Simplifying Progress

Building an AAV8 Platform, Together: Lessons From a Collaborative Development Journey

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Forewords

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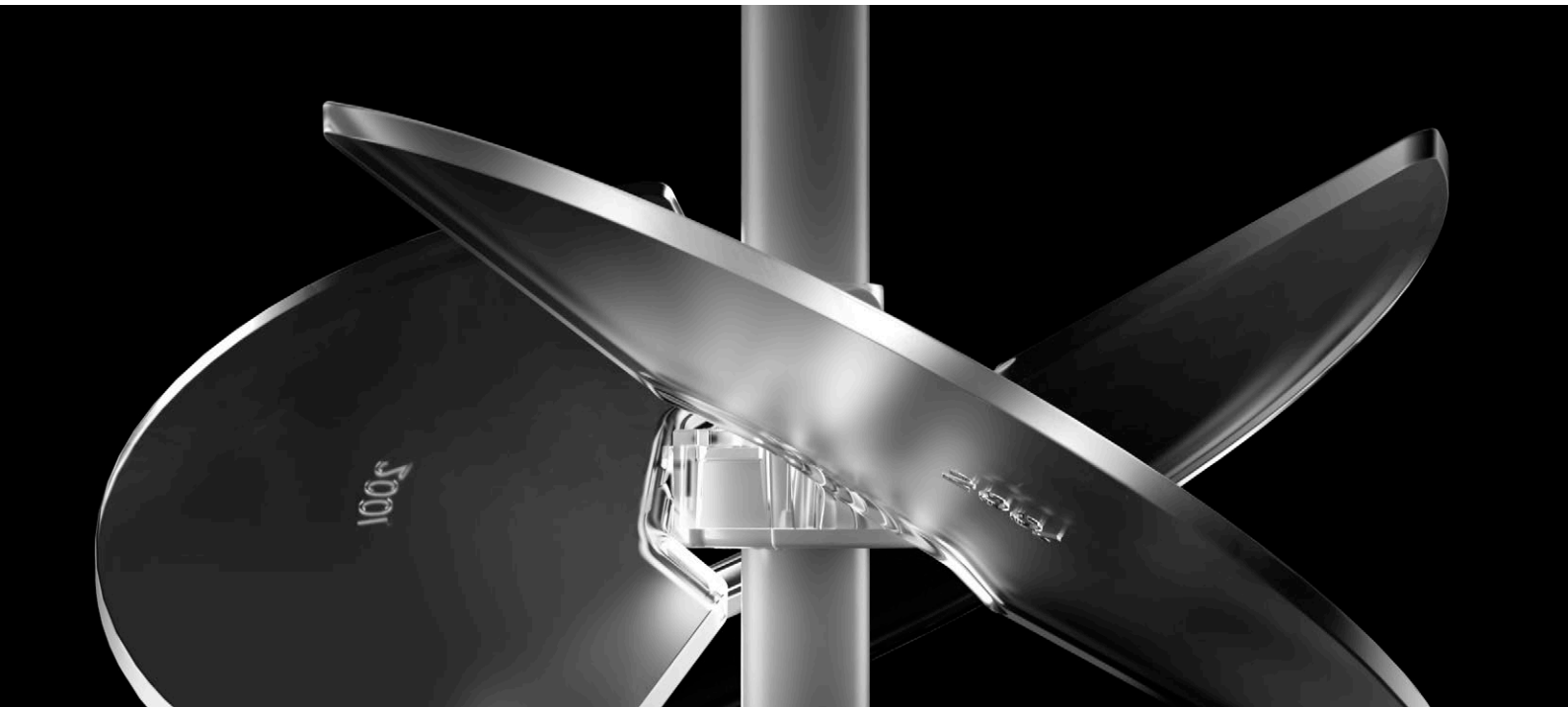
Developing a robust and scalable AAV8 production platform is no small task. It requires careful alignment across upstream and downstream operations, rigorous process development, and the ability to move efficiently from small-scale experiments to manufacturing-relevant volumes. At Matica Biotechnology, we undertook this challenge with the goal of establishing a flexible, end-to-end process that could support our clients' therapeutic programs at both clinical and commercial stages.

This project with Sartorius focused on building and demonstrating an AAV8 platform capable of scaling to a 50 L bioreactor system, while maintaining performance consistency and meeting quality expectations. To accomplish that, we combined our internal expertise in viral vector manufacturing with external technologies and services that allowed us to move quickly and systematically through process design, optimization, and scale-up.

One of the key aspects of this collaboration was the ability to manage complexity without compromising control. From upstream transfection and culture optimization to clarification, tangential flow filtration, and chromatography, we implemented a sequence of well-characterized unit operations that delivered reproducible outcomes and meaningful process insights. Throughout this effort, our team maintained a strong focus on scalability, analytical rigor, and practical implementation.

The work summarized in this white paper reflects the result of a structured, cross-functional approach to platform development. It provides a transparent look at the technical decisions, process performance, and lessons learned along the way. For organizations navigating similar challenges in gene therapy manufacturing, we hope these insights offer a useful reference point and perhaps a starting point for your own platform-building efforts.



The increasing demand for AAV-based therapies places new pressure on developers and manufacturers to establish processes that are not only efficient and scalable, but also adaptable to a rapidly evolving regulatory and commercial landscape. With this project, our shared objective was clear: to build an AAV production platform that could demonstrate technical rigor across all stages of development—and scale to meet real-world manufacturing demands.

Together with Matica Biotechnology, we approached this goal through a structured and integrated process. We began with tech transfer, progressing through early-stage optimization using design of experiment tools in small-scale bioreactors, development of a downstream purification process, and scale-up. Every step was designed with flexibility and reproducibility in mind, with decisions supported by data and guided by scalability.

What made this effort particularly valuable was the comprehensive nature of the work. Rather than optimizing one part of the process in isolation, we developed and connected upstream and downstream operations as a unified workflow. This approach allowed us to understand the interdependencies between steps, evaluate performance at each stage, and ultimately demonstrate a process with strong outcomes, including reproducible titers, effective capsid separation, and significant impurity reduction.

This white paper captures the technical foundation and key takeaways from the collaboration. It is not just a summary of equipment or yields, but a reflection of what's required to build a platform: alignment on process design, clarity in execution, and the flexibility to adapt as challenges emerge. We hope it serves as a helpful resource for others building toward scalable solutions in gene therapy manufacturing.

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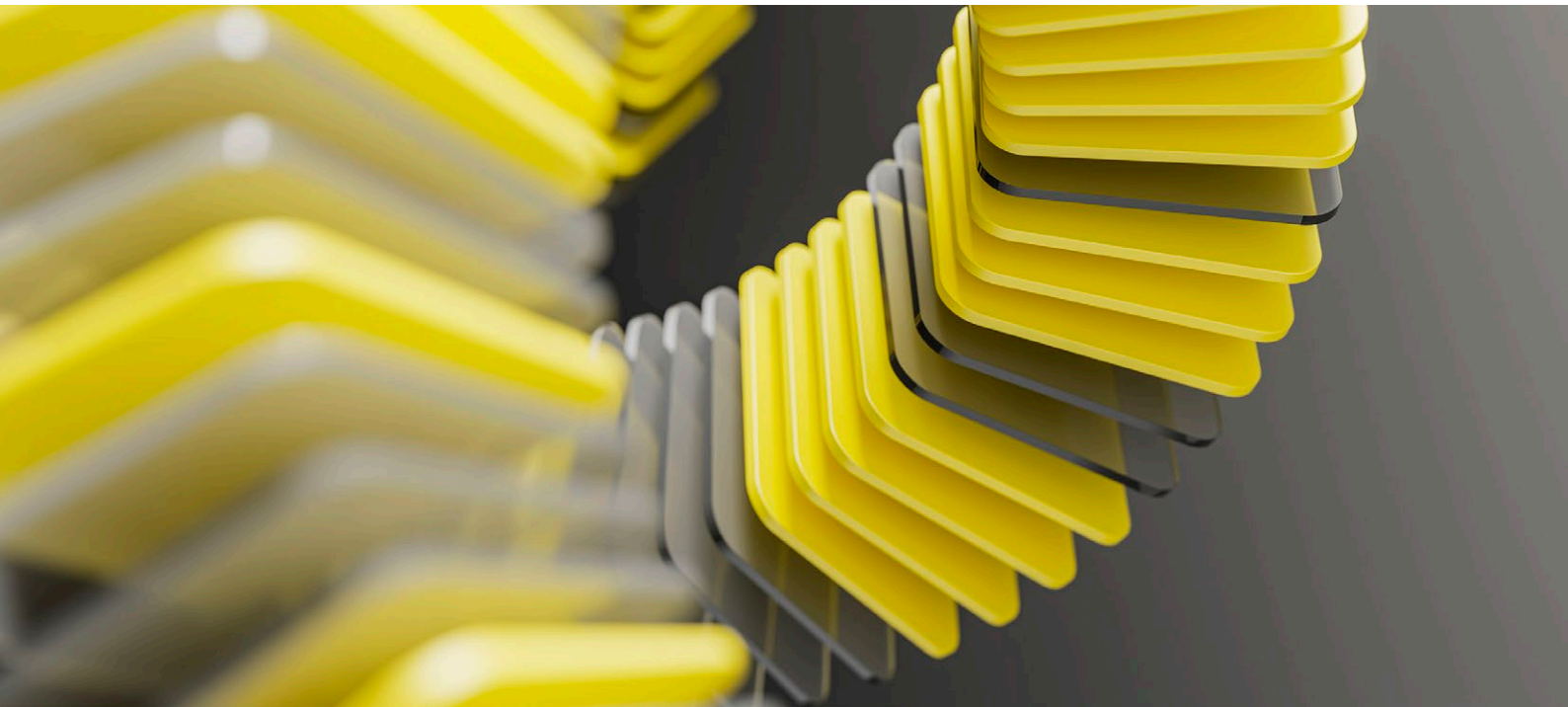


Why Scalable Platforms Are Essential for AAV8 Manufacturing

"Our objective was to demonstrate a truly scalable, end-to-end AAV8 production platform — not just at the bench, but up to 50 liters — with a strong focus on process robustness and analytical validation."

Trent Lyman
Matica Biotechnology

Adeno-associated virus serotype 8 (AAV8) has emerged as one of the leading vectors in gene therapy, with widespread use in clinical trials targeting muscular dystrophy, hemophilia, and retinal diseases.[1] Its ability to deliver genetic payloads safely and effectively has led to increased demand across both preclinical and commercial pipelines.

However, AAV8 production presents known bottlenecks, including variable yields, challenges in separating full and empty capsids, and maintaining product quality at scale. Regulatory expectations and the need for GMP-compliant solutions that accelerate timelines further intensify these challenges.

The market for AAV-based gene therapies is rapidly maturing, with over 700 programs currently being developed and therapies administered to over 3,000 patients,[2] including Luxturna® for inherited retinal diseases and Zolgensma® for spinal muscular atrophy. As more programs approach late-stage development, vector manufacturers are under growing pressure to deliver material that meets stringent regulatory and clinical requirements, often within compressed development timelines. Speed to clinic is particularly important for rare disease programs seeking fast-track or orphan designations.

Moreover, expectations around consistency, scalability, and GMP compliance continue to rise. Regulatory agencies now require detailed control strategies across both upstream and downstream processes, including evidence of effective full | empty capsid separation, host cell impurity clearance, and analytical validation. These pressures are heightened by the fact that many gene therapy developers, especially early-stage biotechs, face infrastructure and resource constraints that make custom, one-off process development inefficient and unsustainable.

The need for reproducibility and transferability across sites and scales is also accelerating demand for platform-based approaches. A well-characterized, end-to-end AAV production platform provides both technical and strategic advantages, reducing development risk, enabling faster tech transfer, and supporting regulatory readiness from the earliest development stages. Market reports show that the cell and gene therapy contract development manufacturing organization (CDMO) space is growing at over 20% CAGR, but capacity alone is no longer sufficient: process maturity and integration are critical.[3]

The collaboration between Matica Biotechnology and Sartorius was developed in response to a shifting market that demands modular, scalable, and GMP-compliant solutions that allow gene therapy programs to advance quickly.

As a CDMO, Matica Biotechnology must rapidly onboard new clients, adapt to varied process inputs, and ensure consistent output across a range of products and scales. Processes tailored to a single therapy or serotype would limit reusability, increase development time for each new project, and complicate regulatory alignment across batches and clients.

In contrast, a well-defined platform enables faster turnaround, reduced development costs, and more predictable scale-up performance. It allows Matica Biotechnology to implement repeatable unit operations with known performance characteristics, streamlining qualification and validation activities. This is especially important for supporting early-phase clients who require both speed and flexibility, but cannot afford the timeline or risk of custom process development.

A platform approach also simplifies tech transfer and operational handover, both internally and for external partners. With standardized equipment, media, analytics, and process conditions, the likelihood of deviations, delays, or retraining is significantly reduced. As gene therapy programs increasingly move toward commercial readiness, the ability to offer a compliant, scalable, and modular AAV production process is a significant competitive advantage.

"The technology transfer strategy was deliberate — starting from Ambr® 250 HT and Univessel® runs, then bridging into the 50 L Biostat STR® system. Shared SOPs and expected outcomes were key to making this seamless."

Franziska Bollmann
Sartorius

Figure 1: *Products Used Within AAV8 Manufacturing*

Flexsafe® RM 20 Basic Bag

Biostat® RM 20

Flexsafe STR® 50 L

Biostat STR® 50 L

FectoVIR®-AAV

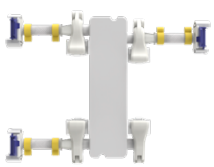
Sartoclear® DL75

Sartopore® 2 (XLG)

Sartocon® Self-Contained Cassette | Hydrosart®

Sartoflow® Expert SU

CIMmultus® SO3



Sartocon® Slice

CIMmultus PrimaS®

Sartoflow® Smart

Sartopore® Evo

The Modular Mindset: How Sartorius Enables Plug-and-Play Development

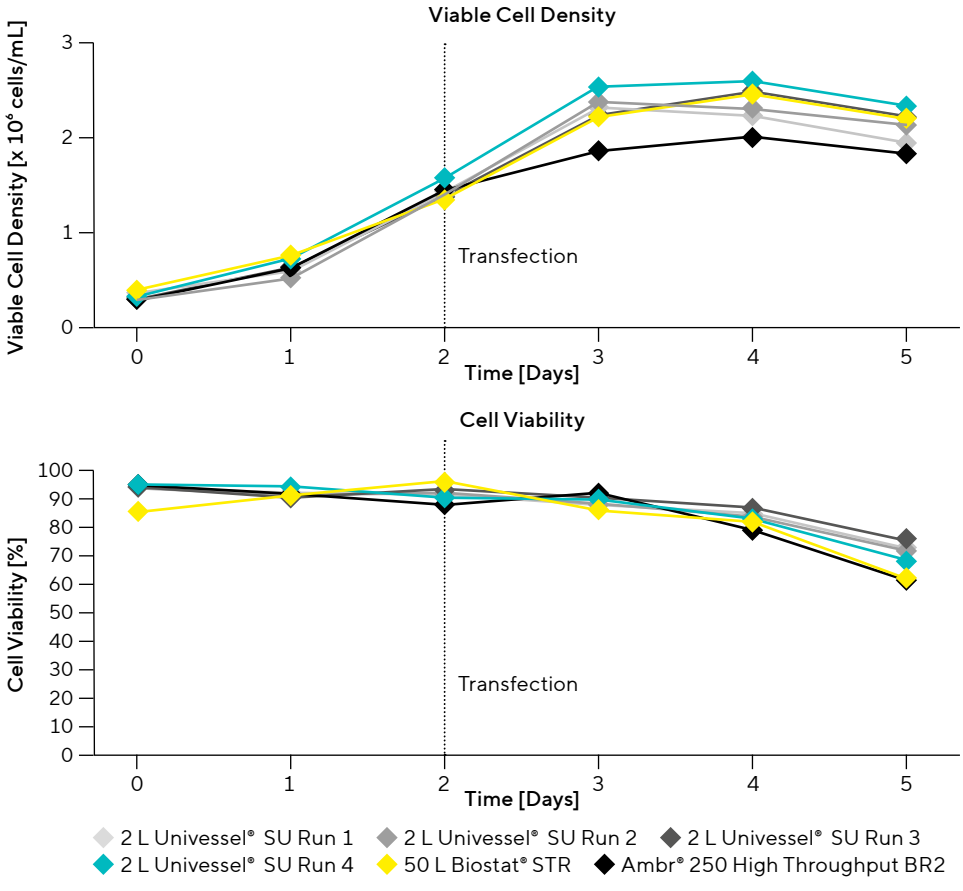
"The success of the tech transfer came down to alignment — not just on tools and data, but on process philosophy. Sartorius made it easy to translate bench insights into GMP-ready operations."

Trent Lyman
Matica Biotechnology

To meet the demands of modern gene therapy manufacturing, developers are turning to modular systems that can adapt quickly, scale efficiently, and maintain compliance without compromising speed. This "modular mindset" is especially valuable in viral vector production, where small changes in upstream conditions can dramatically impact downstream performance. Sartorius technologies played a central role in enabling this kind of flexible, plug-and-play process development across the AAV8 platform demonstrated in this project.

Matica Biotechnology's modular approach began upstream with the use of scalable single-use bioreactors, including the Ambr® 250 High Throughput for early-stage process development and the Biostat STR® 50 L for manufacturing-scale production (Figure 2). These platforms enabled their scientists to evaluate multiple process parameters in parallel and quickly scale up without the need to re-engineer workflows. Using MODDE® software to execute design of experiments (DoE), the team characterized critical process parameters that required precise control to achieve the same results across scales. Specifically, they identified robust setpoints for viral genome titer across agitation and gas flow conditions, as well as the parameters at which the process is most stable. This use of advanced data analysis shortened optimization timelines while maintaining process insight and control.

Figure 2: *Viable Cell Density and Viability Profiles Are Comparable Between All Scales*

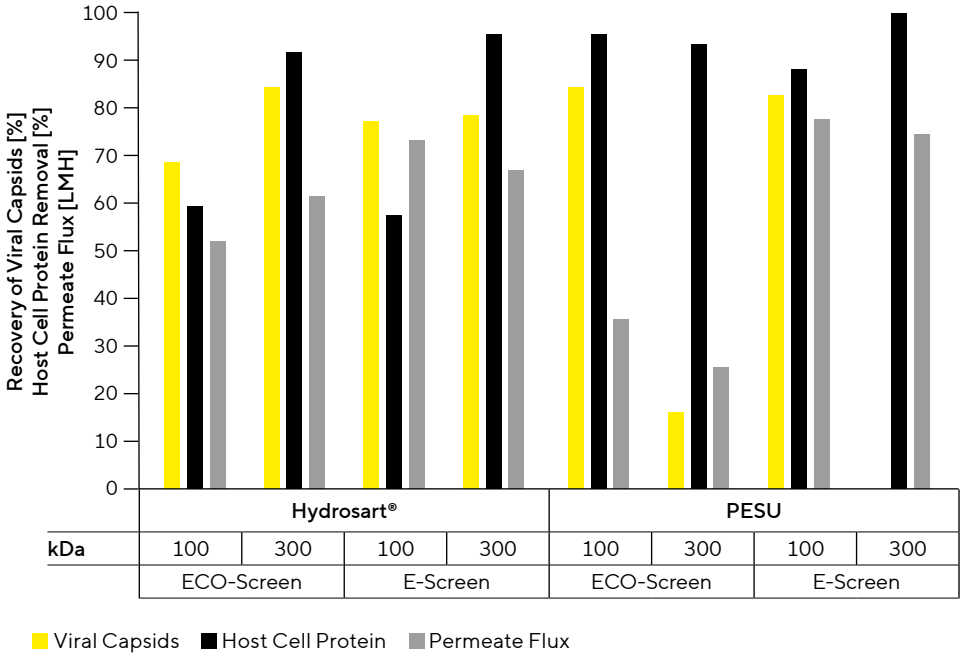


During downstream processing, the modular approach continued with interchangeable filtration and chromatography solutions tailored to each unit operation. Several tangential flow filtration (TFF) membranes were systematically evaluated for their ability to maximize viral recovery, minimize host cell impurities, and provide consistent performance during scale-up (Figure 3).

"We compared multiple TFF membranes and chemistries. Hydrosart® 300 kDa and PESU 100 kDa stood out in capsid recovery and impurity clearance. The ability to fine-tune this was critical for quality."

Trent Lyman
Matica Biotechnology

Figure 3: *Comparison of the Performance of All TFF Cassettes*

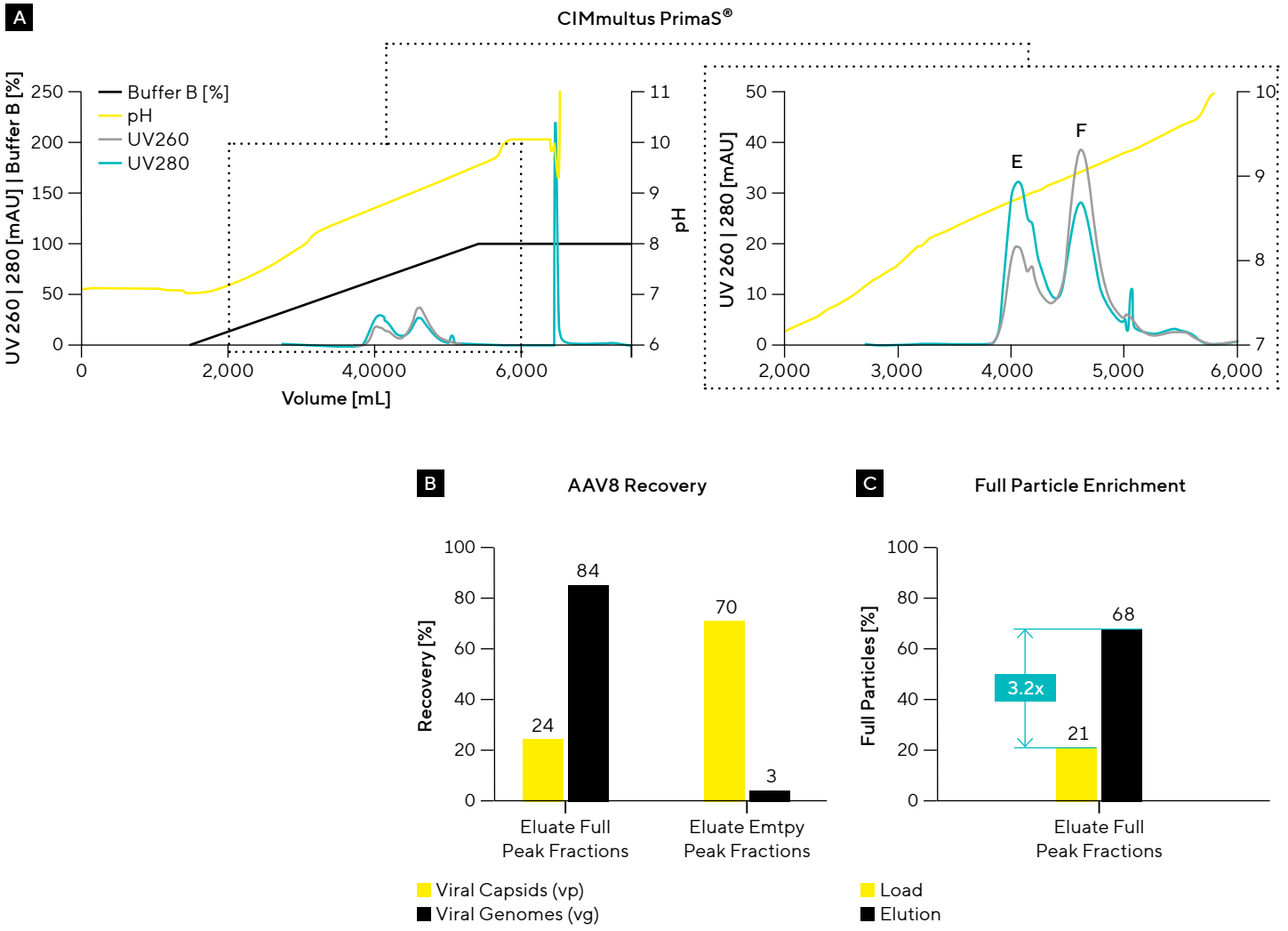


"This wasn't about developing isolated process steps. It was about showing that a unified, modular solution could handle the full journey — from upstream to downstream — with reproducibility and GMP relevance."

Franziska Bollmann
Sartorius

Similarly, CIMmultus® SO3 and PrimaS® monolith columns were implemented for high yield capture and polishing chromatography, enabling strong impurity clearance and >3-fold enrichment of full AAV8 particles (Figure 4).

Figure 4: *Chromatogram of Separation of Full AAV8 Capsids From Empty Capsids Using CIMmultus PrimaS® With a Zoom-in on the Full and Empty Peak Fractions in the Elution Phase (**E** = Empty Particles Peak, **F** = Full Particles Peak).* **(A)** *Recovery of AAV8 Capsids and Genomes in the Full and Empty Peak Fractions* **(B)***, and Enrichment of Full Capsids During Polishing* **(C)**

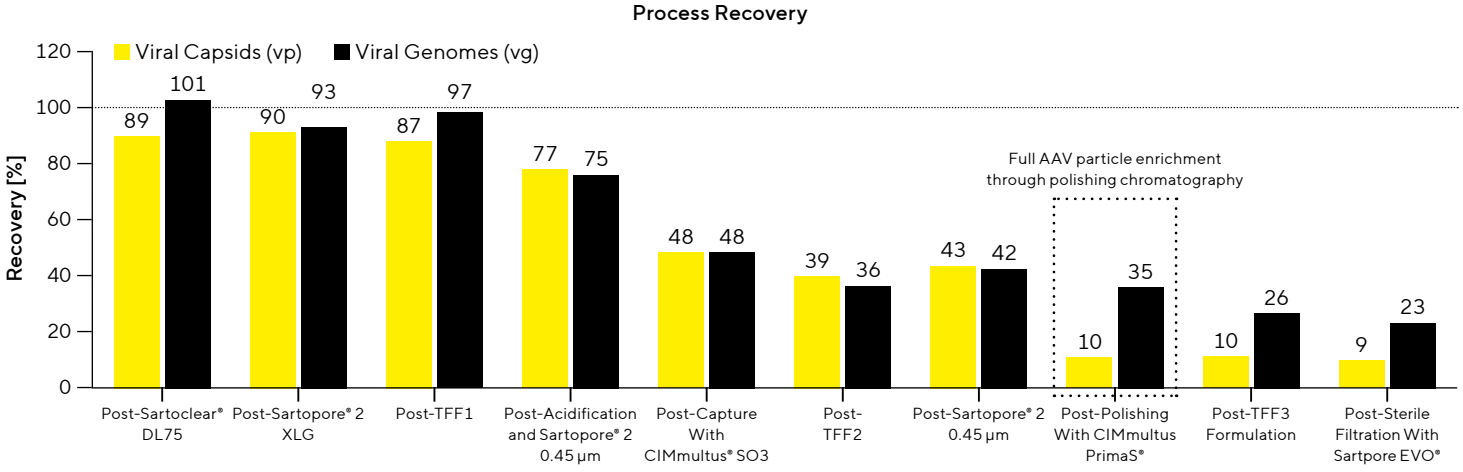


Overall, the process achieved robust recovery of both AAV genomes and particles, reaching values comparable to current industry benchmarks (23% and 9%, respectively; Figure 5). Notably, the relatively low viral capsid recovery was the result of an effective polishing step that efficiently removed empty capsids.

"CIMmultus® PrimaS delivered not just high viral genome recovery, but also impressive enrichment of full AAV particles — more than 3-fold in the 50 L end-to-end run."

Franziska Bollmann
Sartorius

Figure 5: *Process Recoveries of AAV8 Genomes and Capsids From Individual Unit Operations Across the End-to-End Purification Process Relative to the Upstream Titer*



Note. Capsid recovery at polishing chromatography step is low, due to full AAV particle enrichment.

Single-use technologies were foundational to much of the project's speed and agility. The closed-system designs reduced turnaround time and mitigated contamination risk. This feature is particularly critical for viral vector work, which often involves high biosafety requirements. Disposable components also reduced the burden of cleaning validation and supported seamless transitions between batches and scales, helping Matica Biotechnology maintain GMP alignment even in development stages. According to industry research, single-use systems can reduce manufacturing timelines by up to 40% and capital investment by as much as 60%, making them an essential element for facilities seeking both flexibility and efficiency.[4]

GMP Readiness by Design

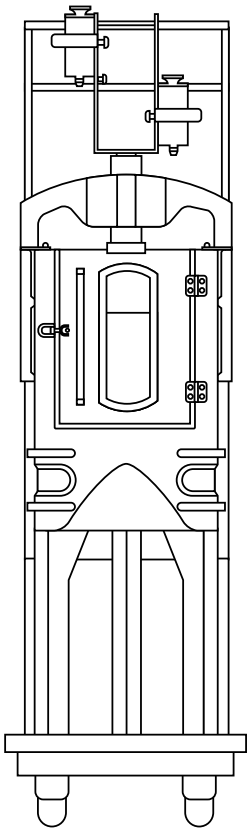
"Achieving around 70% full particles post-polishing was a major milestone. That kind of resolution is essential for both regulatory acceptance and therapeutic efficacy."

Trent Lyman
Matica Biotechnology

In viral vector manufacturing, the ability to scale is only part of the challenge. Processes must also be designed with GMP readiness from the outset, ensuring that materials, methods, and analytical results meet the expectations of global regulatory agencies. For Matica Biotechnology, this meant optimizing titers and throughput while ensuring the process could transfer seamlessly from development to GMP production with minimal rework. This required careful planning around qualification, documentation, and traceability at every stage.

From the beginning, each unit operation in the platform was evaluated for both technical performance and its suitability for GMP environments. Sartorius technologies were selected largely because of their proven track record in regulated biomanufacturing settings, including the availability of qualification packages, standardized SOPs, and validation support. Tools like the Biostat STR® 50 L and Sartoflow® Expert SU were supported by well-defined protocols and robust data packages, enabling faster implementation and alignment with GMP expectations. These systems also offered compatibility with electronic batch records and digital data capture, supporting traceability and audit readiness.

Technology transfer was a key focus throughout the project. As the process moved from small-scale feasibility to a 50 L integrated production run, Sartorius provided consistent instrumentation, interfaces, and training across scales, allowing Matica Biotechnology to scale up without costly revalidations. SOPs and expected results were shared early and used as benchmarks during scale-up and development runs. This ensured alignment across performance, documentation, and risk management, areas that are critical for successful GMP transition.



Single-use systems played a foundational role in contamination control and compliance. Disposable bioreactor bags, filtration capsules, and tubing assemblies helped reduce the risk of cross-contamination and eliminated the need for time- and labor-intensive cleaning validation. Sterile conditions were maintained throughout downstream workflows, supporting bioburden control and enabling operations in less complex facility environments. This is a key advantage in viral vector production, where biosafety is paramount.

Regulatory agencies expect manufacturers to demonstrate control, consistency, and a deep understanding of process variability. By embedding digital tools for in-line analytics and leveraging platforms designed with GMP deployment in mind, Matica Biotechnology was able to generate the data integrity, traceability, and contamination control needed to meet regulatory expectations. The resulting process was scalable and aligned with the quality systems required for clinical and commercial manufacturing.

Accelerating the Timeline

A core goal in developing the AAV8 platform was to compress the typical development cycle without compromising quality or scalability. Several strategic decisions and technical enablers contributed to this acceleration.

One of the most important time-saving strategies was the use of DoE modeling early in the upstream process. By leveraging Sartorius' Ambr® 250 High Throughput bioreactor system and MODDE® software, the team was able to run multiple experimental conditions in parallel and quickly identify optimal process parameters (such as stirrer speed and gas flow rates) for viral genome titer. This structured approach avoided time-consuming trial-and-error experiments, accelerating the establishment of a robust process.

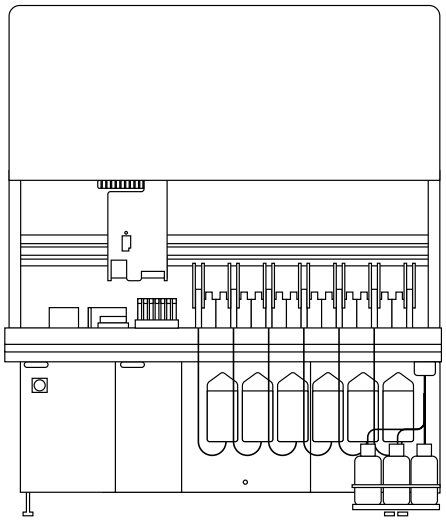
Another major factor was the adoption of single-use systems across both upstream and downstream operations. Single-use bioreactors, filters, and chromatography setups reduced the requirement for cleaning between runs and enabled faster turnaround between development stages. This flexibility was essential for scaling quickly from Ambr® 250 High Throughput to 2 L Univessel® SU to the 50 L Biostat STR® platform, all while maintaining consistent process performance.

Digital tools provided an additional layer of efficiency by enabling rapid data analysis, process monitoring, and transferability. Real-time analytics platforms and standardized data outputs ensured that process knowledge could be captured, compared, and applied across different scales and unit operations. This level of insight helped prevent delays caused by unforeseen variability or inconsistent execution and supported faster decision-making during both optimization and troubleshooting phases.

Finally, the platform was designed from the beginning as a cohesive, modular system, as opposed to a sequence of unconnected steps. This meant that each phase of the project built directly on the previous one, with fewer redundancies and minimal rework. As a result, the full end-to-end process (including upstream production, clarification, TFF, capture, polishing, sterile filtration, and analytics) was demonstrated at 50 L scale in a highly compressed development timeline.

"We demonstrated consistent step recovery across the entire downstream process — between 80% and 100% — which reflects the robustness of the platform."

Franziska Bollmann
Sartorius



"End-to-end, we reached 23% viral genome and 9% capsid recovery. For a scaled-up process like this, that's a strong outcome, especially considering the impurity reduction we achieved."

Trent Lyman
Matica Biotechnology

Platform, Not Project: Enabling Future Therapies

While the immediate goal of this project was to establish a high-performing AAV8 production process, the broader objective was to build a foundation that could extend beyond a single serotype or client program. The resulting platform was designed to be modular, scalable, and broadly applicable, capable of supporting a wider range of viral vector programs.

The upstream and downstream workflows validated in this project are not unique to AAV8. Many of the core elements — including suspension-adapted HEK293 cells, polyethyleneimine (PEI)-based transient transfection, depth filtration, TFF, and ion-exchange chromatography — are relevant across other AAV serotypes, such as AAV2, AAV5, or AAV9. In addition, the use of scalable single-use bioreactors, interchangeable TFF membranes, and a variety of chromatography chemistries for purification provides the operational flexibility to adapt to different genetic elements or expression profiles without redesigning the entire process.

This adaptability is especially valuable in the current gene therapy landscape, where developers are working with diverse gene sizes and serotype combinations that may require fine-tuning but not full reoptimization. With this platform, Matica Biotechnology can onboard new projects faster, using existing process parameters and analytics as a starting point while allowing for targeted optimization as needed. Moreover, the availability of scalable, small-scale screening tools—in combination with DoE strategies—support the rapid development and optimization of robust downstream processes suitable for diverse customer projects.

The platform also strengthens the ability to transfer processes to clients or external manufacturing partners. Standardized unit operations, validated technologies, and documented performance across multiple scales make the process easier to replicate and qualify in different facilities. This is particularly beneficial for clients seeking to move from early-phase material to clinical or commercial production with minimal risk and delay.

By treating this initiative as a platform and not a one-off project, Matica Biotechnology has positioned itself to serve a wider array of gene therapy developers with consistent quality, reduced lead times, and greater operational control. The investment in process integration, documentation, and scalability now enables flexibility where it matters most: in meeting the needs of the next therapy.

Platform Applications: Designed for Flexibility and Scalability

Serotype Flexibility
- Core process adaptable to other AAV serotypes (e.g., AAV2, AAV5, AAV9)
- No need to reinvent upstream or downstream processes

Scalability & Tech Transfer
- Proven scale-up path from 250 mL, to 2 L, to 50 L
- Single-use systems simplify tech transfer to internal or partner facilities
- Standardized SOPs and process data packages support smooth onboarding

Payload Agility
- Supports varied gene sizes and expression cassettes
- Transient transfection parameters easily adjusted for vector-specific demands
- Validated assays that support a range of serotypes and payloads

Applicability Across Projects
- Reproducible workflows minimize development time for new clients
- Cross-project efficiency reduces the cost of customization
- Faster development timelines for early-phase and platform-based programs

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Lessons for the Industry: Partnering for Speed and Success

Below is a guide for building a robust AAV platform with a reliable partner.

1 Define the Platform Vision Early
- ✓ Align on whether you're building a one-time process or a repeatable platform
- ✓ Invest upfront in scalability, analytics, and transferability

2 Choose Technology That Scales Without Reinvention
- ✓ Select tools proven across scales (e.g., Ambr® 250 High Throughput to Biostat STR® 50 L)
- ✓ Prioritize single-use systems to minimize downtime and complexity

3 Treat Digital Tools as Process Accelerators
- ✓ Use DoE and MVDA software to speed up optimization
- ✓ Establish digital traceability to support GMP-readiness from day one

4 Align on Mindset, Not Just Milestones
- ✓ Ensure both teams prioritize transparency, shared decision-making, and speed
- ✓ Prioritize collaborative co-development over transactional outsourcing

5 Anticipate Tech Transfer, Even in Early Development
- ✓ Build documentation and SOPs as you go
- ✓ Design unit operations with future partners and facilities in mind

6 Avoid Common Pitfalls
- ✓ Support a range of serotypes and payloads with validated assays
- ✓ Reduce rework and keep analytics on-track with QC-ready methods
- ✓ Connect upstream and downstream development to avoid scaling in isolation

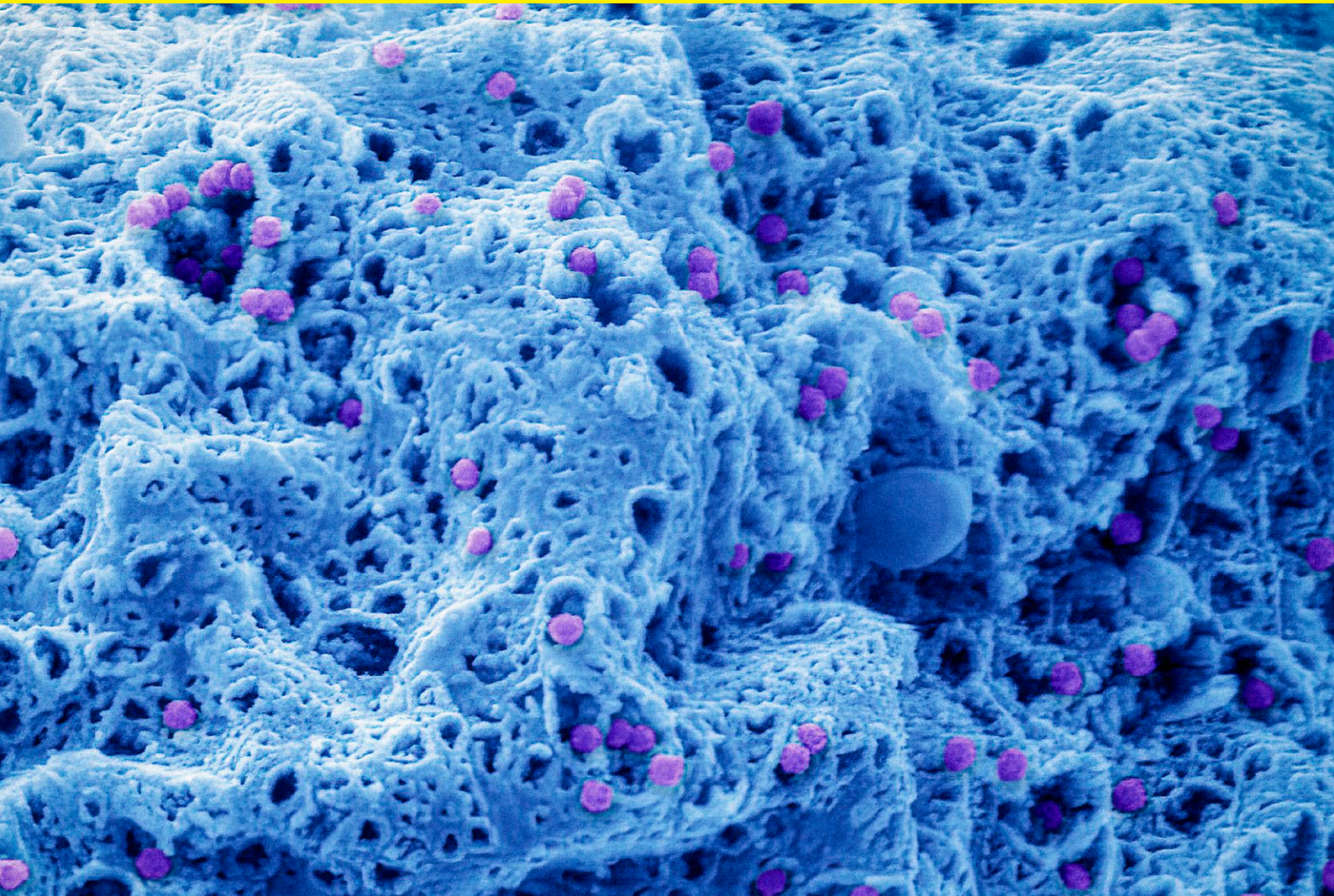
Conclusion

For more information, visit
sartorius.com/cell-gene-therapy

A Blueprint for Platform-Driven Innovation

This project illustrates the impact of treating platform development as a strategic asset rather than a series of technical tasks. By taking an integrated approach from early upstream optimization to downstream polishing and analytics, Matica Biotechnology was able to build a modular, scalable, high-performing AAV8 manufacturing platform that delivers adaptability and speed.

For gene therapy developers and manufacturers navigating similar pressures, this collaboration offers a clear blueprint: invest in scalable systems, design for flexibility, and embed GMP readiness from the start. Sartorius technologies and expertise played a key role in enabling this outcome and are available to support others aiming to turn development into deployable, reproducible platforms. This enabled the development of a robust and future-ready AAV manufacturing platform.



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Dr. Franziska Bollmann, PMP®, is a Senior Program Manager in Separation Technologies at Sartorius, where she manages strategic partnerships for multiple modalities including AAV.

She has 8 years of experience focusing on developing viral vector production processes for gene therapy applications. She is also an experienced project manager, leading global cross-functional project teams in the biotech industry for more than 10 years.

Katy McLaughlin
PhD,
Scientific Content Writer,
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Katy is part of the Marketing Communications team at Sartorius, where she supports the creation of a variety of written pieces, from published articles to web content.

Before joining Sartorius in 2021, Katy was employed as a Post-Doctoral Research Associate at the University of Edinburgh, where she also completed her doctoral studies. Here, she carried out research in genetics and cellular biology and began taking on writing projects, eventually entering into a career as a freelance writer for various biotech companies and agencies.

Paul Cashen
Market Expert Bioprocess Solutions,
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Paul is a Marketing Expert for Bioprocess Solutions at Sartorius, responsible for developing and executing modality-based marketing strategies and driving thought leadership initiatives.

Paul has more than 15 years of experience in the biologics industry, with expertise in downstream processing and analytical development. He specializes in the downstream process development, scale-up and manufacturing of ATMPs, such as lentiviral and adeno-associated viral vectors, as well as process intensification strategies for downstream purification.

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