Simplifying Progress

Keep Your Molecule Moving: Reaching the Finish Line First in Cell & Gene Therapy

How companies in discovery and early-stage R&D can accelerate progress and break barriers to success in a high-stakes field

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Foreword

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Paul is responsible for implementing solutions during late-stage process development and commercial scale-up.

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.

Cell and gene therapies have huge clinical potential, offering new ways to treat diseases that have been difficult or impossible to address in the past. However, those at the early stages of developing these therapies—researchers, entrepreneurs, and startup teams—face unique challenges. Advancing from concept to a safe and effective treatment requires considerable time, persistence, and the ability to navigate operational and commercial hurdles, including non-standardized production processes, managing complex supply chains, and keeping up with changing regulations.

This white paper is for early-stage cell and gene therapy developers who are working to reach their next milestone and overcome barriers to success. Inside, we share data, market trends, and expert advice to help you identify obstacles early, design stronger processes, and make more confident decisions. We also know that resources can be limited for startups and small teams, so we've designed this paper to provide practical insights and strategies that help you work through the real-world challenges of development.

Chapter 1

The Importance of Momentum in Cell and Gene Therapies

Why time is the most valuable currency

The landscape of cell and gene therapy drug development is marked by explosive growth: the global market is expected to exceed $20 billion by 2028, with a compound annual growth rate of more than 30%,[1] fueled by a pipeline of almost 2,000 active programs.[2] However, it is estimated that less than 5% of these therapies will achieve regulatory approval.[3] Success depends on achieving key clinical, financial, and regulatory milestones, which makes it essential for drug developers to consider and implement quality by design (QbD) from the beginning of their drug development journey.

Around three quarters of complete response letters (CRLs) issued by the U.S. Food and Drug Administration (FDA) for cell and gene therapy drugs between 2020 and 2024 were due to manufacturing deficiencies.[4] Demonstrating safety and efficacy is not enough; success also requires a robust chemistry, manufacturing, and controls (CMC) strategy. While the implementation of QbD isn't mandatory, cell and gene therapy developers are strongly advised by regulatory agencies to implement QbD and risk-based control strategies in early development, highlighting the identification of critical quality attributes, critical process parameters, and a CMC strategy as key to manufacturing readiness.[5]

Demonstrating early clinical proof of concept has become a decisive advantage in today's highly competitive cell and gene therapy landscape. Initial success in showing drug safety and efficacy not only strengthens scientific confidence in the drug product but also attracts critical funding. In 2024 alone, venture capital investment into cell and gene therapies reached $15.2 billion,[6] with a large proportion of that investment concentrated in drugs with strong early data. On the other hand, early-stage missteps, such as process variability or inconsistent trial performance, can lead to significant losses in time and funding.[7] This highlights the need for robust data generation that builds trust across clinical and commercial stakeholders.

Maintaining momentum in cell and gene therapy development is imperative. The complexity of the underlying biology, coupled with the challenges in scale-up and ever-evolving regulatory guidance, demands a collaborative and agile approach across all stakeholders. Close integration between research and development and clinical development is essential to help accelerate timelines and ensure therapies are both effective and scalable. This foundation is critical to converting modern-day innovation into future approved therapies that address urgent patient needs, while unlocking a market projected to exceed $50 billion in the next decade.[8]

Rapid market growth
The global cell and gene therapy market is projected to exceed $20 billion by 2028.[1]

Low success rates
Fewer than 5% of the 2,000+ drugs in the pipeline are expected to achieve regulatory approval.[2,3]

Manufacturing gaps
74% of CRLs issued by the U.S. FDA (2020–2024) were due to quality or manufacturing deficiencies.[4]

Chapter 2

Where Are You Getting Stuck?

Five common bottlenecks that stall progress

- **Platform uncertainty:** Key decisions made before early data is available
- **Infrastructure misalignment:** Facilities often rely on legacy systems that lack flexibility
- **Resource limitations:** Small teams managing broad process development activities
- **Regulatory complexity:** Expectations shift as guidance for advanced therapies evolves
- **Operational gaps:** Limited alignment across internal teams and external partners

Despite this rapid growth and clear urgency, multiple bottlenecks continue to stall progress across cell and gene therapy drug development. One of the most critical issues is platform uncertainty. Cell and gene therapy is a diverse field, encompassing delivery methods and modalities such as viral vectors, cell therapies, and nucleic acids. Within each modality, additional factors must be considered, including cell type or virus serotype. Premature commitment to a specific platform before sufficient data is generated can result in costly redesigns and delays.

This challenge is compounded by the fact that most manufacturing facilities are optimized for large-scale commercial production rather than the flexibility needed for early-stage clinical manufacturing or even commercial manufacturing of low-volume therapeutic products. As little as a third of contract development and manufacturing organizations (CDMOs) have reported that they operate above 80% utilization,[9] reflecting a misalignment between capacity and the demands of early clinical transition. Platform ambiguity and rigid infrastructure risk slowing the early momentum of promising drug candidates before they can prove clinical value.

Adding to these challenges are resource constraints and regulatory complexity. Often within the cell and gene therapy space, small, specialized development teams are expected to deliver rapid innovation across scientific, manufacturing, and regulatory domains. Although investment in cell and gene therapy surpassed $15 billion in 2024,[10] the scale of requirements for drug development can lead to difficult trade-offs that increase the potential for delays. At the same time, regulatory pathways for advanced therapies, although evolving, are still not comprehensively defined. Approximately 40% of all FDA clinical holds in recent years have involved cell and gene therapy studies, even though these products represent only about 8% of drugs in development.[11] This regulatory uncertainty requires rigorous early-stage planning and dedicated expertise to navigate submission and feedback cycles without compromising timelines or resource allocation.

Operational fragmentation across internal teams and external partners further complicates the drug development process. When process development, clinical trial management, and regulatory affairs operate in silos, inefficiencies accumulate, causing delays that often only emerge late in the development lifecycle. Addressing these bottlenecks requires a holistic approach that integrates development decisions, infrastructure flexibility, resource planning, regulatory strategy, and cross-functional collaboration from the earliest stages. Without such an approach, even drugs with early clinical promise can falter due to preventable operational failures.

Chapter 3

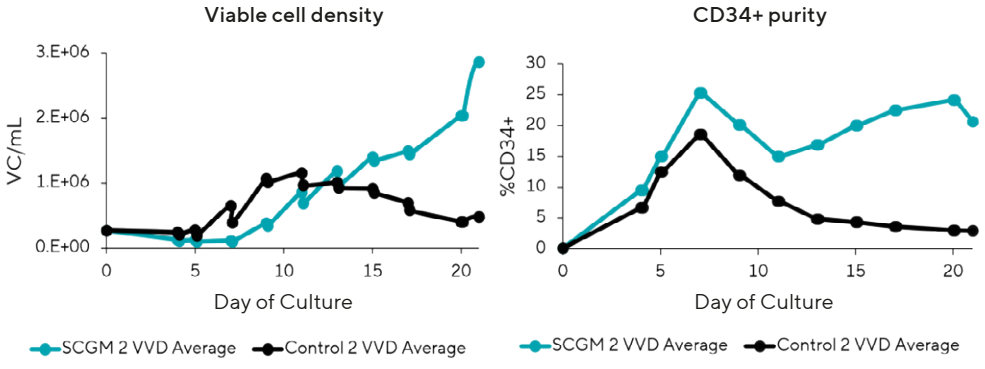
The Strategic Role of Raw Materials

Developing an early raw materials strategy aligned with late-stage requirements

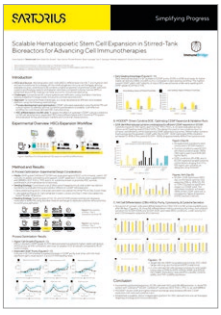
In cell and gene therapies, the final product is often a living cell or viral vector, both of which are highly sensitive to the composition and quality of raw materials such as media, cytokines, and transfection reagents. Variability in raw materials can lead to inconsistent cell growth and phenotypes, variable titers, and vector quality, affecting therapeutic efficacy and patient safety.

Additionally, regulatory agencies such as the FDA and the European Medicines Agency (EMA) require traceability, documentation, and quality control of all raw materials, and are tightening requirements on animal-derived components. Using GMP-grade, high-quality materials that are xeno-free or animal-component-free helps streamline regulatory approval and reduce contamination risks. Figure 1 highlights the impact of using GMP-grade cell culture media on performance in a hematopoietic stem cell expansion process.

Figure 1: Case study from a collaboration with ImmuneBridge showing increased viable cell density and higher CD34⁺ purity when using GMP-grade CellGenix® SCGM compared with research-use-only medium



Note. Feed rate is two vessel volumes per day. This figure is adapted from the poster Scalable Hematopoietic Stem Cell Expansion in Stirred-Tank Bioreactors for Advancing Cell Immunotherapies



Discover how ImmuneBridge optimized cord-blood-derived hematopoietic stem cell expansion and differentiation into NK cells using the Ambr®15 system with CellGenix® GMP SCGM and cytokines, achieving scalable, donor-independent immune cell production for oncology and immunotherapies.

Download the poster

Beyond quality and regulatory compliance, raw materials must support consistent performance across batches and scales as cell and gene therapy products move from clinical to commercial scale. Standardized raw materials reduce the need for revalidation and facilitate tech transfer between sites or CDMOs, improving overall process scalability and avoiding costly delays. Production bottlenecks can also be avoided by building a resilient supply chain. Cell and gene therapy developers must secure reliable sources of critical raw materials through dual sourcing, long-term supplier agreements, and inventory strategies to minimize disruptions.

The diversity and complexity of cell and gene therapy processes confound these challenges. Advanced therapies often require tailored raw materials optimized for specific cell types and modalities. Strategic partnerships with reliable partners enable the co-development of solutions to enhance cell expansion or transfection efficiency, maximizing process efficiency.

Finally, a robust raw material strategy can accelerate timelines and reduce the overall cost of goods (COGs), which is critical in cell and gene therapy processes where manufacturing is already complex and expensive. High-performing raw materials improve productivity, reducing the overall cost per dose, and proper characterization reduces batch failures and troubleshooting time.

Chapter 4

Establishing a Strategy for Your End Goal

What "progress" really looks like in early-stage cell and gene therapy development

Progress in cell and gene therapy development is highly dynamic. At each stage, parameters must be refined, processes optimized, and strategies adjusted to ensure the therapeutic candidate remains viable and competitive. As such, it is critical to ensure the program can adapt. This means being prepared to integrate new data, respond to regulatory feedback, and adjust processes to address the needs of different patient populations.

Planning with flexibility in mind

The most successful development strategies begin with flexibility built into the plan: selecting tools and technologies that can accommodate future shifts and designing workflows that allow for change without compromising quality or documentation. Flexibility becomes especially valuable in circumstances where process changes are likely, such as when the clinical approach is adjusted, unexpected results are received during scale-up, or regulatory expectations evolve.

Prioritizing milestones in the development journey

Instead of attempting to fix every design choice from the outset, it is more effective to structure development around key milestones. These milestones serve as natural decision points where cell and gene therapy developers can pause, evaluate their progress, and make adjustments as necessary, enabling the identification of new opportunities while ensuring continued progress.

Key milestones in early-stage cell and gene therapy development:

1. **Candidate selection and early proof of concept**
   Early decisions about vector, modality, and therapeutic strategy are made
2. **Process and platform design**
   Selection of technologies, materials, and systems that establish the foundation for scalability and adaptability
3. **Preclinical package completion**
   Evaluation of safety and efficacy data before engaging with regulatory authorities
4. **IND preparation and submission**
   Defining the process, documentation, and readiness for first-in-human trials
5. **Technology transfer to manufacturing**
   Transitioning from development to GMP production, aligning on scale, controls, and flexibility
6. **Initial clinical data review**
   Early human data may prompt refinements to dose, delivery, or manufacturing strategy

Where can you adopt flexibility into your process?

Scenario 1:
Early planning phase

At the start of a development program, the focus is on defining the overall strategy. This phase provides an ideal opportunity to incorporate flexibility and scalability into the process design.

Key actions:
- Select modular or platform-based systems that allow future adaptation to changes in vector, format, or scale
- Establish a strategy for raw material qualification, sourcing, and control
- Implement documentation and data management systems designed to expand with program needs
- Define clear checkpoints to enable systematic evaluation and adjustment of the development pathway

Decisions made at this stage can have long-term consequences, influencing both the adaptability of the process and the efficiency of future development activities.

Scenario 2:
Preparing for a regulatory milestone

As organizations approach a clinical submission or progress into a s ubsequent development phase, strategic planning becomes essential to ensure efficiency and regulatory compliance. With the right tools and foresight, this stage can serve to streamline processes and accelerate overall development timelines.

Key actions:
- Establish a documentation strategy that supports data comparability and minimizes the need for rework
- Explore opportunities to conduct development activities in parallel, such as process scale-up and analytical validation
- Generate a robust evidence base to enable future flexibility, supported by consistent data and platform standardization

When approached with comprehensive planning, regulatory transitions evolve from potential sources of delay into structured, progressive steps that drive progress.

Scenario 3:
Refining a late-stage process

At advanced stages of development, processes may appear fully defined, yet unforeseen challenges can necessitate modification. For example, a formulation may not demonstrate the expected stability, or yield variability may emerge. In such circumstances, a combination of flexible process design and robust foundational strategies enables adaptation without significant delay.

Key actions:
- Leverage existing data and product characterization to support process adjustments
- Implement changes through single-use or closed-system technologies to minimize the impact on validation requirements
- Ensure documentation workflows allow for real-time updates and traceability

Even in late-stage development, the use of appropriate tools and a systematic approach enables controlled process refinement while maintaining regulatory compliance and development momentum.

Chapter 5:

External Support in Early-Stage Development

The role of strategic collaboration in transforming development outcomes

Early-stage cell and gene therapy programs typically operate with limited time and small teams. Moving a therapy toward clinical and commercial readiness requires smart decision-making, efficient execution, and the ability to adapt as new data or constraints emerge. While enabling tools and platforms are essential, acceleration often requires partners that deliver technical expertise, process knowledge, and the foresight to de-risk development steps before they become roadblocks.

External support is most valuable when it fills functional gaps, provides specialist input across disciplines, and integrates with internal workflows. This requires moving beyond transactional interactions toward strategic partnerships with organizations that possess a comprehensive understanding of the cell and gene therapy development landscape—from vector selection and upstream process optimization to comparability planning and IND-enabling activities.

Bridge functional gaps with integrated expertise

Many early programs operate with lean teams, where individuals assume overlapping responsibilities across development, quality, and regulatory functions. In such cases, cross-functional guidance can reduce the risk of misalignment and save valuable time. Technical partners can help map a development strategy that anticipates regulatory needs, ensures quality expectations are met, and minimizes rework during scale-up.

This approach is embedded into the Sartorius Innovation Center in Marlborough, Massachusetts—a facility designed to support early-stage developers with access to relevant technologies, collaborative working environments, and established bioprocess workflows. On-site teams help customers rapidly evaluate, adapt, and implement process steps using the same tools that will carry them into GMP production.

When these strategic partnerships function well, they provide structure and clarity to development, supporting internal expertise with practical knowledge and scalable solutions.

"This cutting-edge innovation center enables us to leverage our bioprocessing tools and workflows expertise, ultimately accelerating and simplifying our customers' path to clinical trials."

René Fáber
Head of Sartorius Bioprocess Solutions Division

Customer Case Study—Adeno-associated virus platform development with Matica Biotechnology

A recent collaboration between Matica Biotechnology and Sartorius illustrates how early-stage agility and modular development can accelerate adeno-associated virus (AAV) production timelines without compromising control.

To build and scale an AAV8 production platform, the teams applied a modular concept, treating each unit operation as part of a flexible, end-to-end system. This allowed changes to be incorporated efficiently without reworking the entire process.

Key elements of the approach included:

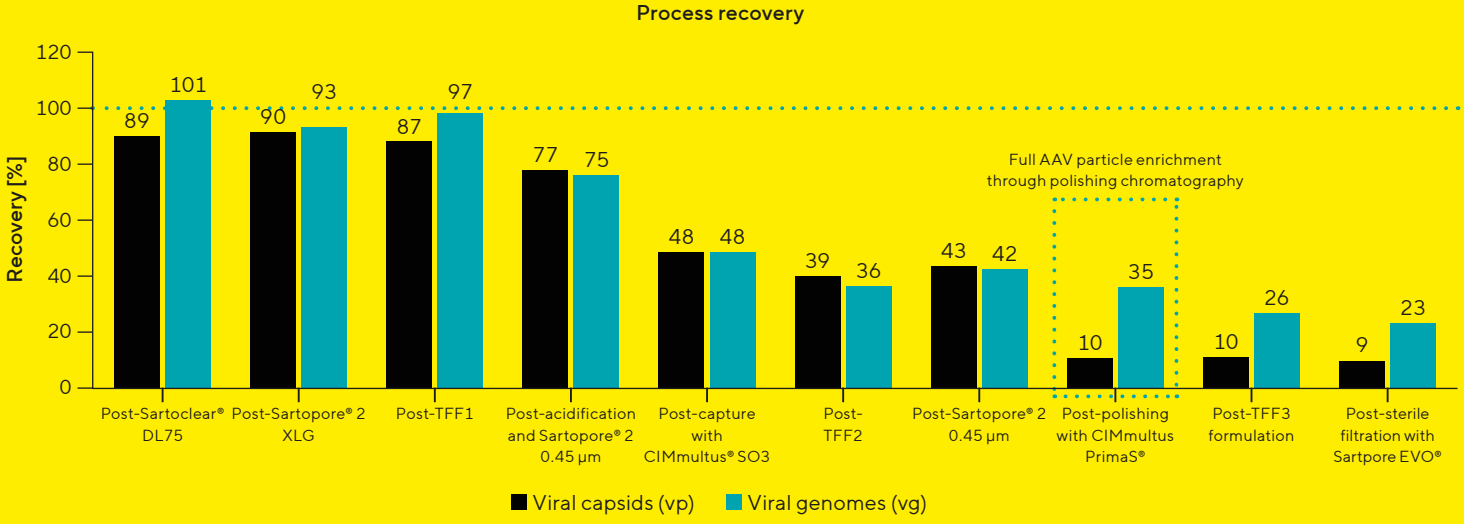
- Design of experiments: Used early to optimize upstream and downstream parameters
- Modular technologies: Enabled rapid configuration and tech transfer readiness
- Quality by design principles: Ensured process understanding and comparability planning from the outset
- GMP readiness: Achieved at the 50 L scale through coordinated design and documentation

The result was a process designed for technical feasibility and regulatory compliance, and was delivered on an accelerated timeline with fewer handoffs. Process recoveries across unit operations are shown in Figure 2.

Learn more about our collaboration with Matica Biotechnology.

Download the white paper

Figure 2: 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.
This figure is adapted from the white paper Building an AAV8 Platform, Together: Lessons From a Collaborative Development Journey

Reducing time to clinical batches

Partners that understand the realities of early-stage cell and gene therapy can also help reduce development timelines in more targeted ways. This includes accelerating material preparation, streamlining documentation and batch records, and guiding process design toward approaches that reduce future comparability risk.

In practice, this might involve:

- Implementing scalable single-use systems early to avoid future redesigns
- Aligning assay development with critical quality attributes from the outset
- Using digital tools to manage traceability and documentation in real time
- Integrating high-throughput experimentation to support rapid optimization

These steps support rapid development while enhancing the confidence in data packages submitted to regulators. When timelines are compressed, small efficiency gains in process design, testing, and decision-making can add up to major time savings without compromising quality.

Conclusion

Success in cell and gene therapy development is achieved through measured decision-making, adaptable strategies, and the ability to pivot when new information arises. The ability to leverage external expertise and implement modular systems to sustain forward momentum becomes a critical differentiator.

Each stage of development represents an opportunity to refine processes, accelerate progress, and strengthen the long-term resilience of the program. By approaching each phase with operational foresight and a commitment to innovation and flexibility, organizations build cumulative momentum that advances cell and gene therapies toward the finish line.

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Further Reading

1. Setting the Standard in CGT: Perspectives on Performance, Scalability and Regulatory Compliance
2. Cell & Gene Therapy in Conversation: Q&A With Seven Experts

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