Testimony of Alice J. Chen, Ph.D

Associate Professor and Vice Dean for Research, Sol Price School of Public Policy
Senior Fellow, Leonard D. Schaeffer Center for Health Policy & Economics
University of Southern California

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Pharmaceutical Pricing That Balances Innovation and Affordability for Patients with Rare Diseases

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Summary of Key Points

- Americans want innovation for rare diseases: these treatments improve the lives of patients, and patients highly value them.
- Innovators need economic incentives to develop rare disease treatments and cures.
- Pharmaceutical prices need to match the value of innovation.
- Blunt price controls are not the answer: while they can enhance patient access to medications today, they do so at the expense of developing novel treatments in the future.
- To strike a balance between incentivizing innovation and making treatments accessible for patients, we need to consider alternative financing mechanisms for drugs that deliver significant long-term value for patients.

Pharmaceutical Pricing That Balances Innovation and Affordability for Patients with Rare Diseases

Chairman Guthrie, Ranking Member Eshoo, and distinguished Members of the Committee, thank you for the opportunity to testify today about patient access to treatments for rare diseases.

My name is Alice Chen. I am a health economist, Associate Professor and the Vice Dean for Research at the University of Southern California (USC) Sol Price School of Public Policy, and a Senior Fellow at the USC Schaeffer Center for Health Policy & Economics. By way of background, I have been studying pharmaceutical markets for a decade, and my research has been widely published in leading economics, medical, and public policy journals. The opinions I offer today are my own and do not represent the views of USC or the USC Schaeffer Center.

Americans want innovation for rare diseases.

Medical innovation plays a pivotal role in improving health outcomes for patients. From organ transplants to cardiovascular surgery, vaccines to antibiotics, medical advances have transformed the range of solutions patients can access, improved quality of life, and dramatically reduced mortality. In many cases, new medical technologies have restored normal or near normal lives to patients with once-dreaded diseases like hepatitis C,[1] HIV,[2] and leukemia.[3]

Pharmaceutical innovation, in particular, has been crucial in addressing unmet patient medical needs. For rare diseases, treatment options are often limited, and new drug developments can provide hope to patients and families facing challenging health conditions. For example, we have seen the development of targeted therapies that directly address the underlying genetic causes of devastating illnesses, including cystic fibrosis, Huntington's disease, ALS, and certain cancers. These innovative treatments are alleviating symptoms and slowing disease progression. They are fundamentally improving the lives of patients.

Moreover, patients highly value these treatments. Early Schaeffer Center research has demonstrated that patients are generally sensitive to out-of-pocket costs: even a $5 cost increase will lead them to take fewer medications for common chronic conditions.[4] However, patients care deeply about specialty drugs for rare, complex diseases and are willing to pay higher prices for those treatments.[5] In economic terms, we call this inelastic demand. Patients with terminal

[1] Karen Van Nuys et al., "Broad Hepatitis C Treatment Scenarios Return Substantial Health Gains, But Capacity Is A Concern," Health Affairs 34, no. 10 (October 2015): 1666–74, https://doi.org/10.1377/hlthaff.2014.1193.
[2] Tomas J. Philipson and Anupam B. Jena, "Who Benefits from New Medical Technologies? Estimates of Consumer and Producer Surpluses for HIV/AIDS Drugs," *Forum for Health Economics & Policy* 9, no. 2 (January 2, 2006), https://doi.org/10.2202/1558-9544.1005.
[3] Wesley Yin et al., "Value of Survival Gains in Chronic Myeloid Leukemia," *The American Journal of Managed Care* 18, no. 11 Suppl (November 2012): S257-264.
[4] Dana P. Goldman et al., "Pharmacy Benefits and the Use of Drugs by the Chronically Ill," *JAMA* 291, no. 19 (May 19, 2004): 2344–50, https://doi.org/10.1001/jama.291.19.2344.
[5] Dana P Goldman et al., "The Value of Specialty Oncology Drugs," *Health Services Research* 45, no. 1 (February 2010): 115–32, https://doi.org/10.1111/j.1475-6773.2009.01059.x.

illnesses also value medical innovation more those who are in good health. Ignoring these patient preferences leads to an undervaluation of treatments for rare disease.[6]

We need incentives for innovators to develop rare disease treatments and cures.

To continue developing the types of innovations that patients value, manufacturers must expect positive returns to their drug development investments. This undertaking is challenging. On average, over 90% of drugs fail.[7] Of the small subset that do succeed, 10 to 15 years are required to progress from initial discovery to market approval.[8]

This high risk of significant financial loss requires difficult tradeoffs. Like any firm, drug manufacturers make decisions based on expected net profits. This means that drug manufacturers will typically pursue drugs with the greatest market potential, as measured by the size of the target patient population, disease prevalence, demand for treatment, and potential revenue streams of a specific drug. Consequently, changing the anticipated revenue stream can significantly impact how many drugs manufacturers decide to investigate, which drugs manufacturers attempt to bring to market, and in which disease areas manufacturers focus their efforts.

Due to the limited number of patients affected, rare diseases inherently present weaker financial incentives for drug innovation. And yet, neglecting rare diseases creates inequities for those unlucky enough to be afflicted by them. That is why our society has created policies—like the 1983 Orphan Drug Act—to encourage rare disease drug development through tax credits, user fee waivers, and special market exclusivity. These additional incentives can expand potential revenue streams and offset some of the challenges associated with developing therapies for rare conditions. These policies have worked well: since 1983, 6,493 drugs with orphan drug designation have entered the development pipeline; of these, 700 have received FDA approval.[9] This is in stark contrast with the only ten FDA approvals for rare treatments in the eight years preceding passage of the ODA.[10]

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[6] Darius N. Lakdawalla et al., "How Cancer Patients Value Hope And The Implications For Cost-Effectiveness Assessments Of High-Cost Cancer Therapies," *Health Affairs* 31, no. 4 (April 2012): 676–82, https://doi.org/10.1377/hlthaff.2011.1300.

[7] Chi Heem Wong, Kien Wei Siah, and Andrew W Lo, "Estimation of Clinical Trial Success Rates and Related Parameters," *Biostatistics (Oxford, England)* 20, no. 2 (April 2019): 273–86, https://doi.org/10.1093/biostatistics/kxx069.

[8] Bernard Lo and Marilyn J. Field, "The Pathway from Idea to Regulatory Approval: Examples for Drug Development," in *Conflict of Interest in Medical Research, Education, and Practice* (National Academies Press (US), 2009), https://www.ncbi nlm.nih.gov/books/NBK22930/.

[9] Narendra Chirmule et al., "Orphan Drug Development: Challenges, Regulation, and Success Stories," *Journal of Biosciences* 49 (2024): 30.

[10] Marlene E. Haffner, "Adopting Orphan Drugs--Two Dozen Years of Treating Rare Diseases," *The New England Journal of Medicine* 354, no. 5 (February 2, 2006): 445–47, https://doi.org/10.1056/NEJMp058317.

Pharmaceutical prices need to match the value of innovation.

Orphan drugs tend to be some of the most expensive drugs on the market.[11] For example, in December 2023, the FDA approved the first cell-based gene therapies for the treatment of sickle cell disease.[12] This treatment extracts cells from a patient's bone marrow, precisely edits a gene with CRISPR technology, and then reintroduces the modified cells into patients. While this one-time treatment can eliminate severe pain symptoms for a patient's lifetime, it comes with a substantial initial price tag of $2.2 million to $3.1 millions.[13] While this high price is unique to a potentially curative therapy, the median orphan drug has a list price of just under $220 thousand per treatment,[14] a much lower figure but nonetheless, a substantial cost.

To strike a balance between ensuring affordability and nurturing ongoing pharmaceutical innovation, prices of new drug treatments need to match the value they deliver. Some technologies have very high prices, while the health benefits they deliver are also high. A value-based pricing approach ensures that manufacturers are not only encouraged to create high-value therapies but also discouraged from pursuing less beneficial drugs.

The following principles should guide pricing policies in the healthcare and pharmaceutical market as it relates to rare disease:

1. Prices should reflect value: The value of a drug should be comprehensively assessed based on the benefits it delivers to patients and their families, and that value should be captured in a drug's price. This evaluation should encompass a wide variety of aspects, including improvements in health outcomes that matter to patients, quality of life enhancements, reduced disease burden on the community, and broader economic considerations such as cost savings associated with reduced hospitalizations, medical interventions, or other resource utilization. It should also incorporate the patient's preferences, namely that health improvements are more valuable for people with severe diseases. While these preferences are ignored in traditional cost effectiveness models, newer, non-discriminatory value assessment models such as the Generalized Risk-Adjusted Cost Effectiveness (GRACE) model more fully account for the preferences and needs of patients.[15]

2. Value assessment should be based on strong evidence: Evaluation of health outcomes should be built on a foundation of strong evidence, from data obtained not only through

[11] Hana Althobaiti et al., "Disentangling the Cost of Orphan Drugs Marketed in the United States," *Healthcare* 11, no. 4 (February 13, 2023): 558, https://doi.org/10.3390/healthcare11040558.
[12] Office of the Commissioner, "FDA Approves First Gene Therapies to Treat Patients with Sickle Cell Disease," FDA (FDA, December 8, 2023), https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease.
[13] "US FDA Approves Two Gene Therapies for Sickle Cell Disease | Reuters," December 8, 2023, https://www.reuters.com/business/healthcare-pharmaceuticals/us-approves-two-gene-therapies-sickle-cell-disease-2023-12-08/.
[14] Althobaiti et al., "Disentangling the Cost of Orphan Drugs Marketed in the United States."
[15] Darius N. Lakdawalla and Charles E. Phelps, "The Generalized Risk-Adjusted Cost-Effectiveness (GRACE) Model for Measuring the Value of Gains in Health: An Exact Formulation," *Journal of Benefit-Cost Analysis* 14, no. 1 (March 2023): 44–67, https://doi.org/10.1017/bca.2023.6.

randomized clinical trials (RCTs) used for drug approval, but also real-world evidence. While RCTs provide rigorous evidence under controlled conditions, it is imperative to understand a drug's safety and effectiveness in real-world settings, where patient populations and treatment settings are more diverse. Moreover, at the time of drug approval, the long-term impacts of a drug are often unknown. Real-world evidence is needed to inform whether observed benefits of innovative therapies persist.

3. Continued research should be rewarded: The value of a drug should extend beyond its primary indication to include benefits patients receive across all potential uses. While the initial drug development process takes at least a decade, identifying additional conditions for which a drug is effective typically requires considerably less time. The expedited identification of follow-on indications is invaluable as it broadens patients' access to existing drug technologies and maximizes the therapeutic potential of these treatments.

This last point is particularly salient for orphan drugs. Under the Inflation Reduction Act (IRA), drugs with an orphan designation as their sole FDA-approved indication will be exempt from future price negotiation. This is clear reinforcement that our society values treatment for rare diseases. But the IRA does not extend this exemption to drugs with multiple indications, whether they are primarily orphan drugs or not. Consequently, this diminishes the incentives orphan drug manufacturers have for exploring potential alternative uses for existing drugs in treating other rare diseases.

Follow-on indications represent a critical pathway for faster and more cost-effective innovation, especially in the realm of rare disease treatment, where the limited sizes of patient markets constrain expected returns. Historically, this has been a common strategy: out of 280 orphan drugs identified between 2003 to 2022, 63 had obtained at least one follow-on indication, and many had obtained more.[16] Incentivizing follow-on indications encourages manufacturers to pursue rare disease treatments when they have the opportunity to expand the original market, which will additionally benefits patients.

It is conceivable that the complications brought on by the IRA can be addressed through small policy improvements, like the ORPHAN Cures Act, that could reinforce our society's desire to protect the interests of patients suffering from rare diseases.

Blunt price controls are not the answer.

While lowering pharmaceutical prices may seem at first like a logical approach in improving patient accessibility, the relationship between a drug's price and what a patient ultimately pays is far from straightforward. The extent to which out-of-pocket costs fall will depend on insurer formulary design and benefit structures. But even if mandating lower prices through government price controls would reliably reduce out-of-pocket expenses, such price reductions would come with a significant trade off: they reduce expected future returns and thereby diminish future drug innovation.

[16] James D. Chambers et al., "Follow-On Indications for Orphan Drugs Related to the Inflation Reduction Act," *JAMA Network Open* 6, no. 8 (August 15, 2023): e2329006, https://doi.org/10.1001/jamanetworkopen.2023.29006.

Blunt price controls are counterproductive from the perspective of improving patient health. Moreover, imposing price controls on drugs with high spending, as the IRA does, can introduce additional unintended consequences. Drugs with high spending are often those with the greatest therapeutic value—which is, after all, what drives their widespread utilization. Lowering the prices of these drugs below the value they provide to patients and their families may save money in the near term, but it will discourage development of future high-value drugs that could significantly enhance patient health.

The Orphan Drug Act changed the landscape of therapeutics available for rare diseases by incentivizing new innovation for millions of Americans. However, additional advances are needed. While we know the molecular mechanism behind 7,000 rare diseases, we have FDA-approved treatments for only 500 of them.[17] By disincentivizing drug development in more than one rare disease area, the IRA works against the priorities of the Orphan Drug Act.

We need new policies that will address affordability while preserving innovation.

Ensuring access to cutting-edge treatments among rare diseases necessitates the exploration of innovative financing mechanisms,[18] such as subscription-based payment models or approaches that amortize the cost insurers pay for a life-saving new treatment based on drug effectiveness. Traditional pricing models may sometimes force a choice between paying a high price that assumes an ideal effectiveness outcome or denying access outright. More flexible payment mechanisms can move the market towards a middle ground, where drugs that realize strong real-world efficacy are rewarded, while those that fail to deliver on their clinical promise are not. These types of solutions aim to create a more sustainable system that prioritizes patient access while simultaneously fostering valuable innovation for patients.

[17] "Rare Diseases," National Institutes of Health (NIH), February 7, 2020, https://www nih.gov/about-nih/what-we-do/nih-turning-discovery-into-health/promise-precision-medicine/rare-diseases.
[18] "Schaeffer Solutions: Developing Innovative Payment Models for Prescription Drugs," *USC Schaeffer* (blog), April 23, 2021, https://healthpolicy.usc.edu/report/schaeffer-solutions-innovative-payment-models-for-prescription-drugs/.