Rare Disease Company Coalition

January 24, 2024

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

Re: Cell and Gene Therapies RFI

Dear Ranking Member Cassidy:

On behalf of the Rare Disease Company Coalition (RDCC), we are writing in response to the Senate Committee on Health, Education, Labor, and Pensions (HELP) Request for Information (RFI) on ensuring access to gene and cell therapies.[1]

The RDCC represents innovative life science companies committed to discovering, developing, and delivering treatments for the one in ten Americans living with a rare disease. RDCC member companies are leaders in rare disease innovation. On average, RDCC members reinvest over half their annual revenue back into research & development (R&D), totaling over $15 billion in 2022. RDCC members have brought 45 treatments to market and are presently working on more than 200 rare disease development programs, many of which would be the first ever FDA-approved therapy for their respective patient communities.[2]

The RDCC commends your longstanding leadership and support for the rare disease community and biotech innovation and your interest in developing policy solutions to ensure that Americans can access life-changing and potentially life-saving cell and gene therapies. As recognized by the RFI, many of these first-of-its-kind treatments under development for rare diseases are gene and cell therapies that, with the appropriate policy framework, could ultimately prove life changing to patients living with a rare disease. Yet, despite the immense potential of cell and gene therapies, the current ecosystem may not be well-equipped to handle the increasing activity and advances within the gene therapy market.

The RDCC thanks the Committee for this opportunity to directly share ideas on how to implement the appropriate policy frameworks that incentivize innovation and ensure timely access to cell and gene therapies to treat rare diseases. Our specific responses to the questions posed in the RFI and policy recommendations are included below for your consideration. We look forward to working with you and the Senate Health, Education, Labor and Pensions (HELP) Committee to advance research and legislation to accomplish these goals.

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[1] Gene Therapy Request for Information (RFI), Issued December 5, 2023, https://www.help.senate.gov/imo/media/doc/gene_therapy_rfi.pdf

[2] Rare Disease Company Coalition, https://www.rarecoalition.com/

I. Which Treatments Should Be Included? (Questions 1-2)

a. Policymakers must recognize the differences between cell therapies, gene therapies, and rare disease therapies and recognize at the outset the novel nature of these treatments.

We strongly encourage the Committee to provide clarity to policymakers about the differences between cell therapies, gene therapies, and rare disease therapies. While there are similarities and often overlap between the three therapies, they are nonetheless distinctly different and will likely require different approaches to ensuring access. Gene therapy is designed to silence a mistake in a gene or replace a faulty gene with a corrected one, whereas in cell therapy, human cells are transplanted into a patient to replace or repair damaged cells.[3] Rare disease therapies are those designed to treat patient populations of 200,000 or fewer in the U.S.[4] While some of these therapies may be cell therapies or gene therapies, not all of them are—other modalities include enzyme replacement therapies and small molecule treatments, among others.

Further, we urge policymakers to recognize the novel nature of these treatments at the outset. Stanford Medicine clarifies, "cells and genetically engineered cells have fundamentally different properties than medicines and surgery—they are 'living drugs' that can heal and replace damaged tissues or diseased organs."[5] It is critical to understand and properly consider these key differences because, as with any groundbreaking and developing technology, cell and gene therapy requires considerable investment in research and development (R&D). Manufacturing gene and cell therapies requires significant customization and process development, which will lead to significant increases in complexity—especially at any level of scale.[6] Furthermore, cell and gene therapy development requires close connections between basic research, labs, and clinical care settings. To make the advances in treatment available to patients in need, we must examine the pathways to diagnosis, pre-conditioning and care made available through the entire health care system.

b. Policymakers should focus on developing clear criteria for inclusion that satisfy FDA requirements.

A rigid delineation between rare and ultra-rare disease may be both too narrow or too broad for use in reimbursement and innovative payment models. A static definition may be difficult to adapt to needed changes as they arise. The RDCC encourages policymakers to consider regulatory flexibilities that are concomitant with the size of the patient population and the relevant disease-specific characteristic.

Regardless of whether a treatment targets a rare or ultra-rare disease—both of which aim to address high unmet medical needs—it is essential that patients receive access to a treatment in accordance with the FDA-approved indication statement. As such, which treatments and patient

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[3] Florian Eichler, MD, "What Are Gene and Cell Therapies?" Published November 11, 2022, *https://www.massgeneralbrigham.org/en/about/newsroom/articles/what-is-gene-cell-therapy*

[4] *SEC. 526 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT, 21 USC 360bb, https://www.govinfo.gov/app/details/USCODE-2022-title21/USCODE-2022-title21-chap9-subchapV-partB-sec360bb/summary*

[5] Stanford Medicine Center for Definitive and Curative Medicine (CDCM), "Why Cell and Gene Therapy?" https://med.stanford.edu/cdcm/CGT.html

[6] *Ibid.*

populations are ultimately included should be determined based on clear criteria that best ensure both the safety and efficacy of the treatments and access for patients.

Ultimately, policy must ensure that both public and private payers uphold the FDA's statutory authority—including for drugs approved through expedited development and review programs—in determining a medical product's safety and efficacy. This includes preventing payers from adopting pricing and reimbursement policies that would disincentivize the use of FDA's expedited development and review programs, and other regulatory tools to overcome barriers to rare disease drug development and speed patient access.

Congress empowered FDA to be the sole arbiter of determining a drug's safety and efficacy, and programs like the Accelerated Approval Pathway (AAP) meet FDA's standard for safety and efficacy just as drugs that receive traditional approval. The AAP addresses urgent and unmet medical needs of patients with serious and often life-threatening diseases by speeding the availability of much-needed treatments. Some payers—including Centers for Medicare & Medicaid Services (CMS), contracted managed care organizations (MCOs), and commercial payers—claim that for AAP drugs a "clinical benefit is not established" and will not authorize treatment.[7] Additionally, many self-insured payers will exclude drugs targeting specific rare diseases. When insurers exclude specific rare disease treatments or drugs approved through the AAP, they prolong the period that a patient's health condition may be deteriorating and undermine FDA's authority in determining safety and efficacy.

II. What is the Current Practice for Patients with Ultra-Rare Diseases or Disorders? (Questions 3-10)

a. Physicians, not payers, should determine medical necessity for patients.

Many commercial payers, including self-insured employers, laser out treatments for rare diseases or gene therapies as a treatment modality, to the detriment of patients that may benefit from such treatments. Ultimately, physicians should determine medical necessity and prescribing of rare disease treatment, not payers. In rare and ultra-rare diseases, physician specialists are experts in their field as they spend years, if not decades, in training, research, and clinical practice. As payers evaluate drugs indicated for rare diseases, whether through an internal review committee or through a public process, physicians with expertise in that rare disease should be consulted to inform the payer's coverage policy to ensure alignment with clinical practice.

Upholding the role of physicians in determining medical necessity also necessitates that any new coverage policy models should support the treatment of patients in the most appropriate clinical setting as determined by their physician. Payers should not restrict or limit access to treatments based on the site of care - policymakers should ensure that timely access is granted regardless of whether a treatment is administered in an inpatient or outpatient setting.

[7] Centers for Medicare and Medicaid Services, A Report in Response to the Executive Order on Lowering Prescription Drug Costs for Americans, May 23, 2023.
https://www.cms.gov/priorities/innovation/data-and-reports/2023/eo-rx-drug-cost-response-report

b. As they stand, ERISA employer plans may allow for discrimination in coverage of rare disease treatments.

Many self-insured employee health plans are not subject to the Affordable Care Act Section 1557, which prohibits discrimination in health care plans and activities, though over half of Americans are enrolled through their employer.[8] Employee Retirement Income Security Act of 1974 (ERISA) employer plans have the flexibility to design their health benefits and arbitrarily approve or deny coverage of treatments.[9] To ensure parity, regulators should hold self-insured plans governed by ERISA accountable to the Transparency in Coverage rule regarding rapid enforcement to ensure plan assets are applied in the best interest of rare disease patients.[10]

c. Medicaid is a vital program for patients living with a rare disease and their families.

Medicaid is a crucial resource for patients and families receiving and treating a rare disease diagnosis. Over half of rare diseases affect children—and 30 percent of those children will not live to see their fifth birthday.[11] As such, Medicaid and CHIP are crucial programs to ensure coverage for some of the most vulnerable patients living with a rare disease and their families. Patients with rare disease diagnoses can require multiple procedures within the nation's best institutions; meanwhile, their caregivers often need to take substantial time away from work, or leave the workforce altogether, due to a heavy burden of medical appointments and/or time required to treat the diagnosis and care for a loved one. In many states, Medicaid also facilitates access to important health services that treated or 'recovering' patients may need to (re-)learn necessary, adaptive life skills. In many ways, those program benefits are essential to families keeping or maintaining a basic, though not extraordinary, quality of life, and being able to function over the whole of their lifespan within society.

III. What is the Future of Access for These Therapies? (Questions 39-53)

a. Alternative payment options can accommodate the needs of both payers and manufacturers where one-size-fits-all policies fall short.

As the RFI recognizes, if a patient cannot access innovative treatments, to them it is as if that innovation never occurred.[12] While that statement focused on affordability, the same is true if federal policy makes the development of these treatments prohibitively expensive to develop and commercialize.

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[8] Patient Protection and Affordable Care Act, Pub. L. No. 111-148 (2010), https://www.govinfo.gov/app/details/PLAW-111publ148.
[9] Employee Retirement Income Security Act of 1974, Pub. L. No. 93-406 (1974), https://www.govinfo.gov/content/pkg/COMPS-896/pdf/COMPS-896.pdf
[10] Transparency in Coverage 85 FR 72158, https://www.federalregister.gov/documents/2020/11/12/2020-24591/transparency-in-coverage\
[11] Global Genes, RARE Disease Fact, https://www.globalgenes.org/rare-disease-facts/
[12] Gene Therapy Request for Information (RFI), Issued December 5, 2023, https://www.help.senate.gov/imo/media/doc/gene_therapy_rfi.pdf

Federal policymakers must work with manufacturers to develop and support novel, alternative payment options that work at scale for improving access to innovative treatments. Policymakers must also recognize that different treatments will likely require different payment structures depending on a variety of factors, such as disease characteristics, socioeconomic issues, and unique delivery platform technology. There is not a one-size-fits-all solution—and both payers and manufacturers should have maximum flexibility to enter innovative payment models. Policymakers' collaboration with manufacturers will also be critical given the reality that all pricing and contracting strategies, as well as manufacturer patient assistance programs, are proprietary and should remain as such.

b. Flexibility in innovative arrangements is critical, as unique disease and therapeutic characteristics will drive contracting models.

Various contracting arrangements from traditional volume-based rebates to innovative arrangements (i.e., subscription models or outcomes-based agreements) are all notable tools to support access. It is critical to recognize that some disease states do not lend themselves to outcomes-based arrangements. Measuring an outcome in a rare or ultra-rare disease that is slowly progressing with a heterogeneous patient population is often infeasible. Measuring a hard clinical endpoint, like survival, may take decades—not a practical time frame for a payer's budget window of three years. We urge policymakers to consider legislation that would allow for much-needed flexibility for value-based arrangements, such as those proposed in the Medicaid VBPs for Patients (MVP) Act.[13]

IV. How Should Federal or State Governments Promote Access to New Models? (Questions 54-57)

a. Payers should provide coverage of treatments to the FDA-approved indication statement, without delay, and not apply arbitrary limitations or restrictions.

When an age limit or specific disease milestone is included in the FDA-approved indication statement, it is imperative that patients receive access to that treatment before the age limit or milestone is reached. Otherwise, patients suffering from a rare disease may further and irreversibly deteriorate. In approving a therapy and determining the indication statement, 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, therefore, drive authorization. Inappropriately applying clinical trial criteria as the coverage criteria and basis for prior authorization undermines FDA's scientific authority.

b. Policymakers should reinforce timely access to treatment and remove administrative barriers that delay access.

Patients living with rare diseases in the United States can experience a range of financial barriers to diagnosis, care, and treatment depending on their type of health insurance. Medicaid is a

[13] H.R. 2666 – 118th Congress (2022-2023): Medicaid VBPs for Patients Act or the MVP Act, https://www.congress.gov/bill/118th-congress/house-bill/2666/text

critical resource for Americans living with a rare disease and coverage decisions have significant consequences for timely access. Restrictive policies and barriers to coverage impose disproportionate and often insurmountable burdens on vulnerable patient populations, who may have no other path to diagnosis and treatment. Americans receiving coverage through government payers should not be disadvantaged compared to those receiving commercial insurance coverage.

In Medicaid, for example, although states are required to cover drugs as long as the manufacturer enters into a Medicaid Drug Rebate Program Agreement,[14] Medicaid agencies have imposed access barriers more restrictive than the FDA-labeled indication, particularly for rare disease therapies due to concerns around cost and budget impact.

Federal law requires that FDA-approved drugs subject to a rebate agreement be covered by each state Medicaid program upon availability.[15] In some states, lengthy pharmacy and therapeutics (P&T) Committees or Drug Utilization Review Boards (DURB), an entity that authorizes and reviews the prescribing, distribution and use of medication, carry out proceedings to generate and implement formal coverage criteria that contradict such a requirement and can hinder access to newly available therapies for patients in need. Each state P&T Committee or DURB follows its own new-drug review law and policy, which in many states permits or even mandates extended review timelines. Such delays can result in unreasonable access restrictions on new drugs. To put it in perspective, more than half of all rare disease patients are children. While not all of these patients will utilize a cell or gene therapy, those that do cannot afford Medicaid's extended delays before they can access a needed treatment as many of their conditions are progressive and life-threatening.

Policymakers should work with the Centers for Medicare & Medicaid Services (CMS) to ensure timely patient access to treatment and to achieve shorter, streamlined drug coverage approval processes. This includes enforcing existing Medicaid outpatient drug coverage obligations for state fee-for-service and contracted managed care organizations (MCOs) to ensure that when a drug is prescribed for its medically accepted FDA-approved indication, and a manufacturer has a signed Medicaid drug rebate agreement, the patient is promptly approved for treatment. CMS should instruct state Medicaid programs (including its MCOs) to reduce burdensome and unnecessary prior authorization processes to facilitate timely access to medicines.

Congress should establish rapid review incentives for new rare disease therapies. While states and MCOs must approve prescription requests when a drug is prescribed for its medically accepted indication, Congress should consider establishing incentives, such as bonus payments, for states to conduct expedient coverage reviews of newly available rare disease therapies through P&T and DURB reviews. For example, bonus payments could be offered if coverage reviews are considered by the next scheduled DURB meeting after availability and in no case later than 90 days.

Beyond that, several state Medicaid programs delay coverage until a unique product specific HCPCS J-code is available for a physician-administered drugs—like gene therapy targeting rare

[14] Sec. 1927. [42 U.S.C. 1396r–8], Social Security Act (SSA), https://www.ssa.gov/OP_Home/ssact/title19/1927.htm
[15] Sec. 1927. [42 U.S.C. 1396r–8], Social Security Act (SSA), https://www.ssa.gov/OP_Home/ssact/title19/1927.htm

and ultra-rare diseases—despite the availability of a miscellaneous J-code, which is common coding billing practice. Depending on the FDA approval date and HCPCS quarterly application cycle, a unique product specific HCPCS J-code can take greater than 6 months to be available. Such a delay in access will adversely affect patients, for many of whom every day is critical. Policymakers should explore requirements for CMS to issue an interim J-code upon approval and to update to a product specific J-code within a specified period.

c. Payers should provide timely approval for patients with rare or ultra-rare diseases who may need to travel outside of their state to receive access to a clinical expert or treatment at a center of excellence (CoE).

Rare and ultra-rare disease patients often see providers in multiple states as there may be a limited number of specialists/experts for their given disease or condition. State Medicaid agencies should have an expedited process to enroll providers in situations when a patient needs to travel to another state for treatment and timely reimburse the out-of-state provider for said treatment. A federal safe harbor should be established to provide more certainty for manufacturers to offer travel support programs so patients who need financial support can travel to a treatment site to receive gene therapy. The Accelerating Kids' Access to Care Act (S. 2372) provides a framework that policymakers should consider ensuring timely access to treatment across state lines.[16]

d. Patients must have a timely and accessible avenue to appeal coverage denials.

The appeals process for denials by payers should be accessible to patients and physicians and should not be overly burdensome. Patients should be informed in a timely manner of the denial of services, with clear guidelines for the appeals process. Like Medicaid and ACA plans, patients with self-insured employer health coverage, whose plan may exclude coverage of treatments for rare and ultra-rare diseases, should be able to access the external review process when coverage for a rare disease treatment is denied for being an excluded benefit.

e. External Review should include the appropriate physician subspecialty.

As previously stated, the treating physician determines medical necessity, and external reviews provide appropriate safeguards for patients to appeal a coverage decision. While external reviews are required to include a physician "who manages the condition," often a rare disease is a subspecialty of a specialty. For example, a neurologist treating epilepsy and sleep disorders does not have the same training or clinical expertise as a neuromuscular physician who treats ALS, Duchenne muscular dystrophy and spinal muscular atrophy. Therefore, a neurologist is not appropriate to be the external reviewer on a case for an appeal reviewing a treatment for a neuromuscular disease. This same analogy could be applied to other rare diseases and becomes even more acute in ultra-rare diseases. In all cases, a rare disease expert with direct experience treating that rare disease should be consulted in the review.

[16] S. 2372, 118th Congress (2022-2023): Accelerating Kids' Access to Care Act, https://www.congress.gov/bill/118th-congress/senate-bill/2372

V. How Should Lawmakers Seek to Evaluate and Accomplish These Policy Goals? (Questions 58-59)

a. Endorse Legislation that Would Benefit Access to Gene Therapies.

Enactment of H.R. 2666, the MVP Act, as passed by the House Committee on Energy and Commerce on May 24, 2023,[17] will ensure patient access to rare disease gene therapies by facilitating widespread use of value-based purchasing arrangements ("VBPs") that allow for meaningful outcomes-based refunds during a warranty period. The bipartisan MVP Act codifies and fills gaps in a Centers for Medicare & Medicaid Services (CMS) rule[18] intended to eliminate the government price reporting barrier that is preventing biopharmaceutical companies from offering VBPs. This bill is consistent with Senator Cassidy's Patient Affordability Value and Efficiency Act discussion draft from 2019, as well as sections 121-123 of S. 2164, the Lower Costs, More Cures Act of 2021.[19] We also suggest endorsing other bills that will support gene therapy access like the Safe Step Act (S. 652; H.R. 2630)[20] and HELP Copays Act (S. 1375; H.R. 830).[21]

b. Oppose the CMS Proposed Drug Price Verification Survey.

It is critical to recognize that some disease states do not lend themselves to outcomes-based arrangements; therefore, measuring an outcome in a rare or ultra-rare disease that is slow-progressing with a heterogeneous patient population is often infeasible. Measuring a hard clinical endpoint, like survival, may take decades, which is not a practical time frame for a payer's budget window of three years. As such, flexibility is critical in which voluntary contracting type a manufacturer and payer engage in.

Additionally, subjecting rare disease therapies to unnecessary scrutiny in the context of the Medicaid program without sufficient context will threaten patient access and reduce manufactures' ability to innovate. The impact of this proposed policy on capital formation is also noteworthy. Both early and commercial-stage rare disease companies rely on private investment to sustain research and development efforts. Clinical-stage rare disease companies are at significant risk, as they do not generate product revenue and, for the most part, are significantly or entirely dependent on capital markets to fund development programs that may or may not result in a commercialized product. Policies, such as the proposed rule,[22] can create uncertainty

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[17] H.R. 2666, 118th Congress (2022-2023): Medicaid VBPs for Patients Act or the MVP Act, https://www.congress.gov/bill/118th-congress/house-bill/2666/text

[18] 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, 85 FR 87000, https://www.federalregister.gov/documents/2020/12/31/2020-28567/medicaid-program-establishing-minimum-standards-in-medicaid-state-drug-utilization-review-dur-and

[19] S. 2164, 117th Congress (2021-2022): Lower Costs, More Cures Act of 2021, https://www.congress.gov/bill/117th-congress/senate-bill/2164/text

[20] S. 652, 118th Congress (2023-2024): Safe Step Act, https://www.congress.gov/bill/118th-congress/senate-bill/652

[21] S. 1375,118th Congress (2023-2024): Help Ensure Lower Patient (HELP) Copays Act, https://www.congress.gov/bill/118th-congress/senate-bill/1375/text

[22] Medicaid Program; Misclassification of Drugs, Program Administration and Program Integrity Updates Under the Medicaid Drug Rebate Program, 88 FR 34238, https://www.federalregister.gov/documents/2023/05/26/2023-10934/medicaid-program-misclassification-of-drugs-program-administration-and-program-integrity-updates

and have a disproportionate impact on rare disease drug development. The information from the drug price verification program could affect the investment environment, where small changes can have an enormous impact on the future for the 95 percent of rare diseases that lack an approved treatment.

We recommend opposing the CMS proposed drug price verification survey that unfairly targets gene therapies.

VI. Conclusion

We greatly appreciate the opportunity to provide the RDCC's perspective in response to the Committee's Request for Information. Should you have any questions, please feel free to contact us at yoko@rarecoalition or katie@kpmgroupdc.com.

Sincerely,

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