PERSONALIZED MEDICINE COALITION

September 16, 2024

The Honorable Ron Wyden
Chairman
United States Senate
Committee on Finance
219 Dirksen Senate Office Building
Washington, DC 20510

The Honorable Mike Crapo
Ranking Member
United States Senate
Committee on Finance
219 Dirksen Senate Office Building
Washington, DC 20510

Re: Hearing on the *Inflation Reduction Act (IRA)* and Support for the *Ensuring Pathways to Innovative Cures (EPIC) Act*, the *Optimizing Research Progress Hope And New (ORPHAN) Cures Act*, and the *Maintaining Investments in New Innovation (MINI) Act*

Dear Chairman Wyden and Ranking Member Crapo,

The Personalized Medicine Coalition (PMC), a multi-stakeholder group comprising more than 200 institutions from across the health care spectrum, thanks you and your colleagues for holding a hearing to examine aspects of the *Inflation Reduction Act (IRA)*. The *IRA* included policies intended to lower prescription drug costs for Medicare beneficiaries and reduce drug spending by the federal government. However, recent studies demonstrate the potential for the *IRA* to result in fewer new therapies being developed to address current and future unmet needs. Due to smaller patient subpopulations, personalized medicines that address the root causes of disease can sometimes be expensive and risky to develop. Medicare's drug price negotiation program established by the *IRA* could have an outsized effect in discouraging the pharmaceutical industry from bringing additional personalized medicines and expanded indications to the market. Bipartisan policy solutions like the *Ensuring Pathways to Innovative Cures (EPIC) Act*, the *Optimizing Research Progress Hope And New (ORPHAN) Cures Act*, and the *Maintaining Investments in New Innovation (MINI) Act* have been introduced to forestall disruption to the innovation ecosystem that has allowed patients and providers to benefit from personalized medicine. PMC supports these solutions and urges Congress to advance these bills.

Personalized medicine is an evolving field in which physicians use diagnostic tests and individual details about a person's health to determine which medical treatments will work best for each patient or use medical interventions to alter molecular mechanisms that impact health. By combining data from diagnostic tests with an individual's medical history, circumstances, and values, health care providers can develop targeted treatment and prevention plans with their patients. Personalized medicine is playing an important role in transforming care and patient outcomes for a range of serious and life-threatening diseases and conditions, helping to shift patient and provider experiences away from trial-and-error medicine and toward a more streamlined process for making clinical decisions.

Statement of Neutrality

PMC's members may present their own views on the Senate Committee on Finance's hearing on the *Inflation Reduction Act (IRA)*. PMC's comments are designed to provide feedback so that the general concept of personalized medicine can advance and are not intended to adversely impact the ability of individual PMC members, alone or in combination, to pursue separate positions with respect to the *IRA* or related issues.

Unintended Consequences of the *IRA* on Personalized Medicine — and Legislative Solutions

Personalized medicines now account for more than a quarter of the new therapies approved since 2015. They have comprised more than a third of new drug approvals for six of the last seven years.[i] Recent approvals have brought a record number of new treatments for rare genetic diseases and new ways to address certain cancers and other diseases, including Alzheimer's disease. Multiple analyses, including those from the Congressional Budget Office (CBO), have called attention to the potential consequences of the Medicare drug price negotiation program established by the *IRA*, such as canceled research and development and disincentives to invest in small-molecule medicines and therapeutic areas that require incremental innovation.[ii,iii,iv,v]

PMC is concerned that the *IRA* could have an outsized effect in discouraging the pharmaceutical industry from bringing additional personalized medicines and expanded indications to the market. Legislative solutions have been introduced in Congress that would reverse some of the unintended consequences of the *IRA*. If enacted, we believe these bills would enable the continued development of next generation treatments for patients with unmet medical needs.

Small-molecule drugs

Under the *IRA*, small-molecule drugs are eligible for Medicare negotiation nine years after approval by the U.S. Food and Drug Administration (FDA) versus 13 years for biologics, or large-molecule, products. Implementation of these differential timelines will disincentivize investment in small-molecule over large-molecule drugs. One analysis estimates 79 fewer small-molecule drugs and 188 fewer indications coming to market over the next 20 years.[vi] These dynamics may impact the growing pipelines of personalized medicines available to patients, including patients from communities already experiencing disproportionately high incidence and mortality rates from diseases like cancer.

Many targeted cancer therapies that deliver personalized medicine to patients are small-molecule drugs.[vii] Small-molecule drugs comprise 70 percent of the drugs already selected for negotiation by Medicare, and small-molecule oncology therapies are expected to be predominantly affected during the Medicare drug price negotiation program's first few negotiation cycles. To reduce the impact of differential timelines for drugs and biologics on clinical development for small molecules and patients who need these critical therapies, **PMC supports the *EPIC Act*, which would establish equal timelines for the negotiation of both drugs and biologics at 13 years.**

Orphan drugs for rare diseases

Only about one quarter of all orphan drugs approved in the last two decades have a single indication.[viii] Researching additional orphan indications for existing rare disease treatments plays an important role in identifying new treatments for patients with rare diseases who do not have treatments available to them. Orphan drugs are excluded from the Medicare drug price negotiation under the *IRA* if they treat only one rare disease or condition. If an orphan product has designations for multiple diseases, even if these are also orphan designations, then it loses its exclusion from negotiation. Furthermore, as soon as a drug is designated for a second disease, even without any associated approvals, it becomes negotiation eligible — and the clock for when a product could be selected for negotiation starts at the date of the drug's first approval, even if the second designation or additional approval occurs many years later.

The *IRA's* narrow exclusion for orphan drugs contradicts the goals of the *Orphan Drug Act* to foster the development of new treatments for rare diseases and could stifle post-approval research into additional orphan indications for rare diseases. Even when making investment decisions among multiple potential orphan indications, manufacturers may be incentivized to prioritize indications for rare diseases with larger patient populations over indications for very rare diseases. To preserve hope for the 95 percent of rare disease communities without disease-specific FDA approved treatments, **PMC supports the *ORPHAN Cures Act*, which would ensure orphan drugs treating one or more rare diseases or conditions are excluded from Medicare drug price negotiation under the *IRA* and clarify that the countdown to price negotiation eligibility would begin only when an orphan drug loses its exclusion.**

Genetically targeted therapies

Genetically targeted therapies (GTTs) work by either delivering healthy copies of genes to target cells, permanently changing the genetic code, or manipulating gene expression. If a GTT silences a gene, it is regulated as a drug, but if a GTT adds to a gene, it is regulated by the FDA as a biologic. Despite differences in their pathways for regulatory approval, GTTs are similar in development time, therapeutic action, and complexity of manufacturing. As part of the Medicare drug price negotiation program, GTTs regulated as drugs would be negotiated after nine years, whereas GTTs regulated as biologics would be negotiated after 13 years. These different timelines under the *IRA* impose an artificial distinction that could lead to a lack of parity in the development of these novel therapies.

Of the dozen or so FDA-approved GTTs, all are personalized medicines. While only a limited number of GTTs are on the market now treating rare disease patients, the underlying technology is expected to generate novel therapies for non-rare diseases in the future. To ensure the even advancement of all GTTs in this promising area of personalized medicine, **PMC supports the *MINI Act*, which would make statutory changes to the *IRA* so that all GTTs are treated as biologics that could be negotiated after 13 years.**

Conclusion

To sustain progress in the development of groundbreaking personalized medicine treatments for the benefit of patients and health systems, Congress must support policies that encourage the advancement of the field. PMC would be pleased to serve as a resource for you and your staff to ensure that the *IRA* does not undermine the potential of personalized medicine. If you have any questions about the content of this letter, you can contact me at cbens@personalizedmedicinecoalition.org or David Davenport, PMC's Manager of Science and Public Policy, at ddavenport@personalizedmedicinecoalition.org.

Sincerely,

Cynthia A. Bens
Senior Vice President, Public Policy

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[i] Personalized Medicine Coalition. *Personalized Medicine at FDA: The Scope & Significance of Progress in 2023.* February 29, 2024. https://www.personalizedmedicinecoalition.org/wp-content/uploads/2024/02/report-3.pdf. (Accessed September 12, 2024.)

[ii] Congressional Budget Office. *CBO's Simulation Model of New Drug Development: Working Paper 2021-09*. August 26, 2021. https://www.cbo.gov/publication/57010. (Accessed September 12, 2024.)

[iii] Vital Transformation. *Build Back Better Act: Total Market Impact of Price Controls in Medicare Parts D and B.* July 28, 2022. https://vitaltransformation.com/2022/07/build-back-better-act-total-market-impact-of-price-controls-in-medicare-parts-d-and-b/. (September 12, 2024.)

[iv] Avalere. *Drug Pricing Bill Could Reduce Manufacturer Revenue by Over $450B*. July 22, 2022. https://avalere.com/insights/drug-pricing-bill-could-reduce-manufacturer-revenue. (Accessed September 12, 2024.)

[v] O'Brien, John. "Branded Drug Report 2023: John O'Brien, NPC." *Chain Drug Review*. January 9, 2023. https://www.chaindrugreview.com/branded-drug-report-2023-john-obrien-npc/. (Accessed September 12, 2024.)

[vi] Philipson, Tomas J. et al. *Policy Brief: The Potentially Larger Than Predicted Impact of the IRA on Small Molecule R&D and Patient Health*. The University of Chicago. August 25, 2023. https://ecchc.economics.uchicago.edu/2023/08/25/policy-brief-the-potentially-larger-than-predicted-impact-of-the-ira-on-small-molecule-rd-and-patient-health/. (Accessed September 12, 2024.)

[vii] Bedard, Philippe L. et al., "Small Molecules, Big Impact: 20 Years of Targeted Therapy in Oncology," *The Lancet*. Vol. 395 (10229): 1078-88. March 28, 2020. https://doi.org/10.1016/S0140-6736(20)30164-1. (Accessed September 12, 2024.)

[viii] Chambers, James D. "Follow-On Indications for Orphan Drugs Related to the Inflation Reduction Act." *JAMA Network Open*. August 15, 2023. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2808362. (Accessed September 12, 2024.)