

TESTIMONY OF JOHN F. CROWLEY, EXECUTIVE CHAIRMAN OF AMICUS  
THERAPEUTICS

HOUSE COMMITTEE ON ENERGY AND COMMERCE  
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

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Chairman Griffith, Ranking Member Castor, Chair McMorris Rodgers, Ranking Member Pallone, and Members of the Subcommittee, thank you for the opportunity to present these comments to the Committee as it examines the very real world and negative effects that the Inflation Reduction Act (IRA) is having on medical innovation and the biopharmaceutical sector broadly and, very specifically, the chilling and immediate effect it is having on smaller, emerging biotechnology companies in the United States. I'll also comment on the negative effects this law is having today, and will continue to have into the future, on patient access to novel, often lifesaving therapies. My comments this afternoon focus in particular on the field of rare disease research and drug development as well as the IRA's disincentives to continue investing in important small molecule technologies.

My testimony comes from a very personal perspective and unintended journey into the world of science and medicine. Twenty-five years ago, our family's life changed. First, our then 15-month-old daughter Megan was diagnosed with Pompe disease, a rare and fatal neuromuscular genetic disorder. At the time of Megan's diagnosis, the neurologist looked down at our then seven-day-old son Patrick, asleep in his infant car carrier, and said that given the genetics of Pompe, there was a 25% chance that he too would be stricken with the disease and would need to be tested. Pompe is a recessive disorder, and there is no history in our family. Weeks later we received the news that Patrick, too, had Pompe disease. We were horrified to learn that most babies with this disease died before the age of two, and few lived to be kindergarteners. The doctor told us that we should enjoy the time we had - and that there was nothing that could be done. We learned that nature is not cruel, just brutally random.

My wife, Aileen, and I quickly moved from shock and grief to determination. First, determined to learn everything we could about this awful disease. Then determined to find anyone anywhere in the world who could help us find a way to save our children. Over the next two years, Megan and Patrick got progressively weaker, needing wheelchairs to maneuver and ventilators to breathe. Finally, realizing that time was our greatest challenge, I quit my job, took a home equity loan and cash advances on our credit card and together with a pioneering researcher, I co-founded a small biotechnology company to develop a medicine for Pompe. It was a daunting task. After overcoming many challenges, and the remarkable work of so many, my company was acquired and I had the privilege to lead the team that developed a lifesaving enzyme replacement therapy and secured the first FDA-approved treatment for Pompe disease in 2006. Megan and Patrick began to receive that therapy in early 2003, and this initial approved therapy, and others that have followed, have helped save the lives of thousands of children and now adults living with Pompe -- including Megan and Patrick. Today, despite the many physical disabilities they still endure caused by years of muscle damage before there was a medicine, Megan and Patrick are thriving young adults. Patrick works in a flower store staffed by people who are living with disabilities. Megan, after graduating from Notre Dame and earning a master's in social work at the University of North Carolina at Chapel Hill, works for the Make-A-Wish Foundation.

While our family's journey has received much attention, we are not alone. What science and medicine provided to our family, and continues to provide, is hope. Millions more living with rare, devastating diseases need that same hope today. And they need it fast.

There are nearly ten thousand rare diseases, only a few of which, like cystic fibrosis and hemophilia,<sup>1</sup> are well known to the wider public. While each rare disease affects fewer than 200,000 Americans, collectively they afflict almost 30 million people in this country.<sup>2</sup> About 95% of these disorders have no treatment, and many are not even being researched. This is a public health crisis of epic proportions.

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<sup>1</sup> <https://www.rarebeacon.org/rare-diseases/what-are-rare-diseases/>

<sup>2</sup> <https://rarediseases.org/wp-content/uploads/2019/01/RDD-FAQ-2019.pdf>

We are on the dawn, thankfully though, of a golden age in genetic medicine. Exciting new therapies, like gene editing, gene therapies and precision-based small molecules offer hope today where for so many, for so many years, there has been none. But we need to break down barriers, encourage massive private capital flows to fund biotech entrepreneurs, incentivize our largest biopharmaceuticals companies to invest in rare disease programs, and much more. But instead of declaring a public health crisis and taking the learnings of and demanding an “Operation Warp Speed” for rare diseases, we are instead now facing a massive headwind brought about by an ill-conceived drug control pricing law with consequences - some intended, some unintended - that are instead curtailing funding, further closing avenues of research and, tragically, taking away hope for many who are most in need.

Once our children were treated, I thought my foray into biotech was over. But I soon realized that that the medicine which saved our children’s lives, was not the best we could do. We needed to innovate again to find an even better way to treat Pompe. And on this journey I learned so much more about the suffering of so many individuals and families living with rare diseases.

It was with that motivation that I, with a handful of others, about 19 years ago founded a second biotechnology company,<sup>3</sup> Amicus Therapeutics, dedicated to finding treatments for many rare diseases. When we founded Amicus, we chose the name “Amicus”, the Latin word for “friend”. We wanted Amicus to be the most patient-focused company in this industry. Every day I ask each of our hundreds of global employees to think: “If you had this disease, or you were the parent of a child with this disease, how would you make your business decisions?” It’s a patient-first mindset that leads to business actions that always keep patients at the forefront. At Amicus, we price our medicines to be at or below competitive FDA-approved products that are already on the market – encouraging payors to grant rapid coverage and to ensure broad access. Importantly, at Amicus we committed with the launch of our first FDA-approved product in 2018, to limiting annual price increases for *all* of our medicines. We’ve also committed to reinvest a share of the revenue from each of our FDA-approved

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<sup>3</sup> <https://www.linkedin.com/in/john-f-crowley/details/experience/>

products back into R&D into new treatments for those exact same diseases until the day that the disease is not just treated but cured.

I care deeply about this mission, but like others in my field, I'm greatly disappointed about laws such as the IRA that make major drug discoveries less likely, especially from smaller emerging biotech companies. The development of a new medicine takes many years of research and faces long odds of success.<sup>4</sup> At Amicus, over the years, we have had many more programs and clinical studies fail than succeed. Drug discovery broadly, and rare disease research especially, are inherently filled with risk. But at Amicus, we would rather be the first to fail than the last to succeed. The Inflation Reduction Act (IRA) makes our challenges even greater. This law applies government price controls to a range of drugs, which is guaranteed to reduce investment in finding new treatments and therapies, as studies from the University of Southern California,<sup>5</sup> the University of Chicago and elsewhere suggest.

And this all now comes at what has been the most difficult two and a half years in the history of the biotechnology industry. There are over 3,000 biotechnology companies in the United States, nearly 1,000 of which are public entities. The vast majority have no approved products or revenues, let alone profitability. These companies, though, develop more than 75% of all new medicines. We are the cradle of biomedical innovation, and the American biotechnology sector is the envy of the world ... and an incredibly important strategic advantage for our nation. However, since February 2021, the enterprise value of all U.S. public biotechnology companies (excluding the top 20, which are profitable) has fallen more than 70%. In the rare disease space alone, more than 100 clinical programs have been canceled in the past 18 months. Smaller biotechnology companies, private and public, are suffering from the macroeconomic environment (especially higher interest rates), a largely inconsistent and very challenging FDA, ongoing political rhetoric and the effects of the IRA. And a great concern among entrepreneurs and investors is that the worst may be yet to come.

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<sup>4</sup> <https://scopeblog.stanford.edu/2014/12/11/finding-cures-for-the-most-challenging-diseases/>

<sup>5</sup> <https://healthpolicy.usc.edu/research/mitigating-the-inflation-reduction-acts-potential-adverse-impacts-on-the-prescription-drug-market/#:~:text=Taken%20together%2C%20these%20provisions%20have,approvals%20during%20the%20same%20period.&text=Lowered%20revenues%20may%20lead%20to,for%20follow%20on%20drug%20innovation.>

Let me speak now about the very real-world impact of the IRA on these emerging biotechnology companies- and ultimately on patients in need today, as well as future “patients” who don’t even know that they are going to need hope one day.

### **IRA’s Negative Effects on Research for Rare Disease**

Developing new drugs is an incredibly risky and capital-intensive endeavor -- only 12% of drugs entering clinical trials ultimately receive FDA approval.<sup>6 7 8</sup> Now consider rare diseases -- which in some cases afflict just a few hundred people.<sup>9 10</sup> Such a small patient population makes it extraordinarily difficult for biotech companies to justify the massive R&D costs required to develop a new treatment. Even if a rare disease therapy proves successful and receives FDA approval, firms often struggle to earn back their upfront investments. And these investments are significant. The average compound requires more than \$2.5 billion to make it to market; all the while, companies must also capitalize the costs associated with all the failed programs in past research programs as well.<sup>11</sup>

Congress sought to help alleviate the lack of investment in rare diseases in 1983 when it passed the Orphan Drug Act. The law gives tax credits to companies who develop novel rare disease

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<sup>6</sup><https://www.m2gen.com/company-news/industry-insights/how-long-do-new-cancer-drug-therapies-take-to-go-to-market#:~:text=On%20average%2C%20it%20takes%2010,the%20Study%20of%20Drug%20Development>

<sup>7</sup><https://www.bio.org/sites/default/files/legacy/bioorg/docs/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO.%20Biomedtracker.%20Amplion%202016.pdf> p. 3

<sup>8</sup> <https://www.cbo.gov/publication/57126#:~:text=Only%20about%2012%20percent%20of,for%20introduction%20by%20the%20FDA.>

<sup>9</sup> <https://rarediseases.org/wp-content/uploads/2019/01/RDD-FAQ-2019.pdf> p. 1

<sup>10</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4543882/>

<sup>11</sup> <https://www.policymed.com/2014/12/a-tough-road-cost-to-develop-one-new-drug-is-26-billion-approval-rate-for-drugs-entering-clinical-de.html>

treatments, also known as "orphan drugs."<sup>12</sup> The legislation has been a resounding success -- FDA-approved treatments for rare conditions have increased over 2,000% since its passage.<sup>13</sup>

But instead of building on the successes of the Orphan Drug Act, many policymakers have done a U-turn, pursuing policies that punish -- rather than reward -- companies trying to find novel treatments for rare diseases. Last year's Inflation Reduction Act (IRA) is just one example. The law permits the federal government to impose severe price caps on an increasingly large share of successfully developed prescription drugs covered under Medicare. The law's authors exempted orphan drugs from the price controls if they treat a *single* rare disease.<sup>14</sup> But medicines that treat *multiple* rare diseases don't qualify for the exemption.

That's a big problem. Drug makers routinely investigate whether a drug already approved to treat one rare condition could possibly treat another.<sup>15</sup> Historically, this "follow-on" research has provided transformational cures to patient communities who don't have access to effective treatments. The IRA is already forcing some drug companies to freeze efforts to find additional applications for existing rare disease drugs. One biotech company already stopped a late-stage clinical trial that would have determined whether a rare heart disease drug would also work for a rare eye condition.<sup>16</sup> In short, the IRA's negative treatment of orphan products is a direct contradiction of the positive, and life-changing, work done by Congress in passing the Orphan Drug Act itself many years ago.

### **IRA Disincentivizes Critical Research for Small Molecule Drugs**

Also of great concern is the IRA's disincentive to invest in small molecule drugs. Small molecule drugs account for about 90% of approved medicines. They're often more convenient because they can be taken orally, whereas biologics are delivered by injection or infusion. But extremely effective and cutting-edge medicines exist in both classes -- and both avenues of

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<sup>12</sup> <https://oig.hhs.gov/oei/reports/oei-09-00-00380.pdf> p. 1

<sup>13</sup> <https://pkdcure.org/saving-the-orphan-drug-tax-credit/> (MATH:  $650-30/30 = 20.667 \times 100 = 2067\%$ )

<sup>14</sup> <https://www.kff.org/medicare/issue-brief/explaining-the-prescription-drug-provisions-in-the-inflation-reduction-act/>

<sup>15</sup> <https://www.cahc.net/newsroom/2023/3/1/how-the-inflation-reduction-act-is-impacting-rare-disease-patients#:~:text=In%20the%20rare,in%20later%20years.>

<sup>16</sup> <https://www.bloomberg.com/news/articles/2022-10-27/alnylam-halts-work-on-eye-drug--citing-new-us-law-over-pricing?sref=C4viNJ4s>

development are complex, expensive and fraught with failure. One is not "better" than the other. And of course, such distinctions mean little to patients, who just want the best medicine available.

Yet the IRA says the government can intervene in the market and set prices on small molecule medicines starting just nine years after FDA approval,<sup>17</sup> compared to 13 years for biologics. This policy slashes the value of any new small molecule drug. That's because about half of drug sales occur between 10 and 13 years after FDA approval.<sup>18</sup> If price controls kick in just before that stage, the drug developer and its backers suddenly stand a much lower chance of recouping their investment. This will sharply slash investment into researching small molecule drugs.<sup>19</sup>

Consider my company's quest to treat Fabry disease, a lysosomal disorder that causes burning pain, hearing loss, progressive damage to renal and cardiac function, clouded vision and impaired circulation.<sup>20</sup> It took 13 years of continuous clinical trials before the FDA approved our small molecule treatment in 2018.<sup>21</sup> The total cost of that research and development came to half a billion dollars.<sup>22</sup>

Investors supported our research because they knew that if we discovered a successful treatment, they could earn a return. They wouldn't have backed us for that long if they thought price controls could take effect less than a decade after the drug's release – in our case, less time on the market than it took to actually develop the product. Lawmakers' decision to single out small molecule drugs has no clinical basis and is bizarre when you consider how central they are to our medical system. Medicines in this category include everything from over-the-counter allergy medications to treatments for cystic fibrosis and HIV/AIDS. My children

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<sup>17</sup><https://thehill.com/homenews/senate/3591223-read-full-text-senate-climate-tax-bill-grows-to-755-pages-passes-key-cbo-test/#:~:text=Senate%20Majority%20Leader%20Charles%20Schumer,excise%20tax%20on%20stock%20buybacks.>

<sup>18</sup> <https://nopatientleftbehind.docsend.com/view/qekzsg4mbpp2ajct>

<sup>19</sup> <https://www.biocentury.com/article/645118/biotech-investors-bracing-for-inflation-reduction-act-s-impacts>,  
<https://www.lek.com/insights/ei/how-inflation-reduction-act-will-impact-biopharmaceutical-industry>

<sup>20</sup> [https://www.ninds.nih.gov/health-information/disorders/fabry-disease#:~:text=Fabry%20disease%20\(also%20known%20as,provide%20energy%20to%20the%20body.](https://www.ninds.nih.gov/health-information/disorders/fabry-disease#:~:text=Fabry%20disease%20(also%20known%20as,provide%20energy%20to%20the%20body.)

<sup>21</sup> <https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-rare-genetic-disorder-fabry-disease>

survived because of scientific research and an entrepreneurial ecosystem that enables breakthrough discoveries. Today, the IRA has made this kind of success story impossible.

### **Lessons from Europe**

I urge Congress to look to Europe to understand what will happen in the U.S. with the price control scheme of the IRA and how patients will bear the brunt of it. The U.S. has drawn more pharmaceutical investment in recent years amid challenges in the European market, but that might no longer be the case as price controls threaten to drive drug companies from the U.S., too.<sup>23</sup>

Previous research has shown a decline in biopharma industry investment in Europe relative to the United States, corresponding to increasing price controls in European countries. Research from Vital Transformation found that every 10% drop in the price of medicines in price-controlled EU markets was associated with:<sup>24</sup>

- 14% decrease in total VC funding (10% early stage and 17% late stage)
- 7% decrease in biotech patents
- 9% decrease in biotech start-up funding relative to the U.S.
- an 8% increase in the delay of access to medicines

Vital Transformation also found that the continued downward pressure on prices in price controls in Europe have led to significant declines in biopharmaceutical industry investments in the Europe Union relative to the United States. For example, by 2019, late-stage venture capital funding in the European Union was just 3% of the level in the United States. From 2003 to 2019, biotech investments in the United States increased sixfold, while they remained static in the European Union. In 2020, the U.S. share of total annual biotech startups was roughly three times greater than the EU share. It is important to note, the U.S. is not entitled to be the leader in biotech investment and development, that is a title our country has earned through hard work and

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<sup>23</sup> "The West's Drug-Price Self-Sabotage." *Wall Street Journal*. January 23, 2023.

<sup>24</sup> <https://vitaltransformation.com/2021/11/the-historical-impact-of-price-controls-on-the-biopharma-industry/>



free market economics, and the future leadership – and the jobs and economic growth that accompany it – is not guaranteed.

### **CMS Is Getting it Wrong and Patients Will Suffer**

Beyond the problems inherent in the statute itself, I want to call Congress's attention to very real and very egregious problems with CMS's implementation of the statute as well. In at least two important circumstances, CMS has stepped well beyond its statutory authority to significantly over-impose the IRA's price control provisions on new and novel products that have not yet even hit the statutory market maturity levels outlined in the statute.

To that end, Congress should increase its oversight of the Centers for Medicare & Medicaid Services (CMS) as the Agency moves forward in implementing the IRA's price negotiation program. Unfortunately, a critical policy that CMS finalized was its decision that, in determining which drugs are eligible for negotiation, it would not treat drugs approved under unique New Drug Applications (NDAs) or Biologics License Applications (BLAs) as distinct drugs but, rather, would combine NDAs and BLAs with the same active moiety/active ingredient together for negotiation purposes. CMS must reverse this policy as it is bad for innovation, bad for patients and not supported by the statute. CMS's approach leaves no incentive for therapeutic advancement and will have significant, negative impacts on treatments for patients for decades. Biopharmaceutical innovation is incremental, relying on sustained and continuous improvements to molecules, pathways and modes of administration to achieve maximum clinical benefit for patients. Researchers cannot take significant leaps and develop new active moieties with each generation of treatment. By combining drugs at the active moiety or active ingredient level, CMS is harming investments into new therapies, including for orphan and hard-to-treat diseases. For the sake of pharmaceutical and biotechnology innovation, and patient access to needed therapies, CMS's current extra-statutory framework cannot stand.

CMS must also clarify how its review of the evidence will inform its setting of the maximum fair price ("MFP") for a drug selected for negotiation. CMS's approach remains unclear and presents

untenable levels of uncertainty. Essentially, CMS has said it will use the net price of the “therapeutic alternatives” of drugs selected for negotiation as a starting point and then adjust this starting point based on its review of the clinical evidence. In addition, CMS has said it may make further adjustments based on other data manufacturers are required to submit, such as “recoupment” of research and development costs. But CMS has not provided a framework for how it will review all this evidence. Nor has the agency indicated how certain evidence or factors will be weighed. This lack of clarity and uncertainty is of great concern. CMS should clarify its standards for evidence review and be transparent and accountable about what evidence drove its decisions in setting the MFP and why. Further, CMS’s review of the evidence should focus on factors that are critical for patients, specifically factors related to clinical benefit and unmet medical need and de-emphasize manufacturer specific data elements such as cost of production and research and development costs.

### **Putting the Costs of Medicines in Perspective**

I believe it’s also critical - in evaluating root causes for high patient costs for medicines at the pharmacy counter - that Congress look to the broader healthcare system and supply chain for aspects of market dysfunction. An important fact that is often overlooked is that prescription medicines account for just 14% of overall healthcare spending.<sup>25</sup> Further, recent data illustrate per capita price growth for prescription drugs well below inflation at 3.1%.<sup>26</sup> Yet for the past several years, that singular focus has been on manufacturers – culminating in draconian price controls in the IRA that will do nothing to address the point-of-sale pain experienced by many patients today.

Each link in the chain between a manufacturer and a patient has an important role, but each also has an important impact on the cost of any medicine as well. The PBM market began as an offshoot of the broader insurance market as a mechanism to help manage spend and access to

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<sup>25</sup> <https://phrma.org/resource-center/Topics/Cost-and-Value/Prescription-Medicines---Costs-in-Context>

<sup>26</sup> Altarum Price Brief June 2023.

pharmaceutical products. From inception, its shortcoming is that singular focus – the downstream effects of the decision to supply or deny a pharmaceutical to a patient generally fall outside of the traditional PBM remit. The denial of a particular medicine, which might then result in the hospitalization of a patient, might save a plan formulary money, but it costs the system elsewhere. The PBM model, however, only has responsibility for that one aspect of savings – not necessarily the hospital spending that unfortunately results. These are incentives important to keep in mind.

And PBMs have grown significantly over the years. The largest six PBMs control almost 96% of the PBM market. The largest three (Optum, Express Scripts and CVS Caremark) themselves control 80% of that market. PBMs manage or administer benefits for around 266 million Americans. And they have become behemoths. The combined revenues of the three largest PBMs are now four times larger than the combined revenues of the three largest biopharmaceutical manufacturers.

With this size and scope comes tremendous market power. In 2021 rebates and discounts from brand manufacturers amounted to \$236 billion. All the while, the net price received by manufacturers has steadily decreased. According to Drug Channels, in the first 3 quarters of 2022 net prices decreased by .8%, following a similar trend over the previous 5 years.

The vertical and comprehensive integration of many PBMs has only added to this market power. PBMs have taken on insurer duties, specificity pharmacy duties, mail order pharmacy duties and increasingly, they even serve as rebate aggregators for smaller – less dominant – PBMs and insurers. In fact, there are even reports of the establishment of offshore rebate contracting entities that manage fees and other transactional aspects of U.S.-based biopharmaceutical purchasing. In short, these entities are enormous, opaque, and profitable.

But at the same time, as net prices continue meager if not negative growth across the sector, patients are increasingly not seeing corresponding relief at the pharmacy counter. There are many reasons for this, many of which are in the control of the PBM and insurer. For instance:

- high-deductible health plans that base patient spending on list prices
- coinsurance that does not account for rebates and discounts passed behind the point of sale
- steering patients to PBM-owned specialty and mail order pharmacies
- tiering of products in a way that favors high list prices (and their associated rebates) over lower costs to patients

In sum, as we evaluate root causes for high patient costs for medicines at the pharmacy counter, we believe it is incumbent on Congress to look across the supply chain for aspects of market dysfunction. For the past several years, that singular focus has been on manufacturers – culminating in draconian price controls in the IRA that will do nothing to address the point-of-sale pain experienced by many patients today. Congress should look at the currently dominant PBM market for additional mechanisms to relieve consumer pain.

### **Conclusion**

I thank the Committee for the opportunity to provide this statement for the record and urge the Committee to take steps to address the significant, negative impacts the IRA is having on current and future treatments and cures. We cannot squander this great opportunity in the years ahead to advance state-of-the-art medicines for people in need - especially the most vulnerable among us. It is a moral imperative for our society. And the United States must not relinquish the great strategic advantage that is American biotechnology.