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What are the biggest roadblocks still standing in the way of cell and gene therapy commercialization?

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Christopher Kistler, Fellow Scientist, Catalent

Several persistent challenges continue to slow the path to commercializing cell and gene therapies. First, speed to market remains a critical hurdle. Development timelines are often extended because teams lack efficient, high-throughput tools that enable them to explore a wide range of process conditions quickly without adding cost or resource burden.

Additionally, process and analytics development life cycles are often decoupled. When scale-down modeling is not combined with real-time analytical insights, progress is slower, leading to rework that costs time and resources.

Next, a lack of flexible, well-characterized platform approaches creates friction during the transition between development and manufacturing. Without platform approaches, teams must redesign core processes for each program. This increases cost, raises risk, and delays technology transfer. It also makes it harder to stabilize supply and maintain consistent product quality at scale.

Finally, the pace of introducing novel unit operations, such as perfusion or intensified processing, remains a constraint. Current process designs do not always translate to the reality of a requirement for increased commercial throughput.

These challenges are familiar to experienced development partners. Addressing them early is essential for advancing complex therapies efficiently and reliably toward commercialization.

Mark Edbrooke, Ph.D., Head of Strategy, N4 Pharma

Cell and gene therapies are an extremely exciting, direct consequence of the incredible progress made in the fields of cell biology and molecular biology over recent decades. However, due to

the complex nature of these types of therapeutics, there are multiple hurdles that still need to be overcome in order to make them commercially viable. These include precise targeting to the correct cell types, cost-effective large-scale production, specialized storage and delivery infrastructure, and rigorous safety monitoring to manage long-term risks.

One particularly promising area for progress is cellular delivery technology. Non-viral systems, such as silica-based nanoparticles, can protect and transport DNA, RNA, or gene therapy payloads, while surface modifications enable cell-specific targeting and reduced immune activation. For example, a new mesoporous silica nanoparticle in development is benign to the immune system and can be loaded with gene therapy cargoes, including plasmids and cDNAs.

Non-viral approaches offer distinct advantages over viral vectors, as they are safer, more versatile, easier to produce at scale, and better suited for repeated administration. By continuing to innovate in delivery science, particularly in nanoparticle engineering, we can make cell and gene therapies safer, more accessible, and commercially viable for a broader range of applications.

Martin Westberg, Vice President and General Manager, Cell Therapy, Cytiva

Both cell and gene therapies have tremendous potential to be effective. For the first time in human history, we are able to treat the cause of disease and not just the symptoms thanks to gene therapy. If we are to democratize gene therapies, we'll need improved manufacturing techniques. We must take all the knowledge we have gained from nearly three decades of manufacturing monoclonal antibodies (mAbs) and apply those lessons where appropriate. While developing standard platforms that can be used across a broad range of applications will be critical to advancing gene therapies, we must also continue working toward well-defined and characterized processes.

Cell therapies are a bit trickier. Because they are so complex and require diverse manufacturing processes, it makes their industrialization and scale-up of the manufacturing process a major challenge. Efficient scale-up requires bespoke equipment, software, and reagents.

Standardizing and industrializing these processes will help alleviate the issues related to cost and access. These issues will only continue to grow as the field moves closer to application in broader oncology indications, as well as indications such as autoimmune diseases. As research continues, we must keep working to automate and standardize these processes.

Kevin King, Senior Director, Immune Cell Operations, BioIVT

Challenges continue to exist within the evolving field of cell and gene therapy, particularly concerning the selection and management of starting materials. A critical question is what constitutes ideal starting material, an issue that has complicated early trials and development.

For allogeneic therapies (using donor cells), success hinges on having highly characterized and well-understood donor selection methods. The process of identifying donors whose cells are consistently reliable, recallable, and possess the necessary functional, killing, and memory capabilities is not always straightforward. Moving forward, providers of these materials must employ diligent, innovative, and investigative approaches to donor selection to improve therapeutic outcomes.

Autologous therapy providers (using the patient's cells) face the challenge of determining, as early as possible, if the patient's cells are healthy enough to support the required therapy. Cell and gene therapies can be lifesaving options for patients, but considering the ethical implications of removing the patient from traditional therapies to begin a cell therapy requires critical understanding of the risks and benefits to the patient.

Ultimately, the cell and gene therapy industry must prioritize ethical, compassionate, and effective donor and patient selection processes to enhance the success of these transformative therapies.

John Nolan, Chief Science Officer, Octaviant Financial

The significant financial burden of gene and cell therapies (GCTs) on true end-payers — combined with risks of inefficacy and uncertain long-term durability — remains the major barrier to commercial adoption. Many pharmaceutical manufacturers still rely on a commercial playbook focused on providing incentives to intermediaries (PBMs/ASOs) than on the actual end-payers who bear financial risk. As a result, payers often face the dilemma of spending hundreds of thousands of dollars, if not millions, on therapies that may not deliver efficacy or long-term durability. While some GCTs boast 90%+ effectiveness, payers whose beneficiaries fall into the 10% of failures must absorb the full financial loss — an opportunity cost to the exclusion of other plan members — plus continue to cover the expense of uncured disease in the beneficiary treated with the GCT. Even if the therapy is initially successful, long-term durability (and cost benefit) remains uncertain as almost no long-term studies exist for GCTs. Thus, when non-curative, but effective and cheaper alternative therapies exist (e.g., factor therapy in hemophilia or insulin in type-1 diabetes), payers will be reticent to authorize a gene or cell therapy. Until manufacturers offer direct financial recourse to true end-payers when GCTs fail, payer resistance to adoption will persist.

Jonathan Haigh, Ph.D., UK Site Lead, FUJIFILM Biotechnologies

While there are still challenges to overcome, the outlook for cell and gene therapy commercialization is highly promising. The industry is navigating a period of adjustment, with early-stage cell therapy (CT) innovators facing tighter funding conditions, but this is also giving way to more strategic partnerships and disciplined investment.

The cost of goods remains a critical obstacle, particularly in CT with smaller patient populations and individualized production. These constraints contribute to higher treatment costs and market access barriers. CDMOs can help address hurdles through novel contracting and partnership models and by adopting new manufacturing technologies. Viral-based gene therapy (VGT) is already benefiting from platformed processes and larger-scale manufacturing, and similar innovations are accelerating within CT — particularly in automation, closed-system production, and scalable process design.

Moving forward, we expect the funding slowdown to ease and consolidation to increase, as seen in biologics. Long-term success will hinge on regulatory incentives, technological breakthroughs, and proving ROI versus traditional modalities. Each regulatory approval and commercial success builds momentum, reinforcing investor confidence and strengthening the case for broader adoption. With continued technological progress, these transformative and curative treatment options for patients will continue to move forward.

Vanee Pho-Conners, Ph.D., Vice President Global Marketing, Mission Bio

Analytics and standardization remain challenges for cell and gene therapies, and improvements are needed both to accelerate development and ensure the quality and safety of commercial batches.

Single-cell multi-omics are critical to understanding what is happening in each modified cell. Until recently, fragmentation of technologies meant that single-cell genotyping and targeted gene expression required separate workflows, leading to complex, disconnected data sets that made it difficult to build a robust pipeline at scale. The technology is finally available to meet the requirements of cost, throughput, and reproducibility, and multiple companies are now using single-assay approaches to generate the clinical multi-omics data required for critical quality attributes, ensuring safety of cell therapies.

The next step is to build towards an industry standard. Patients, developers, and especially regulators need to have confidence in the data packages compiled for CGTs. Standardization will benefit the entire industry and ensure advanced therapies are safe for patient use.

Joseph Sinkule, Ph.D., Chief Executive Officer, Founder, and the Chairman of the Board of Directors, Klotho Neurosciences, Inc.

Manufacturing remains a major roadblock in cell and gene therapy. Manufacturing of the individual plasmids required for the “triple transfection” process to make the delivery vectors like AAV and lentivirus, the manufacturing costs associated with making the plasmids and vectors, and improving the targeting the gene/vector delivery to specific tissues and organs is warranted. The manufacturing of cell therapies is also a major issue as the transport,

manufacturing, and timely return of cell-modified materials remains problematic. However, companies like AAVnerGene, a biotech renowned for its transformative technologies in adeno-associated virus (AAV) manufacturing and tissue-targeted delivery, are emerging to overcome this challenge. At Klotho, a biogenetics company developing cell and gene therapies, we utilize a protein derived from a patented form of the "anti-aging" human Klotho gene (s-KL) and novel delivery systems to transform and enhance the treatment of neurodegenerative and age-related disorders. Recently, we have partnered with AAVnerGene to develop our gene therapy asset. Its technology represents an advancement in the manufacturing of AAV vectors for intracellular gene delivery and significantly speeds up the process.

Tiffani Manolis, Vice President and General Manager of Cell Biology, Thermo Fisher Scientific

Cell and gene therapies offer immense promise to patients, especially those living with diseases once thought incurable, by treating the cause at the genetic level. But to fully realize the potential of cell and gene therapies, we need to accelerate the commercialization of treatments at scale to reach more patients faster.

One of the biggest roadblocks is in the complexity — and costs — of manufacturing these therapies. The complexities of manufacturing cell and gene therapies mean that workflows typically rely on manual processes, which can increase costs and delay timelines. At Thermo Fisher, we help address these pain points by providing end-to-end solutions — from standardized, closed-system manufacturing platforms and scalable viral vector production to integrated analytical and quality testing. By streamlining processes and reducing variability, these solutions help to simplify workflows and reduce time to market.

Another hurdle is the ability to access larger patient populations. Cell and gene therapies, in addition to being complex to develop, are incredibly complex to transport and coordinate to ensure patients receive the right treatment at the right time. They require access to cold chain logistics, real-time temperature monitoring, and specialized staff to ensure therapies are still viable once they reach a patient. This can increase the cost of developing a therapy and limit the availability for therapies in areas where there may not be the infrastructure needed to support reliable delivery.

To overcome these challenges, we need to embrace increased automation and foster collaboration across the industry. By doing so, we can effectively scale and accelerate the commercialization of cell and gene therapies, ultimately increasing access to these life-changing therapies.

Randy Dyer, Vice President, Marketing, Elegen

For many cell and gene therapy programs, a major roadblock is the speed and reliability of DNA supply. Every therapy, whether it's a viral vector, an mRNA vaccine, or an engineered cell therapy, starts with DNA. Yet traditional plasmid-based workflows can take weeks to deliver templates, struggle with long or complex sequences, and introduce variability and contamination risks that can stall programs.

These upstream delays ripple through process development, tech transfer, and GMP manufacturing, ultimately slowing time-to-clinic and commercialization. Cell-free DNA manufacturing offers a way to remove this bottleneck — delivering NGS-verified, IVT-ready DNA, manufactured cell-free and delivered in days rather than weeks, so teams can move faster, scale more efficiently, and bring transformative therapies to patients sooner.

Amy Hay, Chief Business Officer, CTMC

A common misconception is that cell therapies are too expensive or complex to scale. When therapies achieve durable clinical responses, they are cost-effective compared with standard of care. Analysis from the Tufts Center for the Study of Drug Development (CSDD) found that long-term remission and reduced treatments, hospitalizations, and clinic visits can offset the upfront cost. Cell therapies also offer a stronger return on investment, with approval rates three times higher than the average oncology drug.

The bigger challenge today isn't cost but getting the next wave of innovations into the clinic. While scientific progress is improving durability, safety, and vein-to-vein timelines, capital efficiency remains a critical bottleneck. Traditional VC/biotech models often require raising $100M+ to move from concept to initial clinical proof of concept, slowing progress.

CTMC's shared-risk model integrates CMC, regulatory, and clinical development with direct connection to MD Anderson Cancer Center, cutting time to clinical proof of concept and reducing technical and regulatory risk. This approach enables investment capital to go further so funds can be used to advance the next innovative therapy.

Fran Brown, Ph.D., Global Head, Drug Development Science, Certara

There are still multiple roadblocks standing in the way of the successful commercialization of cell and gene therapy products across the whole product life cycle. These range from decreased interest from investors or problems with manufacturing and scalability to both acute and long-term safety concerns, patient identification, and logistical challenges, as well as appropriate reimbursement models.

The sector has seen a marked decrease of investment over the last 2–3 years with many major pharma companies exiting the space. This creates financial headwinds for companies still

progressing programs in the space. Manufacturing scalability and COGS are still a challenge for both cell and gene therapies. Processes are still labor intensive and even small process changes can alter product quality attributes, keeping COGS high. For cell therapies, the predominance of autologous products creates logistically complex personalized manufacture and therapeutic delivery, which limits administration to specialized centers. Acute and long-term safety concerns, especially for gene therapies, have resulted in multiple clinical holds and even restrictions for approved products, such as experienced by Sarepta. Perhaps the biggest roadblocks are access and reimbursement challenges. Before agreeing to support the extreme prices attached on one-time therapies, payers are often looking to see long-term safety and efficacy data, which are often not available at initial approval. In addition, high prices for one-time use often create conflicts with annual budgets and patient turn-over with insurance providers. While there are increasing use cases for outcome-based contracts, these are hard to operationalize.

Thomas Fellner, Ph.D., Head of Commercial Development, Specialized Modalities, Lonza

Cell and gene therapies (CGT) are revolutionizing medicine, offering the possibility of cures for diseases once considered untreatable. However, despite this incredible promise, access remains limited, and there are significant challenges that hinder accessibility and scalability.

Within manufacturing process, drug developers can face several roadblocks. Most cell therapies still require highly customized and patient-specific processes. While this flexibility is crucial, it also introduces complexity, variability, and manual steps that simply do not scale. These challenges result in inefficiencies, inconsistent processes, and increased costs.

A further constraint arises when commercial scalability and cost-efficiency are not integrated into early development. Unlike traditional biologics, CGTs carry a higher risk of commercial failure if scalability and cost-efficiency are not addressed early in development. In another words, CGT development cannot afford to treat scalability and cost-efficiency as afterthoughts.

Looking forward, investments in automation, digitalization, and smarter early-stage strategies will be essential to overcoming these challenges and tackling high-risk, high-variability steps from day one. For example, at Lonza, we are investing in digital infrastructure to streamline data capture and improve traceability across the manufacturing life cycle. Through integrated solutions like these, we are advancing CGT manufacturing toward greater scalability and accessibility, accelerating the delivery of transformative therapies to patients worldwide.