BIO-RAD

Can CDMOs Provide Leadership in Cell and Gene Therapy?

Authors: Marwan Alsarraj and Mark White, Ph.D.

Many cell and gene therapies would never make it to market without the expertise and capabilities of contract development and manufacturing organizations (CDMOs) operating behind the scenes. As these promising biologics continue to gain momentum, we spoke with industry experts to find out how CDMOs are:

- **Adding value through stability and development expertise**
- **Developing meaningful, productive partnerships with innovators**
- **Implementing the latest technologies for cell and gene therapy**

Hear from the experts:

Suparna Taneja-Bageshwar, Ph.D., Principal Scientist and Analytical Development Group Leader, FUJIFILM Diosynth Biotechnologies

Dr. Taneja-Bageshwar has been with FUJIFILM Diosynth Biotechnologies for almost seven years. Previously, she worked as a research scientist at Texas A&M University studying ligand receptor interactions. She has a doctoral degree from India in Biochemistry.

Dan DeVido, Ph.D., Director, Strategic Business Development, FUJIFILM Diosynth Biotechnologies

Dr. DeVido has over 20 years' experience in the CDMO industry. The past 8 years has been with FUJIFILM Diosynth Biotechnologies in commercial and strategic roles, contributing to the growth and development of both the recombinant protein and advanced therapies sectors. He gained his Ph.D. in Analytical Chemistry from Florida State University.

Khanh Ngo Courtney, Ph.D., Director of Biologics, Avomeen

Dr. Courtney's experience extends from R&D to analytical method development, validation, implementation, method transfer, and optimization of test methods for the cGMP setting per USP and ICH guidelines. Her technical background provides the foundation for effective authorship of INDs, BLAs and MAAs for biological therapeutic molecules, as well as responses to requests and questions from the FDA, EMA, and PMDA.

Francesca Vitelli, Ph.D., VP for Cell Therapy and Viral Vector Process Development, Intellia Therapeutics, Inc.

Dr. Vitelli has a deep technical and operational focus and a track record of building, developing and leading cross-functional teams in roles spanning academia, start-up and industry. Previously, she was at Lonza Houston as head of cell therapy manufacturing, and prior, head of viral vector process development for 7 years. She received her Ph.D. from the University of Siena in Medical Genetics.

Cell and gene therapies are poised to usher in a new era of healthcare. As of June 2021, 14 cell and gene therapies have been approved for clinical application in the United States, and over 400 more are in various stages of clinical trials. The hopes of many patients hinge on the success of these various programs, which are designed to deliver a significant advance on existing treatments or even a functional cure.

"It's an exciting time to be part of what is really the genesis of a new era in biologics," says Dan DeVido, Ph.D., director of strategic business development at **FUJIFILM Diosynth Biotechnologies**.

As new cell and gene therapies get approved, innovator companies usually get the credit. But many therapies would never make it to market without the expertise and capabilities of contract development and manufacturing organizations (CDMOs) operating behind the scenes.

These novel biologic therapies, while powerful, are also incredibly complicated to develop and produce. Instead of generating a single molecule or protein complex, scientists handle viral delivery vectors and whole cells—complex biological systems in their own right. Here, CDMOs are uniquely positioned to leverage the latest technologies and industry-wide expertise. They can assist with process development and quality control, produce key components of a therapeutic product, or even take a biomanufacturing workflow from start to finish.

We interviewed four industry experts to understand the unique ways CDMOs participate in and shape the future of cell and gene therapy development and production.

How CDMOs Add Value to the Cell and Gene Therapy Space

"Innovator companies want to leverage as much of CDMOs' analytical and technical expertise as they can," says Khanh Ngo Courtney, Ph.D., director of biologics at **Avomeen**, a Michigan-based CDMO that provides analytical testing and development services. "Time is of the essence—everyone is asking, 'How do I get my products to the market as soon as possible in the easiest, cleanest way?'"

In some cases, CDMOs can help bring cell and gene therapies to market by accomplishing things that innovator companies—especially small biotechs and startups—can't do independently, such as scaling up manufacturing or dedicating entire teams to performing rigorous quality control. In other cases, CDMOs bring subtler value-adds to the table that elevate the quality and reliability of cell and gene therapies.

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> ***– Francesca Vitelli, Ph.D., VP for Cell Therapy and Viral Vector Process Development, Intellia Therapeutics, Inc.***

Securing Supply Chain Reliability

"A key benefit of CDMOs is that they can establish some security of supply for critical materials," says Francesca Vitelli, Ph.D., who formerly led viral vector process and analytical development and subsequently cell therapy manufacturing in the CDMO space and is now the head of cell therapy and viral vector process development at Intellia Therapeutics. "For example, during the COVID-19 pandemic, there has been unprecedented demand for the materials and reagents that go into viral vector vaccines and also into cell and gene therapies. A CDMO may have greater negotiating power than a small, single-product biotech for obtaining those necessities."

Expert Process Development

Since CDMOs work with a wide range of companies and products, they often have top-down insight into best practices that individual developers might not initially think to apply to their own therapeutic products.

"Based on our discussions with developers and our experience in the industry, we at Avomeen have been able to develop platform methods for quality control of gene therapy products based on the best and most frequently-requested analytical methods," says Courtney. "A client can come to us, and we can qualify their sample and their matrix using our proprietary method. If that works out, they can proceed straight into validation for GMP use, which reduces the overall timeline."

Key Elements of Meaningful Partnerships

For complex cell and gene therapy products, innovator companies can't simply submit an order to a CDMO and expect to receive a completed therapy in a few months. There needs to be a back-and-forth partnership for collaborative problem-solving.

But even if you know to look for a partnership, not every CDMO will be a good partner for producing cell and gene therapies. So how should innovators choose? It's crucial that a potential CDMO has the necessary laboratory space and technologies to produce or analyze a specific biologic; however, each expert interviewed also stressed that cell and gene therapy production requires building trust on interpersonal levels.

"If I were giving advice to an innovator company on choosing a CDMO, I would point to a term we use within FUJIFILM: *gemba*, a Japanese word which means essentially 'go see it.' Go visit your CDMO, walk through the facilities, talk to the subject matter experts and the leadership and get comfortable with them from a cultural standpoint."

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The experts highlighted key partnership elements, including transparency, clear communication, and priority alignment between the companies.

Transparency

"Transparency is very important to us and to our cell and gene therapy clients," says Suparna Taneja-Bageshwar, Ph.D., a principal scientist and group leader in virology assay development at FUJIFILM. "CDMOs should always be very upfront about what we are offering, and clients should be clear on exactly what we will be responsible for developing. That's the only way for both parties to be confident at every stage."

Courtney says that in some cases, working with a smaller CDMO like Avomeen can offer unique opportunities for end-to-end process consistency and transparency. "Because we're a smaller organization, the person who develops the initial proposal with the client is the same person who reviews and hands over the final deliverable. So there's no gap between the client's expectations coming into the project and the results they get at the end of the day," she explains.

Clear Communication

Experts stressed that both quality and quantity matter when it comes to communication. The best cell and gene therapies will be produced by innovator-CDMO teams that share process knowledge and check in with each other regularly.

"What we've seen from our gene and cell therapy clients is they want answers very quickly. Answers don't necessarily mean a final analytical result; in many cases, it means timely responding to their emails with project updates, preliminary data, and promptly scheduling how the innovator-CDMO team could reconvene to quickly resolve the issue together," says Courtney.

Priority Alignment

Early conversations to set and manage expectations and priorities are crucial for making a CDMO partnership work. Any development process will contain decision points where it's possible to choose speed over cost or quantity, or vice versa. Clear delineation of developers' and CDMOs' priorities, combined with transparency and communication, makes each of those decision points less stressful and likely more successful.

At the end of the day, both CDMOs and innovators need to be aligned on the number one priority: the patients.

"True success only comes when the innovator is successful in delivering a product that has a positive impact on patients," says Vitelli. "Ultimately, it's about understanding through open dialogue that our objectives are the same."

Implementing the Latest Technologies

Because of their industry-wide perspective, breadth of scientific background in the lab staff, and advanced instrumentation capabilities, CDMOs are often early adopters of advanced technologies. This can lead to significant improvements in processes and therapeutic quality for cell and gene therapies.

"Purchasing the latest technologies, for use from discovery to bioanalytics, gives us so much flexibility to change and influence the cell and gene therapy industry," says Courtney.

"There's an incredible amount of technology coming out of CDMOs to benefit the clients," agrees DeVido. "So much of the gene and cell therapy clinical pipeline is in the preclinical stage, with university spinouts and startup companies, and I think CDMOs are doing a great job bringing technology forward."

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Impressing Regulators

Another key area for leadership and innovation is around managing evolving regulatory frameworks.

"The industry standards for gene and cell therapy so far are way beyond what we've ever seen for other biologic molecules," says Courtney. "When the FDA sees an application that uses a superior assay or other technology, they're going to ask every subsequent applicant to explain why they aren't using that same technology."

Vitelli concurs, zeroing in on *Droplet Digital PCR (ddPCR)* technology as a key advance that regulators are looking for. "The shift to *ddPCR* came from regulators saying that applications showing only qPCR data were not acceptable because of large variation. We can't have something so imprecise used to determine doses. Pivoting to using *ddPCR* for assessing viral titer and other important metrics has increased the reproducibility and reliability of the data, and the product quality at the end of the day."

"*ddPCR* has been added to the cell and gene therapy field because it does not require a standard curve," says Taneja-Bageshwar. "The accuracy, precision, and sensitivity allow us to eliminate uncertainties that we can't afford when producing such delicate products."

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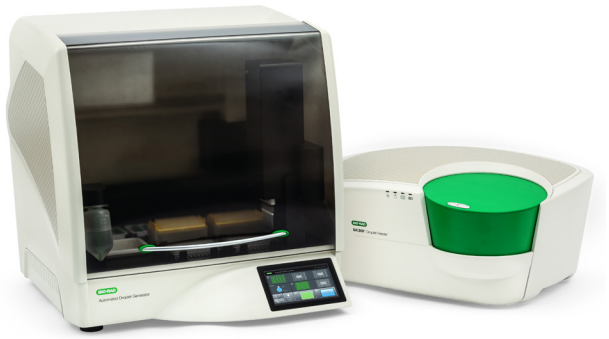

Driving Adoption

CDMOs' early adoption of advanced technologies like *ddPCR* can encourage the innovators they partner with to incorporate those superior technologies into their development workflows.

"I'm always asking clients how they feel about signing on to technology that CDMOs are bringing forward. What's their comfort level? Are they concerned about complications with licensing and so on? It usually depends on the company," says DeVido. "Large biotechs are often already adopting those same technologies themselves, while smaller companies prioritize speed over everything else and are therefore more likely to adopt new advances willingly."