The Great Debate: Internal vs External Manufacturing for Advanced Therapies

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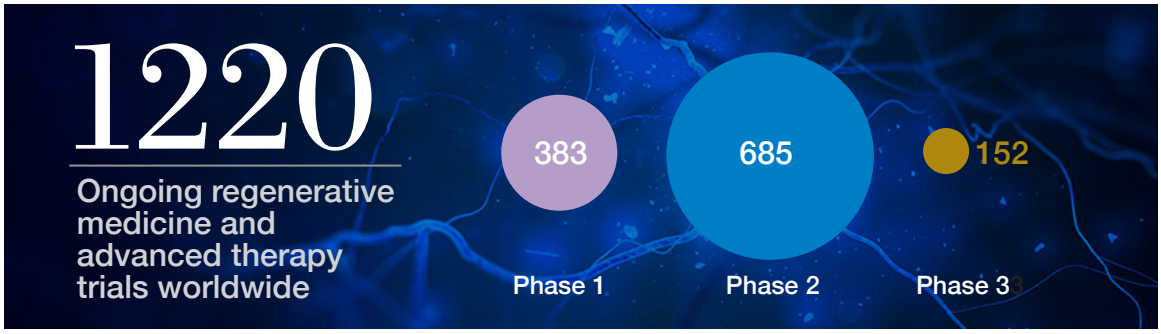
Internal vs External Manufacturing for Advanced Therapies

Determining the right approach to manufacturing is crucial when bringing advanced therapies from clinical development to commercialization. Developers of cell and gene therapy products face unique manufacturing hurdles and overcoming these obstacles requires thoughtful, proactive planning.

On March 31, 2021, Precision ADVANCE, the cell & gene therapy collective,™ hosted The Great Debate: Internal vs External Manufacturing for Advanced Therapies, an expert panel discussion moderated by Arsalan Arif, the publisher and founder of Endpoints News. Precision ADVANCE is an organization of interconnected services and complementary teams focused on the complexities of gene therapies and the resources needed to bring these advanced therapeutics to market.

Current State of the Advanced Therapy Sector

According to the Alliance for Regenerative Medicine, there are currently 1085 gene, cell, and tissue-based therapeutic developers and 1220 ongoing regenerative medicine and advanced therapy trials worldwide. Over 800 of these studies are in phase 2 or phase 3. A watershed year for the sector, 2020 saw nearly $20 billion raised, despite the disruptions of the global pandemic.[1]



“Some may look at the exponential growth of this field and say it is irrational exuberance and too much capital chasing the science,” said Faraz Ali, CEO of Tenaya Therapeutics. “I would actually say that the exuberance is quite rational. The science for gene and cell therapies has matured to a point where we are getting some real results.”

The recent approval of idecabtagene vicleucel for multiple myeloma is the first of a handful of gene therapies expected to be approved in 2021.[2] With more than 3000 patients treated with adeno-associated virus (AAV) gene therapy products over the past 2 decades, there is a growing comfort with safety among regulators, and the risk to benefit ratio seems to be shifting in favor of advanced therapies.

Audrey Greenberg, cofounder of Discovery Labs, pointed out that the level of activity and capital in the sector, coupled with expedited regulatory pathways, has created strain on the system.

“Everyone’s talking about capacity, capacity, capacity,” said Greenberg. “But to me, capacity doesn’t mean just physical space. It also means people, equipment, consumables, and advanced analytical methods that can prove the potency and effectiveness of these treatments, all in a regulatory environment that is complex and ever-changing.”

Overcoming Challenges in Manufacturing

Cell and gene therapies are characterized by cutting-edge research and technology, often requiring multiple drug components and manufacturing modalities to deliver a final product. This complexity results in a fragmented supply chain with very few end-to-end solutions that are conducive to acceptable lead times and business terms. Timelines, funding, and staffing push most small and emerging biotech companies to an external model for preclinical and clinical material. In an environment where demand outstrips supply, however, it may be challenging to secure the right contract development and manufacturing organization (CDMO) partner.

Brian C. Riley, SVP of Technical Operations at Beam Therapeutics, added, “At Beam, the first step of our manufacturing strategy was building the team and technical depth and driving the process and innovation with external partners. Then, we selected partners based on broad evaluation criteria, including culture, capability for manufacturing PD [process development], analytical capacity, lead times, continuity, and cost.”

Developers may also benefit from balancing the risk of their key programs with dual sourcing across all drug components and drug products to help secure their supply chains, not just for clinical manufacturing but also for scale-up to commercial volumes.

For developers using novel approaches or targeting larger indications, making manufacturing a full competency may make sense, as it allows for more control and more rapid iteration due to closer proximity between research and manufacturing.

“Co-locating R&D with manufacturing can help eliminate costly tech transfer efforts and the hurdles that come along with them,” agreed Greenberg. “In addition, adhering to GMP [good manufacturing practice]-grade materials, processes, and analytical methods as early as possible will really speed the path to commercialization and along the FDA timeline.”

Considering Build vs Buy

John Khoury, EVP at Project Farma, introduced the concept of make versus buy business case analysis.

“A make versus buy business cases analysis lays out the short- and long-term strategies of a company, with the objective of delivering a phase-appropriate approach that provides the agility required as the company’s pipeline evolves,” explained Khoury. “The critical foundational points of this analysis are evaluations of the pipeline, portfolio, and platform.”

Ultimately, the goal of a make versus buy business case analysis is to deliver a manufacturing principle that enables scalability and flexibility, while mitigating risk and providing a roadmap.

Bruce Goldsmith, President and CEO of Passage Bio, weighed in by saying, "Models are useful for giving you a structure to think about pros, cons, and risk. But, for us, there is more than just the intrinsic value of owning the asset of manufacturing. By developing an end-to-end understanding of the entire manufacturing process, we can internalize our learning and capture the IP [intellectual property] for the innovation."

While outsourcing offers flexibility and optionality, building and owning the manufacturing capability may give developers more control over their own destinies. The challenge lies in determining when to make that investment. Increasingly, developers may be opting for a hybrid model, with a mix of internal resources and external partners to balance speed to market and supply chain security.

Noted Ali, "For something as novel as cell and gene therapy, you have to think about manufacturing as part of your science, not distinct from it. Manufacturing is your science, and the process is the product."

Innovation

Goldsmith emphasized that the advanced therapy sector is moving forward to next-generation achievements in safety, safety approaches, and delivery. He also mentioned alternative approaches such as moving away from capsids altogether.

"Decades of research are coming to fruition," said Goldsmith. "The stage is set for another transformation that looks at delivery and addresses diseases in a whole new way."

To help developers bring about the next transformation in advanced therapy, the interdisciplinary teams at Precision Medicine Group—including Precision for Medicine, Project Farma, and Precision Value & Health—deliver a comprehensive, integrated approach to driving clinical, manufacturing, and commercial success.

References:

1. Alliance for Regenerative Medicine. 2020: Growth & Resilience in Regenerative Medicine Annual Report.
2. US Food and Drug Administration. FDA approves idecabtagene vicleucel for multiple myeloma. Published March 29, 2021. Accessed November 9, 2021. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-idecabtagene-vicleucel-multiple-myeloma

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Precision ADVANCE, a collection of interconnected services and complementary teams, uniquely focuses on the complexities of clinical, regulatory, manufacturing, and commercial needs to successfully bring cell or gene therapies to market.

Connect with one of our experts. Contact us at **precisionadvance@precisionmedicinegrp.com.**
To learn more about Precision ADVANCE, visit **precisionmedicinegrp.com/advance.**

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