PERSPECTIVES OF VALUE-DRIVEN, INTEGRATED SOLUTIONS IN GENE THERAPY

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Perspectives Of Value-Driven, Integrated Solutions In Gene Therapy

By: **Ratish Krishnan**, Senior Strategy Consultant for Novel Modalities, and **Bruno Souza**, Bioprocessing Marketing Excellence Manager, MilliporeSigma

With rapid market growth and inspiring stories of success, gene therapies boast a promising future for manufacturers and patients alike.[1, 2] Combined with an estimated 7,000 rare diseases without approved therapies affecting more than 25 million Americans, these accomplishments are driving significant interest in gene therapies across the industry.[3] However, realizing their full potential calls on a wide range of capabilities and skillsets that may not be available at every company pursuing these next-generation products. A qualified products and services partner can help address any gaps but could also introduce more problems if they do not offer a holistic approach to gene therapy manufacturing.

Instead, you must find one with an arsenal of solutions and services that can help accommodate and optimize your entire workflow. By unlocking the value of an integrated solutions provider, you can leverage a comprehensive suite of advanced technologies and expertise that will facilitate your path to market and benefit you for the lifetime of your product.

Gene Therapy Success Begins With Good Process Design

Although gene therapies offer new hope to patients by addressing unmet medical needs, they also present many challenges to those companies dedicated to developing and manufacturing them. In addition to clinical uncertainty and small patient populations that may make it difficult to recoup an investment, gene therapies are incredibly expensive to produce. Recent reports estimate the cost of goods/manufacturing for a gene therapy can be anywhere between $500,000 and $1 million, a number that does not take into account other factors, such as R&D, clinical trials, and building commercial infrastructure to support commercial access once a drug is approved.[4]

Viral vectors are a key cost driver of gene therapy products. These gene delivery vehicles, which are used in more than 70% of gene therapy clinical trials worldwide, require specialized skillsets and manufacturing strategies.[5] This calls on experience, capacity, and capabilities not always readily available, particularly in small and emerging biopharma companies. The cost of acquiring those capabilities, whether they are brought in-house or outsourced, can grow quickly, especially when combined with raw materials, equipment, labor, and other costs standard for the production of a biopharmaceutical. Therefore, lowering the price tag for your gene therapy calls on good process design that ensures the most efficient workflow possible through high yield and scalability.

Companies with experience in this space understand these challenges and can offer valuable insight into solutions and technologies that improve vector production upstream as well as reduce viral vectors lost during downstream purification. For example, the most commonly used viral vectors — adeno-associated virus (AAV) and lentivirus — are traditionally produced in adherent cell culture systems using generic, unoptimized media supplemented with fetal bovine serum. Among other issues, this can limit cell growth and overall viral vector productivity and introduce potential contaminants into the manufacturing process. Instead, using suspension cultures with cell lines and chemically defined media can maximize bioreactor production and mitigate contamination risks, which MilliporeSigma estimates can reduce overall production costs by 57% when compared to adherent production processes. That is why we have developed a toolbox of innovative solutions catered to viral vector bioprocessing that includes our comprehensive list of upstream and downstream offerings encompassing all the unit operations, such as the Sf-RVN® Insect Platform for AAV production, Benzonase® endonuclease, and the Millistak+® family of filters, to name a few. Our BioReliance® testing services and viral vector manufacturing facility in Carlsbad, CA, has more than 30 years of experience in viral vector manufacturing and testing as well as a deep understanding of the relevant regulations in this rapidly changing area of the market.

Get an Early Start

While many of the techniques used for gene therapy originated with traditional bioprocessing of monoclonal antibodies, there are distinct differences and highly complex steps, such as plasmid transfection, that can lead to setbacks later during tech transfer and scale-up if your process is not robust enough for commercial manufacturing. A holistic approach to gene therapy manufacturing rather than just looking at one unit operation at a time focuses on establishing a reliable, sustainable, and cost-effective process that will keep pace with the demand as it changes over time.

Delays associated with having to rework your process not only add costs and give your competitors an edge in the market, but most importantly, they also prevent patients from receiving life-changing — and in most cases, life-saving — medication on time. Leveraging the experience of a knowledgeable partner can help prevent costly surprises later by planning for manufacturing challenges early. Overall, they can

help guide your decision-making and ensure you create the most efficient workflow for your next-generation product, reducing the cost of manufacture and, ultimately, the final price tag for the patient.

Key Factors For Partner Selection

As anyone in the industry knows, any variation in the production process of a biologic drug can have an unpredictable and potentially significant impact on the safety and quality of a final product. This unique relationship where "the product is the process" is what makes bioprocessing — and partner selection for products and services — so incredibly challenging. Add in the increased complexity of gene therapy manufacturing, and the need for a holistic approach to product development is more important than ever. Unlike traditional biologics, gene therapies do not have existing process templates to guide development, making expertise and experience paramount. An integrated solutions provider with proven knowledge in this space can build a well-defined process by considering it in its entirety, rather than looking at each individual unit operation. This allows them to optimize and maximize every step, ensuring the most appropriate solution that yields the best final outcome.

For example, if changes are made upstream, it is crucial to understand and prepare for any impacts downstream, calling on collaboration across the entire development team. If you are working with multiple stakeholders that do not communicate, you may not find out about any issues until it is costly and time-consuming to fix them. An integrated solutions provider can also provide access to a variety of experts who can work together to identify and resolve any possible roadblocks. And while expertise and experience are key, there are many other factors you will need to evaluate in a potential partner. This includes an infrastructure that can support and grow with you through each phase of development as well as open lines of communication to ensure support is available whenever it is needed.

An effective way to assess a partner is to have a multidisciplinary team complete a scorecard, which measures the partner's strengths and weaknesses. While cost should be a consideration, the primary factors for evaluation should be those that will offer you a competitive advantage by streamlining your path to market. Quality standards, business principles, and the product family they offer should also fit the needs of the market and be able to accommodate you for the entire life cycle of your product. Flexible solutions that can be easily scaled up as you move through each phase of development are essential. Ask yourself questions like — Can their family of solutions accommodate each phase of production, and does it come with the technical and application support should I need it? What is the level of security and compliance for data management? What is the risk for this partner to exit this market in the next 10 years?

With so many factors to consider, you must make sure you select a partner with a solid reputation and a comprehensive portfolio of products, services, customer support, knowledge, infrastructure, and scientific training to support not only your current needs but also those well into the future.

A Partnership Focused On Longevity

The gene therapy sector is growing at an unprecedented pace, but these products still remain complex and costly to produce. In addition to an innovative family of products designed specifically to address the bottlenecks of gene therapy manufacturing, MilliporeSigma's state-of-the-art facility is equipped to produce viral and gene therapies from clinical to commercial scale. Working with a wide range of customer types, our team has produced more than 500 clinical batches of virus within the last decade to support gene therapy development from clinical through commercialization, including the manufacture of two of the first five FDA-approved cell and gene therapies.

MilliporeSigma is dedicated to meeting patient demand for these life-changing products by ensuring product efficacy, safety, and commercial readiness. Instead of applying a cookie-cutter approach to customer support, Millipore achieves these goals by applying an in-depth analysis of each customer's unique needs and the information they have readily available to design a strategy that is based on a quality first mindset. Our team will work with you to not only solve your problems and supply high-quality raw materials that are chemically defined or animal-origin free but also to ensure you have a better understanding of your own process. This approach is indicative of our dedication to establishing a partnership based on value and expertise rather than a historically transactional exchange driven by only product fit and pricing. As the modern-day biopharma landscape continues to evolve, MilliporeSigma is focused on providing unrivaled support and service that prepares you for your commercialization journey and enables success for the lifetime of your product.

MilliporeSigma is the U.S. and Canada Life Science business of Merck KGaA, Darmstadt, Germany.

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