USC Schaeffer
Leonard D. Schaeffer Center
for Health Policy & Economics

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Sen. Bill Cassidy, MD
Ranking Member
Senate Committee on Health, Education, Labor and Pensions (HELP)

RE: Response to Request for Information on Improving Americans' Access to Gene Therapies

Dear Senator Cassidy:

Thank you for the opportunity to comment on ways to improve and protect access to gene therapies for Americans with ultra-rare diseases.

For more than a decade, researchers at the USC Schaeffer Center for Health Policy & Economics have developed and evaluated innovative pricing structures to ensure access to breakthrough therapies while incentivizing future innovation. Cell and gene therapies for ultra-rare diseases are the next frontier in biomedical advances, offering the potential for substantially improving the lives of many individuals suffering from debilitating conditions. However, the long-term benefits and risks of these new treatments are largely unknown, making financing these treatments precarious for payers and the pharmaceutical companies developing them.

Though data are still accumulating, patient access to gene therapy has been spotty at best. Payers have imposed both explicit and hidden barriers to patient access, an arguably rational response given the still-uncertain benefits of many of these new treatments. At this stage, federal policymakers could play a leadership role in increasing access to therapies through several tools, including:

- Providing the legal framework to allow the creation of financial intermediaries – publicly managed or private, third-party companies – to develop financial instruments to manage risk;
- Developing updated regulatory frameworks that encourage and facilitate outcomes-based or value-based contracts;
- Ensuring generous coverage coupled with predictable and transparent evaluations of value, which will safeguard access and incentives for future innovation.

Below, we provide responses to specific questions asked in the RFI. We welcome the opportunity for further discussion about how to ensure access for these life-changing therapies.

15. What contract options exist for health plans and other payers to mitigate the cost of covering these therapies?

Schaeffer researchers have shown that alternative payment models are necessary for efficient markets in scenarios in which payers and drug manufacturers face asymmetric information, different evaluations of the expected value of a treatment, or when the benefits from treatments accrue over a long time horizon.[1]

[1] Hlávka, J. P., Yu, J. C., Goldman, D. P., & Lakdawalla, D. N. (2021). The Economics of Alternative Payment Models for Pharmaceuticals. *The European Journal of Health Economics*, *22*, 559-569.

Given that there are limited real-world data on the long-term health outcomes from gene therapies, outcomes-based contracts, in the form of drug mortgages or warranties, would mitigate some of the risk health plans and other payers face in financing these therapies.

In outcomes-based pricing, an insurer and a patient would receive rebates in the event the drug ultimately fails to work or stops working. This could be in the form of a direct "money-back guarantee" payment, like a warranty, or instead, a release from the obligation of continuing to make installment payments over time, like a "drug mortgage." Employing financial intermediaries, which we discuss in more detail in response to question 43, would provide the added security of ensuring rebates/payments even if a patient changes payers after the treatment is completed, and even if the pharmaceutical firm lacks the size or financial stability to commit to making rebate payments in the event of widespread treatment failure.

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?

An important role of the federal government to ensure access to these therapies is developing updated regulatory frameworks that encourage and facilitate outcomes-based pricing. While there has been increased interest from the private sector in value-based contracts, concerns about Medicaid's best price rule and other regulatory hurdles have hampered their development.[2] Moving towards a more rational pricing model requires leadership from CMS.

In addition, as was argued in testimony before the U.S. House Ways & Means Subcommittee on Health, generous coverage coupled with predictable and transparent evaluations of value and the implementation of alternative payment models facilitates broad access while still encouraging the development of high-value technologies.[3] While there are unique considerations and challenges for value frameworks for rare diseases, there are models including Generalized Risk-Adjusted Cost-Effectiveness (GRACE), that will incorporate important patient and societal considerations of risk and disease severity.[4,5] In the face of uncertainty about how a drug will perform, using the three-part pricing framework developed at the USC Schaeffer Center might be a feasible solution.[6]

An additional challenge for ensuring access to cell and gene therapies are the resource, technology, and certification costs that health systems and hospitals must incur when providing many of these treatments to patients. While the direct cost of these new therapies is high, the indirect burden of providing the treatment on health systems and hospitals is also substantial. Encouraging investment in these resources and developing programs to encourage additional Centers of Excellence across the country will also benefit patients.

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[2] Sachs, R., Bagley, N., & Lakdawalla, D. N. (2017). Value-Based Pricing for Pharmaceuticals in the Trump Administration. *Health Affairs Forefront*.

[3] Lakdawalla, D.N. (2023). Testimony Before the House Ways and Means Subcommittee on Health Hearing on Examining Policies that Inhibit Innovation and Patient Access. Available at: https://waysandmeans.house.gov/event/health-subcommittee-on-examining-policies-that-inhibit-innovation-and-patient-access/

[4] Jena, A. B., & Lakdawalla, D. N. (2017). Value Frameworks for Rare Diseases: Should They be Different? *Health Affairs Forefront*.

[5] Lakdawalla, D. N., & Phelps, C. E. (2023). The Generalized Risk-Adjusted Cost-Effectiveness (GRACE) Model for Measuring the Value of Gains in Health: An Exact Formulation. *Journal of Benefit-Cost Analysis*, 1-24.

[6] Goldman, D. P., Van Nuys, K., Cheng, W. H., Hlávka, J. P., Pani, L., Chassang, S., & Snowberg, E. (2018). A New Model for Pricing Drugs of Uncertain Efficacy. *NEJM Catalyst*, *4*(6).

Finally, the federal government has an important, indeed singular, role to play in ensuring that these markets are efficient by underpinning them with timely, accurate information equally accessible to all contracting parties. As novel drugs are used in real-world settings, updated information about how those drugs are performing should be made available to patients, payers, and providers in as close to real-time as possible, to enable contracts that reflect up-to-date value assessments. Arguably, the federal government is the only agent who can set up such information markets and ensure fair and equal access to all contracting parties.

40. Should the federal government mandate coverage of these therapies? What markets (e.g. small, large group markets) or plans should be required to cover these therapies?

It seems untenable to mandate or even expect payers to cover very expensive therapies priced as if they will succeed over the long-term but lacking evidence of long-term effectiveness. Innovative financing models, as outlined in our answer to question 43, is a better way to ensure coverage of these therapies.

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

While the potential future savings to the healthcare system are hard to predict, we know the total economic burden of rare and complex conditions is staggering – both for the patient and the healthcare system. For example, sickle cell disease, just one of the more than 7,000 rare diseases known that is particularly salient given the FDA approval of two gene therapies in late 2023, costs the healthcare system $3 billion per year.[7] The lifetime burden of total medical costs attributable to sickle cell disease is estimated to be $1.7 million per patient and patients incur as much as $44,000 in out-of-pocket costs. It is estimated that patients lose more than $800,000 in lifetime earnings due to premature mortality, lower educational attainment and substantially higher unemployment than the general population.[8] In addition, family caregivers have also been found to experience loss of employment and income.

Upfront costs to the healthcare system should be considered in context of the lifetime burden. High value treatments, especially cures, may result in savings to the health system over the long run even if the initial budget impacts are substantial. Value and outcomes-based payment models, as discussed in our response to questions 15 and 43, will pave the way for ensuring access.

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

Using real-world evidence to evaluate "quality-adjusted costs of care" will be critical to understanding the benefits and costs of these therapies for patients and the healthcare system. The quality-adjusted cost of care approach reveals the true costs of healthcare to society by distinguishing between costs that are "paid back" in the form of higher value and costs that simply drive-up expenditures without corresponding

[7] Huo, J., Xiao, H., Garg, M., Shah, C., Wilkie, D. J., & Mainous Iii, A. (2018). The Economic Burden of Sickle Cell Disease in the United States. *Value in Health*, *21*, S108.

[8] National Academies of Sciences, Engineering, and Medicine. (2020). Addressing Sickle Cell Disease: A Strategic Plan and Blueprint for Action. National Academies Press. *Note that Darius Lakdawalla participated on the committee that authored this report.*

value.[9] Through this method, cost growth that drives offsetting value from health gains will be netted out, while any remaining costs represent the "real" increase in society's cost.

It is also important to note that "value" is not simply the opposite of "cost." It does not make sense to reject a treatment simply because it raises total costs, even if it does so substantially.[10] Rather, it makes sense to take on new costs if they lead to corresponding improvements in health, but not otherwise. While it is understandable that health systems, including state Medicaid programs, are fiscally constrained, decisions that focus on cost without considering value may serve as obstacles to the arrival of effective and valuable treatments. The hardest cases are those in which a new therapy increases costs paid by the healthcare system but adds even greater social value; while adoption would increase total net benefit, it cannot be paid for within existing healthcare budgets. In such cases, creative financial solutions are necessary to ensure that society captures the full promise of improved health that novel therapies provide.

43. How should these therapies be financed?

For years, the Schaeffer Center has championed value-based pricing for drugs, where innovators are rewarded the most when they help patients the most.[11] In the context of cell and gene therapies, this requires that payments or rebates be paid over a long period of time, well after the initial date of treatment.

But who should make these payments? Insurers are reluctant to make payments for patients that have long since rotated off their rolls while drug companies worry about taking on the risk of rebate payments. Small drug companies in particular may lack the financial stability to credibly stand behind a "money-back guarantee" in any event.

Given this scenario, financial intermediation could be a market-based solution that allocates risk more efficiently and enables greater access. In short, we imagine a scenario in which a third-party would receive an upfront payment from a manufacturer in exchange for accepting the risk of paying rebates to insurers in the event of treatment failure.

Today, legislative and regulatory barriers make such a solution more difficult. The possibility of significant rebates in the event of treatment failure poses unacceptable risks if those rebates are viewed as "discounts" that then lower maximum allowable prices more broadly, in Medicaid and in 340B drug pricing programs. Therefore, eligible value-based agreements for cell and gene therapies should be exempted from Medicaid and 340B price calculations. We've shown that there is a legal argument for exempting this arrangement.[12]

CMS can issue clarifying guidance concerning its Multiple Best Price Rule which would state that concessions offered in the context of a value-based arrangement would only be applicable to Medicaid under identical circumstances, and that the value-based arrangement need only be offered to a State

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[9] Lakdawalla, D., Shafrin, J., Lucarelli, C., Nicholson, S., Khan, Z. M., & Philipson, T. J. (2015). Quality-adjusted cost of care: a meaningful way to measure growth in innovation cost versus the value of health gains. *Health Affairs*, *34*(4), 555-561.

[10] Lakdawalla, D. N., & Neumann, P. J. (2016). Budget criteria and drug value assessments: a case of apples and oranges?. *Health Affairs Forefront*.

[11] USC Schaeffer Center. (2021). *Schaeffer Solutions: Developing Innovative Payment Models for Prescription Drugs.* Retrieved from: https://healthpolicy.usc.edu/report/schaeffer-solutions-innovative-payment-models-for-prescription-drugs/

[12] Sachs, R., Bagley, N., & Lakdawalla, D. N. (2018). Innovative Contracting for Pharmaceuticals and Medicaid's Best-Price Rule. *Journal of health politics, policy and law*, *43*(1), 5-18.

Medicaid program, but that the State Medicaid program need not accept the offer in order for value-based arrangements to be offered to other payers and for the Multiple Best Price protections to apply. Manufacturers also need protection from triggering best price in 340B. There are a number of ways that regulators could induce program participation. For example:

- Drugs included in the program could be made exempt from the IRA's drug price negotiation program.
- Regulators could ensure that the original payer receives any future rebate payments, even if the beneficiary switches payers.

To be sure, a pathway to Medicaid and/or 340B exemption for cell and gene therapies may put financial pressure on Medicaid programs and providers covering disadvantaged and vulnerable groups. To address this risk, we propose a special risk pool that covers receipt of exemption-eligible cell/gene therapies for the poor, small employers, and seniors with the relevant (and FDA-indicated) conditions. This risk pool could be financed via a tax on profits of health insurers and/or drug companies.

44. How can future payment or coverage models for these therapies be designed in a way that drives down total health costs for the patient?

Patients with rare diseases often face substantial financial burden. It is estimated that the total economic burden in the U.S. was more than $997 billion in 2019, including $38 billion in healthcare costs not covered by insurance.[13]

Ensuring access to curative or high value treatments may help drive down total lifetime healthcare costs for the patient who would otherwise be incurring costs associated with treatment and management of the disease as well as for the healthcare system as a whole. For example, when Sovaldi was approved for the treatment of Hepatitis-C Virus (HCV) in 2013, much was made about the upfront costs of the treatment.[14,15] But even with those high list prices, we argued that the cure was a good deal and health systems should provide broad access.[16] In addition, spillover benefits to patients awaiting transplants for non-HCV-related liver disease would have also been substantial.[17] Unfortunately, a decade later, many patients with HCV are still unable to obtain treatment because of utilization management tools put in place to fix short-term budget issues. A similar trajectory has occurred with patients trying to access treatments for HIV infections.[18] Learning from these mistakes to ensure patients can access valuable new treatments is paramount.

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[13] Yang, G., Cintina, I., Pariser, A., Oehrlein, E., Sullivan, J., & Kennedy, A. (2022). The National Economic Burden of Rare Disease in the United States in 2019. *Orphanet journal of rare diseases*, *17*(1), 1-11.
[14] Knox, R. (2013). $1,000 Pill For Hepatitis C Spurs Debate Over Drug Prices. *National Public Radio.* https://www.npr.org/sections/health-shots/2013/12/30/256885858/-1-000-pill-for-hepatitis-c-spurs-debate-over-drug-prices
[15] Walker, J. (2015). Gilead's $1,000 Pill Is Hard for States to Swallow. *The Wall Street Journal.* *https://www.wsj.com/articles/gileads-1-000-hep-c-pill-is-hard-for-states-to-swallow-1428525426*
[16] Goldman, D., Chandra, A., & Lakdawalla, D. (2014). It's easier to Measure the Cost of Health Care than its Value. *Harvard Business Review*.
[17] Juday, T., Lakdawalla, D. N., & Philipson, T. J. (2016). The Wider Public Health Value of HCV Treatment Accrued by Liver Transplant Recipients.
[18] Drabo, E. F., Hay, J. W., Vardavas, R., Wagner, Z. R., & Sood, N. (2016). A Cost-Effectiveness Analysis of Preexposure Prophylaxis for the Prevention of HIV Among Los Angeles County Men Who Have Sex with Men. *Clinical Infectious Diseases*, *63*(11), 1495-1504.

For the patient, generous and widely available coverage for high-value therapies that improve lives should be a key component of the strategy. Outcomes-based coverage models, including drug mortgages, warranties and other alternative payment systems, provide an avenue for payers and manufacturers to appropriately evaluate effectiveness in the real world but do not require the patient to take on additional financial risk or costs. In our proposed model, private financial intermediaries would enter into an agreement between the manufacturer and the health plan or public payer.

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

We believe that financial intermediation is a viable solution to this issue. A third-party would be paid to take on the risk of paying rebates to insurers in the event of treatment failure. Many of the small biotech firms developing cell and gene therapies do not have the financial capital or stability to take on the risk over the long term, particularly in the event that their drug underperforms.

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

Rare diseases are unique in that they are more challenging to diagnose, partially due to healthcare providers' lack of familiarity with the diseases and their symptoms. As such, the risk of under-diagnosis may exceed the risk of inappropriate utilization, weakening the rationale for utilization management as a tool to manage costs. In addition, recent studies have demonstrated that utilization management can have negative consequences on public health.

49. Should health care providers share in the financial risk of prescribing these therapies to patients? Why or why not?

Health care providers (physicians) should not be burdened with financial risk. Due to the rarity of the conditions being treated, physician group practices will likely see small numbers of patients using any given technology. The "small numbers" problem results in a substantial amount of variation in outcomes. For instance, even if a new therapy has a 50% chance of curing the underlying illness, a physician seeing only two patients with the relevant condition still faces a 1 in 4 chance of both patients failing on treatment. Financial risk is better allocated to stakeholders that can diversify the risks of treatment non-response over larger numbers of patients, such as insurers, manufacturers and/or financial intermediaries that serve both.

55. How could the federal government leverage existing alternative coverage models in order to promote commercial access to these therapies? For instance, interested parties could contemplate changes to independent, non-coordinated excepted benefits, which could allow health plans and payers to subsidize add-on benefits for these therapies.

As described above (response to Question 39), the federal government likely could play an important role in providing timely and accurate information equally accessible to all contracting parties. Potentially, CMS could leverage a framework similar to Coverage with Evidence Development (CED) that could help to facilitate comprehensive, real-world, post-market data collection. While current applications of CED have had significant negative effects on innovation and patient access, changes to CED—such as those we have suggested elsewhere[19]—could provide commercial markets with useful data on these therapies' cost-

[19] Chen, A., Grogan, J., Jacobson, M.… and J. Zissimopoulos (2023). Comments to CMS on Proposed Guidance for Coverage with Evidence Development. USC Schaeffer Center. Available from:

effectiveness. Given the relatively intensive resources, technology and certifications that health systems and hospitals incur in providing many of these treatments to patients, a CED-like approach could facilitate the development of "Centers of Excellence," thereby coordinating and focusing precious health system resources.

We look forward to working with you, the Senate HELP Committee and members of Congress as you pursue improving access to cell and gene therapies.

Sincerely,

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