January 22, 2024
Senator Bill Cassidy, M.D.
U.S. Senate Committee on Health, Education, Labor, and Pensions

Via email to: GeneTherapyCoverage@help.senate.gov

Re: RFI on Improving and Protecting Access to Gene Therapies

Dear Senator Cassidy:

Haystack Project appreciates the opportunity to respond to your Request for Information seeking stakeholder feedback on the unique challenges associated with ultra-rare disease treatments and the role Congress might play in ensuring appropriate access to emerging options that offer disease modifying or even curative potential. Haystack Project has long highlighted the unintended consequences rare and ultra-rare patients bear when reimbursement landscape refinements do not fully consider our patient communities. We have urged Congress, FDA, and CMS to proactively facilitate access to the treatments our patients need while preserving (and refining) the incentive frameworks that have made research and development in ultra-rare diseases financially feasible.

Haystack Project is a 501(c)(3) non-profit organization with a membership of 140+ rare and ultra-rare disease patient advocacy organizations. Our core mission is to evolve health care payment and delivery systems with an eye toward spurring innovation and quality in care toward effective, accessible treatment options for all Americans. We strive to coordinate and focus efforts that highlight and address systemic reimbursement obstacles to patient access in disease states where unmet need is high and treatment delays can be catastrophic.

The Orphan Drug Act has, as FDA recently noted, finally begun to provide treatments for some orphan diseases. Unfortunately, as the RFI noted:

> While progress has been made in promoting access to access to cell and gene therapies more broadly, the small size of the ultra-rare disease population makes access solutions particularly challenging . . .. If a patient cannot afford innovative treatments, to them it is as if that innovation never occurred.

Haystack Project hopes that its comments will be the start of a continuing dialogue with your office. We are eager to contribute the insights and experiences from our patient communities as

you craft policy priorities and work toward a future of hope and progress. Our comments provide a brief background on the unique challenges ultra-rare patients face in accessing treatments. We urge you to consider the access hurdles our patients face with existing treatments as well as the potential exacerbation of these impediments as payers consider new cell and gene therapy options.

LEGISLATION SHOULD PRIORITIZE ACCESS FOR RARE DISEASE PATIENTS AND THOSE REQUIRING CELL AND GENE THERAPIES

As a threshold matter, we are concerned that policy initiatives seeking to solve access impediments should be directed at those facing very rare conditions, regardless of whether those are cell and gene therapies or small molecule or biologics.

We similarly caution against setting a patient threshold in defining "ultra-rare." To the extent that any access-related policy initiative would be limited to disease states with a defined number of impacted patients, we believe that the threshold should be carefully calculated within the context of the "problem" the initiative seeks to address. For example, the ODA was designed to encourage development of treatments for small population conditions and, while set at 200,000 patients, it also included an alternative eligibility standard based on likelihood of recouping research and development costs. Haystack member organizations advocate for conditions impacting fewer than 20,000 patients in the U.S. Their shared experiences reflect a commonality in access challenges as well as lack of (or limited) therapeutic options.

CURRENT PRACTICES AND IMPEDIMENTS

Patient Access Programs

Financial assistance through manufacturers and charitable organization patient assistance programs are crucial to ensuring patients are not denied treatment solely due to financial concerns. Where there is no generic, there is no inducement to take a more expensive drug and health plans' use of copay accumulator programs is an overreach. In most instances, rare and ultra rare diseases have one treatment, no options, and no generics. The recent court decision should be extended to all payers through legislation requiring that patient assistance funds be included in calculations on patient copayments, deductibles, and out-of-pocket maximums.

The more recent and equally insidious practice of "alternative funding" programs are another way self-insured plans avoid costs of specialty drugs. The health plan eliminates coverage for specific high-cost specialty drugs to render individuals needing those drugs "uninsured." This has led to an entirely new set of business entities that are contracted by plans to identify other funding sources and shepherd patients through the process of documenting lack of coverage and financial need to charitable organizations and/or manufacturer patient assistance programs. These programs cause delays in treatments that are critical to our patients, cause

enormous stress, waste patient, caregivers, and physician time. While cell and gene therapies may be the costliest, any solution should address all current treatments for rare diseases. The solution is to ban this practice across all payers.

Formulary restrictions and utilization management strategies

Haystack member organizations have continued to relate their experiences in working with their clinicians and payers to navigate the prior authorization processes and utilization management tools. The most frequently encountered challenges leading to treatment delays include:

- The threshold problem for our patient communities is the tension between where Medicare, Medicaid and many other payers look for evidence supporting medical necessity and where evidence supporting the standard of care in very rare diseases can be found. Payers look to the label and a set of compendia; most treatments for very rare conditions are off-label and too rare to gain inclusion in the compendia – even if the off-label use is the standard of care among disease experts. Patient access programs are not generally available since a manufacturer offering free or discounted drug in this patient population would face off-label promotion scrutiny and potential liability.

  Congress recognized and fixed a similar problem for anti-cancer treatments by defining medically accepted uses to include those that are supported by an expanded set of compendia as well as peer-reviewed literature. Rare and ultra-rare patients need a similar fix so that payers, including Medicare and Medicaid can make coverage decisions that consider, rather than ignore, the available evidence in peer-reviewed literature and, if needed, refer to the opinion of recognized disease-specific experts identified by the relevant specialty society.

Only then can we address utilization management.

- **Step therapy protocols.** Step therapy is a well-accepted, frequently encountered utilization management strategy. This may not be a problem in disease states for which several treatments are available, including generic options. As outlined above, extremely low prevalence conditions rarely have more than one FDA-approved treatment available, and any off-label uses of existing drugs are seldom found in the various compendia and other sources plans commonly rely on to determine coverage. This means that individuals with very rare conditions do not have the same protection from inappropriate step protocols that individuals with common conditions have, and the steps designed for more common diseases are frequently inappropriate within the context of off-label use in rare conditions. This is particularly true when step therapy protocols require failure on a treatment that is not useful in that disease and/or that may be harmful to the patient.

  Haystack does not expect that plans would maintain up-to-date clinical information on every treatment for every rare disease. We do, however, believe CMS should be

required to consider whether plans maintain an expedited review process and permit emergency doses for rare disease patients in determining whether plan designs are nondiscriminatory.

- **NDC "blocks" and "lockouts."** It is relatively common for plans to systematically block coverage of newly approved drugs and biologicals for 6-12 months or longer under the rationale that formulary inclusion requires review of the plan's pharmacy and therapeutics committee. These blocks apply to patients newly seeking treatment as well as to those who have benefited from the treatment through clinical trial participation, open label extensions, and expanded access programs. Haystack recognizes that the mechanism has utility and may be a reasonable approach in more common conditions, however, it has no place in rare and ultra rare diseases.

  In rare conditions declining access to what may be the only on-label is an example of the types of unintended consequences rare disease patients face throughout their health care journey and illustrates how applying policies with seeming equality drives real world inequities that can harm patients. An expedited formulary review process applicable to newly approved treatments for rare diseases would mitigate the disparate impact that blocks and lockouts exact on patients.

  Medicaid FFS and MCOs also do this in effect when P&T/DUR committees review new treatments for formulary placement. Again, this is workable when trying to gain greater discounts among/between competitors, but where there is no competition because there is a first ever treatment for a rare disease, scheduling P&T/DUR reviews effectively does nothing more than effectively delay access like the NDC locks and lockouts. Texas has a process whereby they have access to patients within 30 days and the necessary committees are informed and can review all they want, but after access is flowing. It's a model for the country.

  Medicare and Medicaid managed care policies delaying access until treatment costs are shifted to fee-for-service. Managed care organizations serving Medicare and Medicaid patients are paid on a risk-adjusted basis, and new treatments are not included in the payments to plans automatically. In Medicaid MCOs and Medicare Advantage, access to high-cost treatments is often delayed so that plans can shift the treatment costs to fee-for-service for the first year. In Medicaid, this is accomplished through annual contract negotiations; in Medicare Advantage, cost shifting occurs only when a statutory coverage requirement or NCD requires new coverage. This creates an incentive for Medicare Advantage plans to throw up a flag and call for an NCD every time a high-cost treatment is approved. The CAR-T National Coverage Analysis was initiated by United Healthcare to ensure that the costs for this treatment could be shifted to Medicare during the first year. The idea that on-label as well as off-label treatments are now 'fair game' for NCDs, which result in incredulous delays in treatments for those living with quickly progressing diseases, is unethical. This incentive

for Medicare Advantage plans to throw down an NCD flag at the first sight of a costly drug must be removed.

We expect that this type of delay will increase as an increasing number of cell and gene therapies receive FDA approval.

COVERAGE AND PAYMENT LANDSCAPE

Inpatient access in Medicare and among other payers relying on a DRG payment system

Access hurdles related to reimbursement structures such as inadequate bundled payment rates, high cost-sharing and/or payer coverage restrictions continue to prevent too many patients from receiving what may be the only treatment available to slow the progression or ease the burden of their rare disease.

Haystack Project has repeatedly urged CMS to ensure that when a rare disease patient receives care in the inpatient setting, they receive the care they need, including any FDA-approved treatment, even if the cost of the treatment exceeds the payment to the hospital. Although CMS has reiterated its position that providers are required to treat patients within the standard of care regardless of the financial consequence, many patients with rare and ultra-rare conditions experience a very different reality. This is not a new problem. CMS has periodically responded to Haystack Project and other stakeholders' reports of access delays and denials with assurances that the Agency would consider available options for accommodating higher-cost, low-volume inpatient stays, including in its inpatient prospective payment system rulemaking cycle for FY 2013:

> As stated previously, we acknowledge and recognize the severity of symptoms that patients diagnosed with disorders of porphyrin metabolism may experience. We also are sensitive to concerns about access to care and treatment for these patients. We will continue to monitor this issue and determine how to better account for the variation in resource utilization within the IPPS for these cases.

In last year's proposed rule, CMS appeared interested in identifying and implementing mechanisms that would address access to treatments for rare diseases within the MS-DRG system. CMS noted that rare diseases "pose a unique challenge" and reiterated their continuing preference for "larger clinical cohesive groups within an MS-DRG" to provide "greater stability and thus predictability…" Since a new treatment targeted to a single rare disease within an MS-DRG with dozens or even hundreds of other rare diseases will ever fulfill CMS' need for high volume, we once again urged the Agency to implement an alternative mechanism that would not place structural preferences over patient health.

To date, CMS has not moved beyond the "monitoring" announced over a decade ago and toward concrete action that improves and protects beneficiary access to care in the near-term

and sufficiently reimburses providers for the items and services needed to appropriately treat rare disease patients over the long-term. Any ultra-rare disease treatment, including cell and gene therapies, will face this challenge. Although the New Technology Add-On Payment mechanism offers short-term relief to hospitals, it does not come close to solving the problem over the long term since many rare and ultra-rare conditions are grouped into MS-DRGs with hundreds of other conditions and CMS remains reluctant to re-evaluate DRG assignment for any particular diagnosis that has a low volume of inpatient stays. Delays of over a decade are untenable and Congress should legislate the solutions Haystack has been putting forward for years now, which recognize 'bundled' DRGs do not work for ultra rare diseases.

Medicare Coverage Mechanisms

Initiation of a Medicare National Coverage inquiry on a new FDA-approved treatment can have tremendous consequences for individuals with extremely rare conditions. Patients within a new treatment's labeled indication already fear delays in coverage, regardless of their payer, but this NCA process is particularly onerous, time consuming, and gives all payers an excuse to hold off on coverage. In addition, drug development for extremely rare diseases frequently relies on FDA's accelerated approval mechanism, and treatments achieving approval are more costly than drugs for common conditions. Both of these factors have increased the likelihood that a National Coverage Analysis will be initiated, and that CMS will seek to implement limited coverage under coverage with evidence development (CED).

The Agency for Healthcare Research and Quality (AHRQ) has described CED as "a National Coverage Determination (NCD) that allows patients to access these select medical items and services, with coverage, on the condition that there is prospective collection of agreed upon clinical data." Tere is considerable tension between this access-enabling view of CED and recent CMS efforts to use the coverage mechanism to do FDA's job of directing design of clinical studies, collecting data on outcomes, and analyzing the evidence. One view prioritizes access to promising treatments: the other focuses on Medicare's pool of aged and disabled research subjects.

NCDs generally, and the CED process in particular, delays access to promising new treatments and injects a set of ethical, logistic, and health equity concerns that are particularly inappropriate within the context of treatment for a life-limiting or life-threatening condition. When directed at FDA-approved therapies, it becomes an inflexible utilization management tool, beneficiaries become research subjects, and treatment "decisions" are subjected to randomization and even "blinding" on the precise intervention. It conditions access to safe and effective treatments on factors beyond the patients' control (clinical trial availability, eligibility, and randomization) and their willingness to place their care into the hands of researchers rather than the clinicians managing their condition(s). The Medicare statute supports deeming medically accepted uses as meeting the reasonable and necessary requirements for coverage. These uses should not be subjected to NCD review unless there is sufficient evidence to

conclude that the treatment is either ineffective or harmful. It is unlikely that any recently approved treatment would clear that bar.

OUTCOMES-BASED PAYMENT ARRANGEMENTS

Haystack supports use of outcomes-based payment arrangements for high-cost treatments, including cell and gene therapies as offering the potential for a win/win/win for manufacturers, payers, and patients. The existing statutory and regulatory landscape, including price reporting mechanisms, however, appear to have reduced use of this mechanism to improve access and reduce risk to payers. While manufacturers have found some workarounds with frameworks like warranty models, legislative initiatives that could account for the unique "pricing" status of treatments subject to outcomes-based arrangements are still very relevant and should be accompanied by guardrails to protect patients from burdensome data collection responsibilities, reimburse them for the time, missed work, caregiver costs, and other expenses, and focus on outcomes that are important to patients. Requirements for these arrangements should include:

- Ensuring that manufacturers and payers include patients in Identifying outcomes and endpoints that are meaningful to patients,
- Entities seeking to contract on an outcomes-based payment arrangement should be required to consult with the relevant disease-specific advocacy organization, patients, and caregivers to identify patient-centered outcomes and assess whether the data collection requirements are overly burdensome.
- Critically important is that payment arrangements should not foreclose uses that are medically accepted but not yet on label. This would require manufacturers and payers to maintain separate pricing structures for off-label uses. (See earlier discussion of why off label use in very rare conditions is so prevalent and needed ….)
- Payment arrangements should not result in coverage constrictions beyond the FDA label and medically accepted uses.
- Payers should be required to report on any access requests that have been denied and include the rationale for the coverage denial.
- Any calculation of value should be patient-centered and avoid use of health economic models that adjust value based on patient age, disability, disease progression, or similar factors.

Haystack welcomes the opportunity to discuss other concerns and recommendations for alternative payment implementation.

In addition, we expect that commercial payers may be particularly reluctant to embrace cell and gene therapies given their high cost and the prevalence of "churning" for patients. We expect that existing solutions such as risk pools and reinsurance mechanisms could ease uncertainty and risk but encourage you to examine alternatives through which federal and/or state funding might be available for treatments that reduce future health care costs and disability.

BACKGROUND

Although countless lives have been improved or saved by new therapies enabled by Congress' set of incentives for orphan drugs, significant unmet need predominates in extremely rare conditions and rare cancers:

- Of the approximately 7,000 rare diseases identified to date, 95% have no FDA-approved treatment option.
- Eighty percent of rare diseases are genetic in origin, and present throughout a person's life, even if symptoms are not immediately apparent.
- Diagnosing a patient with a rare disorder is usually a multi-year process involving a series of primary care clinicians, specialists, and diagnostic testing regimens – extreme rarity of a disorder compounds the resources required for diagnosis. Patients often progress to more serious and more costly disease states by the time they receive a diagnosis.
- If a diagnosed condition has no FDA-approved option, treatment often involves off-label use of existing products.
- Approximately half of identified rare diseases do not have a disease-specific advocacy network or organization supporting research and development, and lack of disease-specific natural history severely complicates research toward new, targeted treatments.

Individuals with rare and ultra-rare conditions often require multiple medications, some of which are high-cost, and care from highly specialized clinicians. Approximately 7,000 rare diseases have been identified to date, 90-95% of which have no FDA-approved treatment.

In addition to high health care costs, rare disease patients face substantial challenges from symptom emergence through treatment or management of their condition. In 2021, the Government Accountability Office (GAO) compiled a report to Congress entitled "RARE DISEASES: Although Limited, Available Evidence Suggests Medical and Other Costs Can Be Substantial." The report assessed the challenges rare disease patients face accessing diagnostic and treatment services as well as the personal and economic costs associated with treatment delays. Among its many findings, the GAO found that:

- Rare and ultra-rare disease patients are often unable to access specialists due to geography or failure to receive a referral for follow-up care at initial symptoms.
- Many progress to more severe disease states by the time they receive an accurate diagnosis. The rarer the disease, the more challenging the diagnosis.
- Forty-one percent of rare disease patients also receive at least one misdiagnosis.
- Rare and ultra-rare patients see an average of 4.2 primary care physicians and 4.8 specialists before receiving an accurate diagnosis.
- Patients make an average of 2.4 out-of-state trips related to their rare disease.
- Rare diseases result in emergency room visits an average of 3.7 times and - are hospitalized an average of 1.7 times - for reasons related to their rare disease prior to diagnosis.

- When a rare disease treatment is administered through complex or innovative procedures or requires a period of post-treatment observation and care, there is almost always a limited set of providers offering the treatment. Better out-of-state, out-of-network, and travel cost accommodations are essential to ensuring that patients can receive the care they need.
- Off-label use of treatments indicated for more common conditions are often required to address disease symptoms and/or progression, especially in extremely rare conditions.
- Approximately 7 percent of rare disease patients reported that they were given a false psychological/psychiatric diagnosis that further impeded and delayed their treatment.[1]

Individually, these access challenges can present inconveniences, frustration, and delays in receiving care. Cumulatively, they can present an overwhelming burden for patients and their families. As you know, once a treatment becomes available, timely access is crucial to avoid further disease progression, disability or, for some conditions, death.

Patients suffering from rare diseases that are currently untreatable have maintained hope that the incentives toward innovation, coupled with increased scientific understanding of disease mechanisms, would stimulate progress toward treatment and, eventually, a cure. For innovators and investors, the economic calculation of unmet patient needs balanced against research and development costs, projected risk, and population-based revenue estimates has become increasingly complicated. Reimbursement mechanisms, including refinement of payment and coverage policies can tip the scales for or against pursuing a specific drug candidate for an orphan indication. For patient populations approaching the 200,000 orphan disease limit, current incentives have proven to be sufficiently robust to mitigate clinical trial and reimbursement risks. As affected populations dwindle below 20,000 or even into and below the hundreds, the balance can be far more tenuous. Risks and uncertainties can discourage the investor interest required to take promising therapeutic candidates from bench to market.

Our patient and caregiver communities rely on payers and society in general to lay a strong foundation that gives investors a level of comfort that the costs of research and development can be recouped, either through the price of the new drug, its use in other patient populations, or both. Without this, there is little reason for us to hope they will invest their limited resources in advancing the treatments we need.

Over the past several years, Haystack Project and its member organizations have focused on educating stakeholders and shaping health policy to address longstanding challenges to treatment access and innovation. We have engaged with the Centers for Medicare & Medicaid Services (CMS) through comments on CMMI model proposals, implementation, and refinement of the Medicare Quality Payment Program (QPP) and the Affordable Care Act, as well as throughout annual rulemaking cycles refining policies under Medicare Parts A, B, C and D. In 2019, Haystack Project expressed its increasing concerns that health reform efforts initiated to

[1] GAO Report.

decrease health care costs would fail to consider our patient communities. In fact, since enactment of the Inflation Reduction Act, Haystack Project membership has continued to grow – both in numbers (nearly doubling to 150 ultra-rare disease advocacy organizations) and in the acute sense of urgency on the need to heard, prioritized and accounted for in the policy decisions shaping treatment access and product development for the foreseeable future.

CONCLUSION

Once again, Haystack Project sincerely appreciates the opportunity to respond to your RFI. Given the timeframe for response and its intersection with the holiday season, our groups had limited time to fully consider the full set of questions presented. We are, however, eager to facilitate and participate in discussions with your staff that might further inform future legislation.

If you have any questions or would like additional information, please contact me at Kara.berasi@haystackproject.org or our policy consultant, M Kay Scanlan, at mkayscanlan@consilstrat.com.

Very truly yours,

CEO, Haystack Project