

Leveraging Partnerships and a Unique History to Address Supply Chain and Capacity Challenges in Gene Therapy Manufacturing

By **Wade Macedone** and **Adam Lauber**, Andelyn Biosciences

Andelyn Biosciences has established a unique network of industry experts across the entire development and commercialization spectrum. In addition to historical connections to Nationwide Children's Hospital and the Abigail Wexner Research Institute, the company has added strategic supply agreements/partnerships with Corning Life Sciences and Danaher portfolio companies. As a result, Andelyn has a stable supply chain, real-time access to advanced production technologies, accelerated capacity expansion capabilities, a steady stream of new projects, an expanded brain trust for problem solving, and access to experienced clinical trial operations. This enables the company to offer the flexibility and personalized service of a smaller outsourcing partner – but with security of supply chain well beyond what is typically possible for a company of our size.

Current State of the Biopharma Supply Chain

The supply chain is currently unstable and unpredictable across all industries and markets. The simplest items needed to make starting materials or basic equipment components are in short supply. In the biopharmaceutical industry, those shortages have impacted the quantity and quality of supply. For instance, at Andelyn Biosciences, before we established our current strategic alliances, it was not uncommon to receive several pieces of equipment from a supplier, only to discover that one-quarter of the pieces did not function to specification.

The key issue driving the supply shortages for Andelyn is Operation Warp Speed, the U.S. government program focused on accelerating the manufacturing of COVID-19 therapeutics and vaccines. COVID-19 projects have priority from supply chain and legal perspectives. The supply of non-COVID projects comes second, and the industry's current resistance to accept any amount of risk will eventually lead to more frequent halted production operations.

Limited Options and the Need for Change

The biopharma industry is still relatively young, and thus extensive supply chains for many typically thought of as non-essential ingredients and components are limited to just two or three players with any measurable level of capacity. That leaves limited options. As a result, very few manufacturers have multiple suppliers for nonessential materials and typically single-source them.

Most gene therapy manufacturers have been stockpiling media and other consumables to support their clinical production needs in order to avoid any process changes. The need to demonstrate bioequivalence of materials from different suppliers – and the uncertainty around how to do so for next-generation therapies – has created significant hesitancy among drug manufacturers and their customers. There is real fear of change, the inability to justify the need for it, and the risk of losing data.

Given the current state of the supply chain and the limited capacity available, however, those fears about the risks of change have to be weighed against the potential of program stoppages. Even companies who have stockpiled materials for the production of clinical trial materials will need to make changes in order to move into post-approval commercial manufacturing. One consequence will be a dramatic increase in business for organizations that are able to perform bridging studies for the demonstration of equivalency of gene therapy processes and products.

Fortunately, the industry is recognizing the strain that the current state of the supply chain is placing on the potential for future manufacturing of cell and gene therapies and the urgent need to find a risk-based approach for bridging between materials, components, part numbers, and other things that won't impact efficacy, dosing, or product identity.

The Benefits of a New Strategic Partnership

Andelyn Biosciences realized in the midst of the COVID-19 pandemic the potential for significant ongoing supply chain issues and sought strategic partners that could help alleviate concerns around access to consumables and equipment. The result of that search was a strategic partnership with

Pall Corporation and Cytiva, which are both businesses in the Danaher portfolio, and a significant minority investment from Pall Corporation into Andelyn Biosciences.

Having a strategic supply agreement with Pall and Cytiva – Danaher essentially – and being able to leverage a preferred or tier 1 customer status is a tremendous advantage for a company the size of Andelyn. Generally, that level of supply chain security is only achieved by behemoth CDMOs with buying power and the ability to demand to be served first. *Being able to offer the flexibility and personalized service of a smaller outsourcing partner combined with security of supply places Andelyn in a unique position to effectively serve the gene therapy market.*

The strategic partnership, in addition to providing stability in terms of the supply of consumables and equipment, also assures access for Andelyn to innovative technologies as they are developed and rapid technical support when issues arise. We provide real-time feedback on performance issues for Pall, Cytiva, and other Danaher companies (e.g., Beckman Coulter) – on consumables, equipment, firmware, and software. As a result, Andelyn is able to take real-life hurdles in production yields, efficiencies, and productivity and change them into activity-driven items within Danaher to make equipment changes and optimizations to improve processes almost in a real-time

state. Clive Glover, General Manager, Gene Therapy at Pall Corporation said, “The combined expertise and capability of Pall, Cytiva, and Andelyn to address today's supply chain issues is unmatched. Our collective technical bench-strength and global supply chain reach has already started to provide invaluable advancements to the industry.”

One area of particular interest is increasing the yields of cell and gene therapy manufacturing processes, which are typically low. Boosting yields would drive up efficiencies and drive down costs and thus reduce pricing and enable provision of more of these medicines to patients. The Danaher companies can use Andelyn's direct feedback to develop more integrated, patentable solutions that will benefit their customers, including Andelyn, and give them a market advantage.

The strategic supply agreement with Pall and Cytiva is also accelerating the startup of our new 185,000-ft² manufacturing facility in Columbus, Ohio. An optimized workflow for the specific equipment needed in each manufacturing suite and a favorable purchasing structure have contributed to much less risk and reduced timelines. For instance, Pall has reserved capacity at its UK and Massachusetts production sites to help Andelyn scale to 2,000 liters. This will decrease overhead, material, and labor costs to drive up efficiencies.



In November 2020, Andelyn broke ground on a new 185,000 square foot facility that will include eight customizable product manufacturing suites, six plasmid manufacturing suites, and two suites for the fill-finish of product and plasmids.

Rather than our initial launch date of January 2023, we are now aiming to begin operations in July 2022, which meets the needs of many of our customers for earlier manufacturing capacity in that facility. To have that investor come onboard in March of 2021 and supply equipment so the facility can be launched in under 18 months is practically unheard of. Having the strategic relationships with these suppliers in place is enabling the project to come to fruition much more quickly than we ever thought possible.

Adding to the Advantages of an Existing Relationship

Before formation of the strategic partnership with Pall and Cytiva, Andelyn Biosciences was involved in a partnership with Corning Life Sciences that remains extremely strong today. This partnership focuses on adherent bioreactors and Corning® HYPER-Stack cell culture vessels. We do extensive beta testing for Corning on next-generation HYPERStacks and other adherent bioreactors, the results of which are published. This research with Corning is geared toward bringing more efficient and effective manufacturing solutions to the market and also benefits Andelyn in terms of real-time process and yield improvements. "Corning is determined to support customers such as Andelyn Biosciences, who are conducting critical, life-changing work, during these extraordinary times," said Lydia Kenton Walsh, Vice President of Commercial and Business Operations for Corning Life Sciences. "This is a great example of working together to problem-solve, strategically addressing short-term supply needs, as well as increased security for both organizations through longer-term agreements."

Achieving Speed to Increase Scale and Capacity for Clinical Viral Vector Manufacturing

Another strategic partnership that is accelerating the installation of greater capacity for Andelyn Biosciences is a relationship the company has established with the landlord of our new development facility, which is separate from the new manufacturing facility.

With the Andelyn Development Center, we aim to provide the capacity and scale currently lacking for the production of early tox and preclinical materials that are needed to facilitate entry into the clinic

Being able to offer the flexibility and personalized service of a smaller outsourcing partner combined with security of supply places Andelyn in a unique position to effectively serve the gene therapy market.

for new startups. It will have ~10 times our existing capacity and scale at the Abigail Wexner Research Institute (AWRI) at Nationwide Children's Hospital (NCH) and be operational in Q1 2021. We signed the lease in August 2021, and the rapid build time was made possible by this partnership with our landlord, Van Trust.

Overall, Andelyn has increased current clinical production capacity by 40% over the last year, added additional larger-scale capacity coming online in our existing facility in Q4 2021, further significant large-scale and commercial capacity coming online in Q2/Q3 2022 at our new facility, and a plethora of early-stage development capacity coming onstream in Q1 2022. That capacity is combined with the supply chain security achieved via our strategic partnerships, which provide stable access to media, plasmids, consumables, equipment, software, and much more. As a result, we are positioned to immediately accelerate the development and commercialization of cell and gene therapies for early- to late-stage players.

Building in Flexibility

With the demand for viral vector and related production capacity greatly exceeding supply, it is tempting to expand capacity by leaps and bounds. Andelyn has taken a more pragmatic approach, implementing expansions at the development and large scale in phases so that market evaluation

can guide further investments.

The goal was to build sufficient flexibility so that, once a certain stage of capacity utilization is reached, we have the ability to expand without disrupting current operations. The facilities are also designed with a multi-use approach to enable repurposing if the need arises.

We have a shell adjacent to the new large-scale facility within which we can place additional assets – to the extent that we have visibility into the market and as dictated by equipment lead times – which gives us the ability to pivot and populate additional space as needed and accommodate significant future growth as warranted.

Andelyn also has focused on maximizing the use of our equipment, building in the flexibility to rapidly pivot from one project to the next in order to support customers of all sizes. Stabilization of our supply chain has been a key factor here as well. We can guide and direct customers regarding the materials they will need.

For instance, for a viral vector, GMP plasmids need to be ordered six to 10 months in advance. In particular, we can help early-phase customers navigate supply-chain planning. The extremely tight supply chain for plasmids has, in fact, led us to bring plasmid production in-house in order to increase our supply chain control and facility manufacturing utilization.

A New Plasmid Link

One of the reasons gene therapy developers in particular aren't getting programs into the clinic as quickly as they would like is a lack of understanding regarding the time required to obtain plasmid raw materials. For that reason, Andelyn has been producing research-grade plasmids for the last two years and established technical expertise in plasmid production. We are currently investing time and capacity for clinical-grade plasmid manufacturing, which will be operational in early 2022.

In addition, Andelyn is excited about Danaher's recent acquisition of Aldevron. We are looking forward to partnering with another Danaher portfolio company that can give us some added traction within the tight plasmid supply chain. While it will take some time to work out the details, there is no doubt that our partnership with Danaher will be strengthened through this additional avenue.

Leveraging 15 Years of Experience

Andelyn Biosciences was started 15 years ago by physicians at NCH who 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.

During those 15 years, we have established significant experience in change management and supported more than 150 customers. Our affiliations with the AWRI and physician investigators (PIs) at NCH continue to be invaluable resources as well. With everyone's input, we drive stability with educated changes driven by educated risk assessments.

In the last 12 months, we have built on our existing expertise with the addition of approximately 100 experienced and talented people. Our exciting, mission-based business model has attracted a leadership team from across the industry. We also have working partnerships with Columbus State University and Ohio State University and other organizations in the greater Columbus, Ohio area to develop and enhance our workforce development.

Ongoing Clinical Connections

Our history with and relationship to NCH and the AWRI (NCH is the major shareholder) provide tremendous value for Andelyn and our customers. We have the ability to do tox and IND-enabling studies combined with access to PIs for clinical trials.

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.

Additionally, when PIs in the hospital develop new treatments, Andelyn manufactures the clinical trial batches. The vast majority of successful candidates, although licensed to a third party, stay at Andelyn, because they can leverage the established knowledge base and avoid the need for tech transfer.

Furthermore, how a clinical trial – and specifically the patient and family – is handled for a gene therapy trial is completely

different than how a traditional biologic or small molecule is managed. The knowledge and infrastructure required for its success is quite complicated, but NCH/AWRI has been executing these studies with success for more than 15 years. There is more involved in the logistics of the patient and family than just supplying the product. Having that link to the AWRI and NCH and the specific know-how of the researchers and physicians is a huge advantage for Andelyn, its customers, and patients.

Comprehensive Solution-Focused Network

Andelyn will continue to expand its network to be a competent, full-service solution provider for its customers and patients. We are leveraging our connections with NCH and AWRI, with PIs developing new candidate gene therapies for existing and new indications, and the regulatory group. This network of subject matter experts and their expertise has likely produced more INDs than

any other organization in the world.

The strategic supply partnerships with Pall, Cytiva, and Corning are helping us ensure stable access to key raw materials, single-use components, and processing equipment. Our partnerships with the Danaher portfolio companies and Corning Life Sciences are also helping Andelyn address processing issues and identify opportunities for increasing process efficiencies and productivity through both stepwise and breakthrough technology advancements.

We also have an all-hands-on-deck approach to problem solving from Andelyn Biosciences, the Abigail Wexner Research Institute, and Pall corporation to support our customers' needs. There is a true brain trust available for the most complex problems. *It isn't just Andelyn at this point, but a connection of industry experts that cuts across the entire development and commercialization spectrum. Such a comprehensive network does not exist for any other cell and gene therapy CDMO.* ●

ABOUT THE AUTHORS



Wade Macedone
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.

LinkedIn: www.linkedin.com/in/wademacedone/



Adam Lauber
Chief Financial Officer

Adam Lauber joined as Andelyn's Chief Financial Officer in 2020, bringing a successful track record of managing aggressive growth and successful liquidity events in the outsourced pharma services sector. He started his career with Deloitte's Assurance practice, before joining as the Controller of a WI-based API manufacturer. Over the next decade, he would oversee the company's massive growth to become the diversified integrated global CDMO, Alcam Corporation.

Adam received his undergraduate degree in Accounting, Finance, Investment, and Banking from the University of Wisconsin, Madison, where he also received his Master's of Accountancy.

LinkedIn: www.linkedin.com/in/adam-lauber-58335110/