How to Set up Manufacturing for Biotech Startups

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Deciding when and how to set up manufacturing can be essential to the success of any biotech startup. Experts share their advice on how to approach manufacturing decisions.

Great ideas for potential biotech products, often hatched in small startup settings, seem far removed from the complexities of manufacturing later down the line. Researchers and innovators are focused on lab or virtual work in the early phases and may decide to think about manufacturing later. But key manufacturing questions need to be considered at the right time to avoid compromising development time, complicating the development process, or killing a potential product completely.

What to consider and when

Experts agree the best time to consider manufacturing is as early as possible in the product development timeline. They suggest starting with a critical question: is there an existing process for getting similar product types to manufacturing? If the answer is no, manufacturing might require new technologies or perhaps a platform approach to development, with the implications for cost, complexity, and manufacturing times those bring.

Jeetendra Vaghjiani, Executive Director, Clinical Development and Strategic Marketing, Mammalian, at Lonza Bioscience, highlights some examples. *"Will your new molecule be a straightforward monoclonal antibody, a protein fragment, or something more complex and exotic for final formulation and administration? Knowing the format will drive the process pathway."*

Established product types such as monoclonal antibodies can tap into well-established processes such as platform technologies and analytics. This can speed up critical stages in development such as preparing the right data package for an investigational new drug application with a regulatory agency. However, many new products won't have it so easy.

"The more complex the format is, the more challenging it will be to choose the right protein engineering technology, cell line development, process optimization, and development – not to mention the analytics to evaluate the product, which often must be adapted or developed from scratch," says Vaghjiani.

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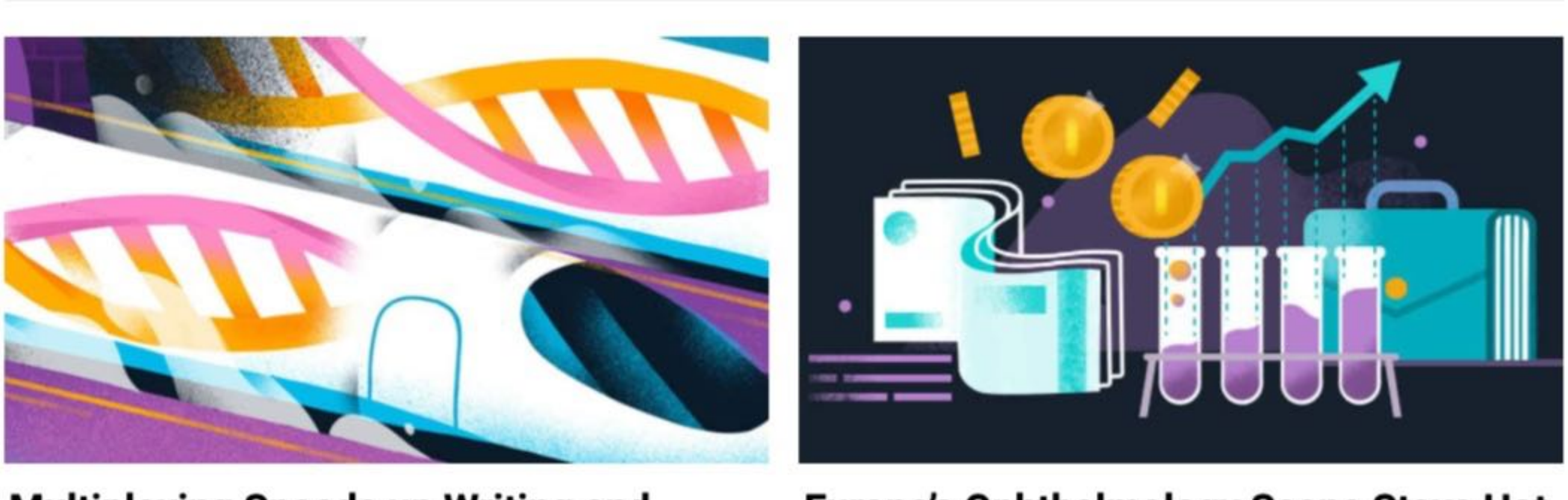

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According to Vaghjiani, there is a key milestone indicating a molecule is ready for manufacturing. This happens when preclinical data demonstrates efficacy for a specific indication or therapeutic area, there are no overt safety issues, and manufacturability of the product is proven.

"We have found if these factors are considered early in the process using in silico and in vitro predictive tools, it can help improve candidate selection and make the pathway to human trials more efficient," adds Vaghjiani.

Outputs from these processes may mean considering an alternative candidate product or *"re-engineering it to de-risk its safety or manufacturability profile while maintaining product activity."* Building in this step early, with the necessary contingency planning, is essential for biotech startups that lack the experience to foresee such obstacles before the manufacturing phase.

Amrik Basran, Entrepreneur in Residence at the life sciences investor Delin Ventures, also highlights the critical question of scale. *"People often fail to consider the complexity of the manufacturing process. What works in small quantities in a lab might not work at scale. Your protein or biologic may have to go through processes it's not seen before, in very high concentrations, temperatures, or volumes. If you leave this too late, by the time you have your lead asset, it's going to take much longer to solve issues flagged up for safety and manufacturability when it comes to working at scale."*

He stresses the need to talk to manufacturers early not only to avoid later cost and complexity, but also to explore potential manufacturing partnerships well in advance.

Leveraging existing expertise, capability, and partnering with a CDMO

Creating a partnership with a contract development and manufacturing organization (CDMO) allows you to outsource the complexity of manufacturing technology, processes, regulatory issues, logistics, and other challenges required to get a candidate to human trials and eventually to commercialization.

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"If it's a standard molecule like a monoclonal antibody that's already well established, you would engage properly with CDMOs while you're still in the preclinical phase," Basran explains. *"Maybe you've got good in vivo data, you've shown the mechanism of action, you've shown efficacy in animal studies, you may have done a bit of toxicity work to prove no major issues. At that point, you can put your tender out and find your CDMO."*

If your product doesn't have a neat fit with an otherwise suitable CDMO, Basran points out they frequently have the means to adjust or develop systems and processes to cater for more specific product needs. Early discussion with a CDMO allows time to modify manufacturing processes or flag other issues that send a product back for adjustments to fit within that CDMO's systems.

Choosing a CDMO partner also flags the question of scale again. "*It is important to choose a CDMO that can offer a range of manufacturing scales, as this can help you manage market variability,"* Jeetendra Vaghjiani points out. *"For example, sometimes going with a CDMO that can offer pilot- as well as large-scale manufacturing can provide better economies of scale as there will be less costly and time-consuming tech transfer involved."*

Partnering with a CDMO experienced in your product type and the regulatory issues involved might also help decide where to manufacture. Some territories require local manufacturing for particular product types or may have other regulations to meet, such as logistics or storage systems, which a CDMO will already have in place.

Manufacturing in-house

Outsourcing the complexities of manufacturing to a partner seems an excellent idea for a biotech startup more focused on research and innovation. But this approach won't always work. When a product is too novel or complex to fit within an existing manufacturing capability, manufacturing in-house might be the right way to go.

James McIlroy, founder and CEO at EnteroBiotix, says his company made a very early decision to manufacture in-house. The firm's intestinal microbiota transfer product, first-in-class within the emerging microbiome therapy field, required unique manufacturing systems and processes that existing CDMOs could not adequately deliver.

However, as McIlroy points out, that didn't mean they had to start from scratch. *"The microbiome has a unique challenge with non-sterile starting materials from human donors, and the complexity of the products. But we looked to existing areas of manufacturing science where we could leverage appropriate expertise, such as biologics generally, and particularly gene therapy, to establish our manufacturing capability."*

EnteroBiotix was initially able to repurpose existing facilities for the company's needs, in a site already designed for industrial use, within a campus with other biotech startups, and in a location with excellent transport links. The company has since constructed new facilities to meet the next stage of its manufacturing requirements, but it has partnered with external providers for specific needs in the past and may again in the future where appropriate. This could happen due to opportunities created by a partnership or a situation where a licensing deal brings external expertise or capability in-house.

As McIlroy explains, the in-house approach offers many other attractive opportunities. *"Doing this in-house means you have complete control over your own timelines, your own destiny, within reason. You retain all the intellectual property and know-how for your core competency and also continue to build your capability all within the business... if we've brought specific subject-matter expertise in-house, we've been sure to augment our own capabilities after that transfer has happened to undertake it later ourselves."*

McIlroy points out that EnteroBiotix's build approach has always been iterative and modular, so they can meet current needs while also maximizing resources and retaining flexibility for those possible future partnerships.

Working within a novel product area without existing blueprints means manufacturing in-house isn't easy. The manufacturing facilities built by EnteroBiotix had to contend with the extraordinary challenges of the pandemic, planning around interrupted supply lines, and getting the right people in place at the right time while working within Covid restrictions. McIlroy believes a key component of their success was and continues to be finding and retaining the right kind of people, enthused by a can-do attitude in a new field.

Ultimately, the choice to go in-house is a difficult one. Investors need a good reason to spend a lot of money on 'bricks and mortar,' so the decision to go bespoke has to offer real business value. McIlroy highlights that his company's ability to control its own processes and capabilities significantly reduces risks such as booking CDMO floor space with massive lead-in times, or production delays caused by unforeseen events that impact external providers. That offers a distinct business advantage. It also means the company is set up for future manufacturing partnerships with biotech startups developing new products in the microbiome field.

Talking to the experts

Making the right decisions about manufacturing at the right time is crucial, and as Basran concludes, it's vital to get the right help. *"It's essential when you're talking about new technologies, new platforms, or where things haven't been tested at scale. If you have no in-house experience, you really need to talk to people early to see where the risks are. It doesn't have to be a CDMO, it can be a consultant in this area who can look at your processes and point out the challenges you have to overcome".*

Cover image via Elena Resko