet this demand.

Drug developers must understand the regulatory and economic dynamics playing out across global and regional markets and must be aware of what's pushing and pulling the industry. This is true when planning to access new or emerging markets around the world, or if a go-to-market strategy is focused entirely on developing a product solely for North America or Europe.

The challenge is to relate current market dynamics and drivers to business and product plans – and use the insights and data effectively to guide critical business decision making.

Biopharmaceuticals driving patient benefit and development complexity

Any discussion of drug development trends, and their impact on manufacturing and strategic outsourcing can't be concluded without mentioning the impact of advancing biopharmaceutical science.

The biologics segment in particular is strongly represented by innovative start-ups and smaller companies with big intellectual capital. These enterprises tend to be entrepreneurial and are generally more intent on successfully meeting early development phases and reaching milestones that keep investors engaged.

Commercial-scale manufacturing is evolving rapidly to meet the growth and advancement of large molecule biopharmaceuticals. Managing the manufacturing scale of these compounds is challenging. Many biologic APIs are effective at very small doses and don't require the volumes or batch sizes of many popular small molecule compounds.

The same could be said for the rise of small molecule inhibitors and antibody-drug conjugates (ADCs) that are creating more targeted approaches to cancer therapy. Production economies are less reliant on scale and more predicated on mastering the complexities involved in processing, aligning optimal chemistries and uncovering upstream and downstream efficiencies of the potential commercial process.

Strategic outsourcing: Becoming the rule rather than the exception

According to Result Healthcare's "Pharma & Biotech 2017 – Review of Outsourced Manufacturing," in light of burgeoning demand for APIs, CDMOs face the real challenge of capturing more value from drug product supply chains. "Overall, the level of outsourcing is 24.6 percent at present, and this is expected to grow," the report states. They predict outsourcing will rise to just over 26 percent by 2021.[6]

Similarly, a 2018 report by analyst firm Visiongain forecasts the overall pharmaceutical contract manufacturing market is growing fast, achieving revenues of $84.0 billion by 2020 at a compound annual growth rate of 6.4 percent from 2015. The market, says Visiongain analysts, is expected to continue to grow from 2016 to 2026 as more pharmaceutical companies strategically outsource manufacturing services.[7]

Pharma's developers are shifting the capital they might normally invest in manufacturing capabilities to better serve their early drug development strategies. This financial strategy shifts both risk and money to the operations side of the ledger in the hope of acquiring access to the expertise required to navigate products from development through to commercial manufacture more efficiently and cost effectively.

Whether regulatory, cultural or financial, most of pharma's emerging and established companies are addressing development risk by focusing on core science and R&D strengths, while collaborating more comprehensively and intelligently with strategic CDMO partners.

More choice, less value?

As the world's regulators focus on drug safety from a manufacturing quality basis, it is increasingly apparent successfully bringing hard-to-make, complex or innovative drugs to market requires a sophisticated and dedicated approach with strong partners.

Most in the industry agree in the future, pharma will engage in more contract services to develop and manufacture their products – not less. But rising demand for these services makes choosing the best partners to achieve successful drug product strategies even more difficult. Why?

For one, as it stands, there are thought to be around 300 pharmaceutical CDMOs supporting the pharmaceutical industry. Despite increasing M&A activity, the market remains highly fragmented. The top five CDMOs collectively account for just 15 percent of the market.[8]

Competition among providers is fierce, and many differentiate themselves by offering particular strengths and capabilities in high demand. Other business drivers, including life-cycle management strategies and the rise of developers leveraging FDA New Drug Application (NDA) 505(b)(2) drug development pathways, are parsing demand among contract suppliers as well, with contractors trying to select the best fit for a CDMO to develop their drug's market or therapeutic value.

However, even though hundreds of contract services providers exist, specific needs for capacity, scale, formulation processing and availability can severely limit the number of CDMOs a developer can choose from.

Stand-alone, end-to-end CDMOs: the "Mega" model expands

The emergence of comprehensive full-service 'Mega' CDMOs offering themselves as end-to-end strategic commercial collaborators are clearly an indicator of how the industry is evolving as well as the desire for long-term partners to manage the full drug development strategy, and reduce go-to-market timelines.

Today, several full-service CDMOs are offering developers the value and risk avoidance they seek, providing secure supply chains, access to scalable, flexible processing and global capacity responsive to demand.

Category champions

End-to-end CDMOs have become a popular business model, but there is evidence the market's outsourcing strategy is shifting to engaging one-stop category champions, that is, contract partners with specific experience developing a particular molecule or drug substance capable of refining these formulations into patient-ready doses. According to an Op-Ed by the editor of Outsourced Pharma, the one-stop model can be faster to market compared to outsourcing to multiple service providers; but the organization still has to manage all the pieces.

Transfers and project transitions can potentially be more seamless he wrote, "but experience says can be doesn't equate to will be." CDMOs, he explains, "are getting better at internal hand off, but they are still hand offs, and not nearly as seamless, coordinated, or systematic as advertised." [10]

Possessing particular technical capabilities to meet market demand has become another driver of CDMO consolidation and acquisition as opposed to acquiring assets for scale. Visiongain points out that market-leading CMOs have grown through acquisitions and site expansions to offer almost all required services on a global scale. However, despite the rise of monolithic CDMOs, Visiongain notes there is still a role to be played by CMOs that can offer specialized capabilities – "particularly those that offer biological drug manufacturing services." [11]

"Experience," explained Outsourced Pharma's editor, "has taught, the best outsourcing outcomes are when drug sponsors meticulously match the technological requirements of the project to specific expertise at specific CDMOs and have an active project management role." [12]

CDMOs and the value of institutionalized excellence

Although engaging CDMOs for drug manufacturing is a proven route for program success, it may not be clear to developers what differentiates one CDMO from another relative to their strategic long-term value as an external partner. Call it Institutionalized excellence characterized by an unbroken legacy of continuous foundational improvement and operational innovation.

A CDMO offers drug developers an inherent value proposition: access to the same people, science, facilities, technical innovation and experience that contribute to the success of the overarching organization.

Institutional experience, fundamental foresight

The institutionalized drug development and commercialization experience of Pfizer Inc. and its people facilitates the foundational foresight Pfizer CentreOne leverages to effectively anticipate the hurdles a compound or product might encounter during scale-up, transfer or commercial manufacturing. For example, if a CDMOs experience includes lessons learned scaling hard-to-make steroids, it's possible they can apply this same experience to optimize a sponsor's long-term drug product strategy too.

With access to global manufacturing expertise, world-leading operational excellence, and contemporary, compliant facilities, foundational CDMOs with efficient, institutionalized approaches are likely much more efficient at implementing effective technology transfers and developing more efficient chemistries at commercial scale.

Many CDMOs strive to offer a full suite of services, from development through to commercial manufacture, to simplify and de-risk the supply chain for their customers. To provide this comprehensive service successfully, CDMOs with foundational institutionalized operations will understand what it takes to go from the lab to clinical scale supply to large commercial production. Any CDMO worth partnering with must have expert knowledge of API synthesis chemistries, excipients, primary and secondary packaging, as well as equipment and operating procedures needed to optimize tech transfers and scale-up routines.

Regulatory experience and a quality organization to match it

Businesses operating in heavily regulated industries, especially pharmaceuticals, should be adept at meeting regulators' expectations. CDMO partners able to demonstrate the ability to efficiently manage compliance in support of drug strategies in prospective new, or international markets will offer a firm foundation for competitive advantage and agility to most drug development strategies.

By possessing a deeper understanding of the regulations that apply to each step of the development and manufacturing journey, an institutionalized CDMO like Pfizer CentreOne offers can often anticipate questions and issues that might arise during drug development and help avoid costly delays because of hard-won experience.

Current Good ~ Practice (cGxP) requirements are ever changing, and they can vary from location to location. Compliance efforts are open to interpretation by manufacturers as well. Pharma companies and their CDMOs need to remain up-to-date with changes they may face during a multi-year development process and then invest resources accordingly. A strategic CDMO partner often invests resources needed to do this as part of its institutionalized effort to sustain operational excellence, in that the organization acts to ensure its own products also meet necessary requirements.

Strong experience with high potency API and hard-to-make finished drug product forms

Pfizer CentreOne is investing to provide expanded access to CDMO services for "high demand" technologies. We offer extensive experience in all phases of drug substance and drug product development and manufacture including:

- Small-molecule API synthesis
- Oral solid dose forms, including highly potent OSDs
- Cortico- and hormonal steroids
- Prostaglandins
- Antibiotics
- Sterile injectables, fill-finish

Aligning drug strategy with collaboration

Developers need to remember that when drug strategy aligns well with the strategic advantages and experience of its outsourcing partners, their drug programs will be stronger and be more resilient over the product's life cycle. Some stand-alone CDMOs may base new technology investments market trends without having built the foundational expertise that can drive project success ahead of the competition.

Strategic outsourcing partners with parent companies that have gone the full distance with their own drug substances and drug products are more likely to reliably deliver drug program success. Engaging a CDMO with institutional experience managing decades-long product life cycles, are more likely to place drug strategies on a solid foundation for success.

Therefore, contract partners with foundational experience moving therapeutics from patent-protected blockbuster exclusivity through second and third generation commercial processes, may be able to articulate and execute more efficient development paths – from greener more efficient synthesis routes to formulation changes supporting scale and other enhancements to achieve efficient, economic drug development and commercial manufacture.

Summary

Pharma's innovators are pushing the envelope with the development of highly-potent API formulations, biologics and other complex hard-to-make compounds. These development pathways are expected to last for decades, especially for OSDs. They also seek better business models to cope with the extremely high costs and lengthy timelines associated with drug development.

More drug owners and developers are turning to CDMOs for the strategic resources, expertise and capacity they need to bring their sophisticated and high-demand drug products to market as economically as possible.

Drug commercialization trends have increased demand for more strategic drug development and manufacturing support from contract services providers. The effort to deliver the depth of services, science and capacity required to support pharma's projects prompted growth and consolidation among CMOs and the emergence of both pure-play and embedded CDMOs.

Choosing the right CDMO to support drug strategy has become one of the more critical decisions drug developers have to make. With so many opportunities and so many CDMOs available, finding the best relationship is often the key to a successful strategic collaboration.

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Whatever your product's market strategy might be, drug owner and drug maker often have to build a common base of knowledge and do it in a timely and prescribed manner. Making more successful drugs begins with a more intelligent collaboration and the sooner both parties can achieve a true and transparent meeting of the minds, the better.

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