March 5, 2026

The Honorable Rick Scott
Chairman
Special Committee on Aging
United States Senate
Washington, DC 20510

The Honorable Kirsten Gillibrand
Ranking Member
Special Committee on Aging
United States Senate
Washington, DC 20510

Dear Chairman Scott and Ranking Member Gillibrand:

On behalf of the Alliance for Regenerative Medicine (ARM), which represents more than 400 members across 25 countries, including emerging and established biotechnology companies, academic and medical research institutions, and patient organizations, I commend the Special Committee on Aging for holding a hearing on how regulatory processes and evolving standards at the Food and Drug Administration (FDA) can unintentionally delay patient access to safe and effective therapies, particularly for individuals living with rare diseases. ARM is the leading international advocacy organization championing the benefits of engineered cell therapies and genetic medicines for patients, healthcare systems, and society. Because approximately 80 percent of rare disorders have genetic causes,[1] cell and gene therapies (CGTs) are critical in targeting the root causes of these diseases rather than treating symptoms and have the potential to transform the lives of afflicted patients.

The FDA's recent reversal of previous agency guidance and rejection of several CGTs for rare diseases has raised concerns over regulatory clarity and predictability at the agency. An efficient and predictable review process at FDA is essential to maintain the U.S.'s biomedical leadership in the face of growing competition from countries like China and to ensure that patients with rare diseases have access to life-saving CGTs. **We urge the Committee to work with the White House, HHS, and the FDA to ensure that practical and actionable steps are taken to address growing concerns over regulatory inconsistencies and late-stage shifts in guidance for CGT rare disease programs at the FDA.**

CGTs can offer life-saving treatment options for patients with rare diseases

The U.S. has introduced more CGT products into the market than any other country and is a world leader in promoting access to CGTs. To date, the FDA has approved 48 CGTs.[2] Research has projected approvals of between 75 and 96 new CGT product-indications by 2033,[3] with estimates of the number of patients receiving CGT treatments increasing approximately tenfold in a similar period.[4]

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[1] Marwaha S, Knowles JW, Ashley EA. A guide for the diagnosis of rare and undiagnosed disease: beyond the exome. Genome Med. 2022;14(1):23. doi: 10.1186/s13073-022-01026-w
[2] U.S. Food and Drug Administration. Approved Cellular and Gene Therapy Products. December 9, 2025. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products.
[3] Cell and Gene therapy (CGT) pipeline deep dive. Center for Biomedical System Design. Tufts Medical Center. 2023. https://newdigs.tuftsmedicalcenter.org/payingforcures/defining-disruption/cell-and-gene-therapy-products-and-%20pipeline/cgt-pipeline-deep-dive/#gsc.tab=0.
[4] Phares S et al. The next decade in cell and gene therapy. *Drug Discovery Today*. January 2026; 31(1). https://www.sciencedirect.com/science/article/pii/S1359644625002648.

It is becoming increasingly clear that the promise of CGTs is bearing fruit for rare disease patients. CGTs are remarkable in that they treat the root cause of disease and have proven to be life-saving for rare disease patients who have few or no other options. Gene therapies seek to modify or introduce genes into a patient's body with the goal of durably treating, preventing, or potentially curing a disease. There are currently 15 gene therapies available for rare genetic diseases and conditions, such as Duchenne muscular dystrophy, sickle cell disease, and two forms of hemophilia. Cell therapies involve the administration of viable, often purified cells into a patient's body to grow, replace, or repair damaged tissue. In 2024, the FDA approved the first-ever adoptive cell therapy – for metastatic melanoma. FDA also approved new cell therapies such as those for advanced synovial sarcoma, a rare type of cancer that often attacks joints, and for dystrophic epidermolysis bullosa, a rare skin condition that causes widespread blistering that can lead to vision loss or permanent scarring.

Congress has long-supported progress in rare disease therapy and CGT development

It takes years and considerable capital to bring new rare disease therapies to market, and companies need predictability to make business decisions, plan future research and development, and attract investors. On average, the development timeline for rare disease treatments is 10-15 years.[5] The cost of bringing CGTs to market is nearly $2 billion,[6] and only 13.8 percent of CGT therapeutic development programs that enter phase 1 of the approval process complete phases 2 and 3 and reach FDA approval.[7] We thank Congress for recent passage of the *Mikaela Naylon Give Kids a Chance Act*, which reauthorizes the Rare Pediatric Disease Priority Review Voucher (RPD PRV) Program and provides crucial incentives for companies to invest in developing treatments like CGTs for children with rare diseases.

Congress has long recognized the importance of policies to address the inherent complexities in developing CGTs and treatments for rare disease populations. Through the *21st Century Cures Act*, for example, Congress authorized the FDA to establish the Regenerative Medicine Advanced Therapy (RMAT) designation program that provides sponsors of CGT products with enhanced FDA interactions. In FY 2024 alone, the FDA approved 73% of RMAT requests, a significant jump from the previous high of 51%. Many RMAT-designated products also hold orphan designation, reflecting the program's impact in accelerating therapies for rare diseases. Moreover, one-third of all RMAT designations granted since the program's inception were awarded in the past two years, underscoring the program's growing role in expediting innovative therapies.

By making RMAT-designated products eligible for accelerated approval, a pathway established by Congress in 1992, the RMAT program also encourages flexible clinical trial designs, novel

[5]Lumsden JM, Urv TK. The Rare Diseases Clinical Research Network: a model for clinical trial readiness. *Ther Adv Rare Dis*. 2023;4:26330040231219272. Published 2023 Dec 26. https://pmc.ncbi.nlm.nih.gov/articles/PMC10752072/

[6] *See* Sabatini MT, Chalmers M. The Cost of Biotech Innovation: Exploring Research and Development Costs of Cell and Gene Therapies. *Pharmaceut Med*. 2023;37(5):365-375. doi:10.1007/s40290-023-00480-0; De Luca M, Cossu G. Cost and availability of novel cell and gene therapies: Can we avoid a catastrophic second valley of death?. *EMBO Rep*. 2023;24(2):e56661. doi:10.15252/embr.202256661.

[7] Wong, C.H., Li, D., Wang, N. *et al.* The estimated annual financial impact of gene therapy in the United States. *Gene Ther* 30, 761–773 (2023). https://doi.org/10.1038/s41434-023-00419-9.

endpoints, and real-world evidence while maintaining FDA standards for safety and efficacy. These flexibilities include the use of surrogate endpoints, which are substitute measures used in clinical trials to predict clinical benefits, allowing for faster drug approvals by the FDA. Gene therapies are especially amenable to the use of surrogate endpoints because the protein product of many gene therapies lies directly in the causal pathway of disease (e.g., a gene mutation causes a lack of protein production that is restored with a functional gene).

Recent actions by the FDA undermine the Trump Administration's bold vision for CGTs

Over the past year, the Trump Administration, including HHS and FDA leadership, have publicly stated unprecedented support for CGTs to ensure America remains a global biotech leader. In 2025, the FDA convened a CGT roundtable and listening sessions with biotech CEOs, providing forums on how accelerate CGT development. The FDA has also proactively outlined multiple new policies to advance the CGT sector, such as the Rare Disease Evidence Principles program (RDEP) to clarify efficacy requirements; a new Plausible Mechanism of Action Pathway for individualized treatments, like N-of-1 gene therapies; and case-by-case flexibilities for chemistry, manufacturing, and controls (CMC) requirements.

Unfortunately, a number of recent negative regulatory actions related to late-stage CGTs have undermined the stated goals of HHS and FDA leadership (see Appendix 1). Over the past four months, the FDA has declined to approve multiple promising CGT medicines – including treatments for rare diseases and conditions like Huntington's Disease, Hunter Syndrome, and Epstein-Barr virus-associated post-transplant lymphoproliferative disorder – by issuing complete response letters (CRLs). Particularly concerning is the inconsistent application of regulatory flexibilities for these rare disease products, despite the fact that nearly all of them received the RMAT designation.

In some of these rejections, the FDA changed the evidentiary requirements for clinical trials at the last minute, reversing commitments it had made just months before to bring these medicines forward. This includes raising last-minute questions about whether a surrogate endpoint predicts clinical benefit or taking issue with the use of natural history studies as a control in the clinical trial design. Randomized, double blind, placebo-controlled trials that are traditionally conducted in conditions with larger and well characterized disease populations are often not appropriate or ethical when considering the challenges and urgency of rare diseases. These CRLs represent a troubling trend where well-established principles of regulatory flexibility have been sidelined in favor of methodological rigor. In fact, the rejection of natural history studies as a valid control runs counter to the Plausible Mechanism Pathway draft guidance just released by the FDA.

Dating back to last year, communication with sponsors has been poor and external engagement has also been lacking. For example, in the past the FDA has assembled a group of outside experts through an Advisory Committee to offer an independent opinion, to hear from patients and families about their experiences with the drug and the condition it treats, and to help resolve scientific disagreements.[3] In 2025, however, the FDA held 65% fewer Advisory Committee meetings for prescription drugs, biologics, and related topics than in 2024, reducing opportunities for external expertise and patient insights to inform FDA decisions, and thus raising questions not only about the adequacy of FDA staffing but philosophical changes.

Historically, collaboration between regulators, researchers, industry, and patients – through transparent knowledge sharing and scientific exchange – has helped drive progress in rare disease treatments while maintaining rigorous standards.

Regulatory inconsistency impacts rare disease patients and the U.S.'s biopharmaceutical leadership

Nearly 900 ongoing clinical trials in the United States are testing CGTs. Each one represents tremendous hope for millions of other patients and their families – not only for those suffering with rare diseases, but also common ones like heart disease, Parkinson's disease, and diabetes. We are concerned that – if not corrected – these patterns of uncertainty risk patient access to life-saving treatments, and this will undoubtedly have a disproportionate impact on rare disease patients. For patients with degenerative conditions, delays in access to treatments caused by FDA's recent regulatory inconsistencies can result in irreversible changes to their functionality or even death. Many rare disease patients simply cannot wait a decade for new trials to be conducted.

These actions that slow the development of urgently needed rare disease therapies also come at a time when China is racing to eclipse the US as the global leader in CGTs. For the first time, in 2025, the Asia-Pacific region surpassed North America in clinical trials for CGTs.[8] And, during the second half of 2025, clinical trials for CGTs grew 20% in China, compared to only 8% in the United States. Clear and predictable regulatory pathways are essential to maintaining U.S. competitiveness in biomedical innovation and for Americans with rare diseases and other high unmet medical needs. Without a serious course correction, U.S. patients will increasingly be denied access to transformative therapies even as these medicines become available to their counterparts in other countries.

ARM recommends several remedies for late-stage rare disease programs

1 in 10 Americans have a rare disease, with 70% of rare diseases beginning in childhood. Of the more than 30 million people living with one or more rare diseases in the United States, 15 million (or 50%) are children. More than 90 percent of the estimated 10,000+ rare diseases still have no cure.[9] Parents raising children with rare diseases face challenges in managing their daily lives as they navigate caregiving roles and uncertainties about the life-course of disease for their children. Their hope is anchored on developers, risking capital and potential for profitability, to innovate cures.

To bring these cures to fruition, innovative breakthroughs like CGTs require not only regulatory flexibilities that address the unique challenges associated with their development, but also a consistent and predictable framework for regulatory oversight. ARM urges a common-sense course-correction at the FDA that puts patients first, addresses regulatory inconsistencies, improves communication, and remedies shifts in guidance that put late-stage rare disease

[8] Alliance for Regenerative Medicine. Reasons to Believe: Innovation, Access, and Sustainability in CGT. January 2026. https://alliancerm.org/wp-content/uploads/2026/01/ARM-CGT-Reasons-to-Believe-January-26-2026.pdf.
[9] *See* National Organization for Rare Disorders. Get to Know the Facts about Rare Disease. December 2025. NRD-2332 RD Fact Sheet_FNL - v2; Global Genes. Numbers: Rare Disease Facts. https://globalgenes.org/rare-disease-facts/.

programs in jeopardy. The FDA has commonly used the following approaches in approving dozens of CGTs over the last decade:

1. Sponsors who were previously aligned with the FDA urgently need a path forward. The FDA should honor the commitments it originally made to companies and patients about what evidence would be acceptable for approval. To facilitate, sponsors should be granted an expedited Type A meeting, with FDA leadership present, to resolve these issues.[10]

2. To prevent unnecessary patient access delays, the FDA should leverage post-market commitments to further establish efficacy after approving the therapies.[11] Through post-market commitments, the FDA can gather additional data from patients after approval to further verify the strong signals that these medicines work.

3. Upon request from the sponsor, the FDA should assemble a group of outside experts, known as an FDA Advisory Committee, to transparently review these therapies and listen to testimony from patients about the benefits-risk considerations for a therapy.[12] If a sponsor requests an Advisory Committee meeting, one should be granted.

We ask the Committee to work with the White House, HHS, and its agencies to ensure that the regulatory flexibilities Congress has authorized are meaningfully and consistently used by the FDA to provide patients with rare diseases access to life-saving therapies like CGTs.

The past decade has shown that a modernized regulatory framework, clear and predictable pathways for sponsors, and open engagement with stakeholders are essential to maintaining the U.S.'s leadership in biomedical innovation. The consistent application of regulatory flexibilities is critical for patients with rare diseases and other high unmet medical needs, where delays in development and approval can mean the difference between life-saving treatment and no treatment at all.

As evidenced by the many powerful testimonies of patients and their advocates heard throughout Rare Disease Week on Capitol Hill, rare diseases profoundly impact the quality of life of affected individuals and their families. The CGT sector holds great promise for transforming the landscape of rare disease treatment by offering the innovative, targeted, and potentially curative therapies these patients deserve. We thank you for your continued focus on improving the lives of those living with rare medical conditions, for some of whom CGTs may be the only treatment option.

ARM strives to be a resource for this Committee. We look forward to working with you to develop additional policy solutions that bring safe and effective regenerative medicines to patients. For questions, please contact ddavenport@alliancerm.org.

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[10] PDUFA VII Commitment Letter / FDA Draft Guidance 2023, *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*

[11] FDCA § 506(c) (21 USC 356(c)), *Expedited approval of drugs for serious or life-threatening diseases or conditions* / 21 CFR 601Subpart E, *Accelerated Approval of Biological Products for Serious or Life-Threatening Illnesses*

[12] Consistent with FDA's longstanding practice under 21 CFR Part 14 and Federal Advisory Committee Act (FACA)

Sincerely,

Mark Battaglini

Mark Battaglini
Chief Strategy Officer
Alliance for Regenerative Medicine

Appendix 1 - Rare disease cell and gene therapy programs in jeopardy

Company	Program	Milestone	Timing/Outcome	RMAT Designation
Atara Biotherapeutics/ Pierre Fabre	Epstein-Barr virus-associated post-transplant lymphoproliferative disorder	**CRL**	January 9, 2026; pursuing Type A meeting	
REGENXBIO	Hunter syndrome	**CRL**	February 7, 2026; pursuing Type A meeting	X
Capricor Therapeutics	Duchenne Muscular Dystrophy Cardiomyopathy	**CSR submitted as part of ongoing BLA review**	February 24, 2026	X
UniQure	Huntington's Disease	**FDA recommends Ph3 RCT with sham brain surgery**	March 2, 2026; pursuing Type B meeting	X

Last Updated: March 5, 2026