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FUTURE FORWARD

HOW YOUR OUTSOURCING STRATEGY SHAPES YOUR DEVELOPMENT JOURNEY

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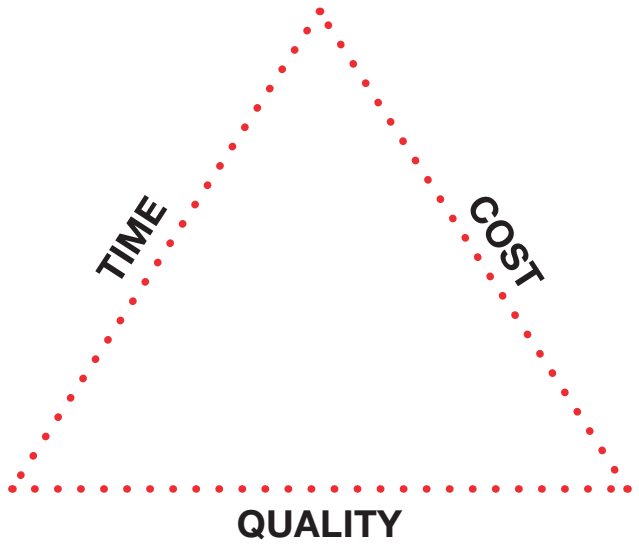
Developing a new therapy is complex. Don’t add to the complexity with the wrong CDMO strategy.

Two common questions for pharmaceutical companies with a new therapy are 1) should we outsource the development program, and 2) if yes, should we work with a single partner or several? Yet, quantifying the value-add of outsourcing can be difficult as no two programs are alike – even if the molecules are similar.

Since the choices you make can have significant impact on the speed, cost and review process of your therapy, it is critical your decision process leads you to the best answer for each investigation. Read on for insights, questions to ask, and decisions that may influence your early development and commercial manufacturing process.



Every development program requires its own careful balance of three critical parameters, while simultaneously adapting to the molecule’s unique needs and challenges.

Your outsourcing strategy should depend on the help you need…

There are risks and advantages to both single- and multi-partner outsourcing strategies. Only through careful matching of needs and capabilities can you determine which is better for your program. Your first step at this stage should be to rank-order the capabilities listed below, understanding that there are inherent tradeoffs in whichever order you choose.

- **Overcoming early development challenges:** if your program is characterized by high potency, low solubility or other molecule challenges, single-source CDMOs tend to have more experience and can likely offer a greater chance of right-first-time results.
- **Regulatory experience:** the need to change a materials source in late stage could have regulatory impact – a larger CDMO with global reach may be better able to find a similar-enough replacement to avoid issues.
- **Multiple markets:** approval in multiple markets may go more smoothly with a single CDMO partner that has extensive regulatory inspection history and experience with harmonizing and translating global data – conversely, you can use regional CDMOs as long as you don't mind the extra management effort.
- **Project Management:** as the number of partners increase, the complexity of managing the program increases as well – and likely the job of project management will wind up with you.
- **Timeline:** if you're working on an expedited timeline (accelerated approval, fast track, etc.) single source may be a better option because an integrated CDMO can pick up time by connecting drug substance (DS) and drug product (DP) processes.
- **Cost:** smaller budgets may tend to favor a multi-partner approach, putting more responsibility on you, but can also increase timeline risk.

Time is the ultimate asset. So, who's faster when?

Key Program Issue	Single-partner	Multi-partner
Pre-clinical speed		✓
Time to start-up		✓
Time between steps	✓	
Time to completion	✓	
Right-first-time	✓	
Time in regulatory review	✓	
Time to to multiple markets	✓	✓
On-time delivery	✓	

...and your endpoint.

Whether you plan to sell your molecule at proof of concept, Phase II, or carry it all the way to market, your likelihood of success could depend on your choice of CDMO partners. Simply put, the further down the development path you travel, the higher the stakes become. And the more critical the experience and track record of your CDMO partner(s) is.

However, don't overlook the fact that even programs headed for an early sale can benefit from more upfront work in solubility and formulation. It more clearly shows the true potential of your molecule and will help the purchaser move to clinical trial faster – both of which can easily translate to a higher sale price.

Endpoint considerations for single-CDMO strategy vs. multiple:

- When development shifts from one provider to another, independent of development phase, information is lost. Scientific information is documented, but the touch and feel, experience, and trade secrets that exist behind every product process are often impossible to reproduce.
- Smaller CDMOs with small-scale API manufacturing and drug product manufacturing equipment may not have the capability, infrastructure, or expertise to scale up to late clinical phase or commercial. Consequently, they may not be looking at risks and challenges for late-stage, larger-scale operations.
- Smaller CDMOs may not be financially stable, which can be risky since many programs take from five to 15 years to progress from pre-clinical to commercial success. This may be less of a concern for earlier endpoints but should still be considered in your review of potential partners.
- There may be tax implications or cross-border issues moving material from one location to another that impact single-source and multi-source partners differently. Global CDMOs can frequently find ways to expedite shipments or reduce tariffs that regional companies cannot.

An unexpected advantage of the single-CDMO strategy

In a recent case, a large pharmaceutical company was acquiring a molecule from a smaller pharma company and wanted some details… from 10 years ago. The seller put them in touch with their CDMO partner to talk about challenges and risks during development.

The selling company was pleased they had worked with a larger, single-source CDMO because it meant there was an experienced name behind their asset, with full records and institutional memory. It's much easier to out-license a molecule with a known history than one whose development partner is no longer in business or has lost everyone who worked on it.

"Molecules never die, they come back. They come back in one form or another, one indication or another."

–Anil Kane, Global Technical and Scientific Affairs, Thermo Fisher Scientific

The final piece: Be future-phase aware when deciding your CDMO strategy.

Since specifics around solubility, dosing, safety and efficacy are often unclear at the beginning of research and development, it makes sense to plan for the worst. That means ensuring your CDMO strategy is ready for anything. Then your development program will be, too.

Potential Issue: Things change once you're in the clinic gathering data.

- What if you need a controlled-release bead?
- What if the dose form is incompatible with the intended patient population?

Solution: Choose a partner who can pivot as your needs change.

Potential Issue: There are dosage problems related to safety or efficacy (specific to oral solid dose).

- Is polymorphism to blame?
- Could spray-drying be a viable solution?

Solution: Choose a partner who helps you solve formulation issues early.

Potential Issue: Forecasts are rarely accurate.

- What if you are first to market and usage skyrockets?
- What if you're not?

Solution: Choose a partner who can flex up or down with you as needed.

The benefit of phase appropriate risks

Challenges like solubility, bioavailability, stability, or clinical efficacy need to be solved in early development, preclinical and Phase I. Others, like the manufacturability of a molecule – whether it's a drug substance or a drug product – can be handled as you go. Document risks and address them later when more material is available, or when more information is uncovered.

	Immediate	Near-term	Medium-term
Timelines	✓		
Safety	✓		
Efficacy	✓		
Developability		✓	
Scalability			✓
Stability			✓
Profitability			✓

Use these checklists to identify potential partners.

In order for a potential outsourcing partner to deliver optimal value, ensure that they are able to meet all your needs. Get concrete, demonstrable answers to these questions and you'll know you're on the right track.

Confirm your potential CDMO partner has:

Right background check list

- ❑ Experience with a similar molecule, similar profile or similar risk profile to yours
- ❑ Experience with your intended dose form
- ❑ Experience with reasonable backup dose forms in case there's an issue
- ❑ A record of proven project management performance for complex molecules
- ❑ A robust quality assurance system to ensure zero-defect results
- ❑ Flexible and adaptable process development & optimization
- ❑ The interest/capability to take on a project with your minimum/maximum batch size

Regulatory experience check list

- ❑ Seasoned regulatory team with expertise focused on ich common technical document (ctd) quality/module 3 for clinical and commercial applications and life-cycle maintenance
- ❑ Multi-jurisdictional experience to support key regions such as: eu, us, and canada, as well as international/rest-of-world registrations
- ❑ Knowledge of the latest regulatory standards
- ❑ Integrated regulatory services with fewer intermediaries, shortened lead times and optimized product knowledge
- ❑ Comprehensive range of cmc regulatory services across all product types manufactured

Early development capabilities check list

- ❑ Technical team to address complex formulation challenges (e.g. Addressing solubility and stability challenges)
- ❑ Ability to build robust processes in early development that enable commercial success
- ❑ Success with optimizing chances of approval
- ❑ Success with implementing strategies to shorten timelines to get to market quicker
- ❑ Access to detailed scientific data for strategic decision making

Commercial manufacturing history check list

- ❑ Efficient global supply chains
- ❑ Success enabling business continuity
- ❑ Experience building in risk mitigation
- ❑ Experience with commercial technology transfers
- ❑ Demonstrated speed and accuracy in execution of technology transfers
- ❑ Experience with clinical trial packaging, storage, transportation.

These points, although seemingly simple, are important measures of a CDMO's ability to meet your program goals. This due diligence can help avoid potential rework and costly delays and help you get to market quicker. Be sure they can provide data, case studies or references for each item as a misunderstanding about current capabilities can have a drastic impact on timeline, quality or cost.

One simple answer.

There are enough challenges in drug development that you don't want to unintentionally add more. For many programs and molecules – independent of end point – a single-CDMO strategy will create the added value you're looking for because it allows the most strategic use of outsourcing.

By working with one global CDMO, you can leverage economies of scale, deep expertise at every phase and a streamlined, collaborative development process that reduces error, downtime and unforeseen risk. In effect, the single-source partnership allows you to find the best possible balance of the competing priorities.

If a single-CDMO strategy is right for you, consider Patheon pharma services as your partner of choice. Our reputation is built on scientific and technical excellence, including specialized capabilities for highly potent and controlled substances, complex formulations, and solubility enhancement. We also offer integrated services for drug development that aligns the development of drug substance and drug product in a coordinated drive toward proof of concept that can reduce development timelines.

With more than 57 locations globally, we provide integrated, end-to-end capabilities through all phases of development, including clinical trial solutions, logistics services and commercial manufacturing.

Interested? Let's discuss how we can help your development program.

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