IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

TEVA PHARMACEUTICALS USA, INC.; TEVA BRANDED PHARMACEUTICAL PRODUCTS R&D, INC, Plaintiffs, v. ROBERT F. KENNEDY JR., in his official capacity as SECRETARY OF HEALTH AND HUMAN SERVICES, *et al.*, Defendants.	§	Civil Action No. 1:25-cv-00113-SLS

BRIEF OF AMICI BAUSCH HEALTH COMPANIES INC., ELI LILLY AND COMPANY, JOHNSON & JOHNSON, PFIZER INC., SANOFI-AVENTIS U.S. LLC, AND BIOTECHNOLOGY INNOVATION ORGANIZATION IN SUPPORT OF PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT

CORPORATE DISCLOSURE STATEMENT

I, the undersigned, counsel of record for Amici Bausch Health Companies Inc., Eli Lilly and Company, Johnson & Johnson, Pfizer Inc., Sanofi-Aventis U.S. LLC, and Biotechnology Innovation Organization, certify that to the best of my knowledge and belief, there are no parent companies, subsidiaries, affiliates, or companies which own at least 10% of the stock of Bausch Health Companies Inc., Eli Lilly and Company, Johnson & Johnson, Pfizer Inc., and Biotechnology Innovation Organization which have any outstanding securities in the hands of the public. The following are parent companies, subsidiaries, affiliates, or companies which own at least 10% of the stock of Sanofi-Aventis U.S. LLC which have any outstanding securities in the hands of the public.

Sanofi S.A. is an indirect parent of Sanofi-Aventis U.S. LLC. Sanofi S.A.'s stock is publicly traded on the NASDAQ under the trading symbol "SNY."

These representations are made in order that judges of this Court may determine the need for recusal.

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INTEREST OF AMICI CURIAE[1]

Amici curiae Bausch Health Companies Inc., Eli Lilly and Company, Johnson & Johnson, Pfizer Inc., and Sanofi-Aventis U.S. LLC are among the leading biopharmaceutical research companies in the world, and the Biotechnology Innovation Organization (BIO) is the principal trade association representing the biotechnology industry with approximately 1,000 members of all sizes (including small startup companies and biotechnology centers, as well as research universities and Fortune 500 companies). As innovators, *amici* invest billions of dollars every year to develop innovative products that prevent, treat, and cure disease, and thus improve and save people's lives. *Amici* share an interest in the adoption and implementation of laws and policies that increase patient access to their groundbreaking medications, while also fostering innovation and promoting the overall public health. After all, the development of new medications and treatments depends in part on the 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 fails to strike the right balance between these considerations, subjecting certain medications to price controls, which in turn discourages innovation and the reinvestment in future breakthrough treatments. The Centers for Medicare & Medicaid Services issued an implementing guidance that stifles innovation even further by sweeping in medications that Congress did not intend to subject to price controls, particularly products that have been recently approved to enter the market. *Amici* explain below how the guidance, if upheld, will result in fewer drugs entering the market and ultimately decrease access to innovative products.

[1] The parties have consented to the filing of this amicus brief. No party's counsel authored this brief in whole or in part. No party, party's counsel, or any person other than amicus and its counsel contributed money intended to fund preparing or submitting this brief.

INTRODUCTION

Pharmaceutical innovators invest billions of dollars every year to develop safe and effective medications that improve and save people's lives. But as is often the case with innovation, success is not guaranteed. Only 0.02% of therapies in development are approved to enter the market, and only a third of those will ever recoup their development costs.[2] Innovators have long relied on free-market pricing and exclusivity rights over their products to make critical development decisions and regain the capital necessary to invest in future lifesaving treatments. The Inflation Reduction Act of 2022 (IRA) dramatically departed from this settled understanding of fundamental market realities. Attempting to lower the cost of Medicare, Congress instructed the Centers for Medicare & Medicaid Services (CMS) to identify top-spend medications that had been marketed for a certain number of years, and then ordered the manufacturers of those medications to "negotiate" with CMS the maximum price they would be allowed to charge Medicare-insured patients.

But there is no "negotiation" in the dubiously named Drug Price Negotiation Program (DPNP). Once CMS identifies a drug, it gets to name its price. Under the DPNP, a manufacturer must agree on the selected medication's maximum price by a certain deadline or else pay a crushing "excise tax" on all domestic sales of that medication for each day on which there is no agreed-upon price. So the "negotiation" between CMS and manufacturers exists only

[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.

"in the Vito Corleone sense—an offer one can't refuse."[3] But that's not all. DPNP's implementation is also insulated twice over. CMS implemented DPNP through guidance—rather than through notice-and-comment rulemaking—which it supposedly can revise on a whim without any input. And to make matters worse, manufacturers cannot administratively appeal or seek judicial review of CMS's selection of medications and determination of the maximum price for selected products. That framework violates the manufacturers' due-process rights by depriving them of property interests without a meaningful opportunity to be heard and an impartial adjudicator.

Apparently unsatisfied with its capacious (and unconstitutional) grant of power, CMS has far exceeded Congress's prescribed limitations on *which* drugs are eligible for price "renegotiation." Congress made a limited number of medications eligible for DPNP price controls. It also specified that they must have been marketed for a set number of years under their respective applications as approved by the U.S. Food and Drug Administration (FDA). Congress then included the ineligibility period—seven years for small molecule drugs and 11 for biological products—in its definition of "qualifying single source drugs," which are what the IRA instructs CMS to rank when selecting the top-spend drugs for price controls. Without this ineligibility period, innovators have little hope to recoup any meaningful part of their multi-billion-dollar investments in research and development (R&D) before CMS slashes the price of their products, which would in turn make the innovation of many new products highly unlikely, if not outright impossible.

[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.

Instead of close adherence to the IRA, CMS's guidance violates the statute's plain text and expands DPNP's reach beyond recognition. Despite Congress tying the selection clock for each small molecule drug or biological product to the approval date for each approved application or license, CMS redefined "qualifying single source drug" to include all of a manufacturer's products with the same active moiety or ingredient. CMS claims it can price-control even *newly approved products* that share the same active moiety as an earlier product that had been marketed for long enough to be "negotiation-eligible" under the IRA. CMS thus effectively does away with the statutory ineligibility period for new products, sweeping in medications that Congress did not intend to price-control.

CMS's guidance has a perverse effect on the development of new products, particularly those with new indications (i.e., new diseases or conditions that can be treated or prevented with a previously approved drug), and with a new composition, delivery method, or device presentation.

Imagine 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 has become the go-to treatment for melanoma since then. That medication, while highly effective, is administered via injection once a week and is known for some significant side effects. The manufacturer then went back to the drawing board and, after years of additional research and testing, developed a new version of the drug—call it Product ABC®—that is just as effective in its treatment of melanoma but much safer and easier to administer. This new product consists of taking a pill once a year and barely has side effects. Around the same time, the manufacturer discovered through further testing that the original drug, Product AB®, not only

treats melanoma but also results in weight loss. In 2024, FDA approved the once-a-year pill to be marketed as Product ABC®, and the anti-obesity indication as Product ABD®.

Because the manufacturer marketed Product AB® as an anti-cancer medication for more than a decade, that medication might be a "qualifying single source drug" and thus eligible for price controls under the IRA. But the same should not be true for Product ABC® or Product ABD®. These new products were *approved* recently under distinct applications. And as a result, the IRA's plain text makes them ineligible for price controls for seven years, thus allowing the manufacturer to recoup its investment. But CMS disagrees. Under its guidance CMS could unilaterally set prices for Product ABC® and Product ABD® from the very moment they enter the market simply because they share "Molecule A" with Product AB®. Never mind that the manufacturer has not been able to market these products under the recently approved applications at a price of its choosing. Never mind the years and hundreds of millions expended to develop and rigorously test the new Product ABC®'s new composition and Product ABD®'s new indication. And if CMS's guidance stands, never mind these new, life-changing products—they simply cannot be made within the bounds of economic rationality.

Amici uniformly oppose the IRA's distortive effect on manufacturers' incentives to innovate in the first place, which itself violates procedural due process. *Infra* § I.A. But at an absolute minimum, CMS must be faithful to the balance Congress struck. As explained below, CMS has exceeded its authority and deviated from that balance. *Infra* § I.B. The result will have devastating consequences for public health by making many new products economically impossible. *Infra* § II. *Amici* urge this Court to grant Teva's motion for summary judgment and reject administrative overreach that will harm public health.

ARGUMENT

I. CMS has implemented an unconstitutional law and exceeded its authority by expanding the types of medicines that Congress made eligible for price controls.

The DPNP "can be broken down into three phases: 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). In the first phase, CMS must identify certain "negotiation-eligible" medications for price controls—ten drugs or biological products for "initial price applicability year" (IPAY) 2026, 15 for IPAY 2027 and IPAY 2028, and 20 for IPAY 2029. *See* 42 U.S.C. § 1320f-1(a)-(b). Then, the manufacturers of the selected medications must "negotiate" with CMS and agree on the maximum price for the products, *id.* § 1320f-2(a)—all 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). And should the manufacturer either refuse to participate or accept CMS's price by the deadline, the manufacturer must pay 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). That tax can rise to 19 times the total daily revenue of that 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).

The one-sided regime that Congress built into the DPNP violates the Constitution. It also makes CMS's adherence to the statutory limitations in the IRA all the more critical to facilitate continued innovation and development of lifechanging treatments for patients. Yet CMS has disregarded those limitations, expanding DPNP's reach to cover more medications than Congress intended and sooner.

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

1. The IRA seemingly cuts off manufacturers and other affected parties from DPNP's implementation. Two statutory 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.[4] And not only has CMS engaged in substantive rulemaking in this manner, but also claims it can revise the guidance without prior notice, depriving manufacturers of the opportunity to explain "the impact that drug price reductions [of selected medications] would have on [their] margins (and corresponding ability to offer particular treatments or remain in business at all)." *Nat'l Infusion Ctr.*, 116 F.4th at 504.

Which brings us to the second feature—Congress's insulation of key determinations from review. The IRA provides that "[t]here shall be no administrative or judicial review" of certain determinations. 42 U.S.C. § 1320f-7. These include CMS's "selection of drugs," as well as determinations of "negotiation-eligible drugs," "qualifying single source drugs," and "a maximum fair price" of the selected medications. *Id.* § 1320f-7(2)-(3). Put together, these two features allow CMS to name its price on the selected medication and reject a manufacturer's

[4] *See also* CMS, *Medicare Drug Price Negotiation Program: Revised Guidance for Initial Price Applicability Year 2026*, at 8-11 (June 30, 2023), https://tinyurl.com/msu4fck4; CMS, *Medicare Drug Price Negotiation Program: Initial Guidance for Initial Price Applicability Year 2026*, at 1-2 (Mar. 15, 2023), https://tinyurl.com/yc5e86cd.

counteroffer—all "without notice and comment and insulated from administrative or judicial review." *Nat'l Infusion Ctr.*, 116 F.4th at 503.

In addition, DPNP is structured to disincentivize negotiation. Consider a manufacturer's options: It could either give in to the agency's demands and agree to pay the proposed price; refuse the offer and choose to pay the excise-tax penalty; or opt out of Medicare and Medicaid altogether, depriving patients and providers of federal reimbursement for all the manufacturer's medications. At the risk of stating the obvious, these are hardly options. "[N]o manufacturer could afford to pay" the excise-tax penalty. *Id.* at 495 (citing Joint Comm'n on Tax'n, 117th Cong., JCX-46-21 *Estimated Budget Effects of the Revenue Provisions of Title XIII – Committee on Ways and Means, of H.R. 5376, The "Build Back Better Act," as passed by the House of Representatives*, at 8 (Nov. 19, 2021)). Nor can any biopharmaceutical company function, much less thrive, if it withdraws its products from federal programs that account for "almost half the annual nationwide spending on prescription drugs," *Sanofi Aventis U.S. LLC v. HHS*, 58 F.4th 696, 699 (3d Cir. 2023)—not to mention that doing so would leave millions of patients without access to critical treatments. To put it bluntly, either paying the excise tax or abandoning Medicare and Medicaid 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). Which means that, once CMS selects a medication for the DPNP, the manufacturer's bargaining power is so limited that it virtually has no choice but to accept CMS's price, no matter how unreasonable or confiscatory—hence, the "offer one can't refuse."

2. Such a one-sided regime violates the Fifth Amendment's Due Process Clause. In a nutshell, the IRA deprives manufacturers of valuable and hard-earned property interests in their products without a meaningful opportunity to be heard and an impartial adjudicator—either on

the front end or the back end. Such erroneous deprivation violates the manufacturers' procedural-due-process-rights "under the *Mathews v. Eldridge* due process test, which balances the private interests at stake, the value of added procedures, and the burdens on the government from the added procedures." *Culley v. Marshall*, 601 U.S. 377, 382 (2024) (citing *Mathews v. Eldridge*, 424 U.S. 319, 334-35 (1976)).

A faithful application of the *Mathews* balancing test reveals the fundamental problems with the IRA. *See Nat'l Infusion Ctr.*, 116 F.4th at 503 (concluding that plaintiff had standing to bring a procedural-due-process challenge to the IRA and had "alleged sufficient facts to satisfy the *Mathews* test"). On one side of the scale is the manufacturers' undoubtedly important interest in their products and business, including the revenue needed to invest and innovate further. *See id.* There is no denying that the DPNP "substantially impacts" those interests by stripping manufacturers of any meaningful bargaining power and effectively forcing them to accept CMS's named price. *Id.* Similarly, the IRA "create[s] a substantial risk of erroneous deprivation" by denying manufacturers the opportunity to challenge, or even weigh in on, CMS's selection of their drugs for price controls. *Id.* On the other side of the scale are the minimal burdens that CMS would face from added procedures like notice-and-comment rulemaking or any kind of back-end review. Those burdens merely "consist[] of the fiscal and administrative burdens inherent in any review process," *id.*, and pale in comparison to the risk of erroneous deprivation that manufacturers face with every CMS determination under the DPNP.

Most fundamentally, the IRA effectively authorizes "executive officials [to] deprive someone of their property without [any] review in an Article III court," and through a "statutory scheme" that, as shown above, is "procedurally deficient" from top to bottom. *Sec. & Exch. Comm'n v. Jarkesy*, 603 U.S. 109, 174 n.4 (2024) (Sotomayor, J., dissenting). Due-process

principles do not tolerate this kind of insulation from judicial review—much less any review. *See id.* (suggesting that judicial review of an agency decision that deprives someone of a property interest may be constitutionally required); *see also id.* at 151 (Gorsuch, J., concurring) (further suggesting that the government can only deprive someone of property through "trial proceedings with their usual protections" in federal court). And so, even if Congress thought it would be inconvenient for CMS to have to defend its drug-selection and pricing determinations in federal court, the Constitution's Bill of Rights "reflects a judgment by the American people that the benefits of its restrictions on the Government outweigh the costs." *United States v. Stevens*, 559 U.S. 460, 470 (2010).

3. And although this one-sided regime is not tolerable at all, it is critical for it to be strictly confined. "Passing a law often requires compromise, where even the most firm public demands bend to competing interests." *N.L.R.B. v. SW General, Inc.*, 580 U.S. 288, 306 (2017). To the extent such judgment is constitutional, both "[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).

Here, it is true that the IRA is imbued with favoritism towards CMS at the expense of innovators. But that is not the entire story. Congress also limited CMS's authority, delineating specific criteria for the selection of "negotiation-eligible" medications and expressly limiting the number of medications that would be subject to the IRA's price controls. And so, to bring it back to the beginning, because the IRA stacked the decks decisively against manufacturers, it is especially critical for this Court to enforce CMS's compliance with the few limitations that Congress prescribed. Thus, whether CMS lawfully selects "negotiation-eligible" medications is

exceedingly important for one simple reason: There isn't much that a manufacturer can do once CMS has selected one or more of its medications for the DPNP.

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

The IRA directs CMS to rank Medicare's top-spend, "negotiation-eligible drugs" and select a certain number for price "renegotiation." 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 … (i) that is *approved* … and is marketed pursuant to such approval; (ii) for which, as of the selected drug publication date with respect to such initial price applicability year, at least 7 years will have elapsed since the date of such approval; and (iii) that is not the listed drug that is approved and marketed under section 355(j) of such title." *Id.* § 1320f-1(e)(1)(A) (emphasis added). The same goes for "biological products," except Congress provided an 11-year ineligibility period as opposed to seven as defined by the "license" FDA issues for biological products, rather than the "approved" new drug application. *Id.* § 1320f-1(e)(1)(B).

Put simply, a "qualifying single source drug" is a drug or biological product that (1) is currently approved and marketed under a specific approved new drug application (NDA) or a biologics license application (BLA); (2) has been marketed under that specific approval or license for a specified time period (i.e., seven years for small molecule drugs and 11 years for biological products); and (3) is not the reference drug or product for an approved and marketed generic or biosimilar. Thus, Congress tied the eligibility of the drugs to their particular applications for FDA "approval," such that a drug might be eligible for price controls only if marketed for at least seven years under that drug's NDA or at least 11 years under its BLA.

CMS's guidance strays far away from the IRA's plain text. It redefines "qualifying single source drug" to include "all dosage forms and strengths of the drug [or biological product] with the same active moiety [or ingredient] and the same holder of" an NDA or BLA, "inclusive of products that are marketed pursuant to different" applications.[5] Put differently, when identifying potential "qualifying single source drugs," CMS will aggregate all of a manufacturer's products that share the same active moiety or ingredient into one fictional "super drug," regardless of whether each distinct product may have only recently obtained FDA approval under its own regulatory application.[6] So a newly approved drug may well be deemed eligible for price controls *before* its seven-year period has expired so long as it shares the same active moiety as another marketed drug from the same manufacturer that the FDA approved at least seven years ago.

Recall Product ABD®. Assume the manufacturer spent $800 million developing the research necessary to support a new indication and estimates that it would need at least ten years to recoup its investment by selling the product at a certain price. By imposing price controls on Product ABD® shortly after it enters the market and slashing its Medicare reimbursement rate in half, CMS makes recoupment of that investment effectively impossible. That ignores Congress's clear directive that manufacturers must have a set period from the application's approval to sell

[5] *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* [hereinafter, *Final Guidance*], at 167-68 (Oct. 2, 2024), https://tinyurl.com/52a6e8c7.

[6] *Id.* at 168-69.

their products free from price controls, thus transforming an already lopsided program into a completely one-sided one.[7]

CMS's aggregation of distinct, separately approved drug products not only defies the IRA but also other federal laws, which also foster innovation by recognizing that distinct products should be treated separately. 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 to enter the market so long as these products are tied to the innovator's distinct NDAs and BLAs. *See* 21 U.S.C. § 355(j)(2)(A)(ii), (iv); 42 U.S.C. § 262(k)-(*l*); *see also* Teva's Mot. for Summary Judgment at 6-7 (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. It is CMS's guidance and its aggregation of different products that breaks with the balance struck by federal laws, including Congress's successful Hatch-Waxman and BPCIA regimes.

* * *

[7] There is another problem with the guidance. In defining "qualifying single source drug," Congress made clear that innovator products cannot be price-controlled once a generic has been "approved" and "marketed." 42 U.S.C. § 1320f-1(e)(1)(A)(iii), (B)(iii). At that juncture, the innovator product fails to meet the definition of "qualifying single source drug" and is no longer "negotiation-eligible." But CMS instead has taken the position that the generic or biosimilar must have engaged in "bona fide marketing" as determined by the agency under the totality of the circumstances. *Final Guidance* at 277-79. This means that, in some cases, an innovator product could still be price-controlled even after the approved generic or biosimilar has entered the market because the generic or biosimilar has yet to meet some imagined and amorphous marketing threshold. By adopting a new standard that allows innovator products to be price-controlled for far longer than Congress intended and by naming itself the sole arbiter of whether that standard is met, CMS again exceeded its authority under the IRA.

CMS's guidance is not entitled to any deference. This Court "must exercise [its] independent judgment in deciding whether [CMS] has acted within its statutory authority." *Loper Bright Enters. v. Raimondo*, 603 U.S. 369, 412 (2024). CMS has not. Here, CMS has taken it upon itself to target many more treatments than Congress intended and drastically slash their Medicare reimbursement rates, often by more than 50 percent.[8] 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 forged ahead with DPNP's implementation, issuing a guidance that 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 drugs that improve and save people's lives. That distorting effect on innovation is too significant to be cast aside.

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

A short primer might help explain better how CMS's guidance threatens innovation.

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, and thus be used to treat more than just one condition. Take tirzepatide medications, which FDA has approved both

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

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 FDA approves a drug for one indication, that drug's manufacturer often begins post-approval research of additional indications.[9] That is for good reason: Post-approval research and development for new indications is "vital to addressing unmet needs for patients."[10] For example, "a medicine approved to treat asthma in adults may be studied post-approval for safety and efficacy in children."[11] Similarly, the manufacturer of a medicine that treats a rare disease may find that the medicine is "relevant to multiple diseases."[12] The benefits of this post-approval innovation are real. One recent study concluded that 63% of medicines first approved as orphan drugs—or drugs approved for only one indication—"were awarded at least one post-approval indication."[13]

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

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[9] 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.

[10] *Id.* at 4.

[11] *Id.* at 3.

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

[13] *Id.* at 2.

Unsurprisingly, patients prefer—and are more likely to take—drugs that are easy to consume. And convenience is essential and can have a real impact for patients.

You are already familiar with Product ABC®, the hypothetical anti-cancer medication that consists of taking a pill once a year to fight melanoma, and which is a much better alternative to Product AB® which instead requires an injection once a week and has significantly more side effects. But there are countless real-life examples of the benefits of such innovation. Take for example Gilead Sciences Inc.'s long-acting anti-HIV medication, lenacapavir, which was lifesaving for many because it required dosing only twice a year.[14] Prior to lenacapavir, many anti-HIV medications required frequent administration.[15] 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.[16] Similarly, Arecor Therapeutics is developing a new version of insulin that accelerates the drug's absorption and thus requires smaller drug amounts for each injection than previous insulin products.[17] Finally, take 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

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

[15] 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.

[16] 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.

[17] 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.

edaravone for daily intravenous (IV) infusion in ALS patients in medical settings.[18] But subsequent R&D resulted in FDA approval of an oral version of edaravone, allowing patients to receive treatment in their own homes.[19] 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 demand and unmet needs spur the 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.[20] This kind of "[d]evelopment of and regulatory approval of new uses of already-approved drugs and biologics is an important source of innovation by biopharmaceutical firms."[21] Likewise, where the drug intake is burdensome and patient adherence to the treatment is low, innovators look into developing a new composition,

[18] FDA News Release, FDA Approves Drug to Treat ALS (May 5, 2017), https://tinyurl.com/2s3a86wb.

[19] 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/58b97czw.

[20] *See, e.g.*, JP Hughes et al., Principles of Early Drug Discovery, Br. J. Pharmacol. 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).

[21] *Id.* at 818.

presentation, or delivery mechanism of the drug, which "[p]olicy makers and interdisciplinary scholars have long recognized [as] pharmaceutical innovation."[22]

Pharmaceutical innovation is not easy. In addition to the scientific knowledge, it takes a lot of 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 may develop the drug composition, presentation, and delivery mechanism they intend to pursue and test in subsequent clinical trials.[23] 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 sometimes can mean restarting the entire R&D process—all the way from the initial research to the testing in animals and then humans.[24]

Drug development typically takes ten to 15 years and costs over a billion dollars on average.[25] For example, since 2016, J&J has invested $77.7 billion in medical innovation through continuous R&D.[26] Similarly, Lilly has invested more than $10 billion *for each* new

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

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

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

[25] 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.

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

FDA-approved molecular entity it brought to market from 2006 to 2014.[27] 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. Pfizer likewise invests over $10 billion in R&D annually.[28] Thus, innovation is complex and expensive, and significant trial and error is involved.[29] There is, after all, no guarantee whatsoever that the manufacturer will succeed. And risk must be incentivized, not discouraged by overreaching guidance. 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 therapeutic use—and only one in three of that minute percentage will ever recoup its development costs.[30]

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

[28] Pfizer Inc., Fourth Quarter 2024 Earnings Teleconference 15-16 (Feb. 4, 2025), https://tinyurl.com/nhhpnw7m.

[29] Pauric Bannigan et al., Machine Learning Directed Drug Formulation Development, Advanced Drug Delivery Reviews 175 12 (2021); *see also* Zeqing Bao et al., Revolutionizing Drug Formulation Development: The Increasing Impact of Machine Learning, Advanced Drug Delivery Reviews 202 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.").

[30] *See supra* note 2.

New indications and new easier-to-administer products that patients will actually take are win-wins for innovators and patients alike.[31] 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 these incentives are aligned, 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 control prematurely—or for that matter, immediately upon approval—a manufacturer is unlikely to recoup its development costs for the newly approved product.[32] This is what likely will happen to our hypothetical manufacturer who might not be able to recoup its R&D

[31] *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.").

[32] 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 potentially answer, unfortunately, might be to limit research and development … funding for niche medication.").

investments that led to the development of Product ABC® and Product ABD®. CMS's guidance does just that. It upends the incentives that make those innovations possible.

As discussed above, CMS defines "qualifying single source drug" to include all of the manufacturer's approved products with the same active moiety or ingredient. *See supra* at 12. This means that new and completely distinct products will become eligible for DPNP's price control at the same time as their already approved counterpart. In doing so, the guidance gets things exactly backwards, leading to reduced investment in subsequent generations of drug development. That is because innovators need sufficient time free from artificial price controls to financially justify their expenditures and be able to reinvest in new R&D.[33] Thus, 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, untreated conditions will remain just that. And as to those conditions for which an approved treatment is already available, patients might have no choice but to rely on certain versions of existing drugs that are hard to administer or use for vulnerable patients, such as the elderly. As a result, the adherence to lifesaving treatment plans will decrease, and so will 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 022406), in 2021. The recently approved XARELTO® is an oral suspension indicated to treat blood clots or reduce the risk of blood clots in children. Although

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

each of these drugs required their own R&D and FDA approval pursuant to separate NDAs, they share the same active moiety. Accordingly, when CMS selected XARELTO®—the initial tablet form of the drug—for inclusion in the DPNP in 2023, the oral suspension form of the drug also became subject to the DPNP's price controls, even though it received FDA approved 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 additional FDA approval—pursuant to a separate BLA (BLA 761044)—to treat Crohn's disease and, three years later, to treat ulcerative colitis. 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 in the R&D of STELARA® and conducted more than 100 clinical trials to identify the safest and most effective uses of STELARA®'s active ingredient. In 2024, FDA selected STELARA® for inclusion in the DPNP, and 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 price controls well in advance of their 11-year ineligibility period expiry (e.g., compare time on market for the STELARA® product treating ulcerative colitis, which was approved in 2019, to the initial STELARA® product, approved in 2009).

This kind of aggregation of different medications is not just unfair but will have lasting effects on pharmacological innovation and patient access. One study estimates, for example, that the DPNP's price controls will "reduce overall annual cancer R&D spending by about $18.1 billion, or 31.8%."[34] 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.[35] Indeed, CMS's implementation of the IRA already has caused manufacturers to "shelve promising new medical treatments."[36] 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 Inflation Reduction Act.'"[37] Likewise, Lilly "was in the early clinical stages of developing a treatment (a BCL2 inhibitor) for certain blood cancers" but had to discontinue development "after careful assessment of the impact of [the IRA] on the program as well as the competitive landscape."[38] Novartis and Genentech also have warned that the IRA's price controls have negatively impacted investment and research into cancer treatments.[39] This is just the beginning. By unduly expanding the definition of "qualifying single source drug" and bundling different products regardless of when

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

[35] 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 33, at 3.

[36] 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.

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

[38] Eli Lilly, The Inflation Reduction Act's Impact on Drug Discovery and Development (Dec. 8, 2022), https://tinyurl.com/2p9k38ud.

[39] *See supra* note 36.

their date of FDA approval, CMS has made things worse for innovators and patients across the country.

CONCLUSION

Teva's motion for summary judgment should be granted.

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