No. 25-5425

IN THE

United States Court of Appeals for the District of Columbia Circuit

TEVA PHARMACEUTICALS USA, INC., et al.,
Plaintiffs-Appellants,

v.

ROBERT F. KENNEDY, JR., in his official capacity as SECRETARY OF HEALTH AND HUMAN SERVICES; MEHMET OZ, in his official capacity as ADMINISTRATOR OF THE CENTERS FOR MEDICARE & MEDICAID SERVICES,
Defendants-Appellees.

On Appeal from the United States District Court
for the District of Columbia
No. 1:25-cv-00113-SLS
Hon. Sparkle Leah Sooknanan

BRIEF OF BAUSCH HEALTH COMPANIES INC., BRISTOL MYERS SQUIBB COMPANY, ELI LILLY AND COMPANY, JOHNSON & JOHNSON, SANOFI-AVENTIS U.S. LLC, AND BIOTECHNOLOGY INNOVATION ORGANIZATION AS AMICI IN SUPPORT OF APPELLANTS

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CERTIFICATE AS TO PARTIES, RULINGS, AND RELATED CASES

A. Parties and Amici

Except for amici who had not yet entered an appearance in this case as of the filing of Appellants' brief, all parties and amici appearing in this Court are listed in Appellants' brief.

B. Rulings Under Review.

Reference to the ruling under review appears in Appellants' brief.

C. Related Cases.

Reference to any related cases pending before this Court appears in Appellants' brief.

CORPORATE DISCLOSURE STATEMENT

As required by Federal Rule of Appellate Procedure 26.1 and D.C. Circuit Rule 26.1, Amici Curiae Bausch Health Companies Inc., Bristol Myers Squibb Company, Eli Lilly and Company, Johnson & Johnson, Sanofi-Aventis U.S. LLC, and Biotechnology Innovation Organization submit the following corporate disclosure statement.

Amici Curiae Bausch Health Companies, Inc., Bristol Myers Squibb Company, Eli Lilly and Company, Johnson & Johnson, and Sanofi-Aventis U.S. LLC, are leading biopharmaceutical research companies. The Biotechnology Innovation Organization is a trade association representing the biotechnology industry.

Bausch Health Companies Inc., Bristol Myers Squibb Company, Eli Lilly and Company, Johnson & Johnson, and Biotechnology Innovation Organization certify that there are no parent companies or publicly held companies that own a 10% or greater ownership interest of their stock. Sanofi-Aventis U.S. LLC is an indirect subsidiary of Sanofi S.A. Sanofi S.A. owns at least 10% of the stock of Sanofi-Aventis U.S. LLC. Sanofi S.A. is a public company traded on the NASDAQ under the trading symbol "SNY."

CERTIFICATE PURSUANT TO D.C. CIRCUIT RULE 29

Pursuant to D.C. Circuit Rule 29(b), undersigned counsel for amici *curiae* represents that all parties have consented to the filing of this brief.[1]

Pursuant to Rule 29(d), undersigned counsel also certifies that this separate brief is necessary. As innovators that invest billions of dollars every year to develop innovative products that prevent, treat, and cure disease, amici have a vested interest in ensuring that federal laws and policies allow crucial pharmacological innovation to continue. Amici are thus well-positioned to explain how the challenged guidance from the Centers for Medicare & Medicaid Services exacerbates the damage that the Inflation Reduction Act of 2022 caused to innovation and will result in fewer drugs entering the market, to the public's detriment.

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[1] No party's counsel authored this brief in whole or in part. No party, party's counsel, or any person other than amici or their counsel contributed money intended to fund preparing or submitting this brief.

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GLOSSARY OF ABBREVIATIONS

BIO	Biotechnology Innovation Organization
CMS	Centers for Medicare & Medicaid Services
DPNP	Drug Price Negotiation Program
FDA	Food and Drug Administration
IRA	Inflation Reduction Act of 2022
NDA	New Drug Application
R&D	Research and Development

STATUTES AND REGULATIONS

All applicable statutes and regulations are contained in the Brief for Appellants.

STATEMENT OF INTEREST

Amici Bausch Health Companies Inc., Bristol Myers Squibb Company, Eli Lilly and Company, Johnson & Johnson, and Sanofi-Aventis U.S. LLC are among the leading biopharmaceutical research companies in the world. The Biotechnology Innovation Organization is the principal trade association representing the biotechnology industry with approximately 1,000 members of all sizes (ranging from small startup companies and biotechnology centers to research universities and Fortune 500 companies). As innovators, amici invest billions of dollars to develop innovative products that improve and save people's lives. Amici share an interest in the adoption and implementation of laws and policies that foster innovation and promote the overall public health. After all, the development of new medications and treatments depends in part on innovators' ability to recoup the costs of their investments and regain sufficient capital to embark on new discoveries.

Amici believe that the Inflation Reduction Act of 2022 unlawfully upends the balance between these considerations when it subjects certain medications to forced sales at prices set by the Centers for Medicare & Medicaid Services (CMS), which in turn discourages

innovation and reinvestment. And CMS has issued implementing guidance that exacerbates these problems by sweeping in medications—in particular, ones that have been recently approved to enter the market—that Congress did not intend to subject to this regime in the IRA. Amici explain how the district court's ruling upholding the agency's guidance, if affirmed, will result in fewer drugs entering the market and ultimately decrease patients' access to innovative products.

INTRODUCTION AND SUMMARY OF THE ARGUMENT

Pharmaceutical innovators invest billions of dollars every year to develop safe and effective medications that save people's lives. But success is far from guaranteed: Only 0.02% of therapies in development are ever approved to enter the market, and only a third of those will recoup their development costs.[2] As a result, innovators have long depended on free-market sales and exclusivity rights over their products to regain the capital necessary to reinvest in future breakthrough treatments.

The Inflation Reduction Act of 2022 (IRA) departed from this settled understanding of fundamental market realities. Attempting to lower the cost of Medicare, Congress first instructed the Centers for Medicare & Medicaid Services (CMS) to identify certain medications that had been approved and marketed for a given number of years.

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[2] *See* Sandra Kraljevic et al., *Accelerating Drug Discovery*, 5 Eur. Molecular Biology Org. Reps., no. 9, 837 (2004), https://tinyurl.com/525p87tp; John A. Vernon & Joseph H. Golec, *Pharmaceutical Price Regulation: Public Perceptions, Economic Realities, and Empirical Evidence* 7 (2008), https://tinyurl.com/2k3hfyw5; U.S. Food & Drug Admin., *The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective* (Nov. 24, 2017), https://tinyurl.com/32xnaus2.

Congress then required the manufacturers of those medications to "negotiate" with CMS a "maximum fair price" for those medications. But the IRA's dubiously named "Drug Price Negotiation Program" (DPNP) allows for "negotiation" in name only. After CMS identifies a drug, it effectively gets to name the price—all with significant limitations on administrative or judicial review. The manufacturer, in turn, must accept the price and provide access to the drug at that price, or else either face crushing penalties or withdraw all its medicines from the Medicare and Medicaid programs entirely. These are choices no drug manufacturer can afford to make. So the "negotiation" between CMS and manufacturers exists only "in the Vito Corleone sense—an offer one can't refuse."[3]

Congress balanced that capacious grant of statutory authority with critical limitations on *which* medications CMS could select for price "negotiation." In particular, Congress defined "qualifying single source drugs"—what CMS must rank when selecting top-spend medications—as including only drugs that had been approved by the

[3] Daniel Hemel, *A Complete Breakdown of the Good, the Bad, and the Ugly in the Inflation Reduction Act*, Slate (Aug. 10, 2022), https://tinyurl.com/3zttxhat.

FDA and marketed for at least seven years.[4] Congress's choice to exclude newly approved medications from price "negotiation" under the DPNP's forced-sale regime shows it wanted innovators to recoup at least some meaningful portion of their multi-billion-dollar investments in new and life-saving drugs.

CMS's implementing guidance contravenes the statute's few but important limitations on this expansive program. The guidance redefines "qualifying single source drug" to include all of a manufacturer's medications with the same "active moiety" (i.e., the part "responsible for the physiological or pharmacological action")—even though that term is found nowhere in the DPNP.[5] CMS claims it can subject even *newly approved products* to the DPNP, so long as those products share the active moiety of an earlier product that had been approved for long enough to be "negotiation-eligible." The guidance effectively does away with the ineligibility period for many new medications.

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[4] In addition to small-molecule drugs, the DPNP also covers biologics. *See* 42 U.S.C. § 1320f-1(e)(1)(A). As relevant here, the DPNP treats small-molecule drugs and biologics in essentially the same way.

[5] *See* 21 C.F.R. § 314.3(b) (defining "active moiety").

The district court upheld CMS's definition of "qualifying single source drug," wrongly concluding that it was consistent with the IRA. In reality, CMS's definition contravenes the plain statutory text and is impossible to square with how Congress treats medications under other federal laws. The district court also ignored the startling ramifications CMS's guidance will have on innovation. The DPNP already stacks the decks decisively against manufacturers, distorting manufacturers' incentives to innovate in the first place. Especially considering the lopsided nature of this regime, it is important that the few statutory limits that Congress put in place be respected. As explained below, CMS's guidance runs roughshod over those limits. Indeed, because CMS's guidance means that many *brand-new* products will be immediately subject to the DPNP, if the district court's decision is affirmed, drug manufacturers will be disincentivized from innovating and developing new products—with devastating consequences for public health. Amici urge this Court to reverse the district court's opinion.

ARGUMENT

I. CMS Exceeded Its Authority By Expanding The Types Of Medicines That Congress Made Eligible For The DPNP.

Congress authorized CMS to select certain top-spend medications for price "negotiation" with limited judicial or administrative review. But Congress also constrained CMS's authority in that one-sided regime by carefully limiting the types of medications it could select. Apparently unsatisfied with an already capacious grant of power, CMS broadened the program beyond recognition, disregarding the few statutory limitations Congress put in place.

A. The DPNP's one-sided regime makes the integrity of the drug-selection phase especially critical for manufacturers.

The DPNP contemplates a three-phase process: the "drug selection phase, the negotiation phase, and (if necessary) the penalty phase." *Nat'l Infusion Ctr. Ass'n v. Becerra*, 116 F.4th 488, 495 (5th Cir. 2024). First, CMS must identify certain "negotiation-eligible" medications every year. 42 U.S.C. § 1320f-1(a)-(b). Then, the manufacturers of the selected medications must "negotiate" with CMS the "maximum fair price" for the products, *id.* § 1320f-2(a)—subject to a statutory ceiling price and Congress's directive to CMS to push for the lowest price

possible, *id.* § 1320f-3(b)(1), (b)(2)(B), and (c); *see also id.* § 1320f-3(b)(2)(C)(ii), (e) (limiting how manufacturers can negotiate). And once CMS names its final price, the negotiation ends. The manufacturer must either accept CMS's final offer or else choose between two untenable options: (1) withdrawing *all* of its products—not just selected ones—from Medicare and Medicaid entirely, or (2) paying an escalating—and crippling—"excise tax" on every domestic sale of the selected medication for each day of "noncompliance." 26 U.S.C. § 5000D(b)-(d).

In practice, there are no alternatives to accepting CMS's price. No biopharmaceutical company can function, much less thrive, if it withdraws from federal programs that account for nearly half of "nationwide spending on retail prescription drugs." Cong. Budget Off., *Prescription Drugs: Spending, Use, and Prices* 8 (2022), https://tinyurl.com/yx7e4wde. That's to say nothing of the fact that companies withdrawing from these programs would leave millions of patients without access to critical treatments. And the excise tax is so expensive that "no manufacturer could afford to pay it." *Nat'l Infusion Ctr. Ass'n*, 116 F.4th at 495. The tax can rise to 19 times the total daily

revenue of a given medication in the United States—including all sales through Medicare and in the private market. *See* Cong. Rsch. Serv., Tax Provisions in the Inflation Reduction Act of 2022 (H.R. 5376) 4 (Aug. 10, 2022), https://tinyurl.com/32wy2fyk. Both options—abandoning Medicare and Medicaid or paying the tax—are the equivalent of a "business death penalty." *Chamber of Com. of U.S. v. Whiting*, 563 U.S. 582, 617 (2011) (Breyer, J., dissenting). Although the DPNP ostensibly allows for "negotiation," in reality, it allows for anything but: Once CMS selects a medication for the DPNP, the manufacturer has so little bargaining power that it has no choice but to sell—and at CMS's price, no matter how unreasonable.

The IRA also deprives manufacturers of important procedural protections. Two features stand out. First, Congress directed CMS to "implement" the DPNP "for 2026, 2027, and 2028 by program instruction or other forms of program guidance." 42 U.S.C. § 1320f note. CMS has read that provision to exempt the program's initial implementation from the Administrative Procedure Act's notice-and-comment requirements, 5 U.S.C. § 553(b), (c), which the Social Security Act otherwise requires the agency to follow in Medicare rulemaking, 42

U.S.C. § 1395hh. *See Nat'l Infusion Ctr.*, 116 F.4th at 495-96.[6] Not just that, but CMS also claims it can revise its guidance without prior notice, depriving manufacturers of the opportunity to explain how CMS's chosen prices for drugs would impact them. *See id.* at 496. Second, Congress has insulated certain key CMS determinations from "administrative or judicial review," including CMS's "selection of drugs" and determinations of "negotiation-eligible drugs" and the "maximum fair price" of the selected drugs. 42 U.S.C. § 1320f-7.

These two features, in combination, allow CMS to name its price on the selected medication and reject a manufacturer's counteroffer—all "without notice and comment and insulated from administrative or judicial review." *Nat'l Infusion Ctr.*, 116 F.4th at 503. The result is clear: The DPNP affords innovators no room to negotiate with CMS and no opportunity for review of critical decisions.

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[6] *See also* CMS, *Medicare Drug Price Negotiation Program: Revised Guidance, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026*, at 8-11 (June 30, 2023), https://tinyurl.com/msu4fck4 ("Revised Guidance"); CMS, *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026*, at 1-2 (Mar. 15, 2023), https://tinyurl.com/yc5e86cd.

B. CMS's guidance unlawfully redefines key features of the DPNP.

Even if this one-sided regime were constitutionally tolerable, it would be critical for CMS to strictly confine its actions to the compromise that Congress struck in the IRA. "Passing a law often requires compromise, where even the most firm public demands bend to competing interests." *N.L.R.B. v. SW Gen., Inc.*, 580 U.S. 288, 306 (2017). And "[c]ourts and agencies must respect and give effect to these sorts of compromises," which reflect Congress's best attempt to deal with "groups with marked but divergent interests." *Ragsdale v. Wolverine World Wide, Inc.*, 535 U.S. 81, 93-94 (2002). Neither the district court nor CMS has done so here.

1. The IRA directs CMS to rank Medicare's top-spend, "negotiation-eligible drugs" and select a certain number for price "negotiation." 42 U.S.C. § 1320f-1(a), (b)(1)(A), (d)(1). But instead of giving the agency boundless discretion to do so, Congress prescribed specific criteria for identifying those medications—that is, the top 50 highest-spend "qualifying single source drugs." *Id.* § 1320f-1(e)(1). Congress defined "qualifying single source drug" as a drug that (1) "is *approved* [by the FDA] … and is marketed pursuant to such approval";

(2) "for which, as of the selected drug publication date … at least 7 years will have elapsed since the date of such approval"; and (3) that is "not the listed drug for any drug that is approved and marketed" as a generic. *Id.* § 1320f-1(e)(1)(A) (emphasis added). Put simply, Congress tied the eligibility of the medications to their particular applications for FDA "approval," such that a drug might be eligible for the DPNP only if it had already been marketed for at least seven years under its new drug application ("NDA"). *See* Appellants' Opening Br. 20-29.

Those limitations reflect Congress's attempt to balance the "competing interests" at issue, *SW General, Inc.*, 580 U.S. at 306—such as manufacturers' need to recoup their investments, which they could then reinvest into researching future medicines, and the government's desire to lower the cost of Medicare. *See infra* 18 (discussing the Hatch-Waxman Act as an example of how Congress has balanced the interests elsewhere). Especially because the IRA stacks the decks so decisively against manufacturers, it is critical for this Court to ensure that CMS complies with the few statutory limitations that Congress prescribed.

Yet CMS's implementing guidance strays far away from this plain text. The guidance redefines "qualifying single source drug" to include

"all dosage forms and strengths of the drug with the same active moiety and the same holder of" an NDA, "inclusive of products that are marketed pursuant to different" applications.[7] Put more simply, when identifying potential "qualifying single source drugs," CMS will aggregate all of a manufacturer's products that have the same active moiety into one fictional "super drug," regardless of whether each distinct product may have only recently obtained FDA approval under its own regulatory application.[8] So a newly approved drug may be deemed eligible for the DPNP *well before* its seven-year period has expired so long as it has the same active moiety as another marketed drug from the same manufacturer that the FDA approved at least seven

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[7] *See* CMS, *Medicare Drug Price Negotiation Program: Final Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2027 and Manufacturer Effectuation of the Maximum Fair Price in 2026 and 2027 for Initial Price Applicability Year 2026*, at 167-68 (Oct. 2, 2024), https://tinyurl.com/52a6e8c7 ("Final Guidance"); *see also* Revised Guidance*, supra* note 6 at 99.

[8] Final Guidance, *supra* note 7 at 168-69. To be sure, CMS treats so-called "fixed combination drugs," 21 C.F.R. § 300.50, slightly differently. *See* CMS, *Medicare Drug Price Negotiation Program: Final Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2028 and Manufacturer Effectuation of the Maximum Fair Price in 2026, 2027, and 2028*, at 167 (Sep. 30, 2025), https://tinyurl.com/2exc6t88.

years ago. That is true even if, for example, the new drug treats a different condition or is administered differently.

2. The district court sided with CMS in part because it reasoned that Teva's interpretation of "qualifying single source drug" could lead to so-called "product hopping"—where manufacturers allegedly alter their products and shift patients to new versions to extend the statutory ineligibility period. JA191. But this "policy concern[] cannot override the text" of the IRA, *Pacific Gas & Electric Co. v. FERC*, 113 F.4th 943, 950 (D.C. Cir. 2024)—which, as discussed, does not allow for CMS's definition of "qualifying single source drug." The concern is also overstated. A newly approved product would not prevent CMS from selecting the original for price "negotiation." Accordingly, there is no actual "extension" of the statutory ineligibility period. Further, if product hopping, which critics claim enables manufacturers to unfairly extend market protections over their products, were a serious problem, one would expect to see fewer generics entering the market. But the empirical data refutes that reality: "Generic competitors over the past 25-30 years have experienced no increasing delays in entering the

market" and have actually "consistently been gaining market share."[9] In fact, "91% of all prescriptions in the United States are filled as generic drugs."[10]

Moreover, product-hopping concerns ignore economic realities. The process of submitting an NDA and obtaining approval for a new product is "both onerous and lengthy." *Mut. Pharm. Co. v. Barlett*, 570 U.S. 472, 476 (2013). Indeed, it takes years for manufacturers to gather the evidence and obtain FDA approval of a modified product. *See id.*; 21 U.S.C. § 355(c); *cf.* 21 C.F.R. § 314.70(b). And that post-approval research and development (R&D) results in products that transform care and add value. Manufacturers would not embark on this costly, uncertain, and lengthy R&D process if they did not believe that the new product was likely to be beneficial for patients to use instead of the original one. Thus, the policy concern that manufacturers would

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[9] Biotechnology Innovation Org., Comments of the Biotechnology Innovation Organization (BIO) in Response to the USPTO Request for Comments on USPTO Initiatives to Ensure the Robustness and Reliability of Patent Rights 6 (Feb. 1, 2023), https://tinyurl.com/yc8t7nzs.

[10] U.S. Food & Drug Admin., Office of Generic Drugs 2022 Annual Report 1 (2023), https://tinyurl.com/3syhfh9z.

engage in product hopping just to avoid being subjected to the DPNP has no basis in fact.

In any event, the district court's logic gives short shrift to the policy concerns on the other side of the ledger. If CMS's guidance is upheld, it will have lasting and detrimental effects on manufacturers' ability to innovate—beyond those the IRA already caused. Take, for example, a manufacturer that discovered a particular molecule ("Molecule A"), which it hoped would be effective in fighting skin cancer. After extensive trial-and-error, the manufacturer developed the medication—call it Product AB®—which FDA approved in 2014 and quickly became a standard treatment for melanoma. Now imagine that scientists also believed that "Molecule A" could yield other benefits. After years of further testing, the manufacturer discovered that its product also results in weight loss. In 2024, FDA approved the anti-obesity indication as Product ABD®. Because the manufacturer marketed Product AB®—the melanoma medication—for more than a decade, that medication might be a "qualifying single source drug" and thus eligible for the DPNP. But the same is not true for Product ABD®, which FDA *approved* recently under a distinct application.

Yet under its guidance, CMS could unilaterally force Product ABD® to be sold at slashed prices from the very moment it enters the market—simply because it shares "Molecule A" with Product AB®. Never mind that the manufacturer has not been able to rely on the free market to advertise and sell the new product under the recently approved application. And never mind the years and hundreds of millions of dollars expended to develop and rigorously test Product ABD®'s new indication. By forcing Product ABD® to be sold at prices set by CMS shortly after it enters the market, CMS makes recoupment of that investment effectively impossible.

CMS's aggregation of distinct, separately approved medications makes it virtually impossible for innovators to recoup a portion of their investments and to continue to innovate, reinvest, and develop new products. Thus, contrary to the district court's logic, it is CMS's guidance, not Teva's interpretation, that would render the IRA "self-defeating." JA191 (quoting *Pugin v. Garland*, 599 U.S. 600, 607 (2023)).

Further, the district court also failed to grapple with the fact that CMS's interpretation cannot be squared with other federal laws, which similarly recognize that distinct products should be treated separately

in order to incentivize innovation. For example, the Hatch-Waxman Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984), and the Biologics Price Competition and Innovation Act (BPCIA), Pub. L. No. 111-148, § 7001, 124 Stat. 119, 804 (2010), authorize an abbreviated path to FDA approval for generics and biosimilars so long as these products are tied to the innovator's *distinct* NDAs or Biologics License Applications (BLAs). *See* 21 U.S.C. § 355(j)(2)(A)(ii), (iv); 42 U.S.C. § 262(k)-(*l*); *see also* Appellants' Opening Br. at 22-23 (discussing the statutory scheme for generic competition). By operating on a product-by-product basis, each law reflects Congress's longstanding commitment to *both* making safe and effective treatments more accessible to patients *and* fostering innovation. CMS's guidance and its aggregation of different products accordingly breaks with the balance struck by Congress's successful Hatch-Waxman and BPCIA regimes.

* * *

In issuing guidance that substantially broadens the sweep of the IRA, CMS has failed to act "within its statutory authority." *Loper Bright Enters. v. Raimondo*, 603 U.S. 369, 412 (2024). CMS has taken it upon itself to target medications beyond those that Congress intended

and drastically slash their prices, often by more than 50 percent.[11] Thus, CMS's (re)definition of "qualifying single source drug" contradicts the IRA's text and the negotiated compromises underlying that legislation. And where, as here, the agency has failed to "respect and give effect to these sorts of compromises," it is this Court's job to vindicate Congress's intent and reject the agency's unauthorized expansion of the statute. *Ragsdale*, 535 U.S. at 94.

II. CMS's Guidance Stifles Innovation And Harms The Public Health.

CMS's guidance discourages the development of new products and harms the public health. By defining "qualifying single source drug" in a manner that bundles different products, regardless of when they are approved to enter the market, CMS has paved the road for having fewer medications that improve and save people's lives. The distorting effect the guidance will have on innovation is too significant to be cast aside.

[11] *See* CMS, *Medicare Drug Price Negotiation Program: Negotiated Prices for Initial Price Applicability Year 2026*, at 2 (Aug. 2024), https://tinyurl.com/yfj2wjn9.

A. Innovating new indications and compositions improves patients' lives.

Before explaining how CMS's guidance threatens innovation, we provide a short primer about the countless ways drug manufacturers continue to innovate even after a drug is initially approved.

Indications. An "indication" is a medical condition that a drug is used to treat or prevent. For example, a drug indication of insulin is Type 2 diabetes. Often, as a result of extensive research and clinical testing, one drug will have more than one indication, meaning that it can be used to treat more than just one condition. For example, the FDA has approved tirzepatide medications to lower blood glucose for patients with Type 2 diabetes *and* to treat obesity and obstructive sleep apnea. Or as in the hypothetical above, the two indications of Product AB® and ABD® are cancer and obesity.

Before or after the FDA approves a drug for one indication, that drug's manufacturer often begins post-approval research of additional indications.[12] That is for good reason: Post-approval research and

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[12] Partnership for Health Analytic Research, *Implications of the Inflation Reduction Act Price Setting Provisions on Post-approval Indications for Small Molecule Medicines* 12 (2023), https://tinyurl.com/mr2yzuft.

development for new indications is "vital to addressing unmet needs for patients."[13] For example, "a medicine approved to treat asthma in adults may be studied post-approval for safety and efficacy in children."[14] Similarly, the manufacturer of a medicine that treats a rare disease may find that the medicine is "relevant to multiple diseases."[15] The benefits of this post-approval innovation are real. One recent study concluded that 63% of medicines first approved as orphan drugs—that is, drugs approved to treat a single rare disease or condition—"were awarded at least one post-approval indication."[16]

Drug compositions, presentations, and delivery mechanisms. A drug's pharmaceutical composition, presentation, and delivery mechanism relate to both how (and how often) the drug is administered (e.g., capsule or intravenous injection) and its physical features. These key characteristics of a medication matter greatly to patients, as they affect the ease of the medication's administration, including how and when a patient consumes it. Unsurprisingly,

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[13] *Id.* at 4.

[14] *Id.* at 3.

[15] *Id.* at 3-4.

[16] *Id.* at 2.

patients prefer—and are more likely to take—medicines that are easy to consume or use. And convenience is essential and can have a real impact for patients.

There are countless real-life examples of the benefits of this innovation. Take for example Gilead Sciences Inc.'s long-acting antiviral medication for HIV prevention, lenacapavir, which requires only twice-a-year dosing.[17] Prior to lenacapavir, antiviral medications for HIV prevention required more frequent administration.[18] Another example is Neurelis's diazepam nasal spray, which treats acute repetitive seizures. The nasal spray served as an easier-to-administer alternative to diazepam rectal gel.[19] Similarly, Arecor Therapeutics is developing a new version of insulin that accelerates the drug's absorption and thus requires smaller amounts for each injection than

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[17] Julia Paik, *Lenacapavir*: *First Approval*, 82 Drugs 1499 (2022), https://tinyurl.com/3unhrj7b.

[18] Giovanni Di Perri, *Pharmacological Outlook of Lenacapavir: A Novel First-in-Class Long-Acting HIV-1 Capsid Inhibitor*, La Infezioni in Medicina, 495, 498 (2023), https://tinyurl.com/mryaf8nn.

[19] R. Edward Hogan et al., *Bioavailability and Safety of Diazepam Intranasal Solution Compared to Oral and Rectal Diazepam in Healthy Volunteers*, Epilepsia (2020), https://tinyurl.com/4mx6hken.

previous insulin products.[20] Finally, consider Mitsubishi Tanabe Pharma America, Inc.'s medication, edaravone, which treats patients with amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease), a motor neuron disease. In 2017, FDA approved edaravone for daily intravenous (IV) infusion in ALS patients in medical settings.[21] But subsequent R&D resulted in FDA approval of an oral version of edaravone, allowing patients to receive treatment in their own homes.[22]

Each of these new products, all of which require separate FDA approvals under their own applications, ensure that patients not only will take but also benefit from the drug. These innovations transform people's lives.

Innovating new indications, as well as the compositions, presentations, and delivery mechanisms of new products. Market

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[20] Arecor Therapeutics plc, *AT278 Ultra-Concentrated Ultra-Rapid Acting Insulin Demonstrates Superiority in Phase 1 Clinical Trial in Overweight and Obese People with Type 2 Diabetes* 1 (May 20, 2024), https://tinyurl.com/2p8k2mjf.

[21] FDA News Release, *FDA Approves Drug to Treat ALS* (May 5, 2017), https://tinyurl.com/bde9p87b.

[22] Mitsubishi Tanabe Pharma America, Inc., *Mitsubishi Tanabe Pharma America Presents 48-Week Results from Global Phase 3 Safety Clinical Study of RADICAVA ORS® (edaravone), an Oral Treatment for ALS* (June 1, 2022), https://tinyurl.com/49neccx8.

demand and unmet needs spur market participants to search for innovative solutions. Pharmacological innovation—including searching for new indications and developing new and improved versions of existing drugs—is no exception. For example, when a disease or condition lacks an adequate treatment, innovators either develop new medications or search for new indications for existing drugs.[23] This "[d]evelopment of and regulatory approval of new uses of already-approved drugs and biologics is an important source of innovation by biopharmaceutical firms."[24] Likewise, where the drug presentation or delivery mechanism is burdensome and patient adherence to the treatment is accordingly low, innovators seek to develop a new composition, presentation, or delivery mechanism of the drug.[25]

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[23] *See, e.g.*, JP Hughes et al., *Principles of Early Drug Discovery*, 162 Brit. J. Pharmacology 1239 (2011), https://tinyurl.com/5n6b8cyz; Joseph A. DiMasi, *Innovating by Developing New Uses of Already-Approved Drugs: Trends in the Marketing Approval of Supplemental Indications*, 35 Clinical Therapeutics 808, 809 (June 2013), https://tinyurl.com/5yhr7s4w.

[24] *Id.* at 818.

[25] Anjali D. Deshmukh, *Redefining Innovation for Pharmaceutical Regulation*, 104 B.U. L. Rev. 577, 583 (Mar. 2024); *see also* Shanta Afrin & Vikas Gupta, *Pharmaceutical Formulation*, StatPearls (2023), https://tinyurl.com/26r2er25.

Thus, drug manufacturers are constantly innovating to find new, better ways to improve patients' health. But pharmaceutical innovation is not easy—or cheap. It requires a great deal of scientific knowledge, time, and money. In searching for innovative solutions, manufacturers make critical decisions early in the drug development process, and those decisions dictate the path to approval. In the development stage, for example, manufacturers determine the drug composition, presentation, and delivery mechanism they intend to pursue and test in subsequent clinical trials.[26] Those decisions matter greatly because FDA's ultimate approval of the medication is generally limited to the indication and version of drug tested during that drug's development. Any subsequent indication or new version must undergo its own approval, which can require companies to restart the entire R&D process—all the way from the initial research to the testing in animals and then humans.[27]

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[26] Gail A. Van Norman, *Drugs, Devices, and the FDA: Part 1*, 1 JACC: Basic to Translational Science no. 3, 172 (Apr. 2016), https://tinyurl.com/4893zahc.

[27] *Id*. at 172, 175.

Drug development typically takes ten to 15 years and costs over two billion dollars on average.[28] For example, since 2016, J&J has invested $90 billion in medical innovation through continuous R&D.[29] Similarly, Lilly invested more than $10 billion for *each* new FDA-approved molecular entity it brought to market from 2006 to 2014.[30] And every year, Lilly re-invests 25% of its revenue into research and development of future medical breakthroughs, including more than $10 billion in 2024 alone. Also in 2024, Sanofi invested approximately €7.4 billion in R&D, and €6.5 billion the year before. Bristol Myers Squibb Company invested more than $11.2 billion in research and development in 2024.

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[28] BIO, *The U.S. Bioscience Industry: A Power Engine for State Economies* 18 (2025), https://tinyurl.com/4f8t827e; *see also* Duxin Sun et al., *Why 90% of Clinical Drug Development Fails and How to Improve It*, 12 Acta Pharmaceutica Sinica B 7, 3050 (July 2022), https://tinyurl.com/zxj4y28p.

[29] Johnson & Johnson, *U.S. Pricing Transparency Report* 2 (2024), https://tinyurl.com/3p52hs4u.

[30] A. Schuhmacher et al., *Changing R&D Models in Research-Based Pharmaceutical Companies*, 14 J. Transl. Med. 105 (2016), https://tinyurl.com/53rkbh9a.

Thus, innovation is complex and expensive, and significant trial and error is involved.[31] There is, after all, no guarantee whatsoever that manufacturers will succeed. And risk must be incentivized, not discouraged. Among other things, manufacturers must balance competing considerations throughout the development process, including whether to trade-off some of the drug's efficacy with its safety (and, if so, how much), while simultaneously accounting for the cost and feasibility of production. Moreover, drugs that secure FDA approval represent only a minute fraction of the therapies developed and put into preclinical and clinical testing. Recall that a mere 0.02% of drugs that go into preclinical testing end up receiving FDA approval for

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[31] Pauric Bannigan et al., *Machine Learning Directed Drug Formulation Development*, 175 Advanced Drug Delivery Revs. 12 (2021); *see also* Zeqing Bao et al., *Revolutionizing Drug Formulation Development: The Increasing Impact of Machine Learning*, 202 Advanced Drug Delivery Reviews 2 (2023) ("However, the design and development of advanced pharmaceutical products is a complex process that requires significant time, resources, and expertise. This complexity arises from numerous factors, including the need to consider various parameters related to the drug, excipients, and manufacturing conditions within a high-dimensional design space.").

therapeutic use—and only one in three of that minute percentage will ever recoup its development costs.[32]

New indications and new easier-to-administer products that patients will actually take are win-wins for innovators and patients alike.[33] Commercial success means that innovators can recoup the return on their investments, reinvest profits on additional R&D, and celebrate the societal benefits of their discoveries. It also means better and improved lives for patients and, in some cases, the difference between life and death. Indeed, a new indication gives hope to millions of patients suffering from otherwise untreated diseases or conditions, and a new drug composition, presentation, or delivery mechanism can offer more effective and safer medication, as well as a treatment plan that patients are more likely to follow. Put simply: When

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[32] *See* Vernon, *supra* note 2 at 7; Kraljevic, *supra* note 2 at 837.

[33] *See* Andrew Powaleny, *3 Things to Know About the Importance of Post-Approval Research and Development*, PhRMA (Dec. 6, 2021), https://tinyurl.com/4xhcnube ("Many of these advances that occur following initial FDA approval have resulted in increased survival rates, improved patient outcomes and enhanced quality of life for patients with cancer, autoimmune diseases and rare diseases, among others.").

manufacturers can adequately recoup their investments, innovation and better patient care invariably follow.

B. CMS's guidance disrupts much-needed innovation.

As just discussed, medications that achieve commercial success after extensive R&D enable the next generation of innovation. By the same token, if a product becomes eligible for price "negotiation" prematurely (or for that matter, immediately upon approval), a manufacturer is even less likely to recoup its development costs for the product and is accordingly less able to reinvest in future innovations.[34] This is what likely would happen to our hypothetical manufacturer: the manufacturer might not be able to recoup the R&D investments that led to the development of Product ABD®. CMS's guidance, in other words, upends the incentives that make innovations like those possible.

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[34] Allison Hickman, *When Eating the Rich Has Consequences: The Potential Long-Term Effects of the Inflation Reduction Act's Drug Price Negotiation Program*, 11 Emory Corporate Governance and Accountability Review Perspectives 14, 17 (2024), https://tinyurl.com/yxzd7zuh ("The question… is how to conduct necessary drug testing trials when they may not make returns on developmental costs because of the future drastic increase in revenue by the implementation of the DPNP. A potential answer, unfortunately, might be to limit research and development … funding for niche medication.").

As discussed above, CMS defines "qualifying single source drug" to include all of the manufacturer's approved products with the same active moiety. *See supra* I.B. This means that new and completely distinct products will become eligible for DPNP's forced-sale regime at the same time as their already approved counterpart. That practical effect of CMS's guidance will lead to reduced investment in subsequent generations of drug development. For it to be even possible to justify continued innovations, innovators need sufficient time on the free market—unencumbered by forced sales—to financially justify their expenditures and arrive at a place where they are able to reinvest in new R&D.[35] By depriving innovators of this much-needed time, CMS's guidance will cause fewer drugs to enter the market, denying patients and their caretakers access to innovative products. Rare and untreated conditions will remain just that. And even as to those conditions for which an approved treatment is already available, patients might have no choice but to rely on versions of existing drugs that are hard to administer or to use—resulting in less patient adherence to lifesaving

[35] Tomas J. Philipson et al., *The Impact of Price Setting at 9 Years on Small Molecule Innovation Under the Inflation Reduction Act*, U. of Chi., at 7 (Oct. 2023), https://tinyurl.com/y8z79hjc.

treatment plans. Thus, CMS's guidance will negatively impact our Nation's overall public health.

Consider XARELTO®, a Janssen Pharmaceuticals, Inc. medication, as an example. In 2011, FDA approved the tablet form of XARELTO® to treat blood clots (NDA 022406). Janssen's subsequent R&D resulted in an additional approval for XARELTO®, pursuant to a separate NDA (NDA 215859), in 2021. The 2021 approval for XARELTO® is an oral suspension indicated to treat blood clots or reduce the risk of blood clots in children. Although the two separate versions of XARELTO® required their own R&D (and accordingly substantial investments of funds by Janssen), and FDA approval pursuant to separate NDAs, they share the same active moiety. Accordingly, when CMS selected the 2014, initial tablet form of XARELTO® for inclusion in the DPNP in 2023, the oral suspension form of the drug also became subject to the DPNP, even though it received FDA approval only in 2021.

Another example is STELARA®, a Janssen Biotech, Inc. biological medication. FDA initially approved STELARA® to treat psoriasis in 2009 (BLA 125261). Further development of STELARA® resulted in

multiple FDA approvals, via supplemental BLAs, for additional indications, including psoriatic arthritis, psoriasis in patients 12 years and older, and psoriasis and psoriatic arthritis in patients six years and older. These versions of STELARA® come in vials or prefilled syringes, allowing patients to receive treatment at home. In 2016, STELARA® received an additional FDA approval—pursuant to a separate BLA (BLA 761044)—to treat Crohn's disease and, three years later, to treat ulcerative colitis. This version of STELARA® is either injected in patients subcutaneously (i.e., through the skin) or administered via an IV. In total, Janssen invested two decades and hundreds of millions of dollars into R&D of STELARA® and conducted more than 100 clinical trials to identify the safest and most effective uses of the drug's active ingredient. In 2024, FDA selected STELARA® for inclusion in the DPNP. Because the later-approved indications of STELARA® share the same active ingredient as the original version of the biological medication (despite having a different BLA), they too were included in FDA's selection. That means that STELARA® products approved after 2009 became subject to the DPNP well in advance of their 11-year ineligibility period expiry. For example, the STELARA® product that

treats ulcerative colitis, which was approved in 2019 after substantial investment by Janssen, became subject to the IRA's forced-sale regime in 2024, rather than 2030.

This kind of aggregation of different treatments is not only unfair but also will have lasting effects on pharmacological innovation and patient access. One study estimates, for example, that the DPNP will "reduce overall annual cancer R&D spending by about $18.1 billion, or 31.8%."[36] In another study, researchers concluded that the IRA's reduction of innovation of small-molecule drugs will result in a loss of 116 million life years due to missed opportunities for health improvement.[37] And these studies were focused on the IRA's consequences, without even accounting for CMS's attempt to sweep more medications prematurely into the DPNP.

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[36] Tomas J. Philipson et al., *Policy Brief: The Impact of Recent White House Proposals on Cancer Research*, U. of Chi., at 1 (June 2022), https://tinyurl.com/nufwucj8.

[37] The study concluded that the absence of small molecule innovation resulting from the IRA will result in 188 fewer small molecule treatments, including 79 fewer new small molecule drugs and 109 fewer post-approval indications for these drugs. *See* Philipson, *supra* note 35, at 3.

These impacts are already being felt. One recent study estimated that following the passage of the IRA, the "average monthly number of industry-sponsored trials on post-approval drugs decreased by 38.4%."[38] Another study suggested that there has been an "overall decline in industry-funded post-approval clinical trials in oncology drugs" following the IRA's passage.[39] And there is evidence that the DPNP already has caused manufacturers to "shelve promising new medical treatments."[40] For example, Alnylam Pharmaceuticals announced that it would not start clinical trials for a rare genetic eye disease treatment, "as the company 'continues to evaluate the impact of the [IRA].'"[41] Likewise, Lilly has publicly stated that the IRA caused it to deprioritize

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[38] Hanke Zheng et al., *The Inflation Reduction Act and Drug Development: Potential Early Signals of Impact on Post-Approval Clinical Trials*, 59 Therapeutic Innovation & Regulatory Science 781, 781 (2025), https://tinyurl.com/mryc2pkr.

[39] Hanke Zheng et al., *Early Impact of the Inflation Reduction Act on Small Molecule vs. Biologic Post-Approval Oncology Trials* at 4, Health Affairs Scholar (2025), https://tinyurl.com/yrpv42ah.

[40] Brad Watts & Katie Mahoney, *Why We're Suing HHS and CMS to Challenge Illegal Price Controls*, U.S. Chamber of Commerce (July 12, 2023), https://tinyurl.com/4nw64v9w.

[41] Jonathan Saltzman, *Alnylam Decides to 'Pause' Drug Trial, Citing New Federal Pricing Law*, Boston Globe (Oct. 27, 2022), https://tinyurl.com/3eucw3e9.

three drugs in development, and would have undermined Lilly's research on existing small-molecule drugs if the IRA had come into effect earlier.[42] Novartis and Genentech also have warned that the IRA's DPNP has negatively impacted investment and research into cancer treatments.[43]

This is just the beginning. By allowing CMS to unduly expand the definition of "qualifying single source drug" and bundling different products regardless of their date of FDA approval, the district court's decision has made things worse for innovators and patients across the country.

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[42] Jessica Merrill, *Lilly Sidelined Three Drugs Due to IRA, CEO Rick Says*, Pink Sheet Citeline Regulatory (June 14, 2023), https://tinyurl.com/3scrudf2.

[43] *See* Watts, *supra* note 40.

CONCLUSION

This Court should reverse the district court.

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I hereby certify that I electronically filed the foregoing with the Clerk of the Court for the United States Court of Appeals for the District of Columbia Circuit by using the appellate CM/ECF system on January 16, 2026.

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