United States Court of Appeals

for the

Third Circuit

Case Nos.
24-1820 & 24-1821

BRISTOL MYERS SQUIBB COMPANY,

Plaintiff-Appellants,

– v. –

XAVIER BECERRA, U.S. Secretary of Health & Human Services; CHIQUITA BROOKS-LASURE, Administrator of Centers for Medicare & Medicaid Services; U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES; CENTERS FOR MEDICARE & MEDICAID SERVICES,

Defendant-Appellees.

(For Continuation of Caption See Inside Cover)

ON APPEAL FROM AN ORDER OF THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF NEW JERSEY IN CASE NOS. 3-23-CV-3335 & 3-23-CV-3818, HONORABLE ZAHID N. QURAISHI

BRIEF OF PIONEER PUBLIC INTEREST LAW CENTER AS *AMICUS CURIAE* IN SUPPORT OF APPELLANTS AND SUPPORTING REVERSAL

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JANSSEN PHARMACEUTICALS, INC.,

Plaintiff-Appellant,

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Defendant-Appellees.

CORPORATE DISCLOSURE STATEMENT

Pursuant to L.A.R. 26.1.1, Amicus Curiae Pioneer Public Interest Law Center ("PLC" or "Pioneer Law Center") hereby discloses that it is a non-profit, non-partisan, legal research and litigation entity organized under the laws of the Commonwealth of Massachusetts that defends and promotes accountable government, economic opportunity, and educational opportunities across the country. Through legal action and public education, PLC works to preserve and enhance constitutional and civil liberties. Pioneer Institute, Inc.is the parent of PLC. PLC does not have any publicly held stock.

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INTEREST AND IDENTITY OF AMICI CURIAE[1]

Pursuant to Fed. R. App. P. 29 and L.A.R. 26.1.1, PLC hereby discloses that it is a non-profit, non-partisan, legal research and litigation entity organized under the laws of the Commonwealth of Massachusetts that defends and promotes accountable government, economic opportunity, and educational opportunities across New England and the United States. Through legal action and public education, PLC works to preserve and enhance constitutional and civil liberties. Pioneer Institute, Inc. is the parent of PLC. PLC does not have any publicly held stock.

[1] The undersigned counsel declares that (1) no party's counsel has authored this brief in whole or in part; and (2) no party, person or entity has contributed money to fund preparation or submission of this brief. The undersigned counsel for the amicus curiae has prepared and submitted this brief on a pro bono basis. Counsel and their law firm do not represent any party in this case or in a proceeding or legal transaction at issue in the present appeal. All parties have consented to the filing of this brief.

INTRODUCTION

Pioneer Law Center respectfully submits this brief pursuant to the district court's April 29, 2024, ruling. As *amicus curiae,* PLC respectfully urges the Court to reverse the New Jersey District Court's decision, enter an order in favor of the Appellants Bristol Myers Squibb ("BMS") and Janssen Pharmaceuticals ("Janssen"), and allow both companies' Motions for Summary Judgment on the Pleadings.

While the Inflation Reduction Act's ("IRA") drug policy provisions were touted as legislation that would lower healthcare costs by reducing the cost of a large basket of medications, the reality is that the IRA will devastate new drug development and innovations. Pub. L. No. 117-169, 136 Stat. 1818. The pricing structures of the IRA create incentives that will redirect research and development dollars to those drugs that are not within the mandatory price negotiation scheme of the act toward those that are either not effected or are less effected by those schemes. By this brief, amicus party Pioneer Law Center hopes to elucidate the negative policy implications of the IRA.

SUMMARY OF ARGUMENT

Pharmaceutical companies provide cutting edge beneficial healthcare to the general public. This includes creating innovative drugs and treatments for diseases and conditions. These treatments and drugs lead to a better quality of life, often

significantly extending an individual's life. However, by implementing the Drug Price Negotiation Program (the "Program") provision of the IRA, the Government vastly diminishes pharmaceutical companies' ability to perform the groundbreaking research and development that is needed for such life-saving treatments.

The lower court incorrectly ruled in favor of the appellee defendants. Credence should be given to the sweeping aftermath of the Program's implementation. There will be a significant reduction in overall revenue, leading to a meaningful decrease in funding that has otherwise historically been available for groundbreaking research and development. Additionally, the reduction of clinical trials and studies will first be multiple designated so-called orphan drugs, namely those dedicated to small populations of patients. Furthermore, the Program will cause pharmaceutical companies to devote more research and development to medications not targeted to the Medicare/Medicaid population, thereby undermining the very intent of the Program. Lastly, small-molecule drug production, which is the most efficient and highly effective for many therapies, will inevitably decrease. In contrast, biologic drugs will be favored due to their longevity in time before being subjected to the restrictions of the Program. The foregoing contortions to drug development programs will deny lifesaving and life-improving therapies to those in greatest need.

ARGUMENT

I. THE IMPLEMENTATION OF THE INFLATION REDUCTION ACT'S DRUG PRICE NEGOTIATION PROGRAM PROVISIONS WILL DEVASTATE NEW DRUG DEVELOPMENT BY DRASTICALLY SLASHING DRUG COMPANIES' RESEARCH AND DEVELOPMENT BUDGETS

The Secretary of Health and Human Services (the "Secretary") administers the Medicare program through the Centers for Medicare & Medicaid Services ("CMS"). Two specific parts of the statute are relevant for the instant analysis: Part B and Part D. Part B explicitly explains coverage for certain drugs administered as part of a physician's service and drugs furnished for use with specific durable medical equipment. Part D describes the regulations and rules for how beneficiaries are provided with prescription drug coverage. When first enacted in 2003, Part D barred the Secretary from intervening in "negotiations with drug manufacturers and pharmacies and [prescription drug plan] sponsors" and from "requir[ing] a particular formulary or institut[ing] a price structure for the reimbursement of covered part D drugs." However, Congress specifically directed the Secretary, as part of the IRA, to create the Program under the auspices of the CMS. In turn, the CMS's mandate is to negotiate maximum fair prices and, to the extent possible, reach agreement with drug manufacturers on an agreed price. Thus, the IRA: (1) creates a maximum price that the government will pay for the drugs selected to be a part of the Program; (2) instructs the CMS to negotiate to the lowest maximum price for each selected drug; and (3) imposes an excise tax on a

drug manufacturer that wishes to remain in the Medicaid/Medicare program but declines to follow the CMS maximum fair price determination for the relevant drug.

The Program will have a vastly negative effect on research and development of new drug therapies. Specifically, the Program will result in (1) a decline in drug manufacturer revenues leading inevitably to a decline in funds available for new drug research and development; (2) a curtailment of clinical trials for treatments related to treating rare diseases for which there are low patient populations; (3) a redirection of research and develop funding to drug therapies targeted to younger patient populations; and (4) a bias towards large molecule over small molecule drugs. We discuss each of these impacts seriatim.

A. A widespread decline in revenue will inevitably lead to a dramatic in reduction in research and development, stifling innovation.

The Program is poised to cause substantial losses in the research and development of new drugs. Significant downward pressure on prices will broadly affect research and development, business growth, and life cycle management. *See* Marie-Lyn Horlacher-Hecht & Andrew Kodesch et al, 3 Keys to Navigating Drug Development Under the IRA, Oliver Wyman, https://www.oliverwyman.com/our-expertise/perspectives/health/2023/june/3-keys-to-navigating-drug-development-under-the-ira.html. Notably, the healthcare consulting firm Avalere has projected a staggering potential deficit of $300 - $450 billion under the IRA. Nick Paul Taylor,

Gilead-backed study warns IRA price negotiations could hit R&D harder than expected, Fierce Biotech (Sep. 6, 2023), https://www.fiercebiotech.com/biotech/gilead-backed-study-warns-medicare-price-negotiations-could-hit-rd-harder-expected. ("The *Chicago Study*"). Since 2018, pharmaceutical companies have, as an industry, devoted 25% of their total revenues toward research and development. *See* Research and Development in the Pharmaceutical Industry, Congressional Budget Office (Apr., 2021), https://www.cbo.gov/publication/57126. Historical evidence forecasts that the decrease in revenue under the Program will lead to a reduction of approximately $75 – $112.5 billion in research and development dollars. *See* John LaMattina, Early Impact of Inflation Reduction Act on Drug Discovery, Forbes (Mar. 6, 2024), https://www.forbes.com/sites/johnlamattina/2024/03/06/early-impact-of-the-inflation-reduction-act-on-drug-discovery/. The most alarming projections by the University of Chicago indicate that the industry could experience an 8% drop in overall revenue. *See The Chicago Study*. This decline is not just a number; it translates directly to a 12.3% reduction in research and development investments. *See id.*

Research and development is the essence of pharmaceutical innovation. *See id.* It fuels the discovery of new therapies and the improvement of existing treatments, directly contributing to advancements in medicine that save lives and

improve the quality of life. *See id.* An 8% revenue drop may appear minimal, but the 12.3% cut in research and development spending is where the true danger lies. *See id.* This reduction means fewer resources dedicated to exploring groundbreaking treatments, fewer clinical trials to test the efficacy and safety of new drugs, and, ultimately, fewer medical breakthroughs. *See id.*

Additionally, while the Congressional Budget Office ("CBO") previously estimated that only 15 out of 1,300 drugs would be affected by the Program, more recent analyses paint a far grimmer picture. *See id.* Multiple studies have revealed significant inconsistencies in the initial findings. *See id*. The University of Chicago estimates that the development of 79 small molecule drugs will be halted, resulting in an estimated 116 million life years lost over the next 20 years. *See id*. This drastic reduction in research and development funding not only impedes the creation of new drugs, it also signals a broader decline in medical progress. *See id.*

Companies such as AstraZeneca and BMS have released statements explaining that clinical trials for certain drugs would have been paused if the IRA had been released earlier. *See* Jordan Cates & Katherine M. Holcomb et al, Medicare price reduction: A paradigm shift in part D access and cost, Milliman (Sep. 12, 2023), https://www.milliman.com/en/insight/medicare-price-negotiation-paradigm-shift-part-d-access-cost#6. These include drugs treating cancer and

neuromuscular diseases. *See id.* A survey conducted by the Pharmaceutical Researchers and Manufacturers of America ("PhRMA") concluded that:

> 78% expect to cancel early-state pipeline projects, 63% said they expect to shift R&D investment focus away from small molecule medicines, 95% said they expect to develop fewer new uses for medicines because of the limited time available before being subject to government price setting and 82% or more of companies with pipeline projects in cardiovascular, mental health, neurology, infectious disease, cancers and rare diseases expect "substantial impacts" on R&D decisions in these areas. This highlights the substantial and far-reaching consequences that the Program could have on the pharmaceutical industry and, by extension, on patient access to innovative treatments.

See Nicole Longo, WTAS: Inflation Reduction Act already impacting R&D decisions, PhRMA (Jan. 17, 2023), https://phrma.org/en/Blog/WTAS-Inflation-Reduction-Act-already-impacting-RD-decisions, (hereinafter "*WTAS"*).

The effects of the Program are widespread. They not only threaten the development of new treatments but also endanger the health and well-being of patients suffering from chronic disease who depend on continuous advancements in drug development. The Program's impact, therefore, must be carefully reconsidered to avoid stifling the very innovation that drives progress in our world-leading healthcare system.

B. The IRA's ambiguity regarding multi-use orphan drugs will, and already has, led to a decrease in trials and research on rare diseases.

Orphan drugs are used to "treat, prevent, or diagnose a disease that affects fewer than 200,000 people in the United States or that will not be profitable within

seven years following approval by the U.S. Food and Drug Administration (FDA)." How the Inflation Reduction Act is Impacting Rare Disease Patients, Council for Affordable Health Coverage (Mar. 1, 2023), https://cahc.net/how-the-inflation-reduction-act-is-impacting-rare-disease-patients/. The FDA has stated that "[o]rphan drugs are desperately needed by patients with rare diseases." *Id.* Congress, recognizing the importance of orphan drugs in treating rare diseases, passed the Orphan Drug Act of 1983, which incentivized drug manufactures to invest in these drugs. *Id.* The act was highly successful, with more than 650 orphan drugs developed since its passage.

The Program undermines and stymies this progress due to its ambiguous language. Under the Program, single-use orphan drugs – which treat "only *one* rare disease or condition" – are excluded from price controls. *Id.* (emphasis added). This attempt to incentivize orphan drug development fails, however, because many orphan drugs are used to treat *multiple* rare diseases. *Id.* In rare drug research, "developers often continue research on approved products for other indications and conditions" because "studying repurposed products can lead to faster access and potentially less expensive therapies for diseases in need of treatments." *Id.* Thus, multi-use orphan drugs are extremely common. *Id.* (stating that "[m]ore than 60 percent of oncology medications approved more than a decade ago, for example, received additional approvals to treat new indications in later years").

The Program makes companies less likely to develop orphan drugs because only single-use orphan drugs are protected from price negotiations. Because the majority of orphan drugs are, or will become, multi-use, "[c]ompanies are unlikely to invest in products that could be subject to limits because they are unlikely to see a return on their investment." *Id.* The rare disease market, in which it is already costly to operate, is therefore made more unfavorable by the Program.

The Program's lack of clarity has already halted crucial, potentially life-saving research. *Id.* Alnylam Pharmaceuticals, Inc. developed Amvuttra, which was approved to treat a rare disease called transthyretin-mediated amyloidosis, which affects the heart. *Id*. The company was researching if the drug could be used to treat Stargardt, an eye disease, but they shut the program down, "cit[ing] the IRA's new price controls as the reason it was stopping work on its potentially secondary use to treat the rare eye disease." *Id.* Another company, Eli Lilly, also blamed the Program for causing them to stop studying potential treatments for blood cancers, stating that the Program had changed the market so vastly, that "when we integrated those changes with this program and its competitive landscape, the program's future investment no longer met our threshold." *Id.*

C. The IRA will have a disproportionately negative impact on seniors.

The elderly population, "which accounts for a significant portion of overall healthcare and pharmaceutical drug utilization in this country," is

disproportionately impacted by the IRA. *See* Dana Goldman & Joseph Grogan et al, Mitigating the Inflation Reduction Act's Adverse Impacts on the Prescription Drug Market, USC Shaeffer (Apr. 13, 2023), https://healthpolicy.usc.edu/research/mitigating-the-inflation-reduction-acts-potential-adverse-impacts-on-the-prescription-drug-market/. Because the Program diminishes revenue, companies are less likely to continue developing drugs "that are less novel but have large consumer market." *See id.* The IRA's price control provisions therefore diminish pharmaceutical companies' incentives to develop drugs intended primarily for elderly patients. *See id.*

Seniors often require a range of treatment options because they may develop resistance to one therapy, they may experience side effects to one therapy, or they may have co-occurring conditions that rule out a particular therapy. *See* Nicole Longo, IRA Threatens Seniors' Access to Robust Treatment Options, PhRMA (Sep. 23, 2023), https://phrma.org/Blog/IRA-threatens-seniors-access-to-robust-treatment-options. According to one study, the Program will limit treatment options for seniors in the future for two reasons. First, seniors will experience more access barriers in the Medicare program. *See* IRA: Patient Options to Therapeutic Options, Hayden Consulting Group (Sept. 4, 2023), https://haydencg.com/post/potential-impact-of-the-ira-on-access-to-therapeutic-options-in-part-d. Second, the Program disincentivizes drug development in certain

classes of medications that are vital to healthcare options for seniors. *Id*. Simply put, any pricing restrictions that result in a reduction in new drug innovation will disproportionately affect seniors because they are the predominant participants in the healthcare system.

D. The Program incentivizes companies to limit their production and research of accessible and affordable drugs in favor of those that offer higher financial viability.

The Program will create perverse economic incentives that will misdirect research and development dollars away from needed therapies and towards those offering higher financial viability. There are two main types of drugs, small-molecule drugs and biologics. Ninety percent of all pharmaceuticals, such as antibiotics and blood pressure medications, are small molecule drugs. They are synthetic medications obtained by natural products. Biologics, such as vaccines, are derived from living organisms or their products. Biologics are "more time-consuming, challenging, and expensive to develop," making them less accessible, and more difficult to administer. For example, insulin is a biologic that must be injected while antibiotics are taken orally as a pill. The Inflation Reduction Act & the Small Molecule Penalty, Council For Affordable Health Coverage (Jan. 12, 2023), https://cahc.net/the-inflation-reduction-act-the-small-molecule-penalty/, (noting that small-molecule drugs are "easy and cheap to reproduce as non-branded generics once the original drug patent expires, increasing availability to patients").

Even though biologics "typically have a much larger price tag" than small-molecule drugs, the Program incentivizes companies to produce biologics. The Program has two different timelines for small molecule and biologic drugs. The timeline harshly restricts the period of time in which companies can profit from small-molecule developments. *See id.* While the Program mandates that the negotiated price for biologics will be implemented 13 years after approval, the negotiated price for small-molecule drugs will be implemented much sooner, after only nine years. *See* Michael Cohen, Inflation Reduction Act Favors Biologics Over Small Molecules: In The Long Term, This Could Partly Undermine Bill's Effort to Contain Costs, Forbes (Jan. 15, 2023), https://www.forbes.com/sites/joshuacohen/2023/01/15/inflation-reduction-act-favors-biologics-over-small-molecules-in-the-long-term-this-could-partly-undermine-bills-effort-to-contain-costs/. Because biologics have an additional four years of protection prior to price controls, "[i]nvestment will shift from small molecules to biologics, disincentivizing innovation and producing more products that are both more expensive and more difficult to administer." *Id.* (noting that biologics, unlike small-molecule drugs, are "typically not available at home, requiring infusion or injection usually in a more expensive setting like a hospital or physician's office").

This irrational penalty on small-molecule drugs will, and already has, caused the termination of small-molecule projects. *See* John Stanford, The IRA Is Already Curtailing Small Drug Development. Here's How To Reverse That, Biospace (Apr. 9, 2024), https://www.biospace.com/the-ira-is-already-curtailing-small-molecule-drug-development-here-s-how-to-reverse-that. Pfizer has announced plans to step away from small molecule treatments in its oncology and to favor the development of biological therapies. *See id;* Greg Slabodkin, IRA Drives Pfizer's Decision to Focus on Biologics, not Small Molecules, Biospace (Mar. 4, 2024), https://www.biospace.com/ira-drives-pfizer-s-decision-to-focus-on-biologics-not-small-molecules. Worryingly, Pfizer expects to decrease the percentage of small molecule drugs in its cancer portfolio from 94% to 35% by 2030. Moreover, the University of Chicago study has concluded that lower research and development spending could lead to the development of 79 fewer new small-molecule drugs over the next twenty years. *The Chicago Study*. Thus, the Program not only favors expensive, less accessible, and more difficult to administer drugs, but also stifles innovation.

The refocusing of drug research away from small molecule medications and toward biologic medications is likely to inhibit development of needed therapies. *See id.* In recent years, small molecule drugs have resulted in vital treatments for diseases such as cancer, neurogenerative, and cardiovascular diseases. *WTAS.* The

Program will create perverse economic incentives that will misdirect research and development dollars away from needed therapies and towards those offering higher financial viability.

CONCLUSION

The implications of the Program are widespread and everlasting. Research indicates that the loss of revenue due to the Program will significantly reduce pharmaceutical companies' investment in research and development. This impact will be most pronounced for small-molecule drugs and orphan drugs. The halt in research on extremely rare diseases will adversely affect around 200,000 people per rare disease. Additionally, there will be a shift to favor researching and developing drugs that focus on a younger population. The ramifications of the Program are too great to ignore and support the Appellants' constitutional claims in the underlying action.

Respectfully submitted,

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CERTIFICATION OF ADMISSION TO BAR

I, Elizabeth J. Sher, certify as follows:

1. I am a member in good standing of the bar of the United States Court of Appeals for the Third Circuit.

2. Pursuant to 28 U.S.C. § 1746, I certify under penalty of perjury that the foregoing is true and correct.

Dated: July 19, 2024

By: /s/ Elizabeth J. Sher

Elizabeth J. Sher

CERTIFICATE OF COMPLIANCE

I certify that this brief complies with the type-volume limits of the United States Court of Appeals for the Third Circuit Requirements for Briefs (https://www2.ca3.uscourts.gov/legacyfiles/chart%20of%20requirements%20for%20briefs.pdf) ("Requirements of Briefs"), as it contains 2,858 words, excluding the parts exempted; (2) this brief complies with the type face and type-style requirements of the Requirements of Briefs because it uses 14-point Times New Roman, a proportional font; (3) the attorneys whose names appear on the brief are either members of the Court's bar, or whose membership is pending, or have filed a motion for admission pro hac vice; (4) the texts of the electronic brief and the paper copies are identical; (5) and that TrendMicro, Trend Service One, was run on the file and did not detect a virus.

/s/ Elizabeth J. Sher

CERTIFICATE OF SERVICE

The undersigned certifies that on this day, she served a copy of the foregoing Amicus Brief of PLC, LLC on counsel of record for the parties hereto through the Court's CM/ECF system.

/s/ Elizabeth J. Sher

Dated: July 19, 2024