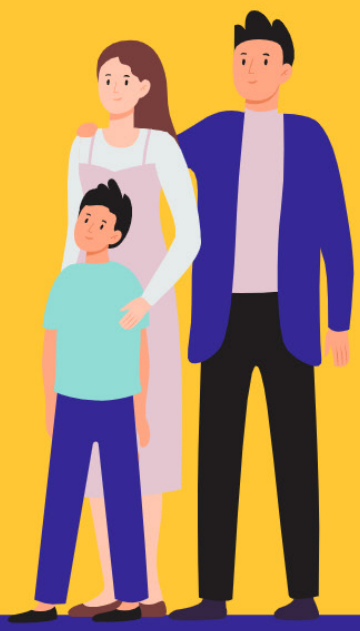
ONE SIZE DOES NOT FIT ALL: UTILIZING MULTIPLE TECHNOLOGY PROVIDERS IN GENE THERAPY MANUFACTURING



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One Size Does Not Fit All: Utilizing Multiple Technology Providers In Gene Therapy Manufacturing

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Despite notable clinical and even commercial success, the demand for gene therapies still outweighs supply. This is because, unlike traditional biologics such as monoclonal antibodies, there is currently no standard blueprint for the development and manufacturing of these novel products. Gene therapies are a relatively new and complex therapeutic modality still in its infancy. Therefore, bringing one to market calls on a customized approach, with the process for each product designed specifically for its unique needs.

In a perfect world, it would be ideal to use one technology provider for all of your manufacturing requirements; however, because the industry is still learning to navigate this burgeoning area, it may be necessary to look at a variety of vendors to find the most advanced solution for each of the different unit operations involved in your gene therapy life cycle. With a diverse and wide landscape of potential partners, it is important to know not only what qualities to look for in a technology provider but also how to traverse the challenges inherent in managing multiple relationships.

Can A Single Technology Provider Meet The Needs Of Your Project?

As advances in science and technology extend the application of gene therapies from ultra-rare diseases to more widespread diseases, the possibilities of what this field can accomplish are expanding rapidly. Viral vectors are the most common gene-delivery mechanism and to date, a total of eight viral-vector-based therapies have already been approved by the FDA, with 25 viral-vector therapeutics in late-stage development and another 120 in Phase II trials as of February 2022.[1] This growing pipeline means that quick and efficient scale-up of viral vector production is more important than ever, with more technology providers throwing their hat in the arena as potential partners for biomanufacturers pursuing these revolutionary treatments.

While the goal is often to reduce the complexity of solution provider relationships, the gene therapy manufacturing template is still evolving and workflows can include 10 or more unit operations that require several different types of products and technologies. As a result, a single technology provider will likely be able to offer superior solutions and guidance in some areas but not all, which could lead to a suboptimal process. And as the industry continues to navigate lessons learned from a pandemic that exposed the cracks in the pharmaceutical supply chain, designing a commercialization strategy around supply from one vendor could leave a biotech vulnerable to shortages and costly delays. Thus, working with multiple partners and where their solutions complement your process best may be the most effective and efficient solution in this evolving area.

Nevertheless, creating a strategy that relies on multiple partners comes with its own challenges. Therefore, a comprehensive evaluation, as early as possible, of each partner is necessary to determine if they are truly committed to understanding your needs and are indeed capable of developing a process to fit those needs.

It's Never Too Soon To Engage With A Potential Technology Provider

With so many factors to evaluate and so much on the line, selecting a partner — or multiple partners — to help bring a new biopharmaceutical product to the market is already a difficult task. However, this can be especially challenging for viral-vector-based therapies, as this is still a new field and drug manufacturers may have difficulties identifying and, thereby, expressing their needs. Therefore, technology and solution providers should know what questions to ask to gain a clear understanding of your expectations and what your end goals may be.

For example, do you plan to make the product yourself or outsource manufacturing to a CDMO? Do you want to manufacture at only clinical or hospital scale, or at commercial scale? These different

endpoints determine the solutions a vendor may recommend. Commercial-scale projects have additional process and compliance requirements that are not needed for the production of clinical drug supply. Often, clinical development does not proceed smoothly, so understanding these interim milestones and potential delays and prioritizing deliverables are keys to developing a strategy to maintain the supply of viral vector.

Ideally, this interaction occurs as early as possible but can take place at any stage. A knowledgeable technology provider will have the foresight necessary to guide you through the decision-making process. While the more context you provide, the better, outlining an early strategy should not require you to divulge proprietary data or more information than you are comfortable sharing. Instead, the vendor should be able to anticipate what potential questions you may have and answer them by leveraging its previous experiences. For example, the team at MilliporeSigma uses its expertise as well as its publicly available case studies as examples to highlight what solutions may fit your process needs. A potential partner that takes the time to get to know your project not only demonstrates they have your best interests in mind but also allows them to effectively evaluate what tools you may need to design the most efficient workflow for your gene therapy product. However, while they have a critical role in doing so, there are also questions you should ask to ensure they can offer the solutions and service you need for the entire life cycle of your therapy.

Begin With The End In Mind

A first step when assessing potential technology providers is to complete a side-by-side comparison of the data available for their products. This can be gathered from documentation created by the technology provider themselves or that has been published in scientific and/or engineering journals. For example, review their upstream and downstream capabilities: What is the maximum titer for cell line A, and how is that different from cell line B? What is the downstream recovery for Technology A versus Technology B? Due to the various nuances in the experiments conducted to gather this information, engaging with the solution provider to help you navigate these comparisons is beneficial.

Consider the depth of a technology provider's portfolio and whether they have the range of products necessary to support every step in the development and manufacturing workflow; however, different technology providers may have differing strengths and strategic directions, leading to the need to work with multiple partners. One of the biggest risks of doing so is data management between multiple vendors. Ensure adequate communication and documentation about the processes and results. Experienced vendors will serve as a key ally in supporting your process development.

Overall, you should approach every technology provider evaluation with your end goals in mind. Even if you seek only small-scale manufacturing now, does the technology provider have the solutions and capabilities to help you scale up to larger volumes should you want to? The newness of gene therapy and the continued successes we see across the industry indicate we are entering a new and exciting frontier for patient care, but it also calls on biomanufacturers to constantly evaluate the solutions they are relying on as the knowledge and technology evolve. You should ask yourself – Do I have the best product for my process? Is my technology provider constantly striving to offer the most advanced services and products possible? A trusted and collaborative partner that can offer not only products but also knowledge based on real-world experiences is invaluable.

Ongoing Commitment To The Future

At MilliporeSigma, we strive to offer our customers end-to-end solutions intended to address the bottlenecks in gene therapy process development and manufacturing. For over 25 years, we have focused on viral and gene therapy manufacturing at our facility in Carlsbad, CA. We have now doubled our capacity with a second facility in order to support large-scale industrial and commercial production for viral vector gene therapies. Our internal laboratories are dedicated to processing novel modalities, and our state-of-the-art M Lab™ Collaboration Centers give pharmaceutical and biopharmaceutical manufacturers the ability to explore ideas, learn innovative techniques, and work side-by-side with our scientists and engineers to solve critical process development and production challenges. MilliporeSigma's Gene Therapy University also offers a unique opportunity to engage in scientific training courses focused on learning more about the basics of viral vector manufacturing. These initiatives coupled with a storied history of quality products allow us to offer our customers a partnership that is not built on transactional exchanges but rather long-term commitments to their future and, most importantly, the patients who depend on them.

REFERENCES

1. https://www.mckinsey.com/industries/life-sciences/our-insights/viral-vector-therapies-at-scale-todays-challenges-and-future-opportunities

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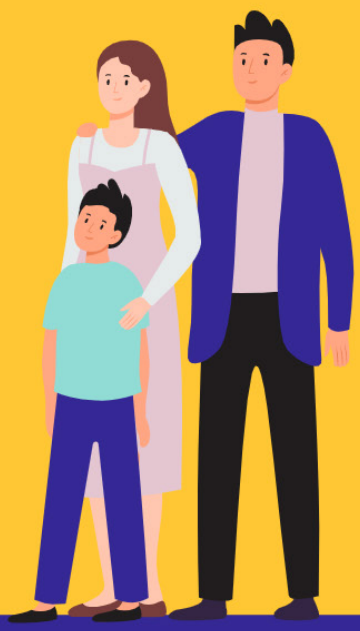

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