Illuminating The Pathway to Efficient Drug Development for Small Biotechs

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Over the last five years, small biotech companies have been a driving force in innovation, accounting for more than 60% of all new prescription drug approvals. As a result of this boom, CDMOs are working to better understand and prepare for the challenges that nascent companies may face on the path to commercialization. Though drug discovery and development come with inherent challenges no matter the size or experience of a sponsor, taking a drug to clinic as a start-up with limited funding is especially difficult. When CDMO teams take the time familiarize themselves with the struggles of these potential clients, they are better positioned to cater toward their unique needs and produce enhanced project outcomes, ultimately serving as key players in the growth and evolution of today's industry. And with that, everyone wins.

Understanding Clientele to Improve the Process

Typically, a small biotech client seeking an outsourcing partner is in the early phases of development with what could be limited funding. Often, they are under immense pressure from investors to meet certain milestones before additional funding is released. Many of these sponsors have taken high risk, high reward approaches to development, despite the possibility of going out of business or losing their funding at any time.

In some cases, a sponsor may have limited understanding in terms of what processes and CMC approaches would work best for their molecule and their relatively small teams. Without proper planning and consideration, these factors could introduce certain challenges for not only the sponsor but also the CDMO. Some examples include:

- **Aggressive timelines** can introduce unnecessary risks and mistakes into development, resulting in delays.
- **Small amounts of API** require development and manufacturing teams to use techniques that require minimal quantities, which can lead to less data and, consequently, limited insight into the product and process.
- **Insufficient knowledge about the material**, how it scales, what degradation factors are present, etc., all elevate risk throughout the development process and can result in frequent process changes.
- **Limited method robustness** makes it challenging to determine whether studies and activities are yielding sufficient information to move forward.
- **Lack of an established regulatory strategy** can result in unnecessary mistakes, repeated activities, and timeline delays.

From the CDMO perspective, approximately 10% of all client projects are smooth from the start, generally because a client has ample experience with their product. On the other hand, around 10% are difficult, requiring CDMOs to tackle issues of API solubility, stability, scale-up, degradation, regulatory strategy, and formulation changes. However, most client partnerships can go either way, meaning that a CDMO's ability to meet the client where they are significantly influences project outcomes.

Strengthening CDMO Offerings

To assist a biotech's successful drug development, there are three key areas CDMOs should focus on: equipment and instrumentation, organization and personnel, and systems and processes.

I. Equipment and Instrumentation

Equipment and instrumentation should be up to date and in line with the latest technological innovations. Since a CDMO's team will be dealing with small amounts of API, it's important to leverage techniques and equipment that are designed to minimize material usage and handle small batches. Though large fill lines will come in handy for large batches, having appropriate fill line sizes at the beginning is important to minimize product loss. The less API a process uses, the better.

II. Organization and Personnel

Assemble a team with the following qualities: technical expertise, flexibility, agility, efficiency, and a willingness to solve problems on the fly. A small, agile working group will help ensure that processes do not get delayed amid endless layers of consultation and approval. Staff should focus on collaborating with sponsors, providing support to teammates, and communicating often and effectively. A strong team will relish the experience of working in a fast-paced, challenging environment.

III. Systems and Processes

One key to effective development is preparing for any risks or obstacles that could come up in advance, Allowing the team to avoid any surprises or delays along the way. Systems and processes will help a CDMO to build a structured but flexible approach for clients. First, conduct a gap assessment, allowing the CDMO team and client teams to identify what is known and unknown about the product. From there, a risk assessment should be conducted to determine what information should be gathered from a phase and risk-appropriate perspective. Conducting these initiatives early will help a CDMO team design a path forward for their client.

Building a Roadmap to Success

The information gathered in the gap and risk assessments will help both CDMO and client identify all pivotal components of development. This includes what to investigate and evaluate, which factors to test for and how best to test for them, and how to pivot based on the outcomes of said investigations. Once the risk assessment is complete, it is time to construct a plan to address any unknowns; this can be developed using a Gantt chart or a decision tree map. This roadmap consists of various tests, activities, and research done via technical papers. Upon completion, it is designed to yield information on what the manufacturing process steps should be. The outcomes of these actions may require changes in materials, excipients, and/or presentation of the drug, which is why CDMO flexibility is vital. Beyond that, it is important to establish reliable methods as early as possible. If a method is unreliable, it could lead to bad data and/or cause project delays.

Early on in a project, set expectations for the client. Start by explaining the approach upfront, allowing for discussion and feedback as necessary. Next, provide the client with a reasonable budget, pricing out known items and providing accurate estimates for standard activities. Ensure that the client knows that

Phase I clinical trial materials are only one of many deliverables. The other component is the development of a control strategy that creates a robust and repeatable process and a solid foundation for future work.

It is important to ensure that analytical methods are in place as early as possible and to avoid offering a firm fill date until the roadmap and tasks have been established; offer a goal fill date for clients and a proposed project schedule based on estimated task duration times. It is also advisable to procure a percentage of the contract fees upfront and/or invest in business insurance to help protect the CDMO organization from unforeseeable financial circumstances.

Discovering Improved Routes to Clinic

It is well understood in the pharma world that it is never easy to create something wholly from scratch, and drug development is no exception. For first-time drug developers and small biotechs, a CDMO with knowledge, experience, and attentiveness can help guarantee a successful development cycle. If a CDMO has the requisite tools, they can develop a plan that reduces project risk and increases the chances of project success. The better the roadmap, the higher the chances of ensuring efficacy and efficiency in a drug's journey to patients.

About William Powers

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