

Keeping Pace With CGT Innovation: Clinical, Regulatory & Commercial Considerations

Panelists:

Paul Bryson, Executive Director, CSL Behring

Doug Danison, Head of Commercial, Cell and Gene Therapy Unit, Bayer

Colleen Delaney, Founder, Chief Scientific Officer & EVP, Research and Development,
Deverra Therapeutics

Tamie Joeckel, Global Business Lead, Cell and Gene Therapy Centre, ICON

Rebecca Kusko, Head of Strategy, Cellino

Moderator: Eliza Slawther, Senior Writer, Citeline

KEY TAKEAWAYS

- Technological advances and past success are motivating companies to explore new applications for CGT therapies.
- Before new CGTs can be commercialized, many challenges must be addressed.
- Financial scalability needs to be evaluated early in the CGT development process.
- Successful CGT development requires early engagement with regulatory agencies to navigate diverse requirements.
- Long-term patient tracking and data capture are essential, but these activities must minimize administrative and treatment burdens.
- Greater collaboration between academia, biotech, and pharma could close knowledge gaps and shorten CGT development cycles.
- The future is bright for CGTs, as long as scalability challenges can be overcome.

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OVERVIEW

Over the last year, the life sciences industry has seen an evolution within the cell and gene therapy (CGT) clinical trial landscape. Target indications for these advanced therapeutics have started to broaden at a faster pace beyond hematological cancers, expanding into areas such as autoimmune, neurodegenerative, and cardiovascular diseases.

To ensure the long-term commercial success of CGTs, life sciences firms must focus on all aspects of the product life cycle from the earliest phase planning to clinical trials to financial and commercial scalability. Technological innovations like artificial intelligence (AI) and automation can help with some challenges, while improved collaboration with regulators and other industry partners will be the key to success with others.

CONTEXT

In parallel with the October 2024 Cell & Gene Meeting on the Mesa, Citeline convened a panel of biotech leaders in Phoenix, Arizona. The panelists described challenges associated with expanding CGTs/technology to new or different indications, shared regulatory issues related to new CGT development, and discussed strategies for market access, reimbursement, and industry collaboration.

KEY TAKEAWAYS

Technological advances and past success are motivating companies to explore new applications for CGT therapies.

A variety of factors are driving CGT companies to explore new target indications, such as:

- **Next-generation gene therapies.** The move to next-generation gene therapies, such as those that are evolved from wild-type viruses, are opening up new indication opportunities. By engineering, inserting or substituting amino acids on an AAV's capsid surface, gene therapies can be targeted more effectively. Manipulating the capsid surface can enable gene therapies to more efficiently cross the blood-brain barrier and other biological barriers. This expands the number of diseases that gene therapies can potentially address.
- **Successful cell therapies.** Allogeneic cellular therapy, such as hematopoietic cell transplants, has been used for years to cure many people of hematologic, non-hematologic, and non-malignant disorders. Autologous CAR T-cell therapies showed that patients can be saved who have no other treatment options.
- **Proof of concept data for stem cell derived therapies.** In the autologous cell therapy space, for example, there are currently three clinical stage induced pluripotent stem cell (iPSC)-derived autologous Parkinson's dopaminergic neuron programs in the United States. That is surprising in a field that used to be very small.

“Autologous CAR-Ts drove home that we can save people who have no other treatment options. That was very inspiring and it level set things. Now as we’re progressing, we’re starting to realize it’s not that easy. There are a lot of issues that are hindering progress.”

Colleen Delaney, Deverra Therapeutics

“With the ability to get past biological barriers, we open up the aperture for diseases that we can go after. We can get higher levels of expression where we want them, to treat diseases that need high levels of therapeutic protein delivered.”

Bethany Mancillia, Capsida Biotherapeutics

Before new CGTs can be commercialized, many challenges must be addressed.

As the targets for new CGTs expand, companies need to overcome hurdles related to clinical trials and delivering products at scale to patients. The panelists identified several areas of concern, including:

- **Managing natural history studies.** For gene therapies that are “first in disease,” companies must establish success markers. In many cases, this means performing a natural history study, which takes time and money. In addition, enrolling patients in these studies can be challenging if participants won’t receive the intervention right away.
- **Identifying patients for clinical trials.** If a good standard of care already exists for a medical condition, it can be difficult to convince patients to try an innovative, less proven therapy based on a disruptive technology that has limited data from clinical trials. Clinical trials with placebo arms can also be challenging. There is the cost of running the placebo arm, as well as managing trial participants who want to get on the treatment if it starts to show a positive effect.
- **Finding trial sites with the appropriate skills and experience.** Historically, CGTs have focused on the oncology space. Oncology centers typically know how to handle cellular products and monitor for infusion related adverse events. Treatment of conditions outside of oncology with CGTs may lead to the use of smaller centers. These sites may be unfamiliar handling products that are preserved or shipped in liquid nitrogen, administering infusions, or identifying potential patient complications. The handholding and retraining at the site level can’t be overlooked.
- **Scaling delivery.** Manufacturing costs, distribution and logistics, and demand predictability can all be difficult to manage for new CGT targets. Even among CGT products that have been commercially available for several years, some of these issues have yet to be overcome. As CGTs move away from oncology and into other indications, an open question is whether the commercialization hurdles will be the same or different than in the past.

Reducing Cell Therapy Manufacturing Costs with Automation & AI

Cellino has invented a closed process for manufacturing cell therapies that’s AI-powered and autonomous. The company’s technology uses light to manage adherent cells. Light passes through a closed system for free. In addition, this approach substantially changes yield. If a small group of cells doesn’t look good, they can be removed from the culture surface using light.

Today, Cellino is focused on iPSCs. In a traditional CGT manufacturing environment, an iPSC biologist can manage 20 cell line clones simultaneously. Using Cellino’s automated system, one iPSC biologist can manage more than 300 cell line clones, supervising the algorithm and lab automation. The final-stage quality metrics are the same or better with the autonomous system. This significantly reduces the cost of goods sold for diseases where autologous therapies make sense.

Patient Delivery Innovations Could Help CGTs Scale More Rapidly

It's important to remember that patient administration is an integral part of scaling a therapy. Without a procedure to transplant CGTs into patients, incentives don't exist to make it happen. Companies working on next-generation gene therapies are identifying capsids that can be delivered intravenously. This would be a scalable delivery approach.

Looking ahead, some industry experts believe that cell therapies with no side effects will be administered in the community. Patients could go to a wellness clinic in a Walgreens or CVS, get an IV infusion for 15 minutes, and then go home.

At some point in the future, industry experts believe that cell therapies that are currently difficult to deliver may be akin to modern forms of injections. This would eliminate many delivery problems. An apt analogy are COVID-19 vaccines, which started as ultra-frozen mRNA vaccines that were very difficult to manage. Today, COVID-19 vaccines are similar to flu vaccines.

“When data is produced that’s impressive, there’s often not a path to scale the technology. It’s in essence a nice science fair experiment. We need to think carefully about how we scale these therapies.”

Rebecca Kusko, Cellino

“You can make as many cells as you want, but you also need the right delivery capacity. You also need to understand the referral pathways so you can get patients to treatment. For CAR Ts and the gene therapies for hemoglobinopathies there are established transplant networks that are a good basis for planning. With CNS therapies delivered direct to the brain, the network doesn’t really exist at scale. It needs to be developed.”

Doug Danison, Bayer

“When a patient’s been going to the same doctor for years and now that clinic can’t administer a therapy, the patient has to get referred to another physician. That creates a lot of pushback at the physician level. We need to find ways to get more sites to administer these therapies.”

Bethany Mancillia, Capsida Biotherapeutics

Financial scalability needs to be evaluated early in the CGT development process.

CGT companies must think about the financial viability of products well before they receive FDA approval. If payers don't believe that a therapy brings enough value to their customers, they won't cover it. The panelists made the following observations:

- **It's essential to understand the payer reimbursement landscape.** Some inpatient therapies are part of a bundled payment with a bundled DRG which may not be financially attractive to sites. In this situation, sites are unlikely to build infrastructure to support a treatment that will lose money.
- **If treatments already exist for an indication, payers may not be motivated to add another to their formulary.** In the CGT field, a lot of development work is done in the same therapeutic areas and for the same indications. When defining a target product profile, it's important to determine early on why a payer would add a therapy to their formulary if it already covers a similar treatment.
- **Getting payer feedback on new therapies can be difficult.** Although vehicles exist outside the U.S. to bring payers together, more work is needed to gather input from those stakeholders in the United States. Despite this challenge, it's essential to have evidence that payers will reimburse for new cell and gene therapies.

“As you think about getting medicines to patients, you also need to consider market access. Regulators will have a perspective on the evidence you need to progress. You need to also ensure that the evidence and statistical plans meet the needs of payers who themselves have a broad set of evidence requirements. You need to think about how you bring payers in the conversation early in development.”

Doug Danison, Bayer

“If you only look at the bar to clear for FDA approval and payers don't think you bring enough value to their customers, they won't cover it. You can't wait until you're post approval to think about financial scalability.”

Rebecca Kusko, Cellino

“You've got to start thinking about commercialization and payor uptake from the very beginning. An ongoing issue with CGT therapies is patient access. While we are getting therapies approved, we are still only reaching a fraction of the patient population post approval. In addition to safety and efficacy, commercialization should be part of the earliest phase considerations and one of the most critical is streamlining and scalability of the end-to-end process.”

Tamie Joeckel, ICON

Successful CGT development requires early engagement with regulatory agencies to navigate diverse requirements.

The panelists shared thoughts about the current regulatory environment, including challenges and opportunities for improvement:

- **The FDA is supportive of CGT development but is encouraged to move faster.** New FDA designations like advanced manufacturing technology (AMT) and regenerative medicine advanced therapies (RMAT) provide CGT development companies with expedited regulatory review. The FDA also offers the START (Support for clinical Trials Advancing Rare disease Therapeutics) program and has established a super office for CGTs.

While these are all positive developments, industry leaders believe that the FDA needs to move faster. Promising opportunity areas include supporting the use of biomarkers in lieu of extensive natural history studies or placebo arms.

- **The lack of harmonization across global clinical trials is difficult.** The regulatory landscape varies widely across regions. No clear answers exist for bringing international regulatory authorities together to simplify the clinical trial process.
- **Uniform regulatory standards could be beneficial but might also create unintended negative consequences.** Global regulatory standards would make it easier for CGT companies to develop compliant business strategies. However, uniform standards might also bring high levels of regulatory scrutiny that could slow CGT innovation.
- **It's never too early to think about potency assays.** Potency assays are a very important part of drug development which must be discussed with regulatory agencies. Some cell therapy companies run into regulatory challenges when they are ready for a biologics license application (BLA), because they don't have a potency assay. A firm may have two potency assays because they are unsure exactly how the product works, or it may be unable to define a potency assay that relates to the mechanism of action.

“I think on the U.S. side, regulation is favorable for gene therapies right now. The FDA needs to continue to do more. We need the FDA to get behind the use of biomarkers in lieu of doing extensive natural history studies or placebo arms.”

Bethany Mancillia, Capsida Biotherapeutics

Long-term patient tracking and data capture are essential, but these activities must minimize administrative and treatment burdens.

Some patients who receive cell and gene therapies must be tracked for many years, while others must be tracked for a lifetime. The panelists made several observations about strategies for long-term patient tracking and data capture:

- **Standardization of global patient registries is needed.** If multiple patient registries emerge worldwide that are disconnected, this will lead to significant complexity. The industry must collaborate to determine how patient registries should work. For transplant patients, the [CIBMTR](#) (Center for International Blood and Marrow Transplant Research) is the gold standard for long-term follow-up.

- Publicizing long-term follow-up information could dispel patient concerns about CGT treatment. Trust in certain patient populations can be a challenge—one example is individuals with sickle cell anemia. Using historical data to address fears and concerns could get patients to sign on to CGT treatments.
- An open question is whether CGT companies are responsible for supporting the mental health component of the patient journey. For many people, health conditions become part of their identity. If they are cured, they may end up leaving communities of other individuals with that condition. This disassociation can have profound effects.

“One of the main challenges—especially in the US—is keeping track of the patients as they change insurance providers and/or jobs over a long term or a lifetime. Considering that many of the patients during the clinical trials likely traveled to the treatment centers, it’s especially important for us to figure out how we can alleviate as much burden as possible on the patient and their caretakers, and figure out how to bring the follow-up to the patients.”

Tamie Joeckel, ICON

“How do we bring a mental healthcare component into the patient journey? What happens to both the patient and their caretakers when you cure a disease that’s been part of someone’s life for years?”

Tamie Joeckel, ICON

Greater collaboration between academia, biotech, and pharma could close knowledge gaps and shorten CGT development cycles.

One panelist noted that on the gene therapy side, it’s important to have a network of academic KOLs (key opinion leaders), especially in rare diseases. These individuals possess a deep understanding of specific diseases.

Another suggested building centers of excellence to connect academics with great innovations with industry resources. These centers would be surrounded by hubs with business development and manufacturing/commercialization process expertise.

One example of a government-funded, innovation-led organization is the UK’s [Cell and Gene Therapy Catapult](#). This organization’s industry advisory group meets monthly to discuss cross-cutting challenges and works together to overcome practical issues like creating standard clinical trial applications. The Cell and Gene Therapy Catapult also has an advanced therapy treatment center network which takes a consortia approach—industry, academia, and clinical sites innovate together.

Examples of CGT Industry Advisory Groups and Collaborative Task Forces

- [The International Society for Cell & Gene Therapy \(ICST\)](#)
- [The International Society for Stem Cell Research \(ISSCR\)](#)
- [American Society for Transplantation and Cellular Therapy \(ASTCT\)](#)
- [Alliance for Cell Therapy \(ACT\) Now](#)
- [The Cord Blood Association](#)
- [The Innovative Health Initiative](#)

“There are a lot of gaps in small biotech and academia. If we can bridge those gaps with people who understand drug development better, it would be great.”

Colleen Delaney, Deverra Therapeutics

“Cell and gene therapy is a space that’s rapidly evolving. From a larger pharma perspective, we need to weigh the risk of overinvestment in a particular technology, and it makes more business sense for us to partner with the academics, biotechs, and startups who are innovating at the cutting edge. They will inevitably have gaps we can help fill and vice versa, and that’s where the opportunity comes in for us.”

Paul Bryson, CSL Behring

The future is bright for CGTs, as long as scalability challenges can be overcome.

CGTs is a field that is taking off like a rocket ship. Continued diversification of target indications is expected to continue in areas like autoimmune disorders, neurology, and more. Looking to the next five to ten years, the panelists made the following observations:

- **To be successful, CGT companies must make headway on scalability.** More work is needed on the last mile. CGTs must be efficient and reach more patients at a reasonable cost. There is optimism that AI and automation can help move the needle.
- **Moving to in vivo delivery of CGTs is very exciting.** Many hope that more therapies can move to first-line treatments. One scenario is that allogeneic cell therapies are available off the shelf and a combination of immune cell therapies will mimic more of the natural immune system.
- **Predictive analytics will identify which patients will be most successful with CGTs.** More data will help CGT development teams identify what types of patients should be enrolled in trials. With this knowledge it will be easier to screen target populations earlier.
- **To ensure that funding continues, it’s essential to demonstrate the commercial viability of CGTs.** CGTs need to be financially attractive to investors. If that’s not possible, funds will flow to small molecules because they seem easier to deliver to the market.

“I feel like investors and others saw the CGT rocket ship. There have been some challenges with profitability as CGTs entered the market. We need to have financial success stories to maintain funding. Someone has to pay the bills for the research to continue. We need to make sure we can make this financially attractive to investors.”

Doug Danison, Bayer

“I think what’s most exciting right now is the idea of moving to in vivo delivery. I hope in five to ten years, we understand where it will work and where it won’t.”

Colleen Delaney, Deverra Therapeutics

BIOGRAPHIES


Paul Bryson

Executive Director, CSL Behring

Paul Bryson is the Executive Director and Global Platform Leader for Cell and Gene Therapy within R&D at CSL. Since joining in 2021, Paul has led the Gene Therapy Platform Strategy Team, acting as a catalyst for focused, strategic platform development. He has spearheaded CSL's early CGT initiatives, advancing multiple programs through IND-enabling studies and driving the evolution of CSL's CGT products across ex vivo and in vivo modalities. Paul is extremely gratified to be able to witness decades of scientific innovation being translated into patients' lives at scale today.

Before CSL, Paul led US operations at TCRcure Biopharma Corp, a pioneering cell therapy startup. There, he oversaw the development of TCR-T and CAR-T therapies for solid tumors, advancing six investigational cell therapies from Discovery to First-in-Human. He holds degrees from Princeton University and Stanford University and completed postdoctoral training at the University of Southern California


Doug Danison

Head of Commercial, Cell and Gene Therapy Unit, Bayer

Doug is inspired by the transformative benefits that biotech innovation can bring to patients, families, physicians, and the healthcare system. He has more than 20 years of pharmaceutical and biotech experience, including roles with Eli Lilly, Amgen, Millennium/Takeda Oncology, bluebird bio, and now Bayer Cell & Gene Therapy (CGT). He has led or overseen the preparation of market access and commercial strategies for products in early development, pivotal study planning, launch, and post launch lifecycle management. He has addressed business challenges from a variety of vantage points including Global, European, and US roles. He has built highly engaged teams, business processes, and a knowledgebase that enables the execution of commercial strategies with a focus on oncology and cell and gene therapies.

As Head of Commercial Strategy and Operations for Bayer CGT, Doug is responsible for connecting large pharmaceutical company commercial scale and footprint with small biotech innovation within the context of an "arms-length" operating model. He enjoys working in new spaces with a high level of uncertainty and the associated challenge of making sense out of ambiguity.



Colleen Delaney

Founder, Chief Scientific Officer & EVP, Research and Development,
Deverra Therapeutics

Dr. Colleen Delaney is Scientific Founder and Chief Scientific Officer, Executive Vice President of Research and Development of Deverra Therapeutics, Inc., a cellular therapy company focused on development of universal donor, off-the-shelf cell therapies for patients with hematologic malignancies and other critical diseases. Additionally, she is the Chief Scientific and Medical Officer for Coeptis Therapeutics. Dr. Delaney is a stem cell transplant physician and an Affiliate and former Professor of the Fred Hutchinson Cancer Research Center, Clinical Research Division, where she was PI of an NIH/government funded laboratory and where she established and became the Director of the Program in Cord Blood Transplant and Cord Blood Research at the Fred Hutch/Seattle Cancer Care Alliance. Dr. Delaney's research interests focus on the development of methods to expand the number of umbilical cord blood stem cells for clinical applications and to also direct these cells to further differentiate into mature blood and immune cells for addition cell therapy products. She has more than 20 years of experience in the development of cord blood derived allogeneic cell therapies from bench to bedside and is an inventor on numerous patents. Over her career, she has raised greater than \$175M in dilutive and non-dilutive capital.

Dr. Delaney received her MSc from Oxford University and her MD from Harvard Medical School and is the recipient of numerous awards, including the prestigious Damon Runyon Foundation Clinical Investigator Award, the Dr. Ali Al-Johani Award in recognition of exemplary clinical medical care and compassion to patients and families, the Seattle Business Journal's Leaders in Health Care Award for Outstanding Medical Research, the Seattle American Women in Science's Award for the Scientific Advancement and Leadership in STEM and she is a 2019 Inductee into the Washington Life Science Hall of Fame.



Tamie Joeckel

Global Business Lead, ICON Centre for Cell and Gene Therapy

Five years ago, Tamie joined ICON's Centre for Cell and Gene Therapy that was formed to provide overarching subject matter expertise and support for their global CGT trials. With over ten years of experience in CGT logistics and site support, she provides operational strategy and consulting for managing the complex supply chain and vendor ecosystem. Prior to ICON, Tamie was SVP at Cryoport and managed the vendor alliances at Vineti. Certified in production and inventory management, she has spent over 40 years in executive management roles encompassing IT, M&A and has pharma experience in both commercial launch and clinical trials. Starting her career at Arthur Andersen as an IT consultant in mergers & acquisitions, she moved to the pharma industry in 2001. As VP of Corporate Development of AmerisourceBergen (now Cencora), Tamie worked with teams responsible for the commercial launch of specialty biologics with a key focus on plasma derived drugs. Working with industry and patient advocacy groups, Tamie spent 3 years on Capitol Hill lobbying for patient reimbursement reform for hemophilia and SCID. As the mother of a grown child with a rare disease, Tamie often jokes that her diverse executive journey in finance, IT & ERP systems led her to the exact place she is supposed to be – which is supporting the product, patient and regulatory journeys in cell and gene therapy.



Rebecca Kusko

Head of Strategy, Cellino

Rebecca Kusko, Ph.D. (Chief of Staff & Head of Strategy): Prior to Cellino, Rebecca spent her last decade in biotech pivoting a small bioinformatics startup into a publicly-traded clinical stage company via business development, corporate strategy, and investor relations. Rebecca received her PhD in Genetics & Genomics from BU School of Medicine, and received her S.B from MIT in Biological Engineering. She is the deputy chair of the FDA lead MAQC Society, an organization focused on best practices for emerging technologies. In her last decade, Rebecca has published more than 50 papers and textbook chapters.



Bethany Mancilla

Chief Business Officer, Capsida Biotherapeutics

Bethany Mancilla is the Chief Business Officer at Capsida Biotherapeutics, a fully integrated gene therapy company developing next generation AAV engineered therapies. Bethany has over 25 years of biotechnology leadership experience in business development, corporate strategy and financing across small and large biopharmaceutical companies. Bethany began her career commercializing innovations and establishing start-up companies from Baylor College of Medicine. She transitioned into emerging biotechnology companies during the genomics era and held increasing roles of responsibility at Gene Logic, a novel drug target discovery company, spear-heading multiple partnerships with leading pharmaceutical companies including Pfizer, Roche, and Lilly. In 2010 she transitioned to VP Business Development for Micromet the developer of the first FDA approved bi-specific T-cell engaging antibody Blincyto® where she had responsibility for US business development and global alliance management. In her role, she forged the strategic partnership with Amgen that led to the company's acquisition by Amgen. As a key member of the Amgen external research and development team, she assumed escalating roles and responsibilities becoming the Vice President of Business Development overseeing a global team of business development executives. In her current position at Capsida, she leads the company's business operations including business development, strategy, corporate communications, and intellectual property management. Since joining Capsida, she has established partnerships providing over \$220M in funding for the advancement of gene therapies for neurodegenerative and neurodevelopmental disorders. Ms. Mancilla received an M.B.A. from the University of Houston and a B.A. from the University of Colorado.



Eliza Slawther

Senior Writer, Citeline (Moderator)

Eliza began reporting on health and medical science in 2018 while completing her Master's degree in Journalism at City, University of London. During her degree program she interned at C+D and on the London Evening Standard's health desk. In the years since, Eliza has written about everything from mid-stage drug development to market access for medicines and devices in the EU and beyond. Her work explores the trials and tribulations of securing reimbursement for medical products in Europe, and Eliza is particularly interested in the challenges of funding innovation in health care. Eliza has lived in London since 2017 and is originally from Cheshire, in the north west of England. She has a BA in English Literature from the University of Manchester and is in the process of completing a second undergraduate degree in Biomedicine from Birkbeck College, an evening university that is part of the University of London.