Alliance for Regenerative Medicine

February 23, 2026

The Honorable Mehmet Oz, MD
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CMS-1832-P
P.O. Box 8016
Baltimore, MD 21244-8016

Submitted electronically via www.regulations.gov

Re: Global Benchmark for Efficient Drug Pricing (GLOBE) Model (CMS-5545-P)

Dear Dr. Oz:

The Alliance for Regenerative Medicine (ARM) appreciates this opportunity to comment on the Global Benchmark for Efficient Drug Pricing (GLOBE) Model proposed rule (the "Proposed Rule")[1].

ARM is the leading international advocacy organization championing the benefits of engineered cell therapies and genetic medicines for patients, healthcare systems, and society. As a community, ARM builds the future of medicine by convening the sector, facilitating influential exchanges on policies and practices, and advancing the narrative with data and analysis. We actively engage key stakeholders to enable the development of advanced therapies and to modernize healthcare systems so that patients benefit from durable, potentially curative treatments. As the global voice of the sector, we represent more than 400 members across 25 countries, including emerging and established biotechnology companies, academic and medical research institutions, and patient organizations.

As outlined in ARM's July 2025 RFI submission ("Ensuring Lawful Regulation and Unleashing Innovation To Make American Healthy Again" (AHRQ-2025-0001)), CGTs have the potential to eliminate or replace costly and burdensome chronic care and avert costs associated with downstream complications of disease progression. This is highly aligned to the Administration's Make America Healthy Again (MAHA) agenda.[2] ARM acknowledges the constructive steps taken by the Administration to support access to existing cell and gene therapies (CGTs) and to promote ongoing innovation, including through the launch of the CGT Access Model, as well as the exclusion of CGTs from packaged payment associated with Comprehensive

[1] https://www.federalregister.gov/d/2025-23702.

[2] Alliance for Regenerative Medicine, comment letter on *Request for Information (RFI): Ensuring Lawful Regulation and Unleashing Innovation To Make American Healthy Again (AHRQ-2025- 0001)*, July 14, 2025, available at: https://alliancerm.org/wp-content/uploads/2025/09/ARM-Comments-on-HHS-RFI-on-Deregulation-AHRQ-2025-0001-FINAL.pdf.

Ambulatory Payment Classifications (C-APCs) reimbursed under the Medicare Outpatient Prospective Payment System.

ARM's membership includes both small and large companies leading the development and manufacturing of cell and gene therapy technologies today. We have seen the promise of these medicines to transform the delivery of care for a wide range of acute and chronic diseases. The robust growth we have seen in CGT innovation relies on a stable market environment with payment policies that promote access to these rapidly evolving technologies and further investment in their potential. **A Most Favored Nation pricing mandate would significantly undermine the constructive steps taken to date by the Administration to support CGTs.** It would diminish patient access to existing cell and gene therapies, as well as introduce significant barriers to continued biopharmaceutical innovation. ARM therefore urges the following:

- **We urge CMS to withdraw the proposed GLOBE model. Importing foreign pricing and payment methodologies risks undervaluing and undermining the long-term health and economic benefits of CGTs.** GLOBE also risks introducing many of the same access challenges observed in non-US OECD countries—where life-saving CGT products have been withdrawn from the market due to inadequate commercial viability—while ceding U.S. biopharmaceutical leadership to China.

- **We believe multiple factors underscore the particular harms MFN pricing would have on CGTs, and ARM urges CMS to exclude CGTs from GLOBE if the agency proceeds with the initiative despite our strong opposition to the model.** CMS specifically sought comment on the merits of excluding CGTs based on supply chain criteria or other factors that warrant their inclusion or exclusion. This request for comment demonstrates the agency's appreciation for the unique nature of CGTs and the adverse effects that an MFN pricing mandate could have on the sustainability of these supply chains and other factors. Exclusion of these therapies from GLOBE and from any other MFN pricing models or policies would be critical to ensuring patient access to CGTs and ongoing innovation and investment in this nascent field.

We greatly appreciate the focus that HHS leadership under President Trump have already brought to the promise of CGTs in the first year of this Administration. ARM reiterates its commitment to collaborating with CMS to develop payment policies that support innovation, protect patient access, and maintain U.S. leadership in regenerative medicine. We discuss our recommendations regarding the Proposed Rule in more detail below.

I. CMS should withdraw the GLOBE model, which will undermine U.S. leadership in biopharmaceutical innovation. This risk is especially pronounced with respect to America's leadership in CGT development, particularly as manufacturers based in China

continue to invest significantly in developing CGT production and R&D capacity.

A. The United States leads the world in biopharmaceutical innovation broadly and CGT product development specifically. Implementing a Most Favored Nation pricing mandate under the GLOBE model risks jeopardizing this position in the face of emergent competition from China.

The U.S. has introduced more CGT products into the market than any other country and is a world leader in promoting access to these therapies. To date, the U.S. Food and Drug Administration (FDA) has approved 48 cell and gene therapies.[3] This includes approvals for gene therapies treating Duchenne muscular dystrophy and hemophilia A, cell therapies for type 1 diabetes and multiple cancer indications, and two gene therapies treating sickle cell disease (SCD).[4] As the promise of CGTs continues to come into focus, the pipeline for both rare and prevalent diseases is accelerating. Most recently, the FDA approved both a new cell therapy and a tissue engineered therapy in December 2025 and could issue approvals of up to three additional cell or gene therapies in the first few months of 2026.[5] Recent research projects approvals of between 75 and 96 new CGT product-indications by 2033,[6] with estimates of the number of patients receiving CGT treatments increasing approximately tenfold in a similar period.[7]

These advances have significant implications not only for patients but also for the Federal health care programs that serve them, representing a significant potential for cost savings to both the state and Federal governments. For example, Medicaid beneficiaries with SCD have five times more emergency department visits and nearly eight times more hospitalizations than Medicaid beneficiaries without SCD,[8] representing a significant cost to both the state and Federal governments. As CGTs can offer potentially curative and durable therapies, they have the potential to

[3] Approved Cellular and Gene Therapy Products, FDA, December 9, 2025, available at: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products.

[4] *See* FDA Approves First Gene Therapies to Treat Patients with Sickle Cell Disease, FDA, December 2023, available at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease.

[5] *See* FDA Approves First Cellular Therapy to Treat Patients with Severe Aplastic Anemia, FDA, December 8, 2025, available at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-cellular-therapy-treat-patients-severe-aplastic-anemia; FDA Approves Nerve Scaffold for the Treatment of Sensory Nerve Discontinuity, FDA, December 3, 2025, available at: https://www.fda.gov/news-events/press-announcements/fda-approves-nerve-scaffold-treatment-sensory-nerve-discontinuity; Sector Snapshot, Q3 2025, Alliance for Regenerative Medicine, December 2025, available at: https://alliancerm.org/wp-content/uploads/2025/11/Sector-Snapshot-Draft-Q3-2025_Published.pdf.

[6] *See* Cell and Gene therapy (CGT) pipeline deep dive, Center for Biomedical System Design, Tufts Medical Center, 2023, available at: https://newdigs.tuftsmedicalcenter.org/payingforcures/defining-disruption/cell-and-gene-therapy-products-and-%20pipeline/cgt-pipeline-deep-dive/#gsc.tab=0.

[7] *See* Phares S et al., The next decade in cell and gene therapy, Drug Discovery Today, January 2026; 31(1), available at: https://www.sciencedirect.com/science/article/pii/S1359644625002648.

[8] *See* Centers for Medicare and Medicaid Services. Sickle Cell Disease Report, March 2023, available at: https://www.medicaid.gov/sites/default/files/2023-03/scd-rpt-mar-2023.pdf.

eliminate or replace the direct cost of chronic care and avert costs associated with downstream complications of disease progression,[9] in line with this administration's stated commitment to address chronic disease.

Even so, access for these products remains challenging and there is much work to be done around improving the innovative payment structures for these therapies, which, as we discuss below, are significantly more expensive and complex to develop and manufacture than traditional drugs. Mandatory importation of foreign prices into the Medicare program will exacerbate these challenges, reduce revenue necessary for research and development, and discourage the private investment necessary to support continued CGT development. The second-order effects of reference pricing mechanisms were illustrated by an analysis conducted by the Congressional Budget Office in 2019 regarding the effects of pending legislation that would have introduced a ceiling price on drugs negotiated by Medicare based on the average price of those drugs in Australia, Canada, France, Germany, Japan, and the United Kingdom. Under this analysis, CBO estimated that implementing a ceiling price on Medicare-negotiated products based on this methodology would result in approximately 8 fewer drugs being introduced to the U.S. market over the 2020-2029 period, and about 30 fewer drugs over the subsequent decade.[10] Imposing MFN pricing policies on CGTs will be detrimental to this continuously evolving class of drugs and undermine the United States' leading role in biopharmaceutical innovation.

A 2025 policy analysis from the University of Chicago similarly estimated that applying the MFN pricing policy to existing drugs in Medicare and Medicaid would reduce U.S. pharmaceutical revenues by 49%. Globally, the analysis found that pharmaceutical revenues were projected to decline by 31%, leading to a nearly 48% reduction in R&D spending. If persistent over a 10-year horizon, this shortfall would result in the loss of 210 new drug approvals, together with 290 post-approval indications, resulting in a combined loss of 500 drugs, or 50 per year. This large cut in innovation is estimated to be associated with a loss of 516 million life-years, corresponding to approximately 6.6 million lives lost worldwide over 10 years.[11]

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[9] *See, e.g.,* Curative Regenerative Medicines: Preparing Health Care Systems for the Coming Wave, Alliance for Regenerative Medicine, November 2016, available at: https://alliancerm.org/wp-content/uploads/2026/02/IN_VIVO_ARM_WhitePaper_CurativeRegenMed.pdf; Regenerative Medicine is Here: New Payment Models Key to Patient Access, Alliance for Regenerative Medicine, August 2018, *available at*: https://alliancerm.org/wp-content/uploads/2018/07/ARM_WhitePaper3_IV1807_LRS.pdf; A Transformative Therapy Value Model for Rare Blood Diseases, Alliance for Regenerative Medicine, January 2020, available at: https://alliancerm.org/wp-content/uploads/2025/09/ARM-Marwood-White-Paper-FINAL.pdf.

[10] Congressional Budget Office & Joint Comm. on Taxation, Letter to the Honorable Frank Pallone Jr., Chairman, Committee on Energy and Commerce, U.S. House of Representatives: Effects of Drug Price Negotiation Stemming from Title I of H.R. 3, the Lower Drug Costs Now Act of 2019, on Spending and Revenues Related to Part D of Medicare (December 10, 2019), available at https://www.cbo.gov/system/files/2019-12/hr3_complete.pdf.

[11] Philipson, Tomas, et al. The Impact on Patient Health of Most-Favored-Nation Pricing of Already Marketed Drugs. The University of Chicago. September 2025. Accessed from: https://bpb-us-w2.wpmucdn.com/voices.uchicago.edu/dist/d/3128/files/2025/09/MFN-Impact-on-Patient-Health-Final-Sep-29.pdf.

ARM believes the U.S. should not implement policies that would cede its global leadership in biopharmaceutical R&D by adopting other countries' price controls. In alignment with the Administration, ARM is particularly concerned about China, which has been successful in attracting CGT developers to initiate clinical trials in its market. For the first time, in 2025, the Asia-Pacific region (n=990) surpassed North America (n=916) in clinical trials.[12] And, during the second half of 2025, clinical trials for CGTs grew 20% in China, compared to only 8% in the United States.

ARM also agrees with the Trump Administration's efforts to encourage domestic manufacturing in the US. However, MFN reference prices could reduce economic and market access incentives for domestic manufacturing of CGTs, which are significantly more expensive and complex to manufacture than traditional drugs. The cost of bringing CGTs to market is nearly $2 billion and typically requires years, or even decades, of research and development.[13] 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, and research projects that only 18 new CGT treatments will be approved between 2020 and 2034, compared to the FDA approving on average 50 new drugs per year. [14] If ex-US prices are used to set US market prices, it may incentivize companies to move manufacturing out of the US to try to lower input costs, thereby undermining the Administration's efforts to support domestic manufacturing.

Instead, the administration should seek to ensure predictable and stable patient access to transformative treatments like CGTs, including through market-based pricing and reimbursement policies that account for the true and full value of these therapies. ARM urges CMS to focus on developing policies that align pricing with the value of a therapy and rewards innovation, rather than importing reference prices that jeopardize patients' access to lifesaving treatments. To these ends, many of ARM's member companies are exploring value-based and outcomes-based arrangements that put a portion of the price of the products at risk, meaning that if the treatments do not perform over the long term for a given patient, there is a reduction in the cost of the therapy. As with the outcomes-based arrangements in the CGT Access Model, these agreements are designed to both reduce costs and improve care quality and access in a meaningful and sustainable way.

B. Importing reference pricing from European markets ignores key differences across markets and how pricing challenges in Europe have limited patients' access to CGTs.

[12] Alliance for Regenerative Medicine. Reasons to Believe: Innovation, Access and Sustainability in CGT. January 2026. Accessed from: https://alliancerm.org/wp-content/uploads/2026/01/ARM-CGT-Reasons-to-Believe-January-26-2026.pdf.

[13] *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.

[14] 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.

Notably, the prices between US and ex-US markets are not directly comparable, as ex-US countries apply confidential discounts and other managed entry agreements as central elements of pricing determinations. Sometimes, a performance-based component is also included. Applying foreign reference pricing mechanisms to CGTs risks undervaluing their long-term benefits and discouraging innovation.

The potential for MFN pricing to restrict patient access to CGTs is illustrated by the experience to date in the European market, where pricing challenges have significantly limited patients' access to CGTs. European countries represent 14 of the 19 GLOBE model reference countries that would be accounted for in CMS's methodology to calculate the Most Favored Nation price for drugs. In fact, 8 of 31 CGTs initially commercialized in the European market have subsequently been withdrawn due to inadequate reimbursement and challenges with commercial viability, resulting in a lack of access to CGTs across entire countries.[15] For example, in 2021, one company withdrew two of its gene therapies from the European market after challenges with achieving appropriate value recognition, specifically for its gene therapy treating the rare inherited blood disorder beta-thalassemia.[16] German payers had failed to agree to a commercially viable price for the gene therapy, as the health technology assessment (HTA) used significantly cheaper life-long blood transfusions as comparators that significantly undervalued the innovative gene therapy option for patients.[17] After Germany and other markets within the EU failed to recognize and pay their fair share for the innovation represented by the gene therapy, the company decided to wind down its European operations entirely, pre-emptively withdrawing a second gene therapy product used to treat cerebral adrenoleukodystrophy (CALD), and focus on commercializing its gene therapies in the U.S.

The threat of unsustainable reimbursement under an MFN pricing scheme is also causing CGT companies to reconsider whether to launch their therapies in other countries. If a product is only available in the U.S., production scale is limited, and it becomes considerably more difficult to lower the cost of goods through manufacturing efficiencies. Thus, in addition to restricting global access to CGTs, MFN policies could unintentionally drive-up costs in the U.S.

Furthermore, a number of common pricing elements in the European market have combined to undermine access to new biopharmaceutical therapies broadly and to CGTs specifically. The reference pricing methodology commonly observed in these markets indexes the pricing for a given medicine in one European market to that of a neighboring market or basket of markets. Thus, a change of manufacturer pricing

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[15] European Medicines Agency, CAT quarterly highlights an approved ATMPs, May 2025, available at: Committee for Advanced Therapies (CAT) quarterly highlights and approved ATMPs Feb-May 2025.

[16] bluebird bio Reports Second Quarter Financial Results and Provides Operational Update, August 9, 2021, available at: https://www.businesswire.com/news/home/20210809005334/en/bluebird-bio-Reports-Second-Quarter-Financial-Results-and-Provides-Operational-Update.

[17] Bruce, Francesca, Lessons From Bluebird Bio: How To Launch Advanced Therapies in Germany, May 19, 2021, available at: https://insights.citeline.com/SC144381/Lessons-From-Bluebird-Bio-How-To-Launch-Advanced-Therapies-in-Germany/.

in one European market can trigger price adjustments in another, ultimately resulting in a cascading erosion of pricing across multiple markets in a way that is entirely disconnected from value.

Europe's challenges with offering adequate reimbursement for CGTs compared to the United States have consolidated the U.S.'s leadership over Europe in patient access to these transformative therapies. Despite being a large market, the EU's restrictive pricing practices have led CGT manufacturers to prioritize market access in the US first, perpetuating access delays or even resulting in complete lack of access to CGTs for patients in Europe.[18] Importing European reference prices would import the same pricing dynamics into the United States that have limited CGT commercialization and patient access in Europe.

II. CMS should exclude CGTs from GLOBE if the agency ultimately proceeds with the initiative.

While ARM strongly opposes the implementation of the GLOBE model and urges its withdrawal, we also affirm that the proposed exclusion of CGTs from GLOBE would be critical to sustaining the economic viability of these medicines if the agency ultimately proceeds with the rule as proposed. CGTs represent a unique class of drugs with complex manufacturing processes and highly specialized supply chains. They also offer the promise of curative outcomes that can offset the costs of alternative therapies and medical complications born by thousands of patients who otherwise rely on chronic care or have no treatment options. Moreover, this exclusion would be necessary to foster patient access to these complex and personalized medicines in more accessible and cost-effective outpatient settings of care.

A. CGTs represent a unique class of medical products, featuring complex manufacturing processes, specialized storage and handling requirements and intensive patient monitoring protocols.

While all pharmaceutical manufacturing is a complex and highly regulated endeavor, manufacturing CGTs and other regenerative medicines is especially complex. CGTs require particularly specialized infrastructure, often times individualized manufacturing, and highly trained clinical teams to administer and implement intensive patient monitoring protocols.

By way of background, even within the general category of CGTs, there are numerous categories of therapies, each presenting specific challenges. For instance, gene therapies often depend on delivery by viral vectors, which are expensive and time-consuming to produce and characterize. Meanwhile, autologous cell therapies rely on collecting a patient's own cells at a clinical facility and then modifying them

[18] Han Y et al. The impacts of pricing and reimbursement policies on access to cell and gene therapies across Europe. *J Community Genet* 17, 23 (2026). https://doi.org/10.1007/s12687-026-00860-4; *See also* Sharma A, Autolus says it won't make money from its cell therapy in Europe until 2027, *Endpoints News*, August 13, 2025 https://endpoints.news/autolus-says-it-wont-make-money-from-its-cell-therapy-in-europe-until-2027/.

to produce the desired therapeutic effect before being re-administered to the patient. From start to finish, this process can take weeks, and the fragile nature of these cells and the resulting product requires highly manual manufacturing and seamless transfer of materials between the clinical site, manufacturers, and other partners. Autologous CGTs require patient-specific cell collection procedures such as leukapheresis. Allogeneic CGTs, which are manufactured from donor tissues, require complex and precise processes to reconstitute and administer them – something most hospitals are not equipped to do without significant infrastructure investment. Allogenic CGTs can also require patient-specific collection services that may also involve additional costs for services related to donor matching.[19]

Across these various diverse categories and others, CGT manufacturers face particular challenges bringing their products to patients. First, CGT manufacturers often rely on a single source supplier for critical equipment and materials, or a single processor of autologous cells. In the case of procuring highly specialized ingredients for CGTs, there is inevitably a smaller number of suppliers, underscoring the fragility of the supply chain for CGTs. In many cases, these developers do rely on sourcing ingredients and key starting materials in the United States, but often U.S.-based developers rely on materials from abroad. A survey ARM conducted with its members found that approximately 35 percent of respondents import key starting materials from abroad into the United States for manufacturing. In addition, it is not uncommon for a manufacturer of a gene therapy to produce a therapy for fewer than 100 patients, or even fewer than 10 patients in a given year, depending on the product's indication. The typically small patient population that may be served makes a manufacturer's demand for ingredients highly variable. Given variable demand and the highly customized nature of manufacturing CGTs, developing domestic sources of ingredients or in-house capabilities can be infeasible at this scale, further underscoring the unique supply chain challenges faced by CGTs.

Another supply chain challenge for CGT manufacturers is that the highly-manual manufacturing of these products is often incredibly time sensitive, and, since these products are "living" medicines, they are also highly fragile. Manufacturing is typically limited to small batches and requires specialized expertise, which significantly increases production costs. The collection of cells for the production of an autologous, ex-vivo CGT product, for example, often comes after months or even years of assessing whether the treatment is suitable for the patient and whether the treatment is covered by insurance. However, once cells have been gathered from a patient at a clinical facility to produce an autologous cell or gene therapy, the timeframe for production and administration to the patient is extremely narrow because the product is custom-produced for that specific patient, placing even greater strain on this fragile system. Even with allogenic therapies which offer the promise of "off the shelf" treatments, manufacturing is limited to

[19] An approach to identifying cell and gene therapy products that would be eligible for this exclusion should account for the highly varied mechanisms of action within this class of drugs. We would recommend a framework that allows for multiple pathways towards identification of eligible products and automatic exclusion of identified products upon FDA approval. More on this framework can be found here.

extremely small batches and the cells are only viable for a very short window (often 24 hours) after reconstitution. In addition, most CGT products also require the deployment of ultra cold chain technology, which requires special handling and storage requirements. These handling requirements and manufacturing processes drive up costs. There are also significant implications if there is a temperature excursion, which sometimes only needs to be very brief to have an impact on the viability of these living medicines. Thus, the time-sensitive nature of the manufacturing process requires complex coordination between the apheresis site, the manufacturer, and the clinical site, and the timing of delivery can often depend on manufacturing capabilities and availability.

Furthermore, because of the patient-specific cell collection services involved in CGTs, Chain of Identity (COI) and Custody (COC) protocols play a critical role in ensuring the right patient receives their own, specifically-manufactured cells. Maintaining COI and COC require investment in and management of robust digital tracking systems. Both COI and COC are crucial for regulatory compliance and ensuring patient safety in CGTs, as they help prevent errors and ensure that the therapy is delivered to the intended patient.

While supply chain considerations are a significant factor, additional factors further support the exclusion of CGTs. In particular, CGTs have uniquely complex and highly individualized Chemistry, Manufacturing, and Controls (CMC) requirements that increase manufacturers' cost of goods sold and, notably, limit opportunities to achieve economies of scale. FDA has established CGT-specific expectations for CMC information to assure product safety, identity, quality, purity, and strength (including potency).[20]

In addition, FDA's CGT guidances emphasize the importance of robust characterization, potency strategies, and lifecycle controls, including expectations for analytical comparability when manufacturing changes occur. These requirements are essential for patient safety, but they require significant and ongoing investment in process controls, raw material qualification, analytical development and validation, and stability programs.[21]

Available published cost data illustrate the magnitude of these manufacturing and CMC burdens, reflecting the inherently labor-intensive, small-batch nature of many CGTs and the extensive testing required to assure product quality. One cell therapy manufacturing costing framework, for example, reported €23,033–€190,799 per batch (i.e., up to around $226,000 in current USD), with yields ranging from 1 to 88 doses, illustrating how yield variability and limited scale can amplify per-dose

[20] U.S. Food and Drug Administration, Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs): Guidance for Industry, January 2020, available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/chemistry-manufacturing-and-control-cmc-information-human-gene-therapy-investigational-new-drug .

[21] U.S. Food and Drug Administration, Potency Tests for Cellular and Gene Therapy Products: Guidance for Industry, January 2011, available at: https://www.fda.gov/files/vaccines%2C%20blood%20%26%20biologics/published/Final-Guidance-for-Industry--Potency-Tests-for-Cellular-and-Gene-Therapy-Products.pdf.

cost and financial risk.[22] These product-level costs sit alongside substantial fixed investments in specialized manufacturing capacity, where public examples of build outs for viral vector facilities meeting standards for Good Manufacturing Practices (GMP) are notably reported in the $65–$75 million range.[23]

In previous comments to the Trump Administration on tariffs and supply chain considerations, ARM has also described the structural constraints that contribute to this cost profile, including reliance on limited or single-source suppliers for critical equipment and materials and the resulting bottlenecks that are difficult to mitigate in the near term.[24] Finally, certain CGT modalities are subject to additional long-term obligations that are costly and not typical for non-CGT products, including the FDA's expectation for 15-year follow-up for certain human gene therapy products, whose intensive monitoring requirements also increase CGT manufacturers' cost of goods sold relative to non-CGT products.[25]

B. <u>The upfront cost of CGTs reflects not only their complex and innovative manufacturing processes but also their potential to provide durable, often curative results. These interventions can eliminate the need for lifelong conventional therapies, underscoring the need to promote patient access</u>.

CGTs are remarkable in that they treat the root cause of disease, and for many CGTs one dose can deliver years, decades, or even a lifetime of clinical benefit. In many cases, the conditions treated by CGTs create a tremendous quality of life burden for patients and their families/caregivers. The cost of care for these patients can reach into the millions of dollars for diseases including hemophilia and sickle cell disease (SCD). Unlike conventional pharmaceuticals, CGTs are typically one-time, durable, and potentially curative therapies that bring hope to patients seeking relief from chronic approaches to their conditions. The Institute for Clinical and Economic Review (ICER) confirmed the high value of one-time durable gene therapies for hemophilia, SCD, spinal muscular atrophy (SMA), metachromatic leukodystrophy (MLD), and more. As an illustrative case: FDA-approved gene therapies for hemophilia A (1) and hemophilia B (2) give significant savings back to the system according to an analysis from the Institute for Clinical and Economic Review (ICER), which serves a drug-pricing watchdog. ICER has found that several

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[22] Ten Ham RMT, Hövels AM, Hoekman J, et al. What does cell therapy manufacturing cost? A framework and methodology to facilitate academic and other small-scale cell therapy manufacturing costings. *Cytotherapy*. 2020;22(7):388-397. doi:10.1016/j.jcyt.2020.03.432.

[23] Santon, D, Avid opens viral vector facility, looks to FY23 to fill GMP capacity, July 8, 2022, available at https://www.bioprocessintl.com/facilities-capacity/avid-opens-viral-vector-facility-looks-to-fy23-to-fill-gmp-capacity.

[24] Alliance for Regenerative Medicine, Comment letter on *Notice of Request for Public Comments on Section 232 National Security Investigation of Imports of Pharmaceuticals and Pharmaceutical Ingredients (Docket No. 250414-0065, XRIN 0694-XC120)*, May 6, 2025, available at: https://alliancerm.org/wp-content/uploads/2025/09/ARM-Comments-on-Commerce-Sec-232-Investigation.pdf.

[25] U.S. Food and Drug Administration, Long Term Follow-Up After Administration of Human Gene Therapy Products: Guidance for Industry, January 2020, available at https://www.fda.gov/files/vaccines%2C%20blood%20%26%20biologics/published/Long-Term-Follow-Up-After-Admin-Human-GT-Products_Jan_2020.pdf.

gene therapies for rare genetic diseases provide value at prices ranging from $2 million to $4 million, particularly when considering long-term cost offsets and the durability of outcomes associated with CGT.[26]

In many cases, CGTs also offer treatments for populations with high unmet need. Many CGTs are indicated to treat rare diseases. The average life expectancy for patients with the rare diseases targeted by approved gene therapies is less than 40 years, or half the normal U.S. lifespan. Notably, for CGTs that treat rare diseases, the small patient population inherently limits the commercial market for the treatment and further complicates the calculation of a market-based reference price. Other CGTs in the pipeline aim to treat subgroups of patients with more prevalent conditions like Parkinson's Disease and heart failure which are significant cost drivers for the Medicare program.

C. <u>The administration of CGTs has only recently begun to see movement to the outpatient setting. This evolution in site of administration has the potential to improve health outcomes and patient access while reducing overall healthcare system cost.</u>

As previously mentioned, CGTs have required specialized infrastructure and patient monitoring requirements that historically necessitated inpatient administration. However, technological improvements in patient risk stratification and remote monitoring have increasingly allowed for administration of CGTs in outpatient settings of care. For example, growth in the outpatient administration of CAR T cell therapies has accelerated significantly in recent years, with 45% of CAR T patients being treated in the outpatient setting in 2025, compared to just 29% in 2024 and just 16% in 2022.[27] Outpatient administration of CAR T cell therapies and other CGTs offers great promise in terms of patient access and care quality.

As CGTs evolve and migrate beyond inpatient administration, the types of providers and sites of services involved in preparatory steps, which require unique labor, resources, and expertise from multiple providers, will continue to diversify. However, GLOBE's standardized pricing approach does not account for these complexities. The implementation of MFN reference pricing could thereby introduce uncertainty for these products just as they are transitioning to lower-cost Part B coverage, potentially limiting investment and further innovation in this space. For new CGT products, this uncertainty could even undermine confidence about whether to launch a Part B CGT product at all.

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[26] *See* Institute for Clinical and Economic Review, Gene Therapy for Hemophilia B and An Update on Gene Therapy for Hemophilia A: Effectiveness and Value, Final Evidence Report, July 26, 2024, available at: https://icer.org/wp-content/uploads/2022/05/ICER_Hemophilia_Final_Report_12222022.pdf; Institute for Clinical and Economic Review, Atidarsagene Autotemcel for Metachromatic Leukodystrophy, Final Evidence Report, October 30, 2023, available at: https://icer.org/wp-content/uploads/2025/06/ICER_MLD_Final-Evidence-Report_ForPublication_10302023_12MonthCheckUp.pdf;

[27] Alliance for Regenerative Medicine, Reasons to Believe: Innovation, Access & Sustainability in CGT, January 2026, available at: https://alliancerm.org/wp-content/uploads/2026/01/ARM-CGT-Reasons-to-Believe-January-27-2026.pdf.

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As outlined herein, ARM is deeply concerned about the potential for GLOBE to undercut investment in American biopharmaceutical innovation and to interrupt patient access to critical medicines, including CGTs, in this country. We urge CMS to withdraw the proposed GLOBE model. Exclusion of these therapies from any MFN model or policy would be critical to ensuring ongoing innovation and investment in CGTs. If CMS proceeds with the GLOBE model, a carveout for CGTs as proposed would be absolutely essential. ARM's advocacy for the exclusion of CGTs from GLOBE should also not be misconstrued as support for MFN policies or for the GLOBE model.

As the CGT pipeline continues to expand into conditions affecting broader Medicare populations, CMS has an opportunity to establish payment policies that support innovative care delivery models, encourage outpatient migration, and maintain reimbursement stability for these breakthrough treatments. ARM is ready to work collaboratively with CMS to develop policies that advance patient access while supporting the sustainable adoption of life-changing therapies for Medicare and Medicaid beneficiaries.

We appreciate CMS's consideration of these comments and welcome the opportunity to discuss these recommendations further. Please feel free to contact David Davenport at ddavenport@alliancerm.org with questions.

Sincerely,

Mark Battaglini

Mark Battaglini
Chief Strategy Officer
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