Nos. 24-1820 & 24-1821

IN THE UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

BRISTOL MYERS SQUIBB CO.,
Plaintiff-Appellant,
v.
XAVIER BECERRA, ET AL.,
Defendants-Appellees.

JANSSEN PHARMACEUTICALS, INC.,
Plaintiff-Appellant,
v.
XAVIER BECERRA, ET AL.,
Defendants-Appellees.

On Appeal from the United States District Court for the District of New Jersey, Nos. 3:23-cv-03335 & 3:23-cv-03818

BRIEF OF AMICUS CURIAE THE BIOTECHNOLOGY INNOVATION ORGANIZATION SUPPORTING APPELLANTS AND REVERSAL

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CORPORATE DISCLOSURE STATEMENT

In accordance with Federal Rule of Appellate Procedure 26.1 and Local Appellate Rule 26.1.1, amicus states as follows:

1. **Is amicus a subsidiary or affiliate of a publicly owned corporation?**

No. The Biotechnology Innovation Organization is a non-profit corporation organized under the laws of the District of Columbia. It has no parent corporation, and no publicly held company has a 10% or greater ownership interest.

2. **Is there a publicly owned corporation, not a party to the appeal or an amicus, that has a financial interest in the outcome?**

None known.

/s/ Daniel G. Jarcho
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STATEMENT OF INTEREST[1]

The Biotechnology Innovation Organization ("BIO") submits this brief as *amicus curiae* in support of appellants Bristol Myers Squibb Co. and Janssen Pharmaceuticals, Inc. ("BMS" and "Janssen"). The District Court's erroneous decision will have significant detrimental effects on the biopharmaceutical industry, including BIO's members focused on developing novel, life-saving prescription medicines.

BIO is the principal trade association representing the biotechnology industry in all fifty States and abroad. BIO has approximately 1,000 members, ranging from small startup companies and biotechnology centers to research universities and Fortune 500 companies. The majority of BIO's members are small companies that have yet to bring products to market or attain profitability. Roughly 80% of BIO's corporate members have annual revenues of under $25 million. These members rely heavily on venture capital and other private investment.

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[1] *Amicus* certifies that all parties have consented in writing to the filing of this brief. *Amicus* also certifies that no party authored this brief in whole or in part or contributed money intended to fund the brief's preparation or submission.

INTRODUCTION

BMS and Janssen assert compelling claims that the Inflation Reduction Act's ("IRA") "Drug Price Negotiation Program" (the "Program") violates the First and Fifth Amendments and the unconstitutional conditions doctrine. Their claims target a Program that imposes extraordinary economic coercion by the Government. The Program strong-arms BMS, Janssen, and other drug companies into providing the Government with access to their drugs at below-market rates (thereby violating the Fifth Amendment). The Program also bullies drug companies to endorse a government message with which they do not agree (thereby violating the First Amendment). The Program effectuates this coercion by requiring non-participating companies to choose between two economically infeasible alternatives: (1) pay an unaffordable "excise tax" (which, although labeled a "tax," is really a crippling monetary sanction that no manufacturer could ever endure) or (2) withdraw their entire drug portfolio from Medicare and Medicaid (an unsustainable option that no manufacturer could ever select).

In this brief, *amicus* illustrates the coercion arising from the second alternative, explaining why drug companies must avoid the economic

devastation associated with exiting the Medicare/Medicaid market. Biopharmaceutical manufacturers rely on Medicare and Medicaid spending for as much as 65% of their annual revenue. They then reinvest billions of dollars of that revenue each year into discovering and developing the next life-saving medication. The illusory "option" for manufacturers to avoid the Program by abandoning more than half the market for the rest of their portfolio is not something a biopharmaceutical manufacturer could ever chose to do—at least not if it wants to continue bringing new, life-saving biopharmaceutical medicines to market.

The District Court's misapprehension of the importance of Medicare and Medicaid is no small error. If the Program is upheld and manufacturers are forced to succumb to the Government's coercive drug-price "negotiation," the Program will yield devastating consequences for the future of biopharmaceutical research and development ("R&D"). By imposing below-market prices on selected drugs, the Program fails to account for the reality that drug costs must account not only for the cost of developing a single drug, but also for the billions of dollars invested in the R&D of drugs that never make it to market. If manufacturers cannot recoup their investments, the Program will result in *fewer* drugs being

developed, *less* investment in biopharma and drug R&D, and *a greater disparate impact* on patients with rare and life-threatening diseases.

Companies that develop and manufacture prescription medications are varied in their circumstances and capabilities. Some are large and established, while others are small and emerging. Each faces unique research challenges and economic dynamics. Some spend years or decades researching and developing myriad biopharma therapies, waiting for a single breakthrough. The Program fails to account for any of that. It imposes a pricing scheme that is blind to market realities and that imposes mandates—masked as "choices"—on how manufacturers must sell and provide access to their drugs. If left standing, the Program will deal a crushing blow for small companies focusing on emerging therapies and rare diseases. The Program's framework is not only unconstitutional; it poses an existential threat to the future of biopharma.

ARGUMENT

I. COMPANIES ARE COERCED INTO PARTICIPATING IN THE IRA'S DRUG PRICE NEGOTIATION PROGRAM BECAUSE MANUFACTURERS CANNOT PRACTICALLY WITHDRAW THEIR ENTIRE PORTFOLIO FROM MEDICARE.

Drug companies are coerced into participating in the Program because manufacturers cannot, as a practical matter, stop selling their products to Medicare and Medicaid ("Medicare").[2] Medicare is the 10,000-pound gorilla in the pharmaceutical market, particularly for the drugs targeted by the Program. As this Court has recognized, "[t]he federal government dominates the healthcare market. Through Medicare and Medicaid, it pays for almost half the annual nationwide spending on prescription drugs." *Sanofi Aventis U.S. LLC v. U.S. Dep't of Health & Hum. Servs.*, 58 F.4th 696, 699 (3d Cir. 2023) (citing Cong. Budget Off., *Prescription Drugs: Spending, Use, and Prices* 8 (2022)).[3] The federal

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[2] Like the District Court below, for simplicity we will refer to Medicare and Medicaid collectively as "Medicare." JA3.

[3] Another district court analyzing the Program has opined that nothing this Court said in *Sanofi* suggests "that drug manufacturers are required to participate in the Program or any other part of Medicare." *AstraZeneca Pharms. LP v. Becerra*, 2024 WL 895036, at *15 (D. Del. Mar. 1, 2024). But like the District Court below, that court failed to observe the market realities for pharmaceutical manufacturers. For the reasons discussed in

Government wields its overwhelming "market power to get drug makers to subsidize healthcare." *Id.* at 699. That overwhelming "market power" means the consequences of avoiding the Program threaten participants' commercial viability altogether.

Because Medicare represents such a large majority of the pharmaceutical market, requiring a manufacturer to withdraw from Medicare to avoid giving up its constitutional rights would be tantamount to requiring the manufacturer to stop selling prescription drugs altogether. Take for example, Janssen's Xarelto, used to "treat[] and help prevent blood clots and reduce[] the risk of stroke." JA793. As Janssen explained to the District Court below, Medicare and Medicaid accounted "for more than 60%" of Xarelto prescriptions in the United States in 2022. JA793. And that is just one product from among the Program's first round of selections. But the constitutional question presented is broader than a single manufacturer or a single product. The Program is designed to target prescription drugs with high Medicare Part

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this brief, pharmaceutical manufacturers are not "free to accept or reject" participation in the Program (*id.* at *16) because their existence depends on revenue from Government purchases of prescription medications.

B and Part D utilization and expenditures. *See* 42 U.S.C. § 1320f-1; *AstraZeneca*, 2024 WL 895036, at *3. In the future, the Program will likely and eventually target prescription drugs that are used almost exclusively by aging patients in the Medicare demographic. As a result, even if the Program is not immediately crippling for the drugs or manufacturers currently targeted by the Program, it surely will be for future innovators looking to develop life-saving medications.

In *Horne v. Department of Agriculture*, the Supreme Court held that the Government effectuated a Taking of personal property when it prohibited raisin growers from selling raisins unless they provided a specified quantity of their crop to the Government free of charge. 576 U.S. 351, 357–67 (2015). The Court rejected the Government's argument that there was no Taking "because raisin growers voluntarily choose to participate in the raisin market." *Id.* at 365. The Taking could not "reasonably be characterized as part of a . . . voluntary exchange" because "[s]elling produce in interstate commerce . . . is . . . not a special governmental benefit that the Government may hold hostage, to be ransomed by the waiver of constitutional protection." *Id.* at 366.

The District Court wrongly distinguished *Horne* on the ground that a pharmaceutical manufacturer's refusal to participate in the Program would result in a prohibition of only some of its sales (those to Medicare), but not all of its sales (as in *Horne*). JA11–12 (citing *Horne*, 576 U.S. at 365). But there is no rule that a Taking only occurs when participation is all-or-nothing. Indeed, *Horne* rejected such a wooden approach. *See Horne*, 576 U.S. at 365 ("[P]roperty rights 'cannot be so easily manipulated.'" (quoting *Loretto v. Teleprompter Manhattan CATV Corp.*, 458 U.S. 419, 439 n.17 (1982))). On the contrary, conditioning an extraordinary amount of sales on participation in a government program can be just as coercive as conditioning all sales.

But below, the District Court summarily rejected BMS's and Janssen's arguments about the coercive nature of the Program by drawing inapt analogies to cases involving totally different markets. For example, the District Court cited (non-Takings) cases considering the markets for non-profit hospitals and nursing homes. *See Baptist Hosp. E. v. Sec'y of Health & Hum. Servs.*, 802 F.2d 860, 862 (6th Cir. 1986); *St. Francis Hosp. Ctr. v. Heckler*, 714 F.2d 872, 873 (7th Cir. 1983); *Minn. Ass'n of Health Care Facilities, Inc. v. Minn. Dep't of Pub. Welfare*, 742

F.2d 442, 444 (8th Cir. 1984); *Livingston Care Ctr., Inc. v. United States*, 934 F.2d 719, 720 (6th Cir. 1991). But those markets are not comparable to the prescription drug market, and the cases analyzing those markets say nothing about the coercive impact of requiring a manufacturer to completely withdraw its entire portfolio from Medicare if it wants to avoid an illegal Taking.

In *Baptist Hospital*, for example, five non-profit hospitals "provided *some* free health care to *non*-Medicare patients" and later sought "reimbursement from the Medicare program for a portion of th[o]se services" by including them as bad debts and charity allowances on their Medicare cost report. 802 F.2d at 862 (emphasis added). Following an administrative review, the district court upheld a decision to not allow the reimbursements as "entirely consistent" with the Medicare Act. *Id.* at 863. The court also reasoned that the decision to not reimburse for charity services did not violate the Fifth Amendment's due process clause in part based on its conclusion that the hospitals' "participation in the Medicare Program [was] wholly voluntary." *Id.* at 870.

Baptist Hospital's conclusion was incorrect even as to health care providers. But the analysis is decidedly different for pharmaceutical

companies. Health care providers can, and do, opt out of participation in Medicare, and the governing regulations even provide a roadmap for doing so. *See* 42 C.F.R. § 405.420. But here, there is no evidence in the record that any manufacturer has *ever* offered its products only to patients not covered by Medicare. For good reason: It is simply not an economically feasible alternative.

There are also other practical differences that greatly impact patients. If a provider chooses not to treat Medicare patients, the impact on those patients is simply that they must drive further or obtain care from a less-preferred physician. But for branded medications like those targeted by the Program, there is only one seller. If that seller opts out of selling to Medicare, Medicare patients in dire need of critical life-saving medications will be left without options. That result would undermine Medicare's core purpose to ensure "adequate health care for a specific group of people." *Baptist Hosp.*, 802 F.2d at 868. And reputationally, a drug company would have a difficult time explaining a decision not to provide life-saving medicines to some of America's sickest patients. The Government has forced manufacturers into a trap they cannot possibly escape.

The District Court cited *Baptist Hospital* in support of its conclusion that "any provider fear[ing] that its participation will drive it to insolvency . . . may withdraw from participation." JA15 (quoting *Baptist Hosp.*, 802 F.2d 860 at 869–70). But that argument misses the forest for a single tree. The problem is not just that participation in the Program might drive a pharmaceutical manufacturer to insolvency, but that *non*-participation would as well. That is why it is unconstitutional to condition participation in Medicare on participation in the Program.

Non-profit hospitals and nursing home providers, like those analyzed in the cases relied on by the Government and the District Court below, are not like the innovators and drug manufacturers targeted by the Program. Hospitals and nursing homes serve small localities, meaning that the impact of being deprived of Medicare patients in a small geographic segment simply means that local providers may "opt not to participate [in Medicare and] are free to serve persons not covered by Medicare and those potential Medicare recipients who are willing to forego Medicare benefits for the services provided." *Baptist Hosp.*, 802 F.2d at 870. That option does not exist for pharmaceutical manufacturers, which provide life-saving medications for patients

nationwide and rely on that nationwide revenue to recoup their huge research and development investments and to fund future investments in developing the next line of life-saving medications. Nor is it reasonable or realistic to expect patients to forego their Medicare benefits to pay for the drugs targeted by the Program. Those products are some of the most widely prescribed medications, primarily because of their extremely high effectiveness in treating severe, life-altering diseases.

The Program is nothing but an illusion of "choice"—manufacturers must either "voluntarily" participate in the Program's "negotiations" or withdraw entirely from Medicare. That is no choice at all. That is coerced participation in a Program that violates the constitutional rights of BMS and Janssen.

II. THE IRA'S DRUG PRICE NEGOTIATION PROGRAM WILL BLUNT INNOVATION AND STIFLE DEVELOPMENT OF NEW OR IMPROVED LIFE-SAVING MEDICATIONS.

The consequences of an incorrect constitutional ruling cannot be overstated. The Program, if upheld, will ultimately result in fewer drugs being developed and less investment in biopharma and drug R&D. And the impact will not be uniform. Patients with rare and life-threatening diseases will suffer the greatest negative impact.

The Program addresses the pricing of each drug in isolation. What the Program does not account for is how pricing fundamentally affects biopharma R&D more broadly. For every drug that makes it to market, nine other drugs come up short, having proved unviable after an enormous financial investment into their exploration and development.

Innovators—including large manufacturers and emerging biotech startups—are willing to take on those risks in a competitive market where they can be rewarded for a successful innovation. But in a world where a company is forced to receive less than fair market value for its products, it must make a very real, and unsettling, choice about whether it even makes economic sense to bring new products to market. The Program's pricing structure disincentivizes investment in therapies for rare and orphan diseases and has already led biotechnology companies to reduce research funding and abandon clinical trials. *See Life Science Investment Tracker*, Incubate, https://lifesciencetracker.com. Simply put, the ultimate, real-world consequences of the District Court's errant decision are decreased innovation, fewer life-saving medications ever making it to market, and a disproportionate negative impact on patients with rare and life-threatening diseases.

A. The Program's pricing structure does not reflect or account for the R&D required to develop life-saving medications, stifling investment in future biotech drug developments.

The Program represents a fundamental misconception of how drugs are developed and priced. It incorrectly derives the Government's price of a medication solely from the R&D costs of that medication alone. In actuality, the price of a drug that makes it to market must compensate and account not only for the cost of that drug but also for the vast number of drugs that never make it out of preliminary research phases or clinical trials. By failing to account for *all* R&D costs, the Program ignores market realities. The direct result: R&D and innovation will suffer, with fewer drugs being developed and even fewer making it to market.

The prevailing rhetoric notwithstanding, the pharmaceutical industry is not excessively profitable. Pharmaceuticals rank just 15th—behind myriad financial sectors as well as tobacco, semiconductors, and software. *See* Daniel Gassull et al., *IRA's Impact on the US Biopharma Ecosystem*, Vital Transformation (June 1, 2023) at 7, https://tinyurl.com/2aa7z8fe ["*IRA's Impact on the US Biopharma Ecosystem*"]; *Margins by Sector (US)*, N.Y. Univ. Stern (Jan. 2024), https://tinyurl.com/nhbxvw4f. The biotech sector—which provides vital

R&D to support the biopharmaceutical industry's drug development efforts—is ranked 92nd. *See IRA's Impact on the US Biopharma Ecosystem*, *supra*, at 7. The reason is simple: Drug development is a cost-intensive, high-risk, yearslong process.

Notably, most drugs never make it to market. In 2021, the Congressional Budget Office estimated that nearly 90% of all drugs entering clinical trials failed to receive FDA approval. *See Research and Development in the Pharmaceutical Industry*, Cong. Budget Off. (Apr. 2021), at 2, https://tinyurl.com/2j3n6u7n ["*Research and Development in the Pharmaceutical Industry*"]. That's not even accounting for development efforts that never even reach the clinical-trial phases. For that reason, the biopharma sector invests a huge component of its revenue on R&D—50% more than the next closest sector (software and internet). *See IRA's Impact on the US Biopharma Ecosystem*, *supra*, at 11. The biopharma sector allocated 28% of revenue toward R&D in 2022, with biotech firms allocating even more—39%. *See id.* In 2019, the pharmaceutical industry invested $83 billion in R&D activities—*ten times* the amount spent in the 1980s (after adjusting for inflation). *See Research and Development in the Pharmaceutical Industry*, *supra*, at 1.

Developing life-saving medications is a time-intense, resource-consuming process with a 1 in 10 success rate.

Each drug that makes it to market stands on the shoulders of nine or ten other drugs that never make it out of clinical trials (and even more that never even get that far). All told, accounting for unsuccessful clinical trials, the estimated median R&D costs per FDA-approved drug between 2009 and 2018 were $1.1 billion. *See* Olivier J. Wouters et al., *Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018*, JAMA (Mar. 3, 2020), https://tinyurl.com/57ff88mb. Companies must therefore account for *all* R&D costs when pricing the drugs that *do* make it to market. The Program does no such thing, with devastating consequences.

By current estimates, the Program's approach to drug pricing and R&D costs will severely impact both biologics and small molecule drugs "with an average reduction in revenue per therapy of $4.9 billion and $4 billion respectively." *IRA's Impact on the US Biopharma Ecosystem*, *supra*, at 2. That loss in revenue will directly result in less R&D investment, meaning fewer life-saving drugs reaching clinical trials, let

alone making it to market. The conservative estimate is that roughly 139 drugs in the next ten years may never be developed. *See id.* at 2, 16.

Manufacturers are already making hard choices to discontinue R&D efforts in the face the new economic realities ushered in by the Program. For example, BMS recently announced a six percent cut in its workforce and that it would invest the targeted savings into opportunities with the "highest potential." Ned Pagliarulo, *Bristol Myers to Cut 6% of Workforce, Trim Drug Pipeline*, BioPharma Dive (Apr. 25, 2024), https://tinyurl.com/yc43z94j. Two-thirds of those savings will come from cuts to R&D for other programs. *Id.* And Pfizer recently announced its intent to reduce R&D efforts for small molecule drugs, specifically citing the disparity in how the Program treats biologics versus small molecule drugs. *See* Greg Slabodkin, *IRA Drives Pfizer's Decision to Focus on Biologics, Not Small Molecules*, BioSpace (Mar. 4, 2024), https://tinyurl.com/358mdnse. Pfizer's CEO recently commented that the Program "will force a lot of us to make strategic moves, not based on where the science is taking us but based on where IRA is taking us." Edited Transcript of Pfizer Inc at Goldman Sachs Global Healthcare Conference (June 10, 2024) at 10, https://tinyurl.com/4hnyrd8z.

The Program will disproportionately impact emerging biopharmaceutical companies. Many associate the term "Pharma" with the largest of the pharmaceutical manufacturers, like BMS, Janssen, Merck, Pfizer, AstraZeneca, and Eli Lilly. But behind those household names—who are responsible for delivering myriad vital drugs to market—are smaller firms of equal import. Those emerging companies typically invest more of their R&D efforts toward developing and testing *new* drugs—a risky, high-stakes operation. *See Research and Development in the Pharmaceutical Industry*, *supra*, at 3. Those emerging firms deliver critical R&D advancements. In fact, the smaller and emerging drug companies—those whose annual revenue is less than $500 million—"now account for more than 70% of the nearly 3,000 drugs in phase III clinical trials." *Id.* at 4 (citing *The Changing Landscape of Research and Development*, IQVIA Inst. for Hum. Data Sci. (Apr. 23, 2019) at 15, https://tinyurl.com/3x3ywb48). They are also to thank for an increasing number of drugs on the market: "Since 2009, about one-third of the new drugs approved by the Food and Drug Administration have been developed by pharmaceutical firms with annual revenues of less than $100 million." *Id.* (citing Ulrich Geilinger & Chandra Leo, *HBM*

New Drug Approval Report, HBM Partners, at 16 (Jan. 2019)). Because smaller and emerging pharmaceutical firms operate with less revenue and tighter margins,[4] they will suffer the most from the Program's economic disincentives.

Nor will the Program's harmful ripple effect remain confined to existing R&D and the decisions that biopharmaceutical manufacturers will inevitably make to reduce development of new medications. It will transform the landscape of investment into biotech, with far-reaching economic consequences. Start-up biotechnology companies are at the heart of new drug development, responsible for advanced, cutting-edge therapies that will transform disease treatment. But that all takes significant financial investment. Because the Program will prevent even major pharmaceutical manufacturers from recouping their R&D investment, investors will be disincentivized to fund the smaller, start-up companies that are on the front lines.

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[4] In 2014, for example, "the 25 largest drug companies received more than 70 percent of industry revenues." *Research and Development in the Pharmaceutical Industry*, *supra*, at 4.

BIO's market research shows that the Program will reduce available capital in start-up firms by 30%, which will in turn restrict the availability of working capital to fund further investments. *See IRA's Impact on the US Biopharma Ecosystem*, *supra*, at 33. That is an impact to the tune of *billions* of dollars. In one study, 76% of respondents at the grassroots level of biotech drug development reported already seeing less funding for small molecule programs compared to biologics because of the Program. *See* Steven Potts, *Measuring the Damage: IRA's Impact on Small Molecule Drug Development*, No Patient Left Behind (Mar. 31, 2024), https://tinyurl.com/mrxm34fp ["*Measuring the Damage*"]. For example, IGM Biosciences, a small clinical-stage biotechnology company, recently reported its concern that the Program's "cost containment measures . . . may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved." IGM Biosciences, Inc. Form 10-Q for Quarterly Period Ended Sept. 30, 2023 (Nov. 13, 2023), at 45, https://tinyurl.com/jzvutsw4.

The economic impacts of decreased R&D will also extend beyond reduced revenue and less R&D expenditures. Revenue loss inevitably leads to job loss. Some models predict a loss of anywhere between 66,800

and 135,900 direct jobs as well as between 342,000 and 676,000 indirect jobs in the U.S. biopharma ecosystem. *See IRA's Impact on the US Biopharma Ecosystem*, *supra*, at 2, 29–30, 40. Indeed, less than a month after forecasting concerns about profitability and product commercialization, IGM Biosciences announced a 22% reduction in its workforce "given the difficult conditions in the capital markets for our industry." *IGM Biosciences Announces Strategic Pipeline Prioritization and Cash Runway Extension*, IGM Biosciences (Dec. 5, 2023), https://tinyurl.com/yyxsj4p9.

Less revenue due to the Program's impractical pricing structure means less revenue to allocate to R&D, leading to fewer research sites, fewer researchers, fewer research programs, and fewer life-saving medications.

B. Patients will suffer because existing medications will not be expanded to additional indications and new medications will not be developed.

By employing a pricing structure divorced from market or business realities, the Program—if upheld by this Court—will inflict serious consequences on the expansion of indications for existing medications and on the development of new medications.

1. The biopharmaceutical industry is already facing cuts to research efforts in the face of the Program's misaligned mandates.

The hard data illustrates the devastating impact that the Program will have on biopharmaceutical innovation. Consider, for example, if the Program had been enacted in 2014. We can use the past ten years of revenue and R&D data to consider the real implications of the Program. And the results are stunning. One study estimates that under the Program, there would have been a 40% drop in revenue from 2014 to 2022. *See IRA's Impact on the US Biopharma Ecosystem*, *supra*, at 2. The same study also identified up to nearly 50 drug therapies that are on the market today that likely would never have made it to market under the Program's economic realities and consequences. *Id.*

The view looking forward is equally devastating. One recent survey of pharmaceutical manufacturers revealed that 78% of those manufacturers are currently planning on cancelling early-stage projects because they "no longer make sense given the short timelines before medicines could be subject to government price setting." *Inflation Reduction Act*, Pharm. Rsch. & Mfrs. of Am., https://tinyurl.com/33cuex9c (last visited July 1, 2024) ["*Inflation Reduction Act*"]. And two-thirds of

manufacturers expect to shut down pipeline projects that haven't yet made it to clinical development. *Id.*

Yet the population that suffers the most isn't manufacturers; it is the patients that need new and expanded medications to improve their quality of life and treat various conditions and diseases. Those patients will suffer because biopharmaceutical companies will have no choice but to reduce their R&D spend because of the inadequate revenue the Program provides. These are revenues that would have supported development opportunities. As mentioned above, the *conservative* estimate is that the Program's revenue reductions will result in roughly 139 drugs over the next 10 years never being developed. *See IRA's Impact on the US Biopharma Ecosystem*, *supra*, at 2. That's not just a prediction; it's already happening. The industry is already seeing companies abandon existing clinical trials, pointing to the Program as a significant influence on their clinical development decisions. *See* Suchita Shah et al., *Navigating the Inflation Reduction Act's Impact on Drug Pricing and Innovation*, Bos. Consulting Grp. (Sept. 14, 2023), https://tinyurl.com/yc7r339d ["*Navigating the Inflation Reduction Act's Impact on Drug Pricing and Innovation*"].

Manufacturers and other members of the biopharma sector cannot ignore economic realities. The Program imposes unrealistic price controls that will slash revenue, directly reducing R&D resources. In that climate, biopharmaceutical companies must make difficult choices—choosing certain diseases to research over others and triaging their shrinking pool of resources. Ultimately, patients will be the ones who suffer as fewer treatments are researched, fewer drugs make it to clinical trials, and fewer products are approved by the FDA.

2. The Program creates disincentives that disproportionately impact patients with rare diseases.

The Program's price structure disproportionately impacts patients who suffer from extremely rare diseases. Although the Program provides a negotiation exemption for orphan drugs that treat only one rare disease, that exemption creates a misaligned incentive. The exemption lasts only for as long as that orphan drug has only one indication.[5] *See Measuring the Damage*, *supra*; *IRA's Impact on the US Biopharma*

[5] An "indication" for a drug refers to the use of that drug for treating a particular disease. Drugs are approved for one indication and may later be approved for additional indications.

Ecosystem, *supra*, at 2. That structure disincentivizes manufacturers from researching additional indications for orphan drugs to expand their scope of treatment. Once a second indication is identified and approved, the drug is no longer exempted from the Program's negotiation mandate.

Put another way, the Program creates an economic incentive for manufacturers *not* to research and identify additional rare diseases that an orphan drug may treat (to preserve the orphan drugs' exemption from the Program's "negotiation" mandate). To maintain that negotiation exemption and preserve R&D resources, manufacturers will face the harsh reality that they must forego additional potential indications for drugs to ensure that they can afford future R&D. *See also NORD's Position on IRA/CMS Drug Negotiation Price Program*, Nat'l Org. for Rare Disorders (Feb. 22, 2024), https://tinyurl.com/ycsvrbxc.

3. The Program fails to account for post-approval R&D for new drug indications.

The Program will also disincentivize post-approval R&D for new drug indications—in addition to the disincentives discussed above specific to orphan drugs. The Program's price-setting provisions can commence "at pre-defined times after a medicine is initially approved," *Inflation Reduction Act*, *supra*, setting a value for a drug that fails to

account for future opportunity, thereby disincentivizing and cutting off that future R&D. There is no incentive for manufacturers to invest in post-approval R&D to develop and identify new indications for medications if the federal Government can unilaterally set a drug's price (and ostensibly determine its value) before any future research and approvals are carried out. *Id.* With drug "values" frozen in time, manufacturers will have no choice but to reduce investment of R&D for additional indications of already-approved medications.

As a practical matter, certain "indications and disease areas with assets . . . require the company to launch with an indication with a small addressable market before launching larger indications." *Navigating the Inflation Reduction Act's Impact on Drug Pricing and Innovation*, *supra*. The Program hurts development in those disease areas because it can establish a medication's price based on the small market at the time of approval, without accounting for a delayed peak in revenue and value after further R&D identifies additional indications and expands the medication's use.

And again, the impact is disproportionate—heavily affecting already-vulnerable patient populations in disease areas like oncology and

immunology. *See id.* Consider, for example, cancer treatments. Of all oncology medicines approved a decade ago, more than 60% received additional approvals *years* after their initial approval. *See Inflation Reduction Act*, *supra*. In fact, most "received a new indication seven or more years after approval." *Id.* Those later indications are critical to cancer patients, offering potentially vital and life-saving treatment options. But yet again, the Program ignores those research and market realities, setting a price benchmark for medications after initial approval and failing to account for (and therefore disincentivizing) future R&D to expand those medications' uses. "Biopharmaceutical companies have no incentive to invest in post-approval research if the government can set the price of a medicine long before companies even complete the additional research and obtain approval for the additional indication." *Id.*

Consider, too, the detrimental impact on innovation and development for small molecule drugs generally. On average, post-approval clinical trials for small molecule drugs start within three years of approval, but the indications based on those trials are not obtained until seven and a half years after the first approval. *See* Julie Patterson et al., *Unintended Consequences of the Inflation Reduction Act: Clinical*

Development Toward Subsequent Indications, 30 Am. J. Managed Care 82–86 (2024), https://tinyurl.com/ms7df6b5. But under the Program, small molecule drugs are eligible for price "negotiation" 7 years after initial approval, with the "negotiated" prices effective at 9 years post-approval. *Id.* This timeline reorients the economic incentives around R&D for small molecule drugs, forcing researchers and manufacturers to shape their development decisions around the Program's price timing and concerns about price erosion, rather than encouraging decisions that are grounded in science and patients' wellbeing. *Id.*

CONCLUSION

For these reasons, and those set forth in BMS's and Janssen's briefs, the Court should reverse the District Court's judgment.

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Respectfully submitted,

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CERTIFICATES OF COMPLIANCE

In accordance with Third Circuit Rules 28.3(d) and 46.1(e), I certify that I am a member in good standing of the bar of the United States Court of Appeals for the Third Circuit.

In accordance with Third Circuit Rule 31.1(c), I certify that the texts of the electronic brief and paper copies are identical and that Microsoft Defender was run on the file and did not detect a virus.

In accordance with Federal Rules of Appellate Procedure 29(a)(4)(G) and 32(g)(1), I certify that this brief complies with the type-volume limitations of Federal Rules of Appellate Procedure 29(a)(5) and 32(a)(7) because it contains 5,221 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(f), according to the word count of Microsoft Word for Microsoft 365. This brief also complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type-style requirements of Federal Rule of Appellate Procedure 32(a)(6) because it has been prepared in Century Schoolbook 14-point font, a proportionally spaced typeface.

Dated: July 19, 2024

/s/ Daniel G. Jarco
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CERTIFICATE OF SERVICE

I hereby certify that the foregoing brief was filed with the Clerk of the Court for the United States Court of Appeals for the Third Circuit through the appellate CM/ECF system on July 19, 2024, which will serve a notice of electronic filing to all registered counsel of record. I also certify that seven paper copies of the foregoing brief were sent to the Clerk's Office via overnight delivery.

Dated: July 19, 2024

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