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INSIGHT BRIEF

Critical Steps to Optimize Viral Vector Manufacturing with CDMOs

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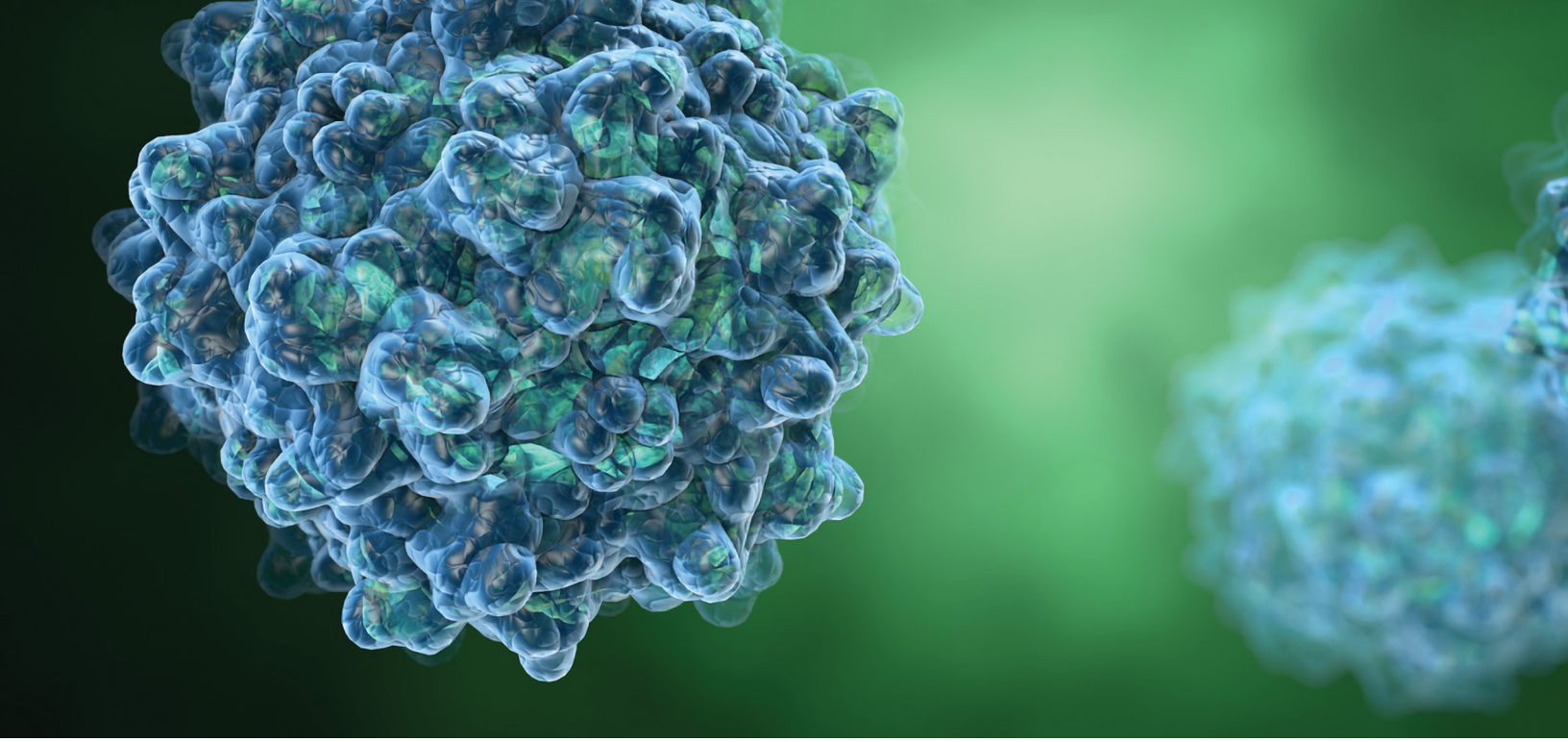
The need for viral vectors is rapidly growing across the cell and gene therapy space, driven by novel therapeutic and oncologic applications. Amid this surge of innovative therapies, the Food and Drug Administration (FDA) and European Medicines Agency (EMA) are updating guidelines to include advanced therapies. Meanwhile, early-stage drug developers can struggle to understand the complexities of large-scale cGMP viral vector manufacture at the required quality standards. As pharmaceutical companies navigate the complex and emerging advanced therapies field, early consultations with the FDA and partnerships with experienced contract development and manufacturing organizations (CDMOs) will ensure delivery of high-quality products to patients on a cost-effective timeline. The following best practices will yield productive collaboration throughout your viral vector production.

Step 1: Align on Process

At the outset of any viral vector manufacturing partnership, a client and their manufacturer need to align on the type of process they are building. There are three common scenarios:

1. **Adoption of platform processes:** Clients use a CDMO's existing platform purification process, standard materials, and analytical methods to manufacture their product.
2. **Process transfer:** Clients transfer their unique, established process to a CDMO for scale-up and cGMP manufacture of their product.
3. **Full process development (PD):** Clients rely on a CDMO to develop their bench-scale process into a robust, scalable, cGMP-compliant process.

Typically, adoption of a CDMO's platform process will help shorten the timelines. Depending on the product and clinical stage, it could take in the region of 12 months to produce, test, and release drug product. Other strategies are contingent upon the client, their product specifications, and the clinical trial stage. For projects that require full PD, FUJIFILM Biotechnologies — a leading CDMO experienced in viral vector manufacturing — adheres to a tried and tested template that begins with a proposal in response to a client's request for proposal, followed by a signed scope of work that includes timeline, methodology, and then a technology transfer into PD.



Ultimately, there is a learning curve to the first cGMP manufacture of any cell and gene therapy product. Often, early-stage customers coming from the research and development (R&D) space anticipate yields and titers equivalent to their bench-scale process. However, large-scale cGMP manufacturing follows specific guidelines, protocols, distinct purification and testing criteria. For early-stage companies, the FDA can provide phase-specific recommendations for your product while a manufacturer will share expertise on best practices and reliable platforms based on regulatory guidelines and previous experiences.

Step 2: Maintain the Balance Between Cost, Quality, and Timeline

At times, we recognize it can be difficult to balance priorities between manufacturing costs, product quality, and timelines for getting the product to clinic/market as fast as possible. Taking the time to guarantee quality and focus on select PD aspects will help avoid obstacles/delays in later stages of process characterization and process validation. Begin by identifying phase-appropriate goals with your partner as early as possible. Reach alignment on chemistry, manufacturing, and controls (CMC) components, analytical methodology, and product specifications to ensure compliance. Early-stage clients with limited funds need to meet regular milestones to raise funds. At FUJIFILM Biotechnologies, we work with both early and late-stage clinical development clients to get their products to patients without compromising on quality.

In many cases, we encourage clients to use established platform methods to maximize efficiency and quality throughout production. However, client requests for product- or phase-specific needs can be considered with early communication and planning. We also recommend that early-stage clients leverage single-use manufacturing systems to eliminate time spent on validation and qualification, allowing them to reach the clinic as soon as possible. During later clinical stages or commercial manufacturing, if required, the process can be seamlessly scaled up to use traditional stainless-steel bioreactors.

Step 3: Establish Trust Between Customer and Partner

Lasting relationships are built on a foundation of trust between a client and their CDMO partner. This process is aided by helpful behaviors from both parties. For the client, it is important to provide reliable, complete information as promptly as possible, including all necessary process details, product specifications, critical process parameters (CPPs), and critical quality attributes (CQAs). Gaps in communications can mean a CDMO needs to

unexpectedly find workarounds to minimize impact on timelines. Transparency and communication will help your CDMO partner plan ahead and avoid pitfalls in later stages. At cGMP scale, last-minute changes will snowball into detrimental effects on your timeline and costs downstream. Seemingly minor changes require updated documents, additional personnel training, and potentially new raw materials. Ensure advanced agreement on protocols and process to avoid any costly adjustments.

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Transparent and on-time communication from your CDMO is equally critical. At FUJIFILM Biotechnologies, we update customers on any challenges that come up in real time and work on mitigation strategies as soon as possible. FUJIFILM Biotechnologies places an emphasis on ensuring that everyone from lab technicians to senior management understand a client's product, including why it is being made, how it can change lives, and why it is scientifically unique or technically challenging. Most importantly, we are aware of the impact our work has on patients' lives and their families. For all of us at FUJIFILM Biotechnologies, our social responsibility to patients is of the highest importance — delays in manufacturing are lost opportunities in getting the products to patients who need them the most. We encourage potential clients to tour our facilities and meet personnel to see these values exemplified in practice.

A Fruitful Partnership

Collaboration between sponsor and CDMO is a critical component to successful viral vector manufacturing. Sponsors must identify and select a partner that they trust to handle difficulties throughout the process. As you consider your milestones, budget restrictions, and product quality aspects, let the expertise of your manufacturer and the FDA/EMA guide your path for getting therapies to patients as soon as possible.

Contact FUJIFILM Biotechnologies to accelerate your viral vector manufacturing.

About the Author

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Ramesh leads upstream, downstream, analytical development, and Manufacturing Science & Technology (MSAT) functions. Ramesh also leads the Science and Innovation projects for FUJIFILM Biotechnologies' gene therapy related programs. Before heading the PD group, Ramesh started at FUJIFILM Biotechnologies as Director, Program Design, Gene Therapy.

Previously, as a Senior Scientist at Boehringer Ingelheim Animal Health, Ramesh's primary research focus was on development of Equine Herpes virus and Canine adenovirus based recombinant vaccines against multiple pathogens (from rabies to FMDV) for use in pets and livestock. Ramesh also worked at NewLink Genetics Corp. & Bioprotection Systems Corp. in Iowa, where he developed adjuvanted and virus-like particle-based vaccines against emerging and re-emerging hemorrhagic fever viruses and infectious diseases — specifically Rift Valley fever virus and Influenza.

After completing his master's in molecular and human genetics from Banaras Hindu University, India, Ramesh graduated with a PhD in Genetics from Iowa State University. Since then, his research and professional focus has been on the development of recombinant viral vectors for use in cell & gene therapy applications and as recombinant vaccines.

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MKT-0193-IB-Rev01