CONTRACT MANUFACTURING

COMMODITY OR COMPETITIVE EDGE?

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The approach to choosing a contract manufacturer can have a significant impact on the success and timing of a development program and ultimately product launch. This should be viewed as a "high-stakes" strategic decision process, and it is critical to start early, cast a wide net, and dig deep in identifying and assessing potential partners.

The Need

Successful drug development requires a wide range of expertise. One aspect that is often overlooked or underweighted as a strategic imperative is ensuring an optimal manufacturing program. Because outsourcing to contract manufacturing organizations (CMOs) or contract development and manufacturing organizations (CDMOs) is increasingly common, there may be a temptation to view these services as a commodity—particularly against the backdrop of multiple competing priorities and finite time and resources. However, as manufacturing requirements and drug delivery technologies continue to evolve, strategic manufacturing decisions are becoming increasingly important and could be key determinants of commercial success.

Potential Challenges

The process of establishing and developing quality manufacturing relationships can pose multiple challenges. The first can be simply finding a manufacturer with capability and sufficient capacity to complete a project in a desired timeframe. This challenge is potentially amplified for small innovator and/or mid-sized specialty pharmaceutical companies, as they have to compete for manufacturing capacity and human resources with larger companies that are bringing larger projects and pipelines to potential manufacturing partners.

While the majority of outsourcing growth is being driven by small innovator companies, our own interactions with contract manufacturers and pharmaceutical manufacturing executives suggest a significant amount of outsourcing is driven by mid-size and large pharma companies. Around 30-40 percent of mid-size and large pharmaceutical companies outsource some portion of their drug product manufacturing, while at least 75 percent outsource some of their active pharmaceutical ingredient (API) manufacturing projects.

The search for a suitable manufacturing partner becomes even more challenging in situations requiring specialized development and manufacturing capabilities, such as high-potency APIs (HPAPIs), cytotoxics,

or biologics, as well as novel delivery formulations such as transdermal or nanoparticle technology.

Among CMOs and CDMOs reporting HPAPI manufacturing capabilities, only about 20 percent report the ability to handle ultra-high potency compounds (occupational exposure limit < 0.1 ug/m^3).[1] Given a potential dearth of certain specialized capabilities, it is essential that innovator companies begin early in development programs to seek a manufacturing partner with the necessary expertise to execute on such projects.

The Stakes

Small innovator companies arguably have the most at stake. Since timely and reliable manufacturing is pivotal in providing product for clinical trials and launch, missteps can delay or derail development programs. The European Medicines Agency (EMA) recently cited the CMO manufacturing Zepatier, Merck's hepatitis C drug, for issues involving record keeping and quality-management systems. This issue is expected to delay the EU launch to Q4 2016, or as far as the end of Q1 2017. In the case of the early-stage innovator company with one or a few lead assets, such delays in revenue generation could put company viability at stake, necessitating a robust manufacturing program to mitigate risk.

The selection of an ideal manufacturing partner also has implications for partnering and business development opportunities. Huron estimates that emerging innovator companies account for roughly 65-70 percent of the global pharmaceutical pipeline, with most of these companies engaging in manufacturing outsourcing. A BIO report on emerging company investment suggests that approximately 45 percent of the emerging company pipeline is partnered with other companies.[2]

1. Roots Analysis, "HPAPIs and Manufacturing Market, 2014 – 2024" (2014)

2. BIO Industry Analysis "Emerging Therapeutic Company Investment and Deal Trends" (2015)

As part of the diligence process in evaluating partnership or acquisition targets, larger companies will evaluate all aspects of a development program, including manufacturing capabilities, which could entail investigation of the FDA's audit reports, factory inspection observations in 483 letters, batch records, and more. Once a manufacturing program for a specific asset has been implemented, major efforts and expenses are required to change manufacturers. From the perspective of the innovator company, then, failure to develop a robust manufacturing program could jeopardize the success of a business development opportunity.

Manufacturing Partners— The Key Differentiator

Finding the ideal manufacturing partner can prove challenging with limited obvious differentiation amongst CMOs and CDMOs. What does an ideal manufacturing partner look like? Beyond technical capabilities, manufacturers should be able to **demonstrate their ability to be committed thought partners who understand the specific needs and recognize potential hurdles associated with a program/molecule**, providing guidance on optimizing project outcomes/timelines. Potential partners should be evaluated not just on the breadth of services offered, but also on their **ability to "connect the dots" between offerings to realize tangible benefits, such as time and cost savings** over the lifecycle of a program and/or product.

Implications for Innovators And Contract Manufacturers

Given the challenges and the high stakes associated with outsourced development and manufacturing, it is critical to **start early, cast a wide net, and dig deep in identifying and assessing potential partners**. This process should involve the delineation of specific and unique needs, proactive research on the landscape of potential CMOs and CDMOs, networking to seek personal input based on first-hand experience, and deep diligence with candidates that make

the "short list." Conversely, **if CMOs and CDMOs wish to participate in the evolving industry "ecosystem," then it is incumbent upon them to clearly articulate and substantiate their value proposition** to emerging innovator companies, from whom an increasing portion of the early- and mid-stage pipeline originates. In the current industry climate, considering its significant potential impact on clinical and commercial success, a robust outsourced manufacturing program should be considered a competitive asset—not a commodity.

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