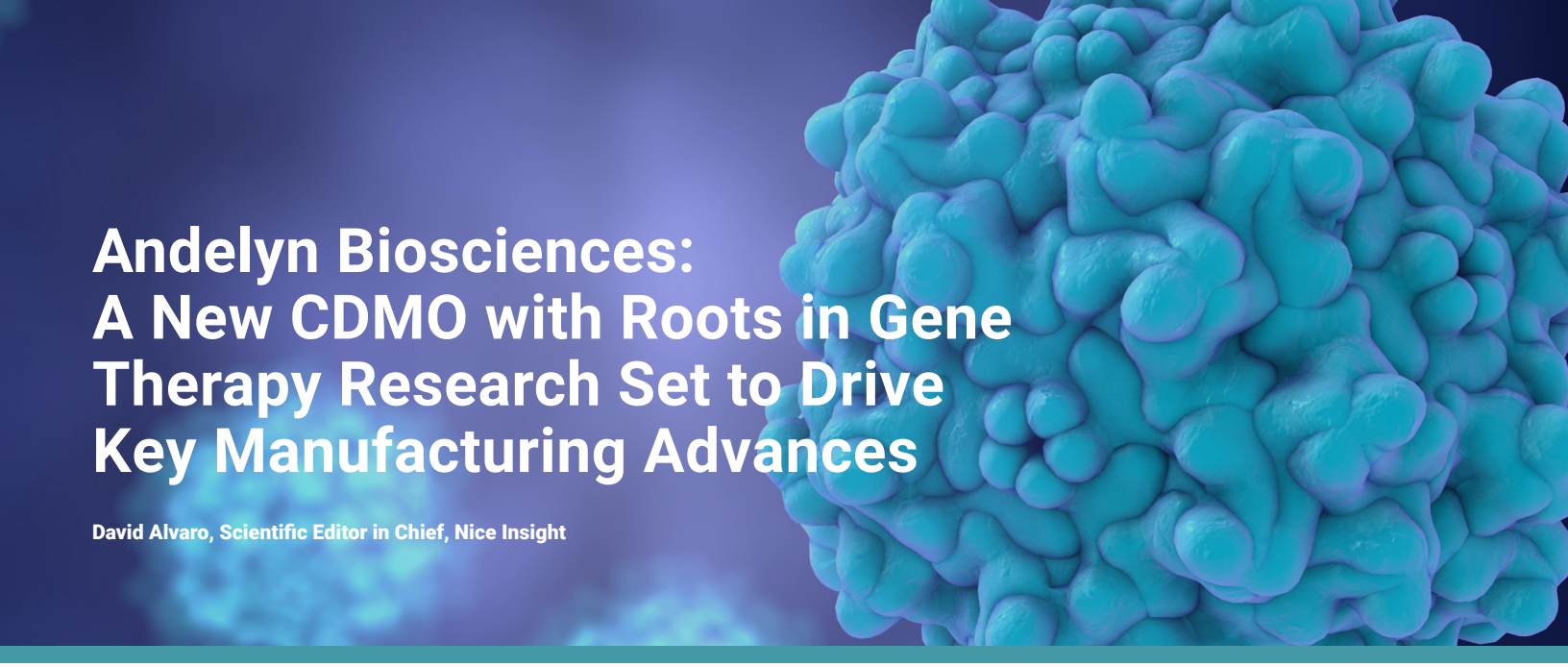

Andelyn Biosciences: A New CDMO with Roots in Gene Therapy Research Set to Drive Key Manufacturing Advances

David Alvaro, Scientific Editor in Chief, Nice Insight

Andelyn Biosciences, a full-spectrum gene therapy CDMO organization that supports clients from preclinical studies through phase III trials, originally spun out of a GMP core established to enable gene therapy clinical programs operating out of Nationwide Children's Hospital. Over the following 15 years, the company has leveraged the expertise acquired through the hospital's gene therapy programs to support the full range of outsourcing services required by other gene therapy developers.

Pharma's Almanac Scientific Editor in Chief David Alvaro met with Andelyn's Chief Executive Officer Mayo Pujols and Chief Operating Officer Wade Macedone to discuss the challenges facing gene therapy developers and how Andelyn's history and unique perspective help drive innovation in the sector.

David Alvaro (DA): In your view, *what are some of the key challenges to the advancement of the gene therapy field? What steps might be taken to address them?*

WADE MACEDONE (WM): The lack of capacity in the field is an issue, as is the logistics of dosing patients. There are very few organizations with the necessary supportive capabilities. It also remains a challenge that gene therapies must bring the patient to the product, as opposed to bringing the product to the patient, which is the case for most other kinds of therapies.

Pricing is also a major point of contention. There are only a few indications – hemophilia, diabetes, sickle cell disease – that presently make any sense to the insurance industry. It's difficult to support specialized gene therapies unless you have the advantage of being able to demonstrate that the gene therapy will reduce medical costs over time. It's a debate that the industry needs to work on, and the ultimate success will probably require solutions in many different areas.

Improving production yields can help increase capacity and drive down costs. Ideally, a cookie-cutter approach, such as what is typical for small molecule generics, would make gene therapies valuable and more affordable to customers in healthcare. However, getting there will be a huge undertaking.

MAYO PUJOLS (MP): The technologies, the know-how, and the shifting platforms that we will see in the next few years are going to enable gene therapies to be mass-produced in a manner analogous to vaccines. Processes are going to be scaled, while platforms will shift from very-small-scale, very-low-yield processes to more efficient, higher-yielding solutions via the development of better cell lines, improved plasmids, larger equipment, and better-designed processes that are ultimately scalable so that we can treat more people.

DA: Can you tell me more about *the genesis and the original vision for Andelyn Biosciences? Have there been some inflection points where the vision evolved?*

MP: This business was started 15 years ago by physicians at Nationwide Children's Hospital that believed in gene therapy but could not find a contract manufacturer that would take on this type of project. It initially provided clinical trial materials only to the hospital, then to other academic centers and hospitals and foundations looking to treat a dozen or fewer patients, and eventually to biotech and biopharma companies.

WM: Nationwide Children's physician–scientists collaborated with hospital and research

Being flexible and approachable and having that patient-centric philosophy goes a long way with our customers. Our compassionate approach coupled with our considerable technical expertise separates us from most of our competitors.

institute leadership to create a small GMP facility to produce viral vectors for gene therapy clinical trials. Having this resource accelerated the hospital's gene therapy program and helped bring some of the brightest minds to Nationwide Children's.

In 2017, the Abigail Wexner Research Institute at Nationwide Children's opened a larger cGMP Clinical Manufacturing Faculty (CMF). Research-grade plasmids were first offered in 2019, and in 2020 a larger bioreactor was added, and manufacturing capability was expanded from phase I and II to include phase III. That year, Andelyn Biosciences was spun off as a standalone entity.

The original vision for that first small GMP facility was to be the GMP core for Nationwide Children's Hospital supporting their early-phase trials. At that time, we were transferring projects to external service providers once they moved beyond phase IIa. but many customers were coming back to us asking for support through phase III.

That led to some internal discussions. We recognized the capacity issue in the industry, and the hospital leadership felt that it was important to do everything possible to bring products to patients in an expedited manner. Today, we're nearly on our tenth phase III audit with customers.

DA: Do you feel like Andelyn Biosciences' history and the unique perspective it has given you confers real benefits to both the company and your customers?

WM: It is a huge benefit, especially to smaller organizations. Most of these programs start small, and, when they become big, they are acquired by a larger biopharma company. That is what the hospital wants – to get those products to market to help patients.

It also makes a difference in attracting and retaining talent for Andelyn. Our organization wholeheartedly believes in that mission, and it keeps people motivated. Money is one thing, and work–life balance is another, but when you tie what we do to a child's life, an adult's life, the work becomes even more impactful. It's quite amazing – if you ever need something to bring you into work every day, that's it.

Additionally, we are often recommended by physicians that have worked with us before. They are familiar with the breadth of our expertise with different serotypes and our ability to support projects from the concept stage forward. That long history with physicians can be really beneficial for all involved.

DA: What different kinds of customers is Andelyn Biosciences currently working with, and how do their needs vary?

MP: The ideal collection of customers for Andelyn is a balance between academia and foundations and biotech/biopharma clients, the latter of which ranges from very small, virtual biotechs to global companies.

As we build additional capacity, we want to ensure that we are fully able to support clients that are a little further along, in phase II or III, and advancing into larger trials to become commercial products. We want to attract those clients without losing sight of the earlier-stage clients we have historically served.

Most of our current clients started with us when they were looking for help producing early research and tox batches that went into their first IND. Once they saw that we had the capability, they had us make phase I and then phase II material for them. Now, we are making phase III material for some of them, and, if they get approved, we will likely be their commercial manufacturer.

WM: I'd love to have large strategic organizations that book out capacity and reserve our rooms, but I don't want to see any room go idle from a manufacturing standpoint. We have targeted a 75% operating efficiency, where our facility will be running 75% of the year. The rest of it should be in changeover from one product to the next or shut down from a project management perspective.

To achieve that, we are in discussions to establish strategic partnerships to help us meet the needs of smaller customers. The idea is that "customer A" can reserve suite 1 for the entire year, even if there will be a few weeks not needed, but those weeks will be filled with other customers' projects, and the time will be charged to those customers.

MP: In terms of what clients need, smaller companies that are just starting out require basic services: the studies required to support their first IND. We've done this about 60 times, so we know what's necessary for an IND. We can guide clients in writing it, provide them the list of studies they'll need to do, and execute the studies for them. We understand the path they need to take to get a product approved and into the clinic.

Larger companies are looking for a partner that has the capacity, reliability, and reputation they can really trust. Sometimes they can't produce enough in-house and come to us for backup capacity and sometimes they need extra batches if more material is needed. And, of course, we continue to produce clinical material for Nationwide Children's Hospital.

DA: Beyond the experience and unique perspective you bring to the table, what else would you identify as the key differentiators for Andelyn Biosciences in the gene therapy CDMO space?

WM: Being flexible and approachable and having that patient-centric philosophy goes a long way with our customers. Our compassionate approach coupled with our considerable technical expertise separates us from most of our competitors. Our connection to Nationwide Children's Hospital is also a huge differentiator. Most CDMO counterparts don't have clinical experience and can't advise on the clinical aspects.

Our experience from the last 15 years is truly unlike that of any other CDMO. For example, few competitors have the serotype experience we do. Every serotype, every indication is different. Every serotype delivers a different payload to a different muscle, for a different approach. AAV9 and rh74 seem to be the most popular serotypes, and there are several organizations that can support those kinds of projects, but it can be a real struggle to find support for any others. We have considerable experience with about 15 different serotypes within Andelyn, from AAV2 to rh74 and everything in between.

Another differentiator is our new facility, which was designed to be fully unidirectional for people, product, and waste. It is 100% fresh air through the facility in each one of

the suites, so that changeover is an engineered effort and not a theoretical concept. It wasn't the cheapest way to build a facility, but it is the most robust. Each suite operates independently, and therefore, unlike what occurs with a ballroom approach, a hotspot in one suite does not halt operations in the entire facility.

MP: Our employees are a real differentiator for Andelyn. We have folks that were here 15 years ago that have the deep know-how that comes with having worked with so many programs and encountering and solving many different issues. They can easily help clients address challenges ranging from low yields to quality concerns.

The other piece is our "white glove" service. We offer very personalized support with respect to meeting customers' needs. Each client gets a personal program manager that intimately knows the specific process and the customer's needs, schedule, and deliverables.

With our history and expertise, we definitely bring things to bear that our competitors cannot, including real flexibility. Because we're small and nimble, we can move things around and find novel solutions to meet people's needs, which often isn't the case with big companies, where slots need to be booked six months to a year in advance. If they're in a rush, we can do a lot more.

Another big differentiator is that we are currently moving into the plasmid manufacturing space. Once that is operational, we will be able to offer support from this key starting material through to viral vector and final product manufacturing.

DA: ***How important are strategic partnerships to your current operations and your future plans?***

MP: Partnerships make it possible for customers to work not just with Andelyn, but with other industry leaders. We recently entered into a partnership with Danaher, which owns both Pall and Cytiva (previously GE Life Sciences). We also have an existing partnership with Corning Life Sciences.

These partners help us to address key production pain points and improve the efficiency, economics, and scalability of our processes. We establish a competitive edge by staying at the forefront of innovation and gaining access to enabling technologies. Our partners benefit from the opportunity to develop and showcase solutions for a wide range of customers with many different issues.

As a result, our customers essentially work with a much broader team than just Andelyn alone. We believe that this approach will attract customers that not only want a reliable and knowledgeable CDMO but want a partner that has an eye to the future and is positioned at the cutting edge of manufacturing technology. We not only have people that truly understand gene therapy development and manufacturing, but also the technology and the partnerships to complete even the most challenging projects.

DA: ***What can you tell me about Andelyn's objectives and strategic goals over the longer term and your ultimate vision for the company?***

WM: Our strategy is to control as much of the supply chain as possible – front end and back end. What tends to require the longest time across the industry now is plasmids – critical upfront raw materials. So, we've taken the initiative to produce research-grade plasmids and are now in the process of getting FDA approval to manufacture phase I/IIa plasmids for our clients. It really comes back to that 75% operating efficiency. If we're going to utilize our capacity, we need to control that critical raw material upfront.

The back end is just as bad; lead times at contract testing organizations can be tens of weeks. To combat this, we are building out our analytical development and quality control laboratories. We've already doubled the capacity in the current facility and are adding capacity to the new build so that we don't have to outsource and can shrink our throughput time.

MP: Given that the industry is moving toward the development of gene therapies that treat indications with very large patient populations, we are also making investments in our new facility so that we have the capacity to produce millions of doses and not just a few hundred or few thousand. We'll definitely be in a unique place to provide that support.

Our journey is going to be very interesting in many ways. I see us becoming a premier CDMO not only in the vector and gene therapy spaces but also in cell therapy and other areas that need these vectors -- and doing so in a way that continuously drives innovation. Five years from now, we will be much more mature. With the new facility, we will be a showcase site for Pall, Cytiva, and Corning. That will make us a very attractive choice, and my hope is that we'll become a household name.

When I joined Andelyn, we had a mission and vision that was created by the committee at the hospital, by the communication team, to be the most reliable, quality-minded, and knowledgeable CDMO. While that is true, it doesn't reflect who we really want to be and what wakes us up in the morning.

Andelyn is a pioneer in the development of gene therapy production processes. We are not the doctor but the treatment enabler. We do this work because we know there's a child or an adult or a family who's getting that treatment and the hope it brings; that has always been our motivator. Being both mission- and vision-driven will help us continue to drive the gene therapy field even further forward.

ABOUT THE AUTHORS

Mayo Pujols, Chief Executive Officer, Andelyn Biosciences

CEO Mayo Pujols has led Andelyn's expansion to a full-service gene therapy CMO since joining the company in May 2020. He's been in the pharma and biotech industry for more than 25 years, including more than five years focused exclusively on cell and gene therapy. Before Andelyn, he led the Global Cell and Gene Technical Development and Manufacturing Division at Novartis, building a global manufacturing network and product pipeline. His experience also includes leadership roles at Celgene, Merck, and MedImmune.

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Wade Macedone, Chief Operating Officer, Andelyn Biosciences

Chief Operating Officer Wade Macedone oversees operations, development, manufacturing, quality, supply chain, and technical affairs for Andelyn, bringing more than 25 years of experience in the pharmaceutical industry. He previously served as Executive Director of Quality and Analytical Development at West-Ward Pharmaceuticals, and before that spent more than 20 years at Boehringer Ingelheim in a variety of leadership roles.

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