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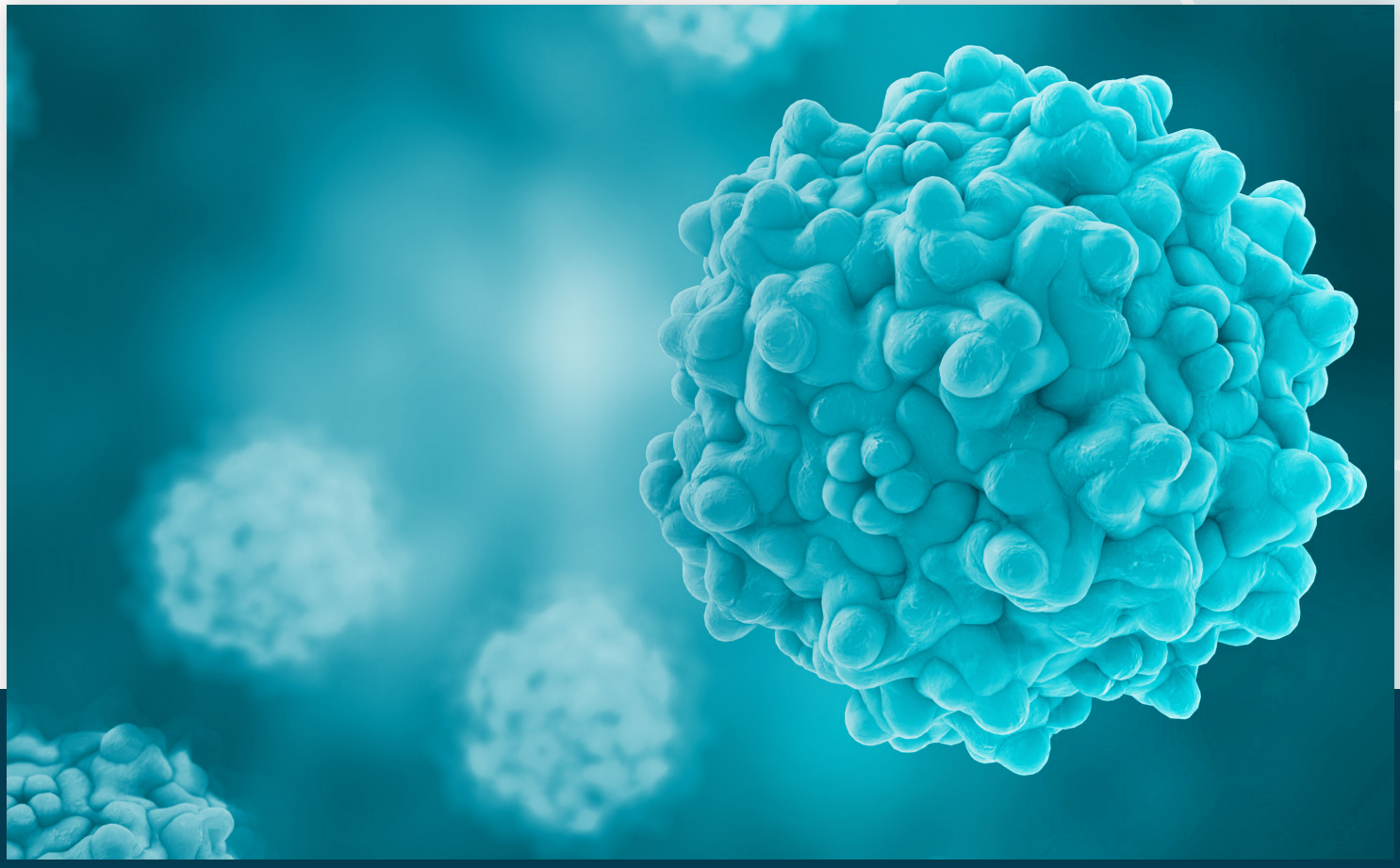

WHITE PAPER

Reducing Risk For Commercial Manufacturing Of Cell And Gene Therapies

By Cyrill Kellerhals
Head of Manufacturing, Andelyn Biosciences

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For any biotherapeutic in development today, a critical element in achieving commercialization is reducing manufacturing risk. Serving as many patients as possible as quickly and resourcefully as possible requires particular focus on three key areas:

Manufacturing

Process Development

Quality Control

Andelyn Biosciences, a gene therapy CDMO spun out of Nationwide Children's Hospital, has amassed the necessary expertise to support complex biologics in achieving late-stage manufacturing readiness by working across these key areas to establish interconnected, optimized manufacturing processes. With three facilities in the Columbus, Ohio area – a plasmid facility on the campus of Nationwide Children's, a new GMP manufacturing facility, and a development center in nearby Dublin, Ohio – Andelyn has the capacity and expertise to provide end-to-end development and manufacturing services.

Andelyn's long and pioneering history with gene therapy modalities and adeno-associated virus (AAV) therapies – researchers at Nationwide developed Zolgensma, the first systemic gene therapy approved by the FDA – enables it to leverage its legacy of expertise for accelerated and agile development and scale-up. Its CDMO services are structured around four core pillars:

Starting Materials
including research, tox, and GMP plasmid manufacturing

Development
including process development, tech transfer, and process optimization

Manufacturing
including research, tox, and GMP of adherent and suspension processes of up to 2,000 L

Fill/Finish
including program-specific fill volumes and vial configurations, CZ vials, and primary labeling and packaging

Leveraging Critical Control Strategies to Optimize Late-Stage Manufacturing

Andelyn has positioned itself for agility by performing the majority of its testing in-house and establishing redundancy for some of its equipment between its development activities and GMP manufacturing. For example, Andelyn utilizes the same bioreactor platforms in its process development lab and manufacturing facility, enabling one-for-one tech transfer for a process. The close proximity of its Ohio facilities also means that involved teams can collaborate very closely during tech transfer activities and establish a cross-functional understanding of how an application performs in both settings. Its manufacturing activities, which encompass adherent and suspension platform and its fill/finish capabilities, both manual and semi-automated, round out a comprehensive approach to end-to-end scale-up and commercialization. Its quality assurance organization oversees every phase of production in these facilities, and its regulatory support experts are on hand to verify every stage of scale-up.

Andelyn's proven platform for industrialization is built on decades of experience in development and GMP manufacturing. It leverages a Design of Experiment (DoE) -based approach to optimize production parameters; this has enabled Andelyn to establish a platform capable of maintaining titers across multiple scales, from 125 mL flasks to 2,000 L bioreactors. With the flexibility to accommodate multiple serotypes and consistently high yields, recovery, and purity across scales, Andelyn can ensure seamless scaling from preclinical to commercial.

The technical challenges that accompany process development and scale-up demand comprehensive strategies. At Andelyn, operators leverage ICH Q8, Q9, and Q10 guidelines as a foundation for its product development and commercialization. It then works closely with clients to foment a strategy tailored to their process performance qualification (PPQ) or biologic license application (BLA) goals. The phase-appropriate approach Andelyn takes for Q8 includes developing a comprehensive process map and description, establishing an analytical testing strategy, performing

raw material assessment, outlining a raw material strategy, performing Process Failure Mode and Effects Analysis (PFMEA), and establishing process controls. For Q9, Andelyn focuses on performing risk assessment, establishing risk visibility across the organization, and creating a business continuity plan. Finally, its Q10 approach is supported by a common electronic platform for managing change control, deviations, and documentation, as well as quality culture initiatives, environmental monitoring, internal audits, supplier management, training, and a quality council.

Ultimately, Andelyn is able to create a vigorous manufacturing paradigm for its clients by following a quality-by-design approach that leverages modular and customized platforms alongside high-throughput technologies and robust analytics. By employing FMEA studies, analytical method qualification, scale-down models, intermediate and media stability, and DoE studies, Andelyn is able to focus on critical parameters to help clients arrive at the optimal end product and manufacture it consistently and at various scales in an expedited and cost-effective manner.

ABOUT ANDELYN BIOSCIENCES

Andelyn Biosciences is a full-service cell and gene therapy CDMO focused on the development, characterization, and production of viral vectors for gene therapy. With more than 20 years of experience, Andelyn's deep scientific expertise has resulted in the production of cGMP material for more than 450 clinical batches and 75 global clinical trials. Andelyn supports customers developing curative cell and gene therapies from concept through plasmid development and manufacturing, process development, and cGMP clinical and commercial manufacturing. Its versatile capabilities include cGMP manufacturing capacity for both adherent and suspension processes up to a 2,000-liter capacity. An advanced digital model, quality system, full regulatory support and supply chain vertical integration help Andelyn accelerate the development and manufacturing of its clients' innovative cell and gene therapies.

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For more information, visit andelynbio.com.