January 22, 2024

The Honorable Senator Bill Cassidy
Ranking Member
U.S. Senate Committee on Health, Education, Labor, and Pensions

Submitted electronically via GeneTherapyCoverage@help.senate.gov

Dear Senator Cassidy,

Arnold Ventures welcomes the opportunity to provide feedback on policy considerations to balance affordability and access to emerging gene therapies. This is a critical issue that is top of mind to patients, taxpayers, and employers, with 3 in 10 adults reporting not taking their medicines as prescribed because of the cost. Arnold Ventures is a philanthropy dedicated to investing in evidence-based policy solutions that maximize opportunity and minimize injustice. We work to develop evidence to drive reform across a range of issues including health care, education, and criminal justice. Our work within the health care sector is driven by the recognition that the system costs too much and fails to adequately care for the people it serves.

Gene therapies are incredibly promising. Over a dozen have been approved by the Food and Drug Administration (FDA) in the US and more than 60 are projected to be approved by 2030. These therapies are often administered just one time and they can cost millions of dollars, which creates affordability concerns for patients and payers. In December 2023, two sickle cell gene therapies were approved by the FDA: Vertex/CRISPR’s Casgevy and Bluebird Bio’s Lyfgenia, which have list prices of $2.2 million and $3.1 million, respectively. There are approximately 100,000 people in the United States with sickle cell disease. If 20,000 people were to receive these new treatments over the next few years, that would cost the U.S. health care system about $50 billion in gene therapy costs alone.

In addition to the budgetary shock generated by these high prices, policymakers and payers have limited data at time of approval to show the extent of a therapy’s clinical effectiveness, safety, and durability. Below we outline considerations for price and evidence generation that can be woven into different payment models.

**Gene Therapy Prices**

*Alternative Payment Models.* There are a variety of payment models that can be developed between manufacturers and payers. We recommend that you review the Health Affairs article *Confronting High Costs and Clinical Uncertainty: Innovative Payment Models for Gene Therapies*, by Caroline Horrow, JD and Aaron Kesselheim, MD, JD, MPH of Brigham and Women’s hospital. It outlines a variety of models and discusses their advantages and disadvantages. The authors note, importantly, that the terms of these agreements need to be mutually beneficial for payers and manufacturers, which can have competing goals and unequal negotiating power.

*Policies that Directly Address High Prices.* To temper the effects of high prices on access, Congress should consider policy levers that lower prices or cap overall expenditures on a given high-cost gene therapy.
Manufacturers often set prices that generate revenues that far exceed the cost of bringing a drug to market. This approach is increasingly unsustainable. We are concerned that some gene therapies will not face meaningful competition that would otherwise reduce their prices over time. Policies can be developed to lower gene therapy prices in a way that mimics price reductions due to competition over time.

**Prices and Patient Population Size.** With respect to defining ultra-rare conditions (URC), the Institute for Clinical and Economic Review (ICER) established a definition following a process of stakeholder engagement that defines an URC as a one where the patient population is fewer than 10,000 in the United States, which we believe to be reasonable.

Manufacturers with therapies serving larger rare disease communities seem to be setting prices that are more defensible for those treating an URC. We believe that manufacturers of therapies to treat rare diseases that have larger patient sizes have room to charge lower prices at launch than we have seen to date and generate generous returns on their investment in new potential therapies. Policies can couple policies that lower prices, or cap overall expenditures, with alternative payment models that address risk-pooling and affordability over time.

**Clinical Evidence Generation**

Evidence of efficacy, safety, and durability can be limited at the time of a gene therapy’s approval. We have several suggestions to bolster evidence generation to address these issues.

Like many clinical trials, there can be issues as to whether the population studied is truly representative of the population who will ultimately use the drug. More needs to be done to ensure that clinical trial inclusion/exclusion criteria and study outcomes are applicable to patients who ultimately use gene therapies. For example, the gene therapy Arsa-cel, used for metachromatic leukodystrophy (MLD), was shown to be associated with more variability in efficacy at later stages of disease than at earlier stages. As a result, the breadth of individuals with MLD intending to use the therapy might not benefit uniformly, necessitating further evidence be generated.

Testing durability in clinical trials before a gene therapy comes to market is challenging. To collect robust data on clinical outcomes and therapeutic durability over time, Congress can require the creation of a comprehensive patient registry. This work has been done previously for a type of cellular therapy through the C.W. Bill Young Cell Transplantation Program, which established an outcomes database that ensures access to registry data and further research. In the case of gene therapy, long-term follow-up requires a similar approach and, importantly, long-term relationships with patients, including relationships with patients that have been historically underrepresented in biomedical research. To decrease clinical uncertainty around results of industry-sponsored trials, and to enable better comparisons across a class of available therapies over time, patients, providers, and the public need timely access to strong evidence that a well-designed registry can provide.

**Conclusion**

Thank you again for the chance to comment and for considering potential policy levers to address affordability and clinical evidence generation. Arnold Ventures welcomes being a resource to you.
as you work to develop federal policies that address these issues. This letter was prepared by Anna Anderson-Cook, Ph.D., Senior Fellow, Andrea Noda, MPP, Vice President of Health Care, and Katherine Szarama, Ph.D., Director of Health Care.

Please contact Mark E. Miller, Ph.D. Executive Vice President of Health Care at Arnold Ventures at mmiller@arnoldventures.org or Andrea Noda at anoda@arnoldventures.org with any questions.

Sincerely,

Andrea Noda

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i Public Opinion on Prescription Drugs and Their Prices | KFF
ii Carolin Horrow and Aaron Kesselheim, Confronting High Costs And Clinical Uncertainty: Innovative Payment Models For Gene Therapies, Health Affairs Vol. 42, No. 11, November 2023
iii Vertex/CRISPR price sickle cell disease gene therapy at $2.2 mln | Reuters; New sickle cell gene therapies pose cost and access questions (axios.com)
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v Horrow and Kesselheim
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viii Microsoft Word - adaptations of value framework for URD 111317 (icer.org)
ix Making Genetic Therapies Affordable and Accessible - IGI (innovativegenomics.org)
xi Horrow and Kesselheim
xi https://bloodstemcell.hrsa.gov/about/legislation