A Customer-Centric Approach to Cell and Gene Therapy Manufacturing

Drew Brennan, Avid Bioservices

Avid Bioservices, a CDMO until now focused on commercial biologics, is expanding into cell and gene therapy. With a new fit-for-purpose facility for viral vector manufacturing currently in the design and construction phase, the company stands poised to fill an observed unmet need in the space by prioritizing a customer-centric approach and emphasizing flexibility while leveraging its exceptional quality record built over 28 years of biologics manufacturing. As many innovator companies grow frustrated with the shortage of available viral vector development and manufacturing capacity, as well as the considerable and often prohibitive costs needed to build internal manufacturing capabilities, Avid offers a chance to outsource to a trusted partner that's also an organizational fit. Drew Brennan, General Manager, Viral Vector Technologies, at Avid Bioservices spoke with *Pharma's Almanac* Editor in Chief David Alvaro, Ph.D., about the drivers motivating the company's entrance into the viral vector space and the unique and differentiating values Avid can offer cell and gene therapy developers.

David Alvaro (DA): What prompted Avid Bioservices to expand beyond your traditional core competencies and explore the viral vector space?

Drew Brennan (DB): The cell and gene therapy market has experienced explosive growth – at approximately 20% year-over-year for the last 3–5 years – with viral vector and plasmid services being in especially high demand. Avid charted this upward trajectory and analyzed the current landscape to determine whether this need was adequately serviced, where there were potential opportunities, and where would we add value to the marketplace. We explored and researched these questions over the last year to determine whether an expansion of our services was the right move for the market and for our customers.

We spoke with many people regarding their experience with CDMOs in the field of viral vector and plasmid DNA, and our key takeaway was that, while capacity continues to ramp up, customer needs are not being fully met. Specifically, we found that quality in late-stage clinical and commercial manufacturing is a major concern.

Cell and gene therapy is a burgeoning market with a lot of investment and capability being built – but it takes more than simply capacity to add value to the customer. Ultimately, it's about the systems in place, including quality systems, regulatory, and

a strong technical group to manage these unique programs. Considering our history and our approach to customer-centricity, we believe that Avid is perfectly positioned to add value to our clients in cell and gene therapy.

DA: What do you see as differentiating Avid from other players in the space?

DB: It all comes down to maturity in manufacturing. Avid has been producing commercial biologic lots for over 15 years with a very strong quality and regulatory record, which contrasts with many of the newer CDMOs in the market that have little or no experience in late-stage clinical and commercial manufacturing. Avid has a stellar track record of consistently producing commercial batches of biologic products with the highest degree of quality that few CDMOs in the cell and gene therapy market can match.

Also, we believe that Avid is of the appropriate size and has the company culture to provide a customer-centric approach, since our organization is much more in line with the size of most of the clients with whom we'll be working. We can also offer a level of flexibility that's not common with other CDMOs.

We believe that this combination represents an unmet need in the viral vector services market, which we know we can address.

DA: I would imagine that this kind of expansion requires a lot of work even before you start building the physical capabilities. Can you tell me about some of the early steps that set the stage?

DB: Building the facilities is the easier part – the key component to ensuring Avid's success is recruiting the right people to fill the right roles in this new organization. Although the company has a long pedigree of GMP commercial manufacturing and a strong quality and regulatory record, we must attract talented individuals with specific viral vector technical experience. We are addressing this through high-quality recruiting in the area of process development and manufacturing sciences, such that we can add technical value to the customer. In fact, we recently announced the hiring of Elie Hanania, Ph.D., our new Vice President of Process Development, to head our technical teams. With nearly 30 years of experience in gene and cell therapy and specifically in viral vector production and analytical development, we are very excited that Elie has chosen to join the Avid team. It will continue to be a huge challenge to onboard the right people in the current environment, but we believe the quality of our message will continue to attract the best candidates.

DA: There's a range of potential approaches and technologies that are available, from the different possible vectors and serotypes within those vectors to deciding whether to pursue suspension versus adherent manufacturing platforms. Can you tell me what Avid has in mind in terms of your focus?

DB: Most of the vectors that are being developed right now are AAVs for gene therapy and lentiviral (LV) vectors for cell therapy applications; Avid will be able to address the large market for both of those viral vectors, as well as others. We are building our viral vector facility from scratch, which affords the opportunity to design in a great deal of flexibility. We will also be leveraging our 28 years of experience in biologics manufacturing and our existing deep talent pool, as well as augmenting the latter with leading talent with experience in both AAV and LV development and commercialization. Ultimately, as with all other services Avid provides, we will be a CDMO that viral vector clients can rely on.

DA: I would imagine that this also requires quite a bit of development on the analytical side of things as well, correct?

DB: Analytical development is the most underrated part of every project related to viral vectors; it's critically important, and we won't be underestimating the need for analytical development. We plan to internalize it, because it's too integral to projects to rely mostly on outsourcing partners. While there may be exceptions for specific assays, for the large majority of analytical methods, we plan on having a team that can work with our customers to develop and validate those methods internally at Avid. That team will include existing Avid analytical development experts augmented by specialists with practical experience in viral vector development and manufacturing, so we will be well positioned to address even the more difficult challenges posed by viral vectors.

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DA: What can you share about Avid's vision and the overall plan for building up these capabilities? What are the early and intermediate steps and the longer-term goals that you're setting the stage for?

DB: Our initial focus is ensuring that we have a high-quality offering in place for the development and GMP manufacturing of viral vectors focusing on drug substance. However, we also plan to offer drug product capabilities at the facility up to a certain number of vials through a semi-automated process. We're looking forward to serving our early clinical-stage customers by providing both drug substance and drug product.

We will introduce process and analytical development services first, so that we can start working with our clients on these development projects initially. Our GMP capability would follow shortly thereafter, so we can again accommodate our customers moving from development into GMP production.

Avid's viral vector business will be housed in a facility in Costa Mesa, California, adjacent to the Orange County Airport and only a 10-minute drive from the existing Avid facilities, and the design and construction have already begun. It will be a standalone viral vector facility for Avid under the Avid Corporate Quality System. We also intend to leverage Avid's existing systems in supply chain, project management, and accounting,

DA: What can you tell me about some of the macro trends within the space that you are following to guide your strategy?

DB: The first trend we're tracking is the improvement of AAV capsids, which will have some significant changes in the next 10 years. We're also closely watching non-viral methods, especially with the onset of mRNA

technology, as well as exosomes, which can be used for gene transfer. I believe there will continue to be a gradual increase in interest and progress in these areas, and we certainly plan to follow these trends closely over the next 5–10 years.

DA: What are Avid's plans for sourcing raw materials, such as plasmids?

DB: Plasmids are obviously a key raw material in the production of a viral vector. Currently, we're concentrating on producing the viral vectors, but we're certainly considering eventually introducing plasmid production and are aware that many companies are fully integrating plasmid and viral vector services. In terms of other raw materials, there's been a shortage in the marketplace that is attributable both to COVID-19 and the explosive continued growth in the market.

Avid has been immersed in biologics manufacturing and is very familiar with the supply chain challenges that have occurred over the past year and a half. I'm confident that we're set up to tackle this issue on the viral vector side, as we would be leveraging the advanced supply chain organization that currently exists at Avid.

DA: Who do you see as the kinds of customers that have the most to gain from partnering with Avid for viral vector services?

DB: Avid can offer a very strong value proposition in terms of organizational fit. Our customer-centric, flexible approach particularly appeals to small and medium-sized biotechs, though we can see potential advantages for clients of all sizes. These customers can rely heavily on the mature manufacturing and quality organizations that exist at Avid, where we have been an effective partner in guiding them through early-stage and late-stage clinical, as well as, ultimately, commercial manufacturing.

DA: Do you see any benefit of adding on the viral vector capabilities that might spill over into your other business?

DB: Yes, I see potential throughout the business, but especially in the production of non-viral vectors, of which some are made in human cells and can be produced within the traditional Avid offering. Anything produced in mammalian cells that are non-viral can be accommodated by our existing service offering. There is some crossover between what we currently do and our upcoming viral vector services.

Quality remains a defining thread that we intend to leverage throughout the organization. While cell and gene activities will take place in a separate building with a process development team with specialization in vector development and scale-up, in terms of the overarching areas of quality and regulatory and supply chain, we're going to be leveraging our significant existing capability.

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DA: What you can tell me about how you see the market potentially changing, both for your customers and within the CDMO space for viral vectors? Where do you anticipate Avid will be positioned in the near term?

DB: As we reflect on recent trends, gene therapy innovator companies building internal manufacturing capabilities stands out. I think one of the motivating factors behind this is a level of frustration with the current CDMO offerings. At more established CDMOs, the lack of capacity is certainly an ongoing issue, which can result in delays getting projects into development and GMP. These innovator companies also lack trust in the ability of some of the smaller CDMOs emerging from academic labs to carry them through to GMP manufacturing and effectively produce their product with the level of quality required for clinical and commercial use.

This level of frustration has led innovator companies to build internal GMP capability, which can be a significant risk because of high start-up and ongoing operational costs, which are often underestimated and which these companies will carry forward. Our goal is to make the decision easier for the innovators to choose to outsource their manufacturing needs, enabling them to focus on creating cutting-edge cell and gene therapy products and to trust a company like Avid Bioservices with its legacy in high-quality commercial manufacturing to scale up and manufacture their products for the benefit of patients worldwide.

ABOUT THE AUTHOR

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Drew Brennan is the General Manager, Viral Vector Technologies at Avid Bioservices, a biologics CDMO based in Tustin, CA. Drew has a B.S. in chemical engineering and an M.S. in cell biology from Rutgers University. Drew began his career developing perfusion bioreactors for monoclonal antibody production before moving into business development. Over his career, he has been responsible for sales of consumables, capital equipment, and CDMO services. In his previous position at Novasep, he was the General Manager of the U.S. sales subsidiary responsible for all Novasep products, including chromatography equipment, chemical synthesis CDMO services, and viral vector CDMO services.

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