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Chairman Guthrie, Ranking Member Eshoo, and Honorable Members of the Subcommittee on Health of the U.S. House Energy and Commerce Committee, thank you for the opportunity to testify about legislative proposals to support patients with rare diseases. I am Jeromie Ballreich, and I am an Associate Research Professor in the Department of Health Policy and Management at the Johns Hopkins Bloomberg School of Public Health. I direct the master's program in health economics. I am a core faculty member of the Johns Hopkins Drug Access and Affordability Initiative, which is a research center evaluating US pharmaceutical policy and incentives for drug innovation. My research focuses on the US pharmaceutical market, pharmacoeconomics, and economic evaluation. The views expressed within my testimony do not necessarily represent the views of Johns Hopkins University.

As a researcher in this field, I recognize the complexity of the US pharmaceutical market and need to balance access, affordability, and innovation. This balance is particularly salient for pharmaceuticals to treat patients with rare diseases. While this committee is evaluating several legislative proposals to support patients with their diseases, my objective for this testimony is to provide an overview of the current state of innovation in the rare disease space and rationale for maintaining the Inflation Reduction Act's (IRA) stipulations around pharmaceuticals for rare diseases.

In sum, the following are my key points:
- **The IRA improves drug affordability**
- **There has been little evidence that the IRA has significantly impacted pharmaceutical research and development**
- **Current Orphan Drug Act incentives help drive innovation in rare diseases**
- **We are benefitting from a tailwind of tremendous scientific breakthroughs for pharmaceuticals to treat rare diseases**

Inflation Reduction Act
According to a 2023 poll, nearly one in three Americans who are taking prescription drugs said they had not taken the drug as prescribed due to costs, meaning that they either skipped a dose, cut a pill, or did not fill a prescription.[i] We as Americans have access to the best pharmaceuticals

available but as the National Academy of Medicine poignantly noted "In the end, drugs that are not affordable are of little value and drugs that do not exist are of no value."[ii]

To address affordability, the President signed into law the Inflation Reduction Act in August 2022. The IRA stipulates several measures to improve prescription drug affordability, including Medicare price negotiations, inflation rebates for drug price increases, and changes to the Medicare standard benefit design.

Medicare price negotiation improves drug affordability by setting a maximum fair price for high spending drugs that have been on the market for several years. The maximum fair price is contingent on whether the drug is a small molecule or biologic, and how long the drug has been on the US market. Drugs with solely orphan indications or those facing generic or biosimilar competition are excluded. CMS will also consider several other factors for negotiating price reductions below the maximum fair price. Medicare beneficiaries who often pay for these drugs using coinsurance, which is a percentage of the drug price, will see lower costs at the pharmacy because of the negotiated prices.

A recent study that I led examined characteristics of the beneficiaries who will benefit from the first set of drugs negotiated and found negotiated prices will impact over 6 million beneficiaries.[iii] These beneficiaries are generally older, have more comorbidities, have considerably higher part D spending, and often face out-of-pocket costs in excess of $100 when filling their prescription for these 10 drugs. The conditions these first 10 drugs affect and many conditions for future drugs to be negotiated are often common conditions amongst Medicare beneficiaries including cancer, diabetes, and blood conditions such as clotting.

Based on how Medicare identifies drugs for negotiation using gross spending in the Medicare program, very few of the anticipated negotiated drugs were developed for rare diseases. That said, many big spending drugs have an orphan indication which will be discussed later in my testimony.

In addition to price negotiation, the IRA also institutes inflation rebates to mitigate drug price increases amongst branded drugs and changes the standard benefit design to cap the Part D maximum annual out-of-pocket for Medicare beneficiaries to $2000. The inflation rebates will certainly improve drug affordability especially for drugs where beneficiaries pay a coinsurance based on the list price. The inflation rebate should have little impact on rare disease development given its relatively small impact on net spending, since much of the drug price increase contributes to a drug rebate bubble.

The benefit redesign will have a significant impact on drug affordability, especially patients who require high-cost specialty drugs. It has been estimated that nearly 10% of Medicare beneficiaries would benefit from the maximum out-of-pocket cap.[iv] Many treatments for rare diseases cost more than thousands of dollars and are on the specialty drug tier of formularies, which means patients often pay 25% of the drug price. The maximum out pocket will help these patients.

Rare Disease R&D
Pharmaceutical research and development in rare diseases has grown tremendously over the past 40 years. The initial policy push for rare diseases came with the Orphan Drug Act of 1983. The Orphan Drug Act stimulates rare disease R&D by providing R&D tax credits, additional market exclusivities for approved orphan indications, and exemptions from user fees. It is still a significant policy stimulus. In 2023, there were 376 drug indications that received an orphan designation, a key milestone for Orphan Drug Act incentives.[v] There were also 90 drugs approved for orphan indications. Both of these numbers are close to the five-year averages of 390 orphan designations and 84 orphan drug approvals. This early evidence suggests little initial impact from the IRA on rare disease R&D.

The robustness of rare disease R&D is further evident in recent industry analysis of drug assets in development. In 2023, gene therapies, which predominantly treat rare diseases, had the second highest number of drug assets in development in the pharmaceutical industry.[vi] An analysis of mergers and acquisitions from 2019 to 2023 identified that companies involved in rare diseases were the third highest source, both in number of deals as well as dollar value for pharmaceutical

mergers and acquisitions.[vii] The upstream R&D investment has led to research by Dr. Rena Conti and others that suggest annual spending on gene therapies will increase fivefold between 2020 and 2026.[viii] This growth of gene therapies is echoed across many industry sources.

What is driving to growth and how will the IRA influence this growth?
As noted in the previous section, the Orphan Drug Act stimulates rare disease R&D. However, much of the growth in potential treatments for rare diseases are in the gene therapy modality. First and foremost, this trend reflects the dividends from the significant public investment in sequencing the human genome. The federal government spent nearly $4 billion on the Human Genome Project through its completion in 2003.[ix] The scientific community and biopharmaceutical industry benefit from this investment not only for the decoding of the human genome, but also through the development and cost reductions of sequencing, training of a workforce, and establishment of research infrastructure in genomics. The NIH continues to invest in genomics research with an estimated $4.7 billion outlays in 2022.[x]

Not only is the biopharmaceutical industry benefiting from the public investment in the science and incentives from the orphan drug act, but they are also pursuing rare diseases due to the risk reward profile and the gratification of changing patients' lives. Gene therapy development is a risky proposition, with many early-stage therapies facing safety concerns. However, the capital required for clinical trials tends to be far smaller than other therapeutic areas such as cardiovascular disease.[xi] Studies have shown that orphan disease trials tend to cost less than non-orphan disease trials largely due to smaller enrollment.[xii] Yet, once an orphan drug is approved, particularly a gene therapy, it often demands a significant price premium. Many current gene therapies on the market cost 100s of thousands of dollars and sometimes in excess of $1 million per treatment course. These high prices are a function of small market size and lack of therapeutic alternatives. The prices also pose a significant problem for patients and payers, raising concerns about affordability and access.

The IRA will certainly impact the biopharmaceutical industry including rare disease innovation. However, it's impact may be far less than what many have feared. First, the Congressional Budget Office estimates that IRA price negotiations will save the Medicare program

approximately $23 billion in 2030.[xiii] While this is significant, it pales in comparison to the estimated $1 trillion US pharmaceutical market in 2030.[xiv] It is hard to reconcile significant business decision changes with an anticipated sub-3% change in annual revenue. Second, there is a concern that the price negotiation clock will limit development in rare diseases, since companies will now pursue larger markets first to maximize revenue before price negotiations are triggered. I agree that there will certainly be changes to product launch strategies, but subsequent rare disease approved indications will increase a products revenue regardless of when in the life cycle the product is. I suspect we will still see drugs tested across lots of indications including rare diseases with hopes of expanding the drugs label, evidence base, and thereby the drugs market. Even with maximum fair price discounts, branded drugs in the US will still be priced higher than many other developed countries, which suggests a commercial opportunity will remain in expanding indications for drugs, particularly cancer drugs.

Conclusion

The IRA improves drug affordability for Medicare beneficiaries. I do not see a significant impact on rare disease innovation from the IRA. **Congress should keep the IRA intact to ensure drug affordability and consider supporting CMMI on their efforts to improve access to rare disease treatments particularly cell and gene therapy.**

[i] https://www.kff.org/health-costs/poll-finding/public-opinion-on-prescription-drugs-and-their-prices/

[ii] Augustine, N. R., Madhavan, G., & Nass, S. J. (Eds.). (2017). *Making medicines affordable: a national imperative*. Washington (DC): National Academies Press.

[iii] Odouard, I. C., Anderson, G. F., Alexander, G. C., & Ballreich, J. (2023). Sociodemographic and spending characteristics of Medicare beneficiaries taking prescription drugs subject to price negotiations. *Journal of Managed Care & Specialty Pharmacy*, 1-10.

[iv] https://www.managedhealthcareexecutive.com/view/impact-of-2025-s-ira-out-of-pocket-cap-on-medicare-part-d-beneficiaries

[v] https://www.accessdata.fda.gov/scripts/opdlisting/oopd/

[vi] Pharma R&D Annual Review 2023, page 23 Citeline

[vii] https://andrewpannu.com/

[viii] Wong, C. H., Li, D., Wang, N., Gruber, J., Lo, A. W., & Conti, R. M. (2023). The estimated annual financial impact of gene therapy in the United States. *Gene Therapy*, *30*(10), 761-773.

[ix] https://www.battelle.org/docs/default-source/misc/battelle-2011-misc-economic-impact-human-genome-project.pdf

[x] https://report.nih.gov/funding/categorical-spending#/

[xi] Moore, T. J., Zhang, H., Anderson, G., & Alexander, G. C. (2018). Estimated costs of pivotal trials for novel therapeutic agents approved by the US Food and Drug Administration, 2015-2016. *JAMA internal medicine*, *178*(11), 1451-1457.

[xii] Jayasundara, K., Hollis, A., Krahn, M., Mamdani, M., Hoch, J. S., & Grootendorst, P. (2019). Estimating the clinical cost of drug development for orphan versus non-orphan drugs. *Orphanet journal of rare diseases*, *14*, 1-10.
[xiii] https://www.cbo.gov/system/files/2022-08/hr5376_IR_Act_8-3-22.pdf
[xiv] https://www.coherentmi.com/industry-reports/united-states-pharmaceuticals-market