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FIRST OPINION

The IRA needs changes to better support patients with rare diseases

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This time last year, members of Congress were working around the clock to draft and pass the Inflation Reduction Act.

One of their goals was to address government spending on health care. But they specifically didn't want to discourage research into rare disease treatments, so they exempted some of these so-called orphan drugs from the law.

Unfortunately, the exemptions aren't working as intended. Unless Congress acts, the IRA threatens to unravel one of America's greatest medical and public policy success stories: the explosion of new treatments for patients living with rare diseases.

As the CEOs of the National Organization for Rare Disorders and the Biotechnology Innovation Organization, the threat to rare disease drug development hits close to home for us. NORD was established 40 years ago by rare disease patients and families to drive advances in care, research, and policy. BIO's vision is harnessing innovation for the millions of patients and families who depend on our success. Both NORD and BIO are deeply concerned about the IRA's threat to rare disease drug development.

In the early 1980s, there were fewer than 40 medicines available to treat these conditions, which collectively



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afflict roughly 30 million people in the United States. Now, the Food and Drug Administration has approved more than 880 drugs — almost half in the past decade. Another 700 potential treatments are under development.

This success has many progenitors. Scientists work tirelessly in research labs. Brave patients put their lives on the line to test potential treatments. Advocacy groups help amplify patient voices and create critical databases for clinical and other researchers. Meanwhile, everyday Americans donate time and money to fight diseases that have touched their lives.

But perhaps most importantly, lawmakers — through the Orphan

Drug Act of 1983 — created new economic incentives for research into diseases that would have otherwise gone unfunded due to the high cost of rare disease drug development and inevitably limited market for treatments, since each rare disease, by definition, afflicts fewer than 200,000 Americans. The act provided tax credits, grants, and market-exclusivity periods to incentivize developers, sparking a sustained wave of rare disease research.

Despite the successes brought about by the Orphan Drug Act, the search for new rare disease treatments is far from over. We know of more than 7,000 rare diseases, and scientists

discover more every year. In total, fewer than 5% of rare diseases have an FDA-approved treatment.

Identifying effective rare disease treatments doesn't always mean inventing a completely new drug. It's a fact little known outside the clinical world, but the best hope for many patients with a rare disease is that a therapy approved for another condition will prove to be effective against their disease as well.

For instance, post-approval research found in 2013 that a drug originally approved in 2009 is safe and effective for treating juvenile idiopathic arthritis, a severe autoimmune disease. A common immunosuppressant used for organ transplants has been approved to treat three rare diseases.

Discovering these additional indications was no easy feat. Only about 1 in 5 orphan drugs — drugs that were first approved to treat a rare disease — are approved for more than one indication, and the second approval on average takes 4.5 years of additional painstaking research.

About 60% of these follow-on approvals are for additional rare, rather than more common, disease.

The IRA will make it much harder to justify conducting similar lifesaving research in the future. The law gave Medicare the authority to negotiate the price of an expanding list of medicines. In an attempt to protect rare disease research, the IRA's authors exempted some orphan drugs from this type of price-setting, but the exemption applies only as long as the drug has orphan designation for just one rare disease from the FDA.

In Section 30 of its guidance, the Centers for Medicare and Medicaid Services — the agency tasked with implementing the price negotiation program — makes it clear that orphan drugs will become eligible for negotiation as soon as the drug receives an additional orphan designation. So, drugs being studied for more than one rare disease will be fair game for negotiation even before they've been FDA-approved

for additional indications, creating huge disincentives to explore uses for additional rare diseases.

This may endanger the development of future therapies for any number of rare diseases. For example, a University of Pennsylvania immunologist is studying an antibody with an orphan designation in hopes of treating a rare malignancy, research that could fall by the wayside. And one pharmaceutical company is already stalling research into a rare genetic eye disease — thanks to the IRA.

This is a disaster for patients. To maintain incentives for rare disease research, orphan drugs approved for only one rare disease should be exempt regardless of the number of diseases for which they are being studied and have received FDA designation.

CMS should immediately reverse course on its recent guidance. But the real solution here lies with Congress. Americans with rare diseases already face long odds. Unless lawmakers act, we could see a heartbreaking shift away from rare disease innovation.