Dr. Alice Chen, Ph.D.
Associate Professor and Vice Dean for Research – USC Sol Price School of Public Policy

Answers to Questions for the Record
Subcommittee on Health
House Committee on Energy and Commerce
Legislative Proposals to Support Patients with Rare Diseases
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The Honorable Robert Latta

1. **The Maintaining Investments in New Innovation Act is intended to provide a clarification on the definition of an advanced drug product. 21st Century CURES recognized the tremendous potential of genetically targeted medicines, many of which represent the only hope for patients with rare and ultra rare genetic conditions. By targeting specific genetics these innovative, accurate and narrowly targeted medicines are able to deliver benefits of improved quality and extension of life. Would you please share how rare these conditions are and why they should be considered an advanced drug product and treated as such under the law?**

   Cell and gene therapies represent the newest frontier in medical development, and they hold the promise to significantly enhance the quality of life for many individuals affected by rare diseases and ultra-rare diseases. While each rare and ultra-rare disease affects fewer than 200,000 Americans, 25 to 30 million Americans are collectively affected by rare diseases.[1] For patients with these diseases, treatment options are limited, and drug developments through cell and gene therapies can provide hope to patients and families facing challenging health conditions.

2. **Can you comment on how existing policies enacted by the Democrats – namely IRA's "Medicaid best price rule" and the American Rescue Plan allow Medicaid rebates to exceed the cost of actually manufacturing the drug – hinders the development of next generation treatments and cures?**

   While policies such as the IRA's Medicaid best price rule may result in some manufacturers lowering price of existing drugs, it may also result in the discontinuation of certain drugs in favor of lower priced alternatives. Both responses will reduce the expected future returns of new pharmaceuticals and thereby diminish incentives for future drug innovation. The resulting impact on innovation will depend on the magnitude of the revenue reduction, as well as the types of drugs that are affected by such a policy. For example, if the drugs affected by such policies are disproportionately higher value drugs, then incentives for innovation for specifically higher value drugs will also fall.

3. **Recent analyses done by independent policy researchers, such as Kaiser Family Foundation, Avalere Health, and Milliman highlight significant disruption in the Medicare Part D market for 2024 as a result of policies in the Inflation Reduction Act (IRA) being implemented. In 2024, the estimated average enrollment-weighted monthly patient premium for Medicare Part D stand-alone drug plans (PDPs) is projected to increase 21% from 2023, and Medicare beneficiaries have access to the lowest number of standalone PDP options and low-income subsidy benchmark plan options in 2024 than any other year since the Part D program started. Further, there are anecdotal reports that suggest that as Part D plans grapple with the plan**

[1] National Institutes of Health. (2023). The Promise of Precision Medicine: Rare Diseases. Accessed from: https://www.nih.gov/about-nih/what-we-do/nih-turning-discovery-into-health/promise-precision-medicine/rare-diseases#:~:text=Rare%20diseases%20were%20once%20considered,30%20million%20Americans%20are%20affected.

liability shifts of the IRA, they are increasingly moving towards use of more coinsurance and narrowing formularies for patients. Dr. Chen, how will these Part D benefit trends that we are seeing in 2024, as a result of the IRA, impact access to the therapies that rare disease patients in my district and across the country need to enhance their health outcomes and live more full lives?

Part D consumers become worse off when Part D plan premiums increase simultaneously with increased cost-sharing and more narrow formularies: consumers receive less insurance coverage while having to pay more for the plan itself and the utilization of pharmaceutical medications when they need it. Patients with rare diseases may be particularly affected as 85% of orphan drugs are placed on the highest cost-sharing tier within Part D formularies. Moreover, 76% of orphan drugs are subject to prior authorization within existing Part D plans.[2] With less plan choice and potentially no coverage for certain orphan drugs, patients with rare diseases may not be able to access the medications they need.

The Honorable Gus Bilirakis

1. **There is a tremendous and undeniable unmet need for children living with rare diseases. Of the 30 million Americans living with a rare disease, half are children - and a third of those children won't live to see their fifth birthday. According to a recently-published FDA study reflecting on the first ten years of the program, "Continued support of product development for children with rare diseases is needed to find treatments for all children with unmet needs." Since the implementation of the Rare Pediatric Disease Priority Review Voucher (RPD PRV) program in 2012, nearly 50 therapies for rare pediatric diseases have reached patients that may otherwise have no available FDA-approved treatment. Over half of RPD PRVs were granted in the last 5 years alone, but an often-cited GAO study only accounts for PRVs granted prior to 2019. Based on the latest available data, can you provide updated information on the anticipated short and long-term impacts that the continuation of the RPD PRV program will have on investment in research and development in the rare pediatric disease space?**

   Unfortunately, this topic falls outside my area of research and expertise. I would be happy to help the committee identify experts who may be in a better position to answer this question, if needed.

2. **Your testimony mentions the need for incentives to be in place to invest in the development of rare disease treatments. I'm proud to be a co-lead on H.R. 7384, the Creating Hope Reauthorization Act, which extends the RPD PRV program at FDA for another four years. Can you explain why streamlining regulatory process at FDA to shorten review time can provide key incentives needed to invest in new research & development opportunities?**

[2] Yehia F and JB Segal. (2020). Predictors of Orphan Drug Coverage Restrictions in Medicare Part D. *The American Journal of Managed Care,* 26(9).

Shortening FDA review times will reduce the cost manufacturers face when innovating. In particular, the period of marketing exclusivity begins when a patent is initially filed, so the ability to bring a drug to market more quickly ensures higher expected revenues for manufacturers. These higher anticipated revenues then provide larger incentives for manufacturers to invest in R&D.

3. **One critique we've heard is the FDA faces an influx of PRV applications as the deadline approaches. Do you believe we should make this voucher program permanent?**

   To assess the value of the voucher program, we need to identify not only the number, but also the value of the new drugs that have come to market due to the program.

4. **What are the challenges associated with rare pediatric clinical trials, and how do PRVs help alleviate those challenges?**

   Rare pediatric clinical trials are challenging because the diseases studied affect such few patients who are often geographically dispersed. These clinical trials necessarily have small sample sizes that make it difficult to draw statistically significant conclusions. Additionally, multi-cite studies are often required to enroll a sufficient number of participants. As such, the costs of rare pediatric clinical trials are high. PRVs reduce the costs manufacturers face when innovating in rare diseases.

5. **Given the length of time it takes to develop a new drug, particularly within rare disease development, can you provide an economist's perspective on what the unintended consequences would be of losing a key incentive such as the PRV program?**

   Removing the PRV program increases the cost manufacturers face when innovating, which in turn reduces the incentives manufacturers have to innovate for rare pediatric disease.

6. **If the PRV program is not reauthorized, what other ways can Congress incentivize investment in rare diseases with high unmet medical need?**

   To incentivize drug development in the risky area of rare disease, there needs to be sufficient rewards for that investment. Those rewards can either come from reducing the costs of research and development or increasing expected revenues from reimbursement.

7. **How has rare disease therapy development become more difficult in recent years, and why do incentives matter more for rare disease companies dealing with small patient populations?**

   Incentives for innovation matter for all manufacturers. However, 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 to increase the incentives associated with developing orphan drugs.

8. **What other steps can be taken to help streamline FDA's regulatory processes to ensure there are consistent pathways for companies looking to develop rare disease treatments?**

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The Honorable Earl "Buddy" Carter

1. **Antimicrobial Resistance continues to be a growing health crisis in our nation and around the world. It is paramount that we continue to marshal the resources of the federal government while supporting the innovation occurring in the private sector to slow the spread of resistance, ensure the development of novel antibiotics to treat these deadly superbugs, and educate the public on this ongoing threat. I commend Mr. Griffith for his bill requiring a GAO report regarding federal efforts on antimicrobial resistance. Addressing AMR is a top priority of mine, which is why I am a cosponsor of the PASTEUR Act, which is so needed to fix the failing market for antimicrobials. Dr. Chen, in your testimony you mention the importance of antibiotics in addition to other medical innovations that play a pivotal role in improving health outcomes for patients. Can you please discuss the importance of tackling antimicrobial resistance.**

   Research at the Schaeffer Center has shown that inappropriate antibiotic prescribing is common. For example, half of the 41.2 million antibiotic prescriptions for acute respiratory infections are inappropriate since they are prescribed where there is no evidence of benefit.[3] The inappropriate use of antibiotics leads to the development of antibiotic-resistant bacteria, which cause 2.8 million infections a year and kill 35,000 people in the US.[4]

[3] Meeker, D, TK Knight, MW Freidberg, JA Linder, NJ Goldstein, CR Fox et al. Nudging Guideline-Concordant Antibiotic Prescribing: A Randomized Clinical Trial. *JAMA Internal Medicine* 2014 174(3):425-431.
[4] Centers for Disease Control and Prevention. About Microbial Resistance. Accessed from: https://www.cdc.gov/drugresistance/about.html.