Alliance for Regenerative Medicine

January 22, 2023

The Honorable Bill Cassidy, M.D.
Ranking Member
Committee on Health, Education, Labor, and Pensions
U.S. Senate
Washington, DC 20510

Dear Senator Cassidy:

On behalf of the Alliance for Regenerative Medicine (ARM), I thank you for your interest in ensuring Americans have access to innovative and life-changing gene therapies and the opportunity to offer input on behalf of our diverse membership in response to your recent request for information.

ARM is the leading international advocacy organization championing the benefits of engineered cell therapies and genetic medicines for patients, healthcare systems, and society. As the global voice of the cell and gene therapy (CGT) sector, we represent more than 400 members across 25 countries, including emerging and established biotechnology companies, academic and medical research institutions, and patient organizations. ARM is working to build the future of medicine by convening the sector, facilitating influential exchanges on policies and practices, and gathering and analyzing data. We engage stakeholders across the private and public sector to enable the development of advanced therapies and to modernize healthcare systems so that patients benefit from CGTs.

In recent years, numerous life-changing and often life-saving – CGTs have been approved by the Food and Drug Administration (FDA) for some of the most difficult-to-treat conditions that affect both children and adults. These include cerebral adrenoleukodystrophy, beta thalassemia, spinal muscular atrophy, hemophilia A and B, Duchenne muscular dystrophy, sickle cell disease and various forms of cancer. These one-time administered, durable, potentially curative therapies can bring decades or a lifetime of benefits to the seriously or incurably ill, and the consequence of advances in CGT have been likened to the eradication of smallpox.[i] As of January 2024, there are nearly 1,000 CGT clinical trials ongoing in the US and nearly 1,900 globally to test the next generation of therapies[ii].

Importantly, our members are focused on somatic cell approached to treat diseases. ARM does not support or condone modifying human germline cells for use in human clinical trials or for human implantation.

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CGTs include: (1) cell therapies, which administer viable, often purified cells into a patient's body to grow, replace, or repair damaged tissue for the treatment of a disease, (2) gene therapies, which seek to modify or introduce genes into a patient's body (*in vivo* or *ex vivo*) with the goal of durably treating, preventing, or potentially even curing disease, (3) gene editing therapies, which insert, replace, remove, or modify DNA at particular locations in the human genome for therapeutic benefit, and (4) tissue-engineered therapies, intended to restore, maintain, improve, or replace damaged tissues or organs through the combination of scaffolds, cells, and/or biologically active molecules. Cell and gene therapies are administered in both the inpatient and outpatient settings in accordance with their approved label and other clinical factors, like the need for myeloablative conditioning therapy. Each of these therapeutic types is associated with unique challenges in manufacturing, supply chain, administration, and requires distinct considerations for regulatory review.

These novel therapies present new opportunities and challenges for America's healthcare system. CGTs address high unmet medical needs, they can be lifesaving; and many have the potential to reduce the need for burdensome and costly chronic care. While Traditional pharmaceuticals typically treat the symptoms of diseases for short periods and may need to be administered regularly over a patient's lifetime, CGTs target the root causes of disease, are typically administered in a single or limited number of doses and with durable and potentially curative treatment effects. However, as you correctly note in your request for information, our current healthcare system is not designed to pay for these durable, potentially curative treatments. Responsive, forward-looking reforms are necessary to align the promise of CGTs with the needs of patients and society.

Accordingly, ARM looks forward to working with you and the Senate Health, Education, Labor and Pensions (HELP) Committee to advance legislation and support research and data collection efforts to ensure patients in the U.S. have timely, equitable access to CGTs. We offer the responses below to the questions posed in your RFI as well as additional policy recommendations for your consideration.

Which Treatments Should Be Included?

CGTs are part of the shift away from a chronic approach to disease management toward a focus on prevention and disease interruption, and they differ from traditional pharmaceuticals in their administration, mechanism of action, and value proposition. For these reasons, CGTs lend themselves to, and in some cases necessitate new, innovative payment and delivery models.

1. How should lawmakers define an "ultra-rare" disease or disorder cell or gene therapies should be eligible for inclusion in new coverage or contracting requirements for those patients with an ultra-rare disease or disorder? What definitions should lawmakers consider?

Although the Orphan Drug Act of 1983 defines a "rare disease" as a disease or condition that impacts 200,000 Americans or less, ARM recommends avoiding the use of a threshold or specific number to delineate rare subsets like "ultra-rare disease "for the context of payment policy. Doing so would be arbitrary and raises policy, practical, and bioethical concerns that we

believe would hurt the rare disease community, patient access and the field at large. Any pre-determined requirements should be concomitant with the relevant disease-specific characteristics.

2. Are there other criteria that lawmakers should consider in determining which therapies should be included in new coverage or contracting models?

ARM works to ensure adequate access to all CGTs. While we do not believe that new models should be reserved for limited patient populations or specific conditions, we explicitly urge legislators and regulators to recognize and incentivize development and access to CGT products that treat rare diseases, acknowledging the unique circumstances that challenge the development and commercialization of such treatments. We support an approach that prioritizes the improvement of the regulatory, access, and reimbursement pathways for companies developing therapies for the most challenging diseases, while doing so in a manner that does not generate unintended consequences for patients in need of treatments for common conditions.

ARM believes it is inappropriate to restrict coverage of CGTs based on the size of the affected patient population or disease indication. Federal policies should preserve the flexibility for CGT developers to voluntarily enter into contracting models with payers that make sense for their purposes rather than attempting to apply a one-size-fits-all approach.

It is also imperative that any new models empower clinical decisionmakers to determine medical necessity and prescribe treatments for their patients; such that coverage, payment, and cost-sharing policies support the provision of timely care in the setting most clinically appropriate for the patient (e.g., hospital inpatient, outpatient). In other words, payers should not arbitrarily restrict access to treatments or steer patients toward or away from particular treatments or sites of care based on aspects of coverage or contracting models or otherwise.

What is the Current Practice for Patients with Ultra-Rare Diseases or Disorders?

Innovative new CGTs are already delivering on their promise for people living with some rare genetic diseases and blood cancers, saving lives and drastically improving quality of life by eliminating the need for ongoing, invasive and costly medical care. With thousands of researchers and scientific innovators working on new treatments, and hundreds of late-stage clinical trials underway, there is tremendous potential for CGTs to further disrupt the status quo of a much broader array of human diseases.

3. How do patient populations currently access and pay for these therapies?

Today, our U.S. healthcare system is consistently working to provide new treatment options to improve and extend life, yet it is built upon medical approaches that largely address the symptoms of illness and provide incremental improvements to quality of life. The focus remains on the management of disease rather than the restoration of health. Consequently, standard-of-care costs for those living with chronic conditions can reach up to millions of dollars over a person's lifetime, despite only delivering partial improvements in clinical outcomes, in addition

to innumerable hours of lost wages and significant non-medical costs for both patients and their caregivers.

For U.S. patients diagnosed with a rare disorder prior to the age of 19, 55.3% utilize public payers for care.[iii] To achieve the promise of CGTs and meaningfully improve health equity in our country, federal policymakers must ensure that patients who rely on government programs for health coverage (e.g., Medicare, Medicaid, the Children's Health Insurance Program, TRICARE, the Veterans Health Administration, and the Indian Health Service) have appropriate access to these innovative therapies.

4. What, if any, federal or state programs do these patient populations use as they seek to pay for and access these therapies and related care? What is the specific benefit to the patient in using these programs? For example, interested parties could contemplate instances where families choose to "spend down" to become eligible for state Medicaid programs, thus ensuring coverage.

Patients have access to CGTs through all payer channels; however, public programs cover a disproportionate share of many rare disease patients. For example:

- Medicaid pays for 66% of all initial hospitalizations for Sickle Cell Disease
- Medicaid covers 58% of all children with Spinal Muscular Atrophy
- Medicaid pays for 30% of all initial infusions for Hemophilia A & B
- 38% of all patients receiving commercially available CAR-T cell therapy treatments are covered by Medicare

In addition to other stakeholder reports, an ARM analysis affirms that Medicaid patients face many barriers to timely access to CGTs.[ivv] Rather than benefiting, we fear that vulnerable patients reliant on Medicaid coverage may be disadvantaged relative to the commercially insured. A December 2023 study conducted by researchers at the Tufts Medical Center Institute for Clinical Research and Health Policy Studies found that Medicaid coverage policies were more restrictive than commercial policies for 8 CGTs.[vi] To combat these disparities and promote greater access for all patients, ARM urges Congress and CMS to ensure that states are compliant with federal requirements for coverage of CGTs.

10. How do vulnerable patient populations demonstrate financial need as they seek to pay for and access these therapies? If not listed as part of the above, what other mechanisms exist to support access for patients who have demonstrated financial need?

Vulnerable patient populations facing financial challenges in accessing CGTs may encounter barriers that require targeted support. This may involve a combination of strategies such as assisting patients with navigating coverage and reimbursement, preparing for affordability assessments, and application support for patient assistance programs, legal assistance and travel or caregiver support.

It's important for healthcare providers, social workers, and patient advocates to work collaboratively to identify and address the unique financial needs of vulnerable patient populations seeking CGTs. Federal programs should enable support strategies tailored to

patients' individual circumstances and streamline access to benefits designed to support individuals with limited financial means.

How Do Plans and Payers Currently Manage Financial Risk?

Given their novelty, the landscape for coverage of CGTs in the U.S. is complex and dynamic. Coverage policies and reimbursement mechanisms for these innovative therapies have been evolving rapidly due to their unique characteristics, the high upfront investment required, and potential for transformative patient outcomes.

11. What does coverage for these therapies typically look like? What does the landscape look like for coverage of these therapies?

Above all, timely access to CGTs in federal programs is the most existential threat to beneficiaries who qualify for these treatments.

Medicaid - As discussed above, Medicaid is an important payer for CGTs, including many approved therapies that treat rare genetic diseases and for other treatments on the horizon that address more prevalent conditions. Given states' budgetary and staff resource constraints and lack of formalized coverage policies in the burgeoning area of CGTs, Medicaid agencies are frequently a challenge for both companies launching new CGTs and hospitals and academic centers treating patients, as well as an access barrier for beneficiaries seeking treatment. Medicaid treatment delays for CGTs are common, and in some instances, beneficiaries must wait months or even over a year to successfully navigate coverage requirements.

Many state Medicaid programs are not complying with the intent of the current requirement under the federal Medicaid statute (Section 1927 of the Social Security Act) that states cover all FDA-approved indications of a product upon FDA approval. Under the Medicaid Drug Rebate Program (Section 1927 of the SSA), a state is required to cover all of a participating manufacturer's products that are subject to a national rebate agreement upon approval by the FDA and available for sale in the state. Each state follows a process prescribed by Section 1927 under which physicians, pharmacists, and other state-appointed individuals deliberate on, publish and implement formal coverage criteria for such drugs. To facilitate this process, federal Medicaid rules require each state to have a comprehensive Drug Utilization Review (DUR) program that assesses the utilization, quality, medical appropriateness, and cost of prescribed medication. States generally run DUR programs through DUR Boards (DURB) and/ or Pharmacy and Therapeutics (P&T) Committees. P&T/DUR proceedings may lead states to place utilization restrictions on reviewed drugs, including prior authorization and step therapy. Although federal law allows states to employ these tools to manage the use of a particular drug, CMS has said in guidance that the effect of these limitations "should not result in the denial of access to effective, clinically appropriate, and medically necessary treatments."[vii] Despite this mandate, there exists considerable variation across states in how and how quickly Medicaid programs cover CGTs. ARM published an issue brief in November 2023 detailing this as one of the most common Medicaid barriers to accessing CGTs.

Unfortunately, we have seen Medicaid and other payers apply additional exclusionary coverage for certain CGT products, beyond their labeled indication or require additional clinical information or assessments as a criteria for approval. These arbitrary policies can result in treatment denials or delays in time to treatment which has devastating impacts on patients. When an age limit or specific disease milestone is included in the FDA-approved indication statement, access to that treatment before that milestone is reached is imperative so a patient does not miss an opportunity for treatment where for many suffering from rare diseases can further irreversibly deteriorate. In approving a therapy and determining the indication, the FDA relies on totality of data, scientific expertise, and risk-benefit profile. Therefore, the population included in the FDA-approved indication is the population that should be the foundation of a payer's coverage policy and drive authorization decisions. Inappropriately applying clinical trial criteria as the coverage criteria and basis for prior authorization undermines FDA's scientific authority. Many rare diseases are complex with very small heterogeneous patient populations. Clinical trials typically control for this heterogeneity using a homogeneous patient population. Medicaid coverage of CGTs in accordance with the FDA-approved indication must be upheld.

Many states have Medicaid policies that can restrict or delay coverage of a new drug before it undergoes Drug Utilization Review (DUR) and/or Pharmacy and Therapeutics (P&T) Committees. Through these reviews, state Medicaid programs decide on the levels of utilization restrictions, such as prior authorization or step therapy, to apply to a new drug, and whether to include the drug on the state's preferred drug formulary. In some states, whether by state law or informal policy, this process can take six months to a year or more from launch, causing uncertainty about the availability of the drug for patients during that delay. As a result, states that delay the review process are in effect denying coverage of that drug for an extended period, thus failing to meet the intent of their statutory obligation to cover the drug upon its entry into the market. Patients, many of whom are children, suffering from conditions do not have the luxury of waiting for Medicaid to make an FDA approved product available after extended delays.

ARM strongly endorses federal or state "time to treat" legislation whereby states must hold their DUR or P&T committee meetings and render a decision on whether a physician administered drug is covered, non-covered, or covered with certain utilization management approaches, within a set timeframe. States should be able to reach a decision within 90 days given that most patients on these therapies are sicker, or often have a rare disease or a disease with unmet need that can be treated by the newly approved CGT. Also, when a Medicaid patient is prescribed treatment for a CGT's FDA-approved, medically accepted indication within this window a state is expected to authorize treatment before it reviews the therapy through a formal P&T/DUR process.

Further, because of the specialization required for the administration of CGTs, manufacturers generally contract directly with providers in a limited number of states that have the appropriate experience and facilities necessary for the administration of their therapies. For this reason, patients seeking CGT treatments, who in many cases tend to be critically ill with medically

complex conditions, often are required to travel beyond their home states to obtain care. Providers seeking to treat nonresident Medicaid beneficiaries must become enrolled in, and credentialed by, the Medicaid program in the patient's home state. Currently, since each state Medicaid program establishes and administers its own credentialing program, the rules and procedures for credentialing can vary from state to state, resulting in a patchwork of state-specific credentialing requirements. These requirements can be onerous, complex, and time-consuming. As a result, certain providers qualified to administer CGTs may be reluctant to complete necessary credentialing procedures to allow the treatment of nonresident beneficiaries, creating avoidable barriers to care for medically complex patients seeking treatment with CGTs.

ARM has endorsed the bipartisan Accelerating Kids Access to Care Act (S. 2372/H.R. 4578) which takes steps to alleviate these administrative hurdles by requiring state Medicaid programs to establish a streamlined enrollment process for some out-of-state clinicians working with children with complex medical needs while maintaining important program integrity checks. We urge Congress to broaden this legislation to apply to specialized providers treating CGT patients of all ages and swiftly pass it.

ARM has also urged CMS to consider establishing a uniform credentialing standard that could be applied for all providers involved in the administration of CGTs. Consistent with CMS's authority under section 1902(a)(16) of the Social Security, Act and similar to the standards CMS has already adopted for medically-fragile children, the establishment of a consensus-based credentialing standard for CGT providers treating patients of all ages that state Medicaid agencies may opt to use will help facilitate access to care among some of the nation's most vulnerable patients. ARM also encourages CMS to issue information regarding best practices to states, comparable to what CMS provided when implementing the ACE Kids Act, to support states in efficiently credentialling out-of-state providers ahead of the anticipated increase in CGT patients.

State Medicaid agencies, like commercial payers, often negotiate single-case agreements to allow for reimbursement when case rates do not exist, either in-or out-of-network. Single case agreements can be useful when patients are being treated at an out-of-state treatment center. However, every intermediary in the system causes further administrative delays.

Manufacturers often need to deal with the patient's resident state Medicaid Agency, the non-resident state Medicaid Agency, the patient's Medicaid Managed Care plan, treatment centers, and referring providers. Access can be delayed by negotiations among these stakeholders regarding payment issues such as 340B discounts, supplemental rebate negotiations, and services included as part of a single case agreement.

Finally, we note that many state Medicaid programs required managed care organizations (MCOs) to set individual and sometimes inconsistent formulary, preferred drug lists, and prior authorization policies, which can inevitably result in a patchwork of complicated and diverse access restrictions to necessary prescription drugs for beneficiaries. Under this framework, access to medications would depend on the different formularies, access restrictions and other

coverage policies administered by each beneficiary's MCO. Unfortunately, multiple MCO formularies can complicate the ability of states to ensure consistent and expedited access to care for patients. However, certain states are beginning to oversee and manage a single, or unified, drug formulary for all Medicaid recipients, including those covered by MCOs.

Medicare – Medicare currently covers more than one-third of all U.S. patients receiving CAR T-cell therapy, and with more gene therapies indicated for conditions afflicting older adults in the FDA approval pipeline, Medicare will become an increasingly prominent payer of CGTs.

Medicare coverage already lags behind product availability because the Medicare administrative contractors (MACs) only review CGTs for coverage determinations once the product is FDA approved and commercially launched. To ensure that Medicare patients have timely access to newly approved CGTs, CMS must require MACs to conduct timely reviews, and if MACs issue a local coverage determination (LCD) or CMS issues a national coverage determination (NCD) those should be done in a timely manner.

Additionally, the current Medicare bundled payment methodology unfortunately disincentivizes hospitals from adopting new or novel treatment modalities not already reflected in their costs, which in turn can limit beneficiaries' access to new CGTs. ARM urges Congress and CMS to reform the new technology add-on payment (NTAP) program, as outlined below, to foster continued innovation and encourage the use of advanced medical technologies like CGTs to treat Medicare patients.

23. Please share any other relevant information in regard to health plan or other payer coverage of these therapies.

A 2021 study of U.S. commercial payer medical policies found that more than two-thirds of health plans restrict coverage of CGTs and are substantially more restrictive in their coverage of CGTs as compared to other orphan products.[viii]

Patients and healthcare providers often encounter challenges related to prior authorization requirements and coverage denials for CGTs, which can result in harmful and sometimes fatal care delays. Coverage determinations and utilization management practices must be evidence-based, developed with input from appropriate medical specialists, and ultimately the medical necessity and appropriateness of a CGT should be determined by the patients' treating clinicians. Lawmakers should continue to explore policies that streamline prior authorization and protect patients from inappropriate coverage denials and unscrupulous utilization management practices that prevent the timely provision of necessary medical care.

How Do Supply Chain Intermediaries Price and Design Contracts?

The supply chain for manufacturing CGT medications differs significantly from traditional pharmaceutical supply chains, primarily due to the complexity, sensitivity, and personalized nature of these advanced therapies.

29. What are typical contract designs between the drug manufacturer, wholesaler, and distributor as they seek to provide access to these therapies? What special supply chain considerations have to be made for these therapies as the drug manufacturer, wholesaler, and distributor seek to distribute these therapies?

There is no broad standard across the CGT sector regarding manufacturing and contracting with distributors or wholesalers. Rather, manufacturing and contracting processes often reflect a combination of the following:

Personalized Nature of some CGTs:

- Customization: Cell therapies such as aulogous CAR-T's or TILs involve modifying each individual patients' cells, making the supply chain more complex compared to traditional off-the-shelf pharmaceuticals.
- Small Batch Sizes: Production volumes are typically smaller. This contrasts with the economies of scale often achieved in traditional pharmaceutical manufacturing.

CGT Manufacturing Process:

- Biological Components: CGTs involve living cells or genetic material, which adds a layer of complexity to the manufacturing process. The biological nature of these components requires specialized handling and quality control measures.
- Multiple Processing Steps: The manufacturing process can involve multiple steps, including cell isolation, genetic modification, expansion, and purification. Each step requires precision and adherence to strict quality standards.

Cold Chain Supply Process:

- Temperature Sensitivity: Many CGTs are highly sensitive to temperature variations. Maintaining a consistent and controlled temperature throughout the supply chain is crucial to preserving the integrity and efficacy of these therapies.
- Cryopreservation: Some therapies require cryopreservation at ultra-low temperatures for stability. This demands specialized equipment and logistics to ensure the safe transport and storage of frozen materials.

Logistics Challenges:

- Time Sensitivity: Due to the personalized nature of these therapies, there is often a time-sensitive element. Timely delivery is crucial to ensure the product reaches the patient within the optimal administration window.
- Global Distribution: CGTs may be manufactured in one location and administered in another. Manufacturing and administration are more complex than with small molecules because only a limited number of sites are able to conduct those activities.
- Global distribution adds complexity, and providers need to navigate regulatory requirements, customs procedures, and transportation logistics.

Regulatory Compliance:

- Regulations: The supply chain must adhere to Good Manufacturing Practice (GMP) standards to ensure the safety, efficacy, and quality of the therapies. Extensive analytical characterization uses many different assays and must occur for each lot, including potency requirements specific to CGTs and the comparability assessments that must be conducted after manufacturing process often changes.

Specialized Equipment:

- Closed Systems: To prevent contamination and maintain the sterile conditions required for these therapies, closed systems and aseptic processing are often employed, necessitating specialized equipment.

How Do Physicians Provide Access to These Therapies?

Initiating a CGT for a patient is a significant deliberative and consultative process between the physician, the patient and typically the patient's family. Physicians discuss many clinical, financial and access considerations with prospective CGT patients before even reaching a prescribing decision.

34. How does a physician or health system initiate the process of prescribing a patient with an ultra-rare disease or disorder one of these therapies?

As mentioned elsewhere and extensively documented by researchers and patient advocates, the decision to initiate CGT treatment is preceded by a diagnostic journey typically involving many tests and many consults with other specialists. The so-called diagnostic odyssey for a patient diagnosed with a rare disease, especially one that may be treated with a CGT, can be a challenging and lengthy process. This often prolonged and complex journey often begins when a patient experiences unusual or unexplained symptoms. If the symptoms are uncommon or not easily diagnosed, the patient may be referred to specialists such as geneticists, neurologists, or other experts, depending on the nature of the symptoms.

Genetic and genomic sequencing tests, including multi-gene panels, whole exome sequencing and whole genome sequencing, may be conducted to identify clinically relevant genetic variants. Clinicians, such as genetic counselors and specialist physicians, work together to interpret the data and link genetic findings to the patient's clinical presentation. Results of genetic and genomic sequencing tests often directly inform clinical decision making and utilization of precision therapies. Lack of understanding regarding insurance coverage can impede patients' ability to obtain requisite genomic or genetic sequencing tests. For example, the Medicaid Early Periodic Screening, Diagnostic, and Treatment (EPSDT) benefit required for beneficiaries under age 21 and is intended to ensure that patients receive appropriate and necessary health services; however, states' application of this coverage is inconsistent, and some states classify genetic and genomic diagnostics as experimental while others consider them approved. Federal policymakers should ensure that states abide by Medicaid EPSDT coverage requirements and advance policies that increase sequencing availability for all patients, which will promote more timely and appropriate access to CGTs.

Once a diagnosis has been made, treating physicians must not only consider a patient's clinical eligibility but also their insurance and financial status as well as the logistics for treatment.

Some patients may need to travel long distances and, potentially, out-of-state to receive CGT treatment. As explained elsewhere, the intricacies of CGTs may limit the number of COEs offering these complex therapies and as a result, some Medicaid patients may be required to travel out of their home states for treatment. A provider willing to treat out-of-state Medicaid patients is required to bill and accept payment from the patient's home state Medicaid program. However, the provider is only authorized to bill for such services if they are credentialed by and enrolled in that state's Medicaid program. Each state generally develops and administers its own credentialing rules, and the credentialing process can be complex, time-consuming, and expensive to complete. ARM urges Congress to work with CMS to develop a minimum national credentialing standard for providers seeking to administer CGTs to out-of-state beneficiaries of all ages. ARM supports efforts to streamline the Medicaid credentialling process, like Congress did for children with the Accelerating Kids' Access to Care Act (S.2372/H.R. 4758), to facilitate the treatment of CGT patients by out-of-state providers and reduce unnecessary delays and other barriers to care for these patients.

Many CGTs require lengthy hospital admissions and even outpatient therapies require patients to remain within proximity to the treatment center throughout the process and for a period after receiving the therapy to monitor for adverse reactions. ARM supports increased flexibility from federal regulatory agencies to enable manufactures to offer patient assistance programs (PAPs) that help patients and their caregivers afford travel, lodging and ancillary medical services incidental to CGT treatment.

Finally, as detailed elsewhere in this response, the decision to prescribe is only the beginning of the access journey as the patient and their treating clinicians must navigate the complex coverage policies and utilization review protocols imposed by insurers. CGTs often cannot reverse morbidities to the underlying condition to be treated. For this reason, extended treatment delays that may be caused by deferred coverage decisions or protracted prior authorization permanently hamper the impact of the therapies. In other cases, delays in access may cause a patient to age out of the drug's indication, permanently eliminating their opportunity to seek any relief from their disorder.

35. Do physicians or health systems bear any financial risk as part of prescribing a patient with an ultra-rare disease or disorder these therapies?

Currently, CAR-T and gene therapies are predominately provided in the hospital inpatient setting. This means that the hospital purchases the therapy and then seeks reimbursement from the patient's insurance company. In doing so, the hospital assumes significant financial risk as the reimbursement rate is intended to cover not only the cost of providing the therapy, but also many of the ancillary services associated with administering the therapy. ARM has long advocated that the current hospital inpatient reimbursement methodology does not adequately reimburse hospitals for assuming the financial risk of providing CGTs.

It is important to note that some CGTs are provided in an outpatient setting. Setting of care may vary based on treatment modality, payer policy, patient complexity, and other factors. The provision of CGTs on an outpatient basis may trend upward in the future, in keeping with a desire to transition to outpatient settings where appropriate to improve patient access to care and potentially reduce health system cost and patient out-of-pocket costs. Historically, some ancillary services associated with CGT administration have not been reimbursed separately, which exposes the provider to financial risk. In both inpatient and outpatient settings of care, the provider must also invest considerable amounts in preparing their facilities and staff for unique CGT protocols, and it is imperative that reimbursement is adequate to incentivize uptake of new CGTs and sustain patient access to these innovative treatments.

Medicare - In 1983 when Congress created the Inpatient Prospective Payment System (IPPS), regenerative medicine and advanced technologies were closer to science fiction than the clinical reality they are today. As such, Congress likely did not find the need to include a mechanism or methodology that adequately reimburses hospitals for providing these types of new and innovative technologies. However, in an effort to recognize the value of new technologies, Congress, in 2000, required CMS to establish a mechanism that recognizes the costs of new medical services and technologies in the inpatient setting for discharges beginning on or after October 1, 2001.

Specifically, Congress instructed CMS to "provide for additional payment…in an amount that adequately reflects the estimated average cost of such service or technology." Further, Congress instructed CMS that this additional payment might be satisfied by means of a new technology group known as an "add-on payment," that is, a payment adjustment or any other similar mechanism for increasing the amount as long as it represents the estimated average cost of such service or technology. ARM believes that without further improvements to the NTAP program, CGTs will be out of reach for many Medicare beneficiaries and further, biotechnology companies could be discouraged from developing CGTs for the Medicare population due to insufficient eligibility criteria and reimbursement.

To ensure it meets its legislative intent, ARM recommends that CMS increase the frequency of NTAP applications to promote more immediate uptake of new CGTs, which can be delayed due to the singular opportunity for biotechnology companies to obtain an NTAP designation.

ARM urges Congress to increase the NTAP rate to 80% to provide equilibrium in payment rates. This ensures comprehensive and sustainable CGT care delivery options. According to a not-yet-published analysis of Medicare hospital data conducted by ADVI Health, at the current 65% rate, nearly 50% of cases submitted under the "CAR-T and Other Immunotherapies" billing group (MS-DRG 018) are yielding net negative margins when calculating Medicare reimbursement minus actual costs. It is unfitting for CMS to expect institutions to provide care at a significant financial loss.

ARM also continues to advocate that CMS be flexible in establishing reimbursement policies that result in accurate payment, promote innovation, and ensure timely access for Medicare beneficiaries to CGTs. ARM believes that the current construct of MS-DRG 018 ("Chimeric Antigen Receptor (CAR) T-cell and Other Immunotherapies") protects the stability of the relative weight, and appreciates the Agency's historic statements that it will continue to evaluate "the creation and assignment of multiple MS–DRGs for cell and gene therapy cases: One to cover patient care costs, the other to cover product costs across therapeutic product categories." However, as more therapies come to market ARM urges CMS to further detail the circumstances under which it will create new MS-DRGs for CGTs. ARM believes that this information will provide transparency and predictability to manufacturers supporting their commercialization efforts in the inpatient site of care. In doing so, CMS will hopefully maintain the goal of ensuring a stable and accurate provider reimbursement and therefore, patient access to all novel therapies.

Medicaid – As previously discussed, the majority of commercially available CGTs are currently administered in the inpatient setting and similar to Medicare, Medicaid programs typically pay providers a bundled rate that in many cases can be inadequate to cover the hospital's cost of purchasing innovative new therapies. As a result, hospitals and other providers can be strongly disincentivized to administer newly available CGTs to Medicaid patients and may impose patient quotas or prioritize treating patients with other sources of coverage.

Mentioned previously, numerous states have recognized that Medicaid bundled payments are inadequate for inpatient-administered CGTs and have adopted methodologies to pay separately (i.e., reimburse the hospitals directly for their cost of purchasing the therapy). This approach ensures that hospitals have adequate resources to administer CGTs to Medicaid patients while also allowing states and the federal government to collect a rebate from the manufacturer under the MDRP. Separate payment is also a requisite first step in enabling state Medicaid agencies and CGT manufacturers to enter into voluntary outcomes-based payment arrangements. Congress should direct CMS to issue guidance to states on how to implement separate payment for CGTs under existing Medicaid authority.

ARM strongly opposes CMS' recent proposed expansion of the definition of a Medicaid "covered outpatient drug" (in Medicaid proposed rule CMS-2434-P), which would remove the incentive for states to pay separately for CGTs and undermine efforts to expand value-based payment arrangements in Medicaid. We urge Congress to voice concerns to CMS regarding this misguided and unprecedented reinterpretation of the MDRP.

Policymakers should explore new Diagnosis Related Group (DRG) methodologies addressing increased reimbursement requirements for CGTs. Consistent with our comments above regarding Medicare's MS-DRG 018, appropriately structured AP-DRGs could address payment inequities across states. Most states utilize a contractor to set AP-DRG rates. States, CMS, and providers could collaborate with third parties to ensure consistency across states, incentivizing

them to utilize the same AP-DRG year or new AP-DRGs designed with CGTs in mind. These updated DRGs could alleviate some of the financial uncertainty faced by COEs in states that have not yet accepted a methodology of separate payment.

What is the Future of Access for These Therapies?

39. What is the appropriate role of the federal government in ensuring access to these therapies in the commercial market? How can any steps taken on the federal level ensure expanded access while not hurting innovation in this area?

ARM encourages early engagement and collaboration between the developers of CGTs and public payers. This can involve pre-submission discussions to align on coverage and reimbursement considerations. For many potential patients, CGTs represent the best or only available treatment option for debilitating, degenerative, and often fatal diseases. CGTs are fulfilling an urgent and unmet medical need and delayed access can jeopardize patients' health, their eligibility to receive a therapy, and their treatment outcomes.

Congress empowered the FDA to be the sole arbiter of establishing the safety and efficacy of drugs and biologics; therefore, federal policymakers should resist efforts by payers to duplicate or subvert FDA's regulatory review process for the purposes of determining how to cover or pay for approved products. In recent years there have been efforts to restrict coverage or reduce payment for therapies approved by the FDA with Accelerated Approval designation. Such attempts undermine the intent of the Accelerated Approval pathway – to bring treatments to critically ill patients with unmet needs more quickly – and inconsistent coverage and payment policies risk exacerbating health disparities, particularly for patients who rely on federally-funded programs.

Finally, positive coverage decisions and adequate reimbursement structures have a cascading effect on commercial payers and state Medicaid agencies, directly impacting access to CGTs. Many commercial payers and state Medicaid agencies often reference Medicare reimbursement rates as a benchmark (+/-) to build their own case rates. For this reason, it is critical that Medicare's MS-DRG rates fully encompass the value of novel CGTs. Commercial payers and state Medicaid agencies also look to Medicare for coverage policy direction, notably many watched CMS' national coverage analysis of CAR-T to inform their coverage policies after the first CAR-T cell therapies were approved.

40. Should the federal government mandate coverage of these therapies?

All American patients in need should have timely and equitable access to lifesaving and life-changing CGTs. The federal government plays a critical role in ensuring Medicare and Medicaid beneficiaries can access FDA-approved CGTs in accordance with their approved indication. This includes establishing and enforcing appropriate coverage policies that prevent treatment delays and adequate reimbursement so that products are commercially-viable and that hospitals or other providers do not incur financial losses when delivering CGTs to patients.

41. What are the anticipated costs or savings to health systems, plans, payers, or patients as a greater number of these therapies become available?

Many of the diseases targeted by approved gene therapies are relatively expensive. For example, a severe hemophilia B patient requires more than $21 million in lifetime care costs when using the current standard of care.[ix] Lifetime healthcare costs for a severe sickle cell disease patient range from $4 to $6 million.[x] A patient with transfusion-dependent thalassemia requires $5.4 million in lifetime costs on average.[xi] Gene therapies, due to their single administration and durable nature, can save healthcare system resources in the medium to long term. The Institute for Clinical and Economic Review (ICER), for example, has confirmed the cost-offset of recently approved gene therapies for sickle cell disease, hemophilia B, and transfusion-dependent thalassemia.[xiixiiixiv]

The diseases targeted by gene therapies are devastating and often deadly. For example, the average life expectancy for rare diseases targeted by approved gene therapies is 40 years, which is half the average U.S. lifespan, and for some rare pediatric diseases life expectancy is much lower. This illustrates the high unmet medical need that gene therapies address, the impact on patients' length and quality of life, and the potential societal benefits of extending life and restoring the ability of caregivers and even patients to return to work and living fuller lives.

42. How should anticipated benefits from these therapies be evaluated against the potential costs of these therapies?

Every effort should be made to ensure patients have access to transformative new therapies in a timely manner while incentives for innovation remain in place, so that undue challenges in market access and commercialization do not hinder the pace of innovation for this new class of transformative therapies.

An independent scientific evaluation of the clinical and economic evidence should be conducted first, without considering price or payment model, to understand the total benefits of a new technology. ARM has been clear that traditional HTA frameworks in both the U.S. and Europe are not flexible enough to appropriately evaluate potential cures and do not capture the full product value due to issues including: the short-term timeframe for assessing affordability versus the long-timeframe for assessing value; variability in willingness to pay based on degree of unmet medical need; and the subjectivity of incorporating contextual considerations such as caregiver and societal impacts into a quantitative framework.

The most common value assessment approach requires that the analyses occur prior to regulatory approval which denies patients, providers, and health insurers a comprehensive understanding of a treatment's potential benefits and risks. This practice is premature and limits the amount of data and information that can be incorporated into the assessment and upon which an evaluator can base its conclusions. Post-marketing trials, such as confirmatory studies for accelerated approval drugs, and real-world evidence from registries and other data

generation methodologies can provide invaluable data on a drug's benefits and risks derived from longer-term use for a more complete picture of a drug's impact. In the absence of these data, evaluations begin with a premise of insufficient evidence of clinical benefit which inherently biases the review towards a finding of low cost-effectiveness. This is especially true of accelerated approval drugs in which clinical benefit is verified through post-approval trials. Identifying a value-based price benchmark at the time of a drug's approval to influence payer decisions and launch price reflects a narrow focus on cost constraints and access restrictions. This practice is at odds with the reality that certain data are not yet available at the time of launch and the importance of obtaining such information to yield an accurate assessment of both short and long-term value which will lead to maximizing value for patients.

Tufts' NEWDIGS projects that total U.S. gene therapy revenue will reach $7.5 billion in 2030, which represents about 0.1% of projected healthcare spending and 1.3% of projected prescription drug spending in 2030.[xvxvi] This projected gene therapy revenue is 1.8% of the total economic burden of rare disease in the U.S. in 2019, according to economic analysis conducted by the EveryLife Foundation.[xvii]

To compare the financial impact of gene therapies against other durable procedures, the U.S. in 2020 conducted about 3,500 heart transplants at a cost of about $1.6 million each, and 9,950 allogeneic bone marrow transplants at a cost of $1 million each, according to Milliman's triennial report on organ and tissue transplants.[xviii]

43. How should these therapies be financed?

CGTs are unique and highly complex, as are the patients they are intended to treat, and there is no one-size-fits-all financing approach that adequately addresses the diverse needs of patients and healthcare systems. Thus, there are a variety of financing structures that are common within this sector.

An approach to managing the costs of CGTs that is gaining popularity is the use of value-based arrangements (VBAs) or outcomes-based arrangements (OBAs). Such arrangements aim to align reimbursement with the effectiveness of the product in providing a clinical benefit, rather than the quantity of medicine consumed. VBAs and OBAs can bring CGTs to more patients by ensuring access to new therapies while supporting payers in managing their budgets. They defray the cost density of the one-time administered, durable CGTs and mitigate the risk to payers when they are making these considerable upfront investments. ARM and its members have long recognized the need for alternative payment models to make CGTs more available to patients in the U.S. and have actively engaged with CMS to discuss policies that promote the widespread adoption of VBAs and OBAs.

In February 2023, the Department of Health and Human Services (HHS) announced that the Center for Medicare and Medicaid Innovation (CMMI) would be developing a voluntary model designed to provide facilitation for the adoption of OBAs by state Medicaid programs for CGTs

with certain disease indications. The Cell and Gene Therapy (CGT) Access Model, as outlined in the Secretary's report and a subsequent blog post, would establish a multi-state approach for pursuing and administering OBAs in Medicaid. Instead of states individually pursuing agreements with manufacturers, state Medicaid agencies would have the option of assigning CMS to structure and coordinate multi-state OBAs with participating manufacturers. CMS would, in turn, take on the responsibility of implementing financial and clinical outcome measures agreed upon in the OBAs, reconciling the data, and monitoring and evaluating the results. The model also has the potential to address several of the Medicaid access barriers outlined above by alleviating cross-state credentialling challenges, establishing flexibilities under the anti-kickback statute and beneficiary inducement of civil monetary penalties allow manufactures to cover the cost of patient and caregiver travel via patient assistance programs, and supporting the collection and aggregation of data to operationalize OBAs. ARM has provided ongoing input to CMMI to inform their development of the CGT Access Model, including stressing the importance of preserving flexibility in the design OBAs for individual products, and we eagerly await additional information. ARM is supportive of the CMMI model aim to increase equitable access to CGTs; however, the impact of the CMMI model will be limited (by design). Therefore, we urge CMS to consider the more widespread policy initiatives articulated elsewhere in this letter to protect all Medicaid and Medicare beneficiaries' access to CGTs and provide regulatory certainty to the biotechnology companies developing them.

As articulated above, CMS has proposed a change to the MDRP regulations that could undermine its own progress towards encouraging the adoption of VBAs by redefining Medicaid "Covered Outpatient Drugs" (COD) in a manner that vastly expands the scope of the MDRP while eliminating incentives for states to pay hospitals separately for CGTs or enter into voluntary OBAs with manufacturers. Under CMS' approach, any drug, including CGTs, whose costs are separately called out on a hospital claim for payment would be considered a COD. This seemingly technical change could have a devastating impact on Medicaid patients' access to CGTs if implemented. ARM urges Congress to engage with CMS to halt implementation of this problematic provision in the 2023 MDRP proposed rule.

Additionally, Medicaid payments for CGTs should be set at levels ensuring that hospitals and other providers are adequately compensated for providing these innovative therapies to Medicaid patients and do not risk significant financial losses. Congress should enact legislation to provide enhanced funding for separate payments for CGTs though an increased federal Medical Assistance Percentages (FMAP) or other means.

45. Which entity should accept the majority of the financial risk when providing access to these therapies? Why?

Appropriately structured OBAs or VBAs could address payer uncertainty regarding real-world efficacy that supports the durability and value of these cutting-edge therapies. These agreements are designed to support risk-sharing by aligning financial incentives with the real-

world performance of the treatment. These arrangements shift some of this risk to the manufacturer by linking payment to the therapy's actual performance in improving patient health. Manufacturers are incentivized to continually improve the efficacy and safety of their therapies. The prospect of higher reimbursement tied to better outcomes encourages ongoing research and development efforts to enhance the overall performance of the treatment.

However, VBAs/OBAs can present implementation challenges for manufacturers because of their impact on certain price reporting metrics as discussed extensively below. Further, state Medicaid agencies would benefit from federal policy guidance and operational support to negotiate and implement voluntary VBAs or OBAs with CGT manufacturers.

46. What role should utilization management tools play in providing access to these therapies?

Current utilization management policies can unfortunately impose unnecessary burdens on patients, providers, and payers, often leading to delayed or denied care for patients. The planned course of treatment is the result of careful consideration and collaboration between patient and physician. Then, significant time and resources are devoted to completing prior authorization requirements to ensure that the patient will have the requisite access to the prescribed therapy. Utilization management programs must therefore have a clinically accurate foundation to promote credibility and for provider adherence to be feasible. The prior authorization process should minimize delays in care for patients, be transparent to all stakeholders, and focus on expediting access to appropriate care.

47. How quickly should these covered therapies be made available to patients?

CGTs should be covered upon approval by the FDA in accordance with their labeled indication. States often don't begin the Medicaid coverage policy development process until a candidate is identified, and by then, it is often too late for certain patients with unmet medical needs. Some Medicaid programs employ a coverage review process that can take between 180 to 365 days to conclude. To mitigate this challenge, Congress could work with CMS to shorten the time between FDA approval and Medicaid coverage decisions. Further, Congress could direct the GAO to review the time it takes state Medicaid programs to provide access to all recently approved CGTs.

48. What other considerations should be made around benefit design to ensure access to these therapies (e.g. deductibles, cost-sharing)?

Coverage and reimbursement policies should be site-neutral and support patients and their clinicians in determining the most appropriate care setting. As previously noted, cell and gene therapies can be administered in both the inpatient and outpatient settings. Cost-sharing must be considered in the development of a benefit structure and should include input from patient perspectives.

50. What role should patient assistance programs play in providing access to these therapies?

In many cases, CGT treatments are available in only a limited number of hospitals or COEs nationwide. Travel, lodging and related expenses, especially those incurred for out of state travel, are particularly burdensome for low-income patients in need of CGT treatments. Manufacturers support patients in overcoming financial hurdles via Patient Assistance Programs (PAPs). However, since such PAPs may implicate the Anti-Kickback Statute (AKS), manufacturers may be deterred from offering such assistance given the risk of sanctions. One solution would be the enactment by Congress of a statutory AKS safe harbor applicable to such PAPs.

Additionally, Congress should consider increased funding to states to enhance their non-emergency travel benefits for CGT patients and their caregivers in need of such support.

51. Are additional regulatory requirements or flexibilities needed to promote health plan or payer coverage of these therapies?

ARM has endorsed the bipartisan Accelerating Kids Access to Care Act (S. 2372/H.R. 4578) which takes steps to alleviate administrative hurdles by requiring state Medicaid programs to establish a streamlined enrollment process for some out-of-state clinicians working with children with complex medical needs while maintaining important program integrity checks. Explained previously, this legislation would help alleviate delays that Medicaid patients face when seeking CGTs at out-of-state COEs. We urge Congress to broaden and pass this legislation so that it applies to specialized providers treating CGT patients of all ages.

ARM urges CMS to consider establishing a uniform credentialing standard that could be applied for all providers involved in the administration of CGTs. The establishment of a consensus-based credentialing standard for CGT providers treating those of all ages that state Medicaid agencies may opt to use will help facilitate access to care among some of the nation's most vulnerable patients. ARM also encourages CMS to issue information about best practices to states for efficiently credentialling out-of-state providers and to use its enforcement discretion to ensure that states are complying with Medicaid coverage requirements for CGTs and ancillary medical services that are incidental to the administration of CGT.

52. How should policymakers consider other eligibility criteria for access to these therapies for populations such as individuals with long-term disabilities or complex medical needs who are eligible for Medicaid based on disability? What role should commercial insurance play in the long-term for covering these patients who may no longer have the disability that made them Medicaid eligible?

Most patients treated with CGTs experience disability or have unique medical needs. Patient churn and portability pose unique challenges to the effective implementation of OBAs in healthcare. These challenges can impact the continuity of care, the assessment of treatment outcomes, and the overall success of risk-sharing arrangements. Loss of patient follow-up, difficulty in tracking outcomes, fragmented data systems, complexity in attribution models, risk

of selection bias, administrative burdens and privacy and consent issues are concerns often attributed to patients pursuing eligibility for CGTs.

Addressing these challenges requires collaborative efforts among healthcare providers, payers, regulatory bodies, and biotechnology companies to establish standardized data-sharing protocols, enhance interoperability, and develop strategies for tracking patient outcomes across care transitions. Additionally, clear guidelines and frameworks for managing patient churn within the context of outcomes-based agreements are essential to overcome these challenges and ensure the success of risk-sharing arrangements.

53. Please provide feedback on payment and contracting options for health plans, payers, and manufacturers that would provide access to these therapies for patients. These contract options could include value-based models, warranties, annuities, shared savings models, or other risk-based contracting models. Please provide any relevant examples based on existing models.

As articulated above, ARM believes that OBAs can be a helpful tool to improve patient access to these cutting-edge therapies; however, many legacy regulatory requirements require modernization to allow widespread adoption of these arrangements. ARM strongly urges Congress to enact H.R. 2666, the Medicaid VBPs for Patients (MVP) Act to address the following barriers to widespread adoption of VBAs/OBAs:

- Price reporting - According to the Medicaid Drug Rebate Program (MDRP) statute, manufacturers must provide states and the federal government a rebate on all covered outpatient drugs. Refunds or rebates under a VBA could re-set the CMS "Best Price" rule, creating a significant disincentive to VBA adoption. While CMS issued a regulation in 2020 to address this by creating a "Multiple Best Prices" policy, the agency's solution is administratively challenging for both manufacturers and states. As a result, adoption has been limited to date.

  This regulation, which would be codified by the MVP Act, provides a more streamlined solution to ensure manufacturers do not owe outsized rebates for offering steep discounts, or even full refunds, in the event a product fails to satisfy the applicable outcomes measures under a VBA. The MVP Act similarly ensures that Average Sales Price calculations are not distorted due to discounts offered in good faith under a VBA, avoiding inappropriate pay cuts to Medicare physicians.

- Antikickback statute - The federal anti-kickback statute (AKS) prohibits the knowing and willful payment to induce or reward patient referrals, or the generation of business involving any item or service payable by the federal health care programs (e.g., drugs for Medicare or Medicaid patients). Depending on how VBAs are structured, they could potentially run afoul of the AKS.

The MVP Act provides a safe harbor from anti-kickback laws for VBAs between manufacturers and state Medicaid programs, to avoid unintentionally dissuading the uptake of these patient focused arrangements.

- Inpatient drugs - Products furnished in the inpatient hospital setting are not considered covered outpatient drugs subject to MDRP rebates unless there is separate payment for the drug.

The MVP Act requires CMS to issue guidance clarifying how VBAs, and the associated supplemental rebates, can be applied to products administrated in the inpatient setting through separate payment for such drugs. As discussed above, Medicaid paying separately for the CGT allows the hospital to receive the bundled payment for services and a separate reimbursement amount for the CGT. The reimbursement amount can be paid at invoice, actual acquisition cost or average sales price, whichever is the lesser amount. This policy can be federalized, or CMS can be directed to inform states that they may pay separately under a simple state plan amendment (SPA). Currently, only a minority of states have adopted such a policy.

Additionally, to facilitate VBA adoption by state Medicaid programs, Congress should increase the federal share for state expenses associated with the adoption of VBAs, while also directing CMS to provide states with technical assistance and support to states when requested. Several states have approved SPAs for VBA supplemental rebate agreements between manufacturers and Medicaid. However, the National Association of Medicaid Directors (NAMD) noted that the "administrative burdens and demands on state staff resources to implement multiple best prices is significant" and many state Medicaid programs still lack the resources to adopt VBAs. Along these lines, ARM is cautiously optimistic that CMMI's forthcoming Cell & Gene Therapy Access Model could reduce the burden of negotiating VBAs for participating state Medicaid agencies. However, it is ARM's view that States and manufacturers must be allowed to freely negotiate such voluntary agreements with minimal federal intervention but a reasonable amount of oversight and guidance.

Lastly, it is critical for policymakers to address VBA portability issues for Medicaid patients. The outcomes used to establish payment terms under VBAs often take months, or even years, to materialize and measure. In the meantime, the patient may have transitioned to coverage by another payer (i.e., insurance provider). This is a particular issue for Medicaid, where patients tend to fluctuate in and out of coverage depending on their income. The uncertainty as to whether a given patient will remain enrolled in Medicaid for the full duration of the VBA can disrupt and even derail negotiations between manufacturers and state Medicaid programs. For VBAs structured as installment payments, such that the payer is liable for ongoing installment payments only if the therapy continues to demonstrate its intended effect, the state would remain liable to the manufacturer for remaining payments without regard to whether the patient remains a beneficiary in Medicaid.

How Should Federal or State Governments Promote Access to New Models?

Along with the medical community, the federal government has started to embrace shifts in contemporary medical practice towards the use of CGTs. Federal and state policies should presereve the flexibility for CGT manufacturers to *voluntarilty* enter into alternative models, such as OBAs, that are collaboratively designed with consideration of the unique characteristics of each product and the patient population it is intended to treat.

57. How could the federal government promote greater transparency and competition amongst intermediaries to promote access to these therapies? For instance, interested parties could contemplate how greater flexibility in contracting could impact coverage of these therapies. In addition, interested parties could contemplate how different statutorily defined pricing mechanisms (e.g. Average Wholesale Price, Average Sales Prices, Wholesale Acquisition Cost) might need to be adapted in order to promote access to these therapies. With regard to statutorily defined pricing mechanisms and definitions, ARM believes that adaptations should be made to enable VBAs and OBAs that promote patient access to CGTs.

The Medicaid 'Best Price' (BP) is one such example where the government has taken action to modernize reporting –

In December 2020, CMS finalized the rule *Medicaid Program; Establishing Minimum Standards in Medicaid State Drug Utilization Review (DUR) and Supporting Value-Based Purchasing (VBP) for Drugs Covered in Medicaid, Revising Medicaid Drug Rebate and Third Party Liability (TPL) Requirements,* which allows manufacturers who enter into VBPs to report multiple best prices. Before the BP rule, Medicaid's BP reporting requirements severely hindered the use of VBP arrangements in both Medicaid and the commercial space, as the lowest price offered in any market would have to be offered to state Medicaid programs. For example, if a manufacturer sought to offer a commercial plan an outcomes-based contract, where the manufacturer rebates 80% of the drug to the payor if a therapy fails the patient, the manufacturer would have to offer an 80% rebate to all states – an artificially low cost, regardless of whether the drug produces desired outcomes for Medicaid patients or there was a VBP in place.

While the BP rule is a positive first step, perverse incentives to adopt VBPs still exist due to the Average Sales Price (ASP) and Average Manufacturer Price (AMP) methodologies. Including prices for products that had a large rebate due to a failure to meet endpoints in the calculation artificially lowers the average. ARM strongly supports the Medicaid VBPs for Patients (MVP) Act (H.R. 2666), as it codifies the BP rule and makes critical changes to the AMP and ASP legacy provisions that were codified well before CGTs were a reality to accommodate VBPs.

ARM is confident that meaningful improvements in clinical outcomes and cost reduction can be accomplished though ensuring patients can access safe and effective CGTs. CGTs can heal people suffering from complex medical conditions with limited or no treatment options and bend the health cost curve toward lower long-term costs and higher quality outcomes. This trend is already evidenced by several approved and marketed first-generation regenerative medicine products that have reduced patients' utilization of hospital care, clinical and professional services, and nursing and home healthcare. Newly approved therapies also show

tremendous promise. We look forward to partnering with Senator Cassidy and other members of the HELP Committee to advance policies that drive toward the shared aims of better health outcomes, better population health, and lower healthcare costs.

I would also like to express ARM's appreciation for your ongoing interest in regulatory improvements and take this opportunity to highlight two FDA issues affecting the development of CGTs.

First, ARM supports appropriate staffing levels for the Center for Biologics Evaluation and Research (CBER), especially the Office of Therapeutic Products (OTP). While OTP has made some gains in staffing under its increased hiring authority under Prescription Drug User Fee Act (PDUFA) VII, the explosive growth in CGTs over the last six years has resulted in difficulties for OTP staff in being able to communicate with sponsors in a timely and effective fashion that will take time to overcome. The private sector competes for highly talented staff, resulting in retention challenges, as well. The high rate of hiring of new staff, combined with the complexity and rapidly evolving nature of the CGT field, produces a need for faster, more comprehensive new staff training. For these reasons, we encourage Congressional support of robust funding for CBER.

Second, we applaud Congressional and FDA initiatives to increase the efficiency of development through expedited programs for CGTs, including the Regenerative Medicine Advanced Therapy (RMAT) designation and accelerated approval. ARM supports efforts to maximize the impact of the RMAT program in expediting CGT development and is currently undertaking an assessment of the program's impact on the sector. We look forward to sharing our findings with you and the rest of the Committee in the near future. ARM is encouraged by CBER's expressed interest in increasing the use of the accelerated approval pathway for CGTs. Accelerated approval streamlines CGT development while maintaining FDA standards for safety and efficacy. A distinction between accelerated and traditional approval is the trial endpoint (a surrogate endpoint that is reasonably likely to predict the clinical benefit of how a patient feels, functions, or survives). Gene therapies are especially amenable to 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). As discussed in our RFI response, ARM has concerns that this positive regulatory environment could be offset by potential reimbursement challenges for products receiving accelerated approval. We urge Congress to support federal coverage and reimbursement policies that promote the innovation that the accelerated approval pathway can provide.

Again, we thank you for your continued focus on improving the lives of patients suffering from complex medical conditions, for some of whom CGTs may be the only treatment option and urge you to consider ARM's recommendations for ensuring access to these transformative therapies.

ARM welcomes the opportunity to meet with you to discuss these recommendations in greater detail and answer any questions you may have.

Sincerely,

Erica Cischke, MPH
Vice President, Government Affairs
Alliance for Regenerative Medicine

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