IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TEXAS
AUSTIN DIVISION

NATIONAL INFUSION CENTER ASSOCATION, on behalf of itself and its members; GLOBAL COLON CANCER ASSOCATION, on behalf of itself and its members; and PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA, on behalf of itself and its members, Plaintiffs, vs. XAVIER BECERRA, in his official capacity as Secretary of the U.S. Department of Health and Human Services; the U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; CHIQUITA BROOKS-LASURE, in her official capacity as Administrator of the Centers for Medicare and Medicaid Services; and the CENTERS FOR MEDICARE AND MEDICAID SERVICES, Defendants.	Civil Action No. 1:23-cv-00707

PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT

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INTRODUCTION

For decades, Medicare has relied on a market-based system for reimbursing drug purchases, helping to make America the world leader in pharmaceutical research and development. This system has benefitted patients (who receive cutting-edge medicines that extend and enhance their lives), manufacturers (who earn competitive returns for successful products), and providers (who receive reimbursement for administering innovative drugs).

In the Inflation Reduction Act of 2022 (IRA), Congress attempted to replace that time-tested system with government-dictated prices. If enacted forthrightly, this new scheme would have come at a high political cost because price controls harm innovation and patient care. To avoid the likely backlash, Congress adopted a complex and entirely novel structure that, at every turn, seeks to avoid accountability and oversight, obscuring the fact that drug prices are being dictated by government *fiat*.

Here is how the so-called "Drug Price Negotiation Program" (Drug Pricing Program or Program) works. Contrary to its name, the Program involves no genuine "negotiation" at all. Instead, it *compels* manufacturers to accept prices that the Centers for Medicare & Medicaid Services (CMS), a sub-agency of the Department of Health and Human Services (HHS), unilaterally chooses. The law establishes a price ceiling that may not be exceeded, while affording the agency complete discretion to choose as *low* a price as it wants: The agency could decide that an innovative, lifesaving medicine that cost $10 billion to develop is worth just $1 per dose.

In any genuine negotiation, the seller would be free to decline to sell at such an unfair price. But Congress blocked that option. If manufacturers do not agree to participate in the sham "negotiation," or do not accede to whatever price the agency ultimately demands, they are subject to a crippling "excise tax." This supposed "tax" is staggering, starting at a multiple of daily revenues and rapidly escalating to *19 times* the manufacturer's *total U.S. revenues* for the drug in

question (not merely its Medicare revenues). The manufacturer's only alternative is to exit Medicare and Medicaid altogether, not just for the drug in question, but for *all* the manufacturer's drugs—depriving patients nationwide of access to critical medicines and foreclosing nearly half the U.S. drug market. That faux "negotiation," backed by the very real threat of a crippling "tax," serves no legitimate purpose other than obscuring Congress's price-fixing scheme.

Next, Congress insulated this scheme from meaningful accountability. On the front end, the agency claims that it need not engage in notice-and-comment rulemaking regarding the Program's administration. The agency accordingly has already made key implementation decisions—including decisions that stretch the Program beyond the statutory text—without accounting for the views of affected parties. And on the back end, the IRA's text purports to foreclose altogether administrative and judicial review of critical agency decisions. As a result, the agency can decree any price it wants for a manufacturer's drug and then force the manufacturer to "agree" that it is "fair," without any meaningful ability to reach a different deal, walk away from negotiations, or challenge how the agency reached its decision. Patients and providers are shut out as well, even though government-set prices determine providers' reimbursement rates and patients' access to innovative treatments. Concealing its true operation through euphemisms, and totally lacking in accountability, the IRA is a law like none other.

These unprecedented aspects of the Drug Pricing Program render it unconstitutional in at least three ways. *First*, Congress delegated unconstrained authority to the agency, in violation of the separation of powers and the nondelegation doctrine. Price-setting statutes have a historical pedigree, but the IRA is unprecedented because it vests the agency with complete discretion to set prices as low as it wants (regardless of whether the prices are reasonable). Further, it leaves key interpretive and policy decisions to the agency's unfettered choice—essentially allowing the

agency to rewrite the statute as it sees fit, without meaningful judicial oversight.

Second, the excise-tax penalty violates the Eighth Amendment's Excessive Fines Clause. Failing to agree on a negotiated price ordinarily is not considered unlawful or even wrongful conduct. But if a manufacturer fails to agree to the government-imposed price for one of its products, the manufacturer is penalized with a daily excise tax—on *all* of its nationwide sales of the product, not just Medicare sales—that starts unbearably high and quickly escalates into the stratosphere. Indeed, the penalty is so onerous that the Joint Committee on Taxation and the Congressional Budget Office (CBO) both estimated that it will raise "no revenue" because no manufacturer could ever afford to pay it.

Third, exempting key agency implementation decisions from public input and insulating them from judicial review violates the Fifth Amendment's Due Process Clause. The law directly implicates patients, whose access to essential drugs may be thrown into jeopardy; manufacturers, who have invested billions developing drugs that may suddenly be rendered unprofitable; and providers, who face slashed reimbursement rates that could drive them out of business. Yet the agency insists that the IRA gives interested stakeholders *no* meaningful notice-and-comment rights (on the front end) or ability to challenge legally erroneous decisions in court (on the back end).

If allowed to stand, this law will dramatically slow innovation, reduce the availability of new medicines, and undermine public health, causing grave harm to patients, pharmaceutical manufacturers, and healthcare providers. The National Infusion Center Association (NICA), the Global Colon Cancer Association (GCCA), and Pharmaceutical Research and Manufacturers of America (PhRMA) respectfully ask this Court to grant summary judgment, to declare the Drug Pricing Program unconstitutional, and to enjoin its implementation.

BACKGROUND

A. Pharmaceutical Innovation Requires Investment in Research and Development

The process of developing new drugs is lengthy, risky, and expensive. *See* Ex. 1, Expert Decl. of Craig Garthwaite ¶¶ 16–29; Ex. 2, Decl. of Adam Gluck ¶ 10. Today, companies are developing hundreds of new medicines to treat cancers, pediatric conditions, and rare diseases. *See* PhRMA, *Medicines in Development 2021 Report: Rare Diseases* 1 (Dec. 2021), https://bit.ly/3go50j8; PhRMA, *Medicines in Development 2022 Report: Women* 2 (Mar. 2022), https://bit.ly/3EzupyG; Am.'s Biopharmaceutical Cos., *Medicines in Development 2020 Report: Children* 1 (Jan. 2020), https://onphr.ma/2PSX4FN. Researchers also are working on hundreds of novel cell and gene therapies. *See* Am.'s Biopharmaceutical Cos., *Medicines in Development 2020 Update: Cell and Gene Therapy* 1–2 (Feb. 2020), https://onphr.ma/3fY6wSX. And—of particular importance to the older population Medicare covers—companies are developing cutting-edge treatments for Alzheimer's Disease. *See* PhRMA, *Continued Progress Toward New Treatments for Alzheimer's Disease Provides Hope to Millions* 1 (Mar. 2022), https://onphr.ma/42zq8pt. Recent studies indicate that, to develop just one new drug, manufacturers spend an average of over $2 billion. *See* Garthwaite Decl. ¶ 25. Some drugs for complex conditions require over $10 billion in research and development investment. *See* Alexander Schuhmacher et al., *Changing R&D Models in Research-Based Pharmaceutical Companies*, 14 J. Translational Med., no. 105, at 3–4, (Apr. 27, 2016), https://bit.ly/2PWRKRC. And the necessary investments are increasing. Over the last 60 years, drug research and development costs have risen 8.6% annually, even after adjusting for inflation. *See id.* at 3.

Manufacturers also face long odds. Only one in 5,000 compounds that enters preclinical testing will achieve FDA approval, a failure rate of 99.98%. *See* Sandra Kraljevic et al.,

Accelerating Drug Discovery, 5 Eur. Molecular Biology Org. Reps. 837, 837 (2004), https://bit.ly/2Y2gwEK. Of the therapies approved for patient use, only one-third will even cover their development costs, much less provide returns sufficient to allow for continued investment and innovation. *See* John A. Vernon & Joseph H. Golec, *Pharmaceutical Price Regulation: Public Perceptions, Economic Realities, and Empirical Evidence* 7 (2008), http://bit.ly/3UR06de.

Notwithstanding the low success rate, the U.S. biopharmaceutical industry invested an estimated $122 billion on research and development in 2020 alone, representing almost 60% of global pharmaceutical research and development spending. *See* Garthwaite Decl. ¶¶ 10, 16. To justify this level of investment, the expected returns for medicines that do make it to market must be high enough to counterbalance the substantial likelihood of failure. And manufacturers must make investment decisions based on predictions about expected returns a decade or more before the product will launch and begin earning revenues. *See id.*; Gluck Decl. ¶ 11.

Successful pharmaceutical innovation benefits not just manufacturers, but providers and patients as well. Providers are in the business of extending and improving patients' lives by administering treatments that pharmaceutical manufacturers make—including innovative new drugs and therapies. Administering innovative drugs and biologics and obtaining reimbursement based on market prices is the foundation of how providers keep their doors open and serve their patients' needs. Ex. 3, Decl. of Brian Nyquist ¶¶ 9–10. Patients, in turn, depend on pharmaceutical innovation to save, extend, and improve their lives. *See* Ex. 4, Decl. of Andrew Spiegel ¶¶ 9–13, 19; Nyquist Decl. ¶¶ 4, 6.

B. Medicare Traditionally Encouraged Pharmaceutical Innovation

A key driver of pharmaceutical innovation has been the market-based reimbursement traditionally afforded by Medicare. "Medicare stands as the largest federal program after Social Security," providing "health insurance for nearly 60 million aged or disabled Americans, nearly

one-fifth of the Nation's population." *Azar v. Allina Health Servs.*, 139 S. Ct. 1804, 1808 (2019); *see* Garthwaite Decl. ¶ 87. As relevant here, Medicare includes two major prescription drug programs. First, Medicare Part B covers medically necessary and preventative healthcare services, including drugs administered by a physician. *See* 42 U.S.C. §§ 1395k(a)(1), 1395x(s)(2)(A); Garthwaite Decl. ¶ 33. Medicare Part B is administered by CMS and, with certain exceptions, has long reimbursed providers based on market prices. Medicare Part B reimbursement rates generally reflect the drug's "average sales price"—which incorporates the volume-weighted average of all manufacturer sales prices to U.S. purchasers, with certain exceptions—plus a specified percentage (currently 6%). *See* 42 U.S.C. § 1395w-3a; Garthwaite Decl. ¶¶ 36, 38.

Second, Medicare Part D allows Medicare beneficiaries to enroll in privately operated plans covering self-administered prescription drugs. *See* 42 U.S.C. § 1395w-102; Garthwaite Decl. ¶ 35. Drug prices in Part D also are market-based. Part D plans are administered by private plan sponsors, which negotiate prices with manufacturers. *See id.* ¶¶ 36–37. Moreover, the Part D statute provides that, "[i]n order to promote competition under [Part D]," HHS and CMS "may not interfere with the negotiations between drug manufacturers and pharmacies and [prescription drug plan] sponsors." 42 U.S.C. § 1395w–111(i); *see* Garthwaite Decl. ¶ 49. For decades, then, Medicare has encouraged a market-driven approach that has fostered incredible innovation.

Although Medicare's market-based approach benefits patients globally, it helps Americans most directly. Manufacturers generally launch new drugs in the United States first; accordingly, U.S. patients are often the first to receive lifesaving pharmaceuticals. For example, 80% of medicines approved by the FDA in 2021 were available in the United States before any other country. *See* Garthwaite Decl. ¶ 10. Foreign countries with drug-price controls have seen drastic reductions in research and investment, as well as delays in patients' access to advanced treatments.

See Joe Kennedy, *The Link Between Drug Prices and Research on the Next Generation of Cures*, Info. Tech. & Innovation Found. (Sept. 9, 2019), https://bit.ly/3fSIysc; PhRMA, *Global Access to New Medicines Report* 8, 11–36 (Apr. 2023), https://bit.ly/3OR7GEx.

C. The IRA Upends Medicare's Market-Based Reimbursement Mechanisms

The IRA upends Medicare's market-based system. The statute directs HHS to establish a "Drug Price *Negotiation* Program." 42 U.S.C. § 1320f(a) (emphasis added). But in reality, the Program empowers HHS to control drug prices not by negotiation, but by administrative *fiat*.

1. HHS Ranks and Selects "Negotiation-Eligible Drugs"

Beginning in 2023, the IRA directs HHS to rank "negotiation-eligible drugs" based on Medicare's "total expenditures" for them (first in Part D, later in Part B as well) over a specified twelve-month period. *Id.* § 1320f–1(b)(1)(A). Drugs with the highest total expenditures during the specified period are to be ranked the highest. *Id.*

The "negotiation-eligible drugs" that HHS must rank encompass many of the most innovative drugs and biological products available. The IRA defines "negotiation-eligible drugs" as the 50 "qualifying single source drugs" with the highest total expenditures under Parts B and D. *Id.* § 1320f–1(d)(1). A "qualifying single source drug" is defined as one that (1) is marketed under a new drug application or a biologics license application, (2) has been approved by FDA for at least 7 years for drugs or 11 years for biological products, and (3) is not the reference drug for an approved and marketed generic drug or biosimilar product. *Id.* § 1320f–1(e)(1).

Once "negotiation-eligible" drugs have been identified and ranked, the IRA directs HHS to "select" an increasing number of the highest-ranked drugs for negotiation and "publish a list of [them]." *Id.* § 1320f–1(a). Part D drugs will be selected starting in 2023, with "maximum fair prices" taking effect in 2026; Part B drugs are added to the selection process beginning in 2026, with maximum prices taking effect in 2028. *Id.* § 1320f–1(a)(1), (3). Ten Part D drugs will be

selected for 2026, fifteen Part D drugs for 2027, fifteen Part D and Part B drugs for 2028, and twenty Part D and Part B drugs for 2029 and each year thereafter. *Id.* § 1320f–1(a)(1)–(4). This process is cumulative: A selected drug remains selected until HHS determines that an approved generic or licensed biosimilar has been marketed. *Id.* § 1320f–1(c)(1).

HHS must publish the first list of selected drugs by September 1, 2023. *Id.* § 1320f(d)(1), 1320f–1(a)(1). At least one drug manufactured by a member of PhRMA will be included on the first list, as well as subsequent lists. *See* Ex. 5, Decl. of Kristen Bernie ¶¶ 13–15; Garthwaite Decl. ¶ 70; Ex. 6, Decl. of Patrick Costello ¶ 19; Gluck Decl. ¶ 9.

2. HHS Sets "Maximum Fair Prices" Through Sham "Negotiations"

Once drugs are ranked and selected, the IRA directs HHS to "enter into agreements with manufacturers" whereby the parties "negotiate to determine (and … agree to) a maximum fair price." 42 U.S.C. § 1320f–2(a)(1). Manufacturers of drugs included on the first list of selected drugs must enter into these "agreements" by October 1, 2023. *Id.* §§ 1320f(d)(2)(A), 1320f–2(a). The ensuing "negotiations" then must conclude by August 1, 2024. *Id.* §§ 1320f(d)(5), 1320f–3(b)(2)(E).

To conduct the "negotiations," the statute directs HHS to "develop and use a consistent methodology and process … that aims to achieve the lowest maximum fair price for each selected drug." *Id.* § 1320f–3(b)(1). The "negotiation" process includes an HHS "offer," a manufacturer "counteroffer," and an HHS "[r]esponse." *Id.* § 1320f–3(b)(2)(C)–(D). But that is where any resemblance to genuine negotiation ends.

To begin with, HHS can demand any information it wants on pain of massive penalties. The statute commands manufacturers to give HHS a host of closely guarded trade secrets and other proprietary information, including the manufacturer's research and development costs, market data, and costs of production and distribution. *Id.* §§ 1320f–2(a)(4)(B), 1320f–3(e)(1).

Manufacturers also must "compl[y] with" whatever *other* requirements HHS deems "necessary for purposes of administering the program." *Id.* §§ 1320f–2(a)(5), 1320f–6(c). These onerous requirements are enforced by $1 million-per-day civil penalties—*plus* the crippling excise tax discussed below. *Id.* §§ 1320f–2(a)(4)–(5), 1320f–6(c); 26 U.S.C. § 5000D(b)(4).

The IRA then sets no meaningful constraints on what prices HHS can mandate. With one minor exception, the statute does not limit how *low* a price HHS can demand. 42 U.S.C. § 1320f–3(b)(2)(F). But it does place a "ceiling" on how *high* a price HHS can offer. *Id.* § 1320f–3(c). For the Program's first year, the ceiling is calculated as a percentage of a baseline price (generally, the inflation-adjusted non-federal average manufacturer price in 2021). The ceiling ranges from 75 percent of that benchmark for recently approved drugs, down to just 40 percent for drugs that have been approved for over 16 years. *Id.* § 1320f–3(b)(2)(F), (c)(1)(C)(i). In other words, the IRA mandates a first-year *minimum* discount of 25-to-60 percent. For subsequent years, the ceiling can be even more restrictive—the statute directs HHS to use either the calculation above or an alternative calculation if it is lower. *Id.* § 1320f–3(c)(1)(C)(ii).

Below the applicable "ceiling," HHS has free rein to set prices as it pleases. At most, HHS must "consider" specified "factors," including research and development costs, production and distribution costs, prior federal financial support, data on patents and regulatory exclusivities, market data and revenue and sales volume data, and information about alternative treatments. *Id.* § 1320f–3(e). Yet the IRA sets no criteria for how to weigh these considerations, nor does it require HHS to disclose in any meaningful way how it balanced those factors in setting prices. And the statute's low-ceiling, no-floor design gives HHS every incentive to drive prices as low possible.

Once HHS has imposed a "maximum fair price" and that price becomes effective, the manufacturer must provide "access to such price to" a wide array of individuals, pharmacies,

providers, and other entities participating in Medicare. *Id.* § 1320f–2(a)(1). Manufacturers that fail to do so must pay a penalty of *ten times* the difference between the price charged and the price imposed by HHS, multiplied by the number of units sold. *Id.* § 1320f–6(b).

3. Noncompliant Manufacturers Must Pay a Crippling "Excise Tax"

The hammer the IRA uses to force manufacturers to "agree" to a "maximum fair price" is a so-called "excise tax." In ordinary negotiations, parties that fail to reach agreement regarding price can simply walk away. *See* Garthwaite Decl. ¶¶ 42, 81. But under the IRA, manufacturers cannot do that. Instead, the statute imposes a steep penalty for every day the manufacturer has not, by the applicable statutory deadline, (1) entered into an "agreement" to negotiate a maximum fair price for a negotiation-eligible drug, (2) "agreed" to a maximum fair price, or (3) submitted the information HHS demands for the "negotiation" process. 26 U.S.C. § 5000D(b). Congress labeled this penalty an "excise tax," but it is intended to coerce rather than raise revenue.

The size and scope of this "tax" is staggering. It applies to *all* U.S. sales of the drug in question, not just Medicare sales. *See id*. The tax is calculated based on a formula representing an "applicable percentage" of the drug's total cost (price plus tax). *Id.* § 5000D(d). The applicable percentage starts at 65% and then increases 10% for each quarter of noncompliance until it reaches 95%. *Id.* As the Congressional Research Service explained, "[t]he excise tax rate" thus "range[s] from 185.71% to 1,900% of the selected drug's price depending on the duration of noncompliance." Cong. Rsch. Serv., *Tax Provisions in the Inflation Reduction Act of 2022 (H.R. 5376)*, 4 (Aug. 10, 2022), https://bit.ly/3sbHYBy. In other words, the tax *starts* at nearly double the manufacturer's total daily U.S. revenue for the drug, and quickly escalates to *19 times* revenue. A summary of predecessor legislation described the excise tax as a "steep, escalating penalty." Title Summary, H.R. 3, at 1 (2022). Indeed, though the statute calls it a "tax," both the Joint Committee on Taxation and CBO estimated that the tax would raise "no revenue" because no

manufacturer could ever afford to pay it. Joint Comm'n on Tax'n, *Estimated Budget Effects of the Revenue Provisions of Title XIII – Committee on Ways and Means, of H.R. 5376, The "Build Back Better Act,"* at 8 (Nov. 19, 2021), https://bit.ly/3plC4cd; *see* CBO, *Estimated Budgetary Effects of Public Law 117-169*, at 5 (Sept. 7, 2022), https://bit.ly/3JOiq3r (similar). Instead, manufacturers will have no choice but to "agree" to whatever "maximum fair price" HHS demands.

The IRA provides that the excise-tax penalty may be "[s]uspen[ded]," but only if the manufacturer terminates three types of agreements with HHS. 26 U.S.C. § 5000D(c). Terminating those agreements would eliminate coverage under Medicare Part D, Medicare Part B, *and* Medicaid—not just for the manufacturer's drugs subject to the IRA's Drug Pricing Program, but for *all* of the manufacturer's drugs. *See id.*; 42 U.S.C. § 1396r-8(a)(1).

Withdrawing from Medicare and Medicaid altogether is not feasible for manufacturers. To begin with, "[t]he consequence of" withdrawing from Medicare and Medicaid "would be catastrophic for almost any manufacturer." Garthwaite Decl. ¶ 84; *see id.* ¶¶ 85–88. "Through Medicare and Medicaid, [the federal government] pays 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). Medicare and Medicaid account for a hefty portion of many manufacturers' revenue. *See* Bernie Decl. ¶ 11; Garthwaite Decl. ¶ 87; Costello Decl. ¶ 20; Gluck Decl. ¶ 13. In addition, withdrawing from Medicare and Medicaid would cause millions of patients to lose access to medicines they depend on. Pulling the rug out from under patients who have come to rely on medicines for a course of therapy would raise ethical concerns and would be "anathema" to manufacturers' "mission." Gluck Decl. ¶ 13; *see* Costello Decl. ¶ 20; Garthwaite Decl. ¶ 88.

Even if a manufacturer were able, let alone willing, to shoulder those financial, ethical, and reputational costs, the IRA delays manufacturers' ability to exit from Medicare Part D—and thus

compels them to participate—for between 11 and 23 months. *See* 42 U.S.C. §§ 1395w–114a(b)(1)(C)(ii), 1395w–114c(b)(4)(B)(ii), 1395w–153(a)(1). CMS recently issued nonbinding guidance stating that, if manufacturers withdraw, the agency will take administrative actions to reduce that exit delay down to 30 days. *See* CMS, *Medicare Drug Price Negotiation Program: Revised Guidance for Initially Price Applicability Year 2026* [hereinafter *Revised Guidance*], at 120–21 (June 30, 2023), https://bit.ly/3JLSSUH. But the agency's statutory basis for those promised administrative actions is dubious at best, and manufacturers cannot rely on them—particularly since the agency could seemingly change its mind at any time. *See infra* Part I.

4. The IRA Limits Notice-and-Comment Rulemaking and Judicial Review

Despite the Drug Pricing Program's unprecedented burdens on manufacturers and serious repercussions for providers and patients, affected parties have no say in how HHS implements key parts of the Program, and they are deprived of legal recourse regarding numerous critical decisions.

On the front end, before implementation decisions are made, there is no right to participate in the implementation process. The Administrative Procedure Act sets forth general requirements for notice-and-comment rulemaking, which the Social Security Act requires HHS to follow in substantive rulemaking under Medicare. *See* 5 U.S.C. § 553(b), (c); 42 U.S.C. § 1395hh. The IRA, however, provides that HHS "shall implement [the Drug Pricing Program] for 2026, 2027, and 2028, by program instruction or other forms of program guidance." *Id.* § 1320f note. CMS has read that language to exempt the Drug Pricing Program from notice-and-comment requirements during the Program's formative years. *See* CMS, *Medicare Drug Price Negotiation Program: Initial Memorandum for Initial Price Applicability Year 2026* [hereinafter *Initial Guidance*] at 2 (Mar. 15, 2023), https://bit.ly/3m0cDPG; *Revised Guidance* at 8–11.

On the back end, after implementation decisions are made, the IRA purports to insulate critical decisions from review. For example, the statute provides that "[t]here shall be no

administrative or judicial review" of many key HHS determinations, including "[t]he selection of drugs," "the determination of negotiation-eligible drugs," "the determination of qualifying single source drugs," and "[t]he determination of a maximum fair price." 42 U.S.C. § 1320f–7(2)–(3).

D. CMS Implements the IRA Through Guidance

In March 2023, CMS issued initial guidance on the Drug Pricing Program for 2026. The Initial Guidance confirmed CMS's view that the Program "is not subject to the notice-and-comment requirement of the Administrative Procedure Act or the Medicare statute." *Initial Guidance* at 2. And while CMS "voluntarily" solicited comments on some aspects of the Initial Guidance, it adopted other aspects as final. The aspects finalized without notice-and-comment encompass some of the Program's most critical elements, including "the requirements governing the identification of qualifying single source drugs, the identification of negotiation-eligible drugs, the ranking of negotiation-eligible drugs and identification of selected drugs, and the publication of the list of selected drugs." *Id.* at 4. CMS also claimed the unconditional right to "make changes to any policies, including policies on which CMS has not expressly solicited comment." *Id.* at 2.

In June 2023, CMS issued revised Program guidance for 2026. Among other changes, CMS altered some aspects of the Initial Guidance that it had previously issued as "final," without any solicitation of comments. *See Revised Guidance* at 97. As noted, the Revised Guidance also discusses a mechanism to expedite manufacturers' exit from Medicare Part D, purportedly reducing the 11-to-23 month statutory delay to 30 days. *See id.* at 120–21.

ARGUMENT

Summary judgment is appropriate where "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). Here, Plaintiffs are entitled to judgment as a matter of law on all three of their claims. The Drug Pricing Program violates the separation of powers and the nondelegation doctrine; it violates the Eighth

Amendment's Excessive Fines Clause; and it violates the Fifth Amendment's Due Process Clause.

I. THE IRA VIOLATES THE SEPARATION OF POWERS AND THE NONDELEGATION DOCTRINE

Article I, section 1 of the Constitution provides that "[a]ll legislative Powers herein granted shall be vested in a Congress of the United States." Congress accordingly may not "delegate to [other branches] powers which are strictly and exclusively legislative." *Wayman v. Southard*, 23 U.S. (10 Wheat.) 1, 42 (1825). Indeed, "[t]hat congress cannot delegate legislative power to the [executive branch] is a principle universally recognized as vital to the integrity and maintenance of the system of government ordained by the constitution." *Marshall Field & Co. v. Clark*, 143 U.S. 649, 692 (1892). The Supreme Court has twice struck down statutes as violating these principles. *See A.L.A. Schechter Poultry Corp. v. United States*, 295 U.S. 495 (1935); *Panama Ref. Co. v. Ryan*, 293 U.S. 388 (1935). The Fifth Circuit did so again just last year. *See Jarkesy v. SEC*, 34 F.4th 446, 459–63 (5th Cir. 2022), *cert. granted*, No. 22-859, 2023 WL 4278448 (June 30, 2023). As the Supreme Court recently unanimously confirmed, Congress may not "transfer[] its legislative power to another branch." *Gundy v. United States*, 139 S. Ct. 2116, 2121 (2019) (plurality op.); *see id.* at 2130 (Alito, J., concurring in the judgment) (similar); *id.* at 2133–35 (Gorsuch, J., dissenting) (similar).

The nondelegation doctrine reflects larger separation-of-powers principles. The Framers "divided the powers of the new Federal Government into three defined categories, Legislative, Executive, and Judicial." *Seila L. LLC v. CFPB*, 140 S. Ct. 2183, 2202 (2020) (quotation marks omitted). Beyond that, "the Framers bifurcated the federal legislative power into two Chambers: the House of Representatives and the Senate, each composed of multiple Members and Senators." *Id.* at 2203. "The resulting constitutional strategy is straightforward: divide power everywhere except for the Presidency, and render the President directly accountable to the people through regular elections." *Id.* Congress "contravenes this carefully calibrated system" if it "vest[s] significant

governmental power in the hands of a single individual accountable to no one." *Id.* "[A]ccountability evaporates if a person or entity other than Congress exercises legislative power." *Jarkesy*, 34 F.4th at 460.

The IRA violates the separation of powers by delegating to HHS unconstrained discretion to set Medicare drug prices as low as it chooses. While the statute directs HHS to "consider" certain "factors," it provides *no* guidance on how the agency must weigh those factors and sets *no* concrete limits on the agency's ultimate discretion—other than a minimum discounted "ceiling" price the agency must achieve and a directive to "achieve the *lowest* maximum fair price." 42 U.S.C. § 1320f–3(b)(1), (c), (e) (emphasis added). Unlike historical federal price-setting statutes, the IRA is not limited to wartime exigencies or the unique problems of common carriers; and because it imposes no floor or other meaningful constraint on prices, the IRA does not require prices to be "just and reasonable," as previous price-control statutes have done. *See, e.g.*, Pub. L. No. 421, §§ 2, 302, 56 Stat. 23 (1942); 15 U.S.C. § 717c; 16 U.S.C. § 824d. Instead, the IRA gives HHS unconstrained authority to replace market prices for Medicare's most beneficial drugs with lower prices of the agency's unfettered choosing. But Congress cannot commit to an agency's untrammeled discretion command-and-control authority over vast swaths of the economy. *See Jarkesy*, 34 F.4th at 462.

Furthermore, key terms in the IRA are sufficiently open-ended to allow HHS to claim authority to make fundamental policy choices—essentially allowing the agency to rewrite the statute as it sees fit. In addition to its already expansive price-setting authority for negotiation-eligible drugs, CMS also has claimed authority to determine when multiple products qualify as one qualifying single source drug for purposes of determining whether the products qualify for price controls in the first place. *See Revised Guidance* at 11–12. CMS likewise reads the statute not to specify what it means for a generic drug or biosimilar product to be "marketed," such that the reference drug or biological

product would not be negotiation-eligible. *See id.* at 72–78. And CMS has asserted wide discretion to determine what is included in the "total expenditures" that determine HHS's rankings. *See id.* at 97 & n.29; 88 Fed. Reg. 22,120, 22,260 (Apr. 12, 2023). While these issues encompass only parts of the IRA's expansive Drug Pricing Program, they are not the sort of minor matters where an administrative agency may be empowered to "fill up the details." *Wayman*, 23 U.S. (10 Wheat.) at 43. They are "important subjects, which must be entirely regulated by the legislature itself." *Id.*

Where Congress "mandate[s] compliance with … requirements for notice and comment," that may "weigh[] in favor of [upholding] a delegation." *United States v. Garfinkel*, 29 F.3d 451, 459 (8th Cir. 1994) (citation omitted). But the IRA conspicuously *lacks* that procedural safeguard. In the Program's formative years, the statute does not require notice-and-comment rulemaking—or even the solicitation of *any* external input. And the draconian excise tax prevents manufacturers from protecting themselves against arbitrary agency decision-making during the "negotiation" process.

Finally, "judicial review is a factor weighing in favor of upholding a statute against a nondelegation challenge." *Id.* Congress thus traditionally avoids nondelegation problems by "provid[ing] an administrative agency with standards guiding its actions such that a court could ascertain whether the will of Congress has been obeyed." *Skinner v. Mid-Am. Pipeline Co.*, 490 U.S. 212, 218 (1989) (quotation marks omitted). But here, the IRA purports to insulate critical agency decisions from judicial review. *See* 42 U.S.C. § 1320f–7.

The elimination of judicial review in the Drug Pricing Program presents a serious nondelegation problem. In *Touby v. United States*, 500 U.S. 160 (1991), for example, the Supreme Court upheld a delegation scheme limiting judicial review, but only because the statute merely "postpone[d] legal challenges … until the administrative process ha[d] run its course." *Id.* at 168. Here, the IRA purportedly *eliminates* judicial review over critical administrative decisions. Giving

HHS unreviewable authority to resolve basic statutory-interpretation questions is tantamount to permitting the agency to rewrite the statute—a *legislative* function. "[J]udicial review perfects a delegated-lawmaking scheme by assuring that the exercise of such power remains within statutory bounds." *Id.* at 170 (Marshall, J., concurring).

Without judicial constraint, HHS could attempt—with impunity—to simply ignore binding statutory constraints on its price-setting authority. For example, HHS could select a product for negotiation even though it is *not* negotiation-eligible under the statute. If the manufacturer challenged that unlawful decision in court, HHS could respond by citing the IRA's judicial review bar, which provides that "[t]here shall be no … judicial review" of "[t]he selection of drugs" or "the determination of qualifying single source drugs." 42 U.S.C. § 1320f–7(2)–(3). This is just one statutory requirement HHS could ignore while claiming that no judicial review is available to correct its overreach. HHS has a "capacious portfolio of authority" under the IRA, which makes "[t]he constitutional problem … more acute." *Cmty. Fin. Servs. Ass'n of Am., Ltd. v. CFPB*, 51 F.4th 616, 640 (5th Cir. 2022), *cert. granted*, 143 S. Ct. 978 (2023).

Standing alone, each of these defects undermines separation-of-powers principles. Taken together, they create a "novel structure," *Free Enter. Fund v. Pub. Co. Acct. Oversight Bd.*, 561 U.S. 477, 496 (2010), that concentrates "significant governmental power" in an administrative agency "accountable to no one," *Seila*, 140 S. Ct. at 2203, to set prices for nearly half of nationwide prescription drug sales. That result is fatal to the Drug Pricing Program. "Perhaps the most telling indication of a severe constitutional problem with an executive entity is a lack of historical precedent to support it." *Id.* at 2201 (cleaned up). Plaintiffs are aware of no other statute that grants such sweeping power to an administrative agency while *also* barring both front-end input via notice-and-comment rulemaking *and* back-end accountability via judicial review.

II. THE IRA VIOLATES THE EXCESSIVE FINES CLAUSE

The Eighth Amendment provides that "[e]xcessive bail shall not be required, nor excessive fines imposed, nor cruel and unusual punishments inflicted." The Excessive Fines Clause "limits the government's power to extract payments, whether in cash or in kind, as punishment for some offense." *United States v. Bajakajian*, 524 U.S. 321, 328 (1998) (citation omitted). It applies not only to criminal fines but also to civil fines designed "in part to punish." *Austin v. United States*, 509 U.S. 602, 610 (1993); *see Hudson v. United States*, 522 U.S. 93, 103 (1997). "[T]he touchstone of the constitutional inquiry under the Excessive Fines Clause is the principle of proportionality: the amount of the [fine] must bear some relationship to the gravity of the offense that it is designed to punish." *Bajakajian*, 524 U.S. at 334.

The IRA's "excise tax" triggers and violates the Excessive Fines Clause. It is designed to punish noncompliance with the IRA's sham negotiation process, and it is wildly disproportionate to the "offense" of refusing to agree that a government-dictated price is "fair."

A. The IRA's Excise Tax Is Punitive

The IRA's excise tax triggers the Excessive Fines Clause because it is punitive in nature. In assessing whether a "tax" operates as a penalty, the Supreme Court has adopted a "functional approach," under which labels are not dispositive. *NFIB v. Sebelius*, 567 U.S. 519, 565 (2012). In the related context of the Double Jeopardy Clause, courts determine whether a tax is punitive by considering its size and purpose. *See Dep't of Revenue of Mont. v. Kurth Ranch*, 511 U.S. 767, 780 (1994); *Dye v. Frank*, 355 F.3d 1102, 1105 (7th Cir. 2004). And "[i]t matters not whether the scheme has a remedial purpose, even a predominantly remedial purpose" because "the Excessive Fines Clause applies to *any* statutory scheme that serves *in part* to punish." *Tyler v. Hennepin Cnty.*, 143 S. Ct. 1369, 1381 (2023) (Gorsuch, J., concurring) (cleaned up).

Here, the IRA's excise tax is unquestionably punitive. A summary of predecessor

legislation accurately described it as a "steep, escalating *penalty*." Title Summary, H.R. 3, at 1 (2022) (emphasis added). Not only does the statutory scheme serve "in part" to punish, that appears to be its *sole* purpose: Prior to the IRA's passage, the Joint Committee on Taxation and the CBO both told Congress that the tax would raise no revenue *at all*, since no rational manufacturer would ever dare trigger it. *See supra*, at 10. Instead, the tax serves to coerce manufacturers into participating in the IRA's sham negotiation process and, failing that, to punish them harshly. Indeed, the relevant section of the tax code is entitled, "Designated drugs during *noncompliance* periods." 26 U.S.C. § 5000D (emphasis added); *see id.* § 5000D(b) (subparagraph entitled "Noncompliance periods"). "Deter[ring]" noncompliance "has traditionally been viewed as a goal of punishment." *Bajakajian*, 524 U.S. at 329. At the very least, the excise tax "cannot fairly be said *solely* to serve a remedial purpose." *Tyler*, 143 S. Ct. at 1381 (Gorsuch, J. concurring) (cleaned up). Therefore, "the Excessive Fines Clause applies." *Id.*

The sheer size of the tax penalty further demonstrates its punitive nature. The tax rate starts at 186% of a drug's total U.S. revenues, and, after 271 days, reaches 1,900%. 26 U.S.C. § 5000D(b)(1)–(4). That enormous levy would cause significant financial harm to manufacturers. *See* Garthwaite Decl. ¶¶ 66, 84–87; Bernie Decl. ¶ 10. Indeed, for every $1 billion in annual net revenues for a drug, a manufacturer would incur *$19 billion* in penalties after a year. Garthwaite Decl. ¶ 66. And if the drug "accounts for approximately 13 percent or more of its manufacturer's total net revenues, applying the excise tax over a full year . . . would result in an excise tax liability of 100 percent of the manufacturer's total net revenues." *Id.* ¶ 85. By any conceivable measure, that is an "exceedingly heavy burden," *NFIB*, 567 U.S. at 565, confirming that the tax is punitive and does not "solely" serve a remedial purpose, *Tyler*, 143 S. Ct. at 1381 (Gorsuch, J. concurring). *See Bajakajian*, 524 U.S. at 337–40 (concluding that a significantly less onerous excise tax was

grossly disproportionate and punitive).

While the excise tax directly punishes noncompliant manufacturers, its harms extend more broadly. Without it, manufacturers could more effectively resist lowball "offers" from HHS that do not align with a medicine's value, allowing prices and reimbursement rates to continue to reflect market forces. In other words, the excise tax is an integral part of the IRA's scheme for imposing government-dictated prices. As such, the excise tax not only punishes manufacturers, but also reduces reimbursements to providers and limits patients' access to innovative treatments.

B. The IRA's Excise Tax Is Grossly Disproportionate

The IRA's excise tax violates the Excessive Fines Clause because it is wildly disproportionate to the "offense" it seeks to punish. While the Eighth Amendment does not require strict proportionality between the punishment and the gravity of the offense, it forbids "gross disproportionality." *Bajakajian*, 524 U.S. at 336. The Supreme Court has considered three general criteria: "the degree of the defendant's reprehensibility or culpability; the relationship between the penalty and the harm to the victim caused by the defendant's actions; and the sanctions imposed in other cases for comparable misconduct." *Cooper Indus. v. Leatherman Tool Group, Inc.*, 532 U.S. 424, 435 (2001) (citations omitted). Federal courts have applied these factors to many kinds of penalties. *See, e.g.*, *Yates v. Pinellas Hematology & Oncology, P.A.*, 21 F.4th 1288, 1314–16 (11th Cir. 2021) (treble damages and statutory penalties); *United States ex rel. Drakeford v. Tuomey*, 792 F.3d 364, 387–90 (4th Cir. 2015) (punitive damages and civil penalties). These factors establish that the excise-tax penalty is grossly disproportionate to the "offense" of failing to participate in the IRA's compelled-negotiation process.

First, the supposed "offense" being punished—a manufacturer's refusal to express its agreement to a price imposed by HHS—does not entail any "reprehensibility or culpability." *Cooper Indus.*, 532 U.S. at 435. Noncompliant conduct under the IRA involves no "threat of

violence," "trickery," or "deceit," nor does it involve "indifference to or reckless disregard for the health and safety of others." *BMW of N. Am. v. Gore*, 517 U.S. 559, 576 (1996). Indeed, failing to agree on a price for the lawful sale of beneficial medicines ordinarily is not even considered wrongful, much less unlawful. At a minimum, this conduct is less culpable than that at issue in *Bajakajian*, where the Supreme Court held that forfeiting $357,444 in currency was grossly disproportionate to the offense of failing to report that same amount of currency to customs inspectors. *See* 524 U.S. at 337–40. The Court held that the defendant had "a minimal level of culpability" because his "crime was solely a reporting offense," since "[i]t was permissible to transport the currency out of the country so long as he reported it." *Id.* at 337, 339. Here, a manufacturer's refusal to accept an offer it views as unfairly low is not culpable at all.

Second, there is no reasonable relationship between the size of the penalty and any harm caused. As in *Bajakajian*, the "offense" at issue is "unrelated to any other illegal activities," it "affect[s] only … the Government," and it does not involve "fraud on the United States." *Id.* at 338–39. Even if the government has an interest in ensuring that drugs are sold for no more than HHS's mandated price, the tax vastly exceeds any alleged harm. A noncompliant manufacturer faces a penalty of multiple times its *total daily revenues* for *all U.S. sales* of the drug—a figure that dwarfs the difference between HHS's price and the actual sales price, and is significantly more disproportionate than the penalty struck down in *Bajakajian*. The penalty also has no aggregate limit; the tax is assessed for *each day* of noncompliance. The excise tax thus "has absolutely no correlation to any damages sustained by society or to the costs of enforcing the law," and "any relationship between the Government's actual costs and the amount of the sanction is merely coincidental." *Austin*, 509 U.S. at 621–22 & n.14 (brackets omitted).

Third, PhRMA is not aware of *any* other statute that imposes similarly severe sanctions on

comparable "misconduct." There are no other statutes that impose any penalties at all—much less crippling penalties on this scale—for the mere failure to agree to a price mandated by the government. That alone shows that the IRA's excise-tax penalty is grossly disproportionate and unconstitutional. Considered in combination with the other novel and severely punitive features of the excise "tax," this unprecedented use of "the power to destroy," *McCulloch v. Maryland*, 17 U.S. (4 Wheat.) 316, 431 (1819), is plainly unconstitutional.

III. THE IRA VIOLATES THE DUE PROCESS CLAUSE

The Fifth Amendment provides that no person shall "be deprived of life, liberty, or property without due process of law." The government violates that prohibition where it (1) deprives a plaintiff of a protected liberty or property interest (2) without adequate procedures. *See Swarthout v. Cooke*, 562 U.S. 216, 219 (2011). Here, the IRA deprives manufacturers, providers, and patients of protected interests, while affording them no opportunity to be heard and barring judicial review.

A. The IRA Burdens Protected Interests

The "'property' interests subject to procedural due process protection are not limited by a few rigid, technical forms," *Perry v. Sindermann*, 408 U.S. 593, 601 (1972), and "extend well beyond actual ownership of real estate, chattels, or money," *Bd. of Regents of State Colls. v. Roth*, 408 U.S. 564, 571–72 (1972). The government can create such interests through statutes, express or implied contracts, "policies and practices," or "rules and understandings" that are "promulgated and fostered by [government] officials." *Perry*, 408 U.S. at 601–03. While the government "may elect not to confer a property interest" in the first place, "it may not constitutionally authorize the deprivation of such an interest, once conferred, without appropriate procedural safeguards." *Cleveland Bd. of Educ. v. Loudermill*, 470 U.S. 532, 541 (1985) (citation omitted).

The IRA impairs manufacturers' patent rights, as well as their right to offer access to their products at prices set by voluntary agreements.

First, Federal law provides that "patents shall have the attributes of personal property," 35 U.S.C. § 261, and more than a century ago, the Supreme Court "indisputably established" that "rights secured under the grant of letters patent … [are] property," *William Cramp & Sons Ship & Engine Bldg. Co. v. Int'l Curtis Marine Turbine Co.*, 246 U.S. 28, 39–40 (1918). The Court has reaffirmed this principle numerous times since. *See, e.g.*, *Horne v. Dep't of Agric.*, 576 U.S. 351, 359 (2015) (patent "confers upon the patentee an exclusive property in the patented invention" (quotation marks omitted)); *Hartford-Empire Co. v. United States*, 323 U.S. 386, 415 (1945) ("That a patent is property … has long been settled.").

In granting property rights, "[t]he federal patent system … embodies a carefully crafted bargain"—namely, that in return for "the creation and disclosure of new, useful and nonobvious advances in technology," inventors obtain "the exclusive right to practice the invention for a period of years." *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 150–51 (1989). The time-limited "right to exclude" gives the patentee "pecuniary rewards," thereby "encouraging innovation. Indeed, the encouragement of investment-based risk is the fundamental purpose of the patent grant." *Biotechnology Indus. Org.* (*BIO*) *v. District of Columbia*, 496 F.3d 1362, 1372 (Fed. Cir. 2007) (quotation marks omitted).

"By penalizing high prices—and thus limiting the full exercise of the exclusionary power that derives from a patent—the [IRA] re-balance[s] the statutory framework of rewards and incentives … as it relates to inventive new drugs." *Id.* at 1374. Because of the long lead times for developing cutting-edge medicines, manufacturers must make investment decisions based on the prospect of *future* sales. *See* Garthwaite Decl. ¶¶ 14, 18, 77(d); Costello Decl. ¶ 18; Gluck Decl. ¶¶ 14–15. For products that were patented or in development at the time of the IRA's passage, manufacturers invested in reliance on the principle that, "[u]pon grant of the patent, the only

limitation on the size of the carrot should be the dictates of the marketplace." *King Instruments Corp. v. Perego*, 65 F.3d 941, 950 (Fed. Cir. 1995); *see BIO*, 496 F.3d at 1272 ("Importantly, the patent system provides incentive to the innovative drug companies to continue costly development efforts.") (citation omitted). In upending that principle, the selection of a manufacturer's drug for government price controls under the IRA deprives that manufacturer of its property rights.

Second, the IRA also disrupts the "treasured" common-law right to offer access to one's products at prices set by voluntary agreements, not government dictates. *Cedar Point Nursery v. Hassid*, 141 S. Ct. 2063, 2072 (2021). That right is more than "a mere subjective 'expectancy.'" *Perry*, 408 U.S. at 602. For decades, Congress and the Executive Branch allowed and encouraged manufacturers to sell their products at market prices. When Congress created Medicare Part D in 2006, Congress even *prohibited* HHS from "interfer[ing] with the negotiations between drug manufacturers and pharmacies and [prescription drug plan] sponsors." 42 U.S.C. § 1395w–111(i). Manufacturers thus have a "legitimate claim of entitlement" based on years of "rules and understandings, promulgated and fostered by" the federal government. *Perry*, 408 U.S. at 602–03.

The IRA's Drug Pricing Program deprives providers and patients of protected interests as well. Providers have a protected interest in being reimbursed on a non-arbitrary basis at a lawful rate. *See Rock River Health Care, LLC v. Eagleson*, 14 F.4th 768, 774 (7th Cir. 2021); *Furlong v. Shalala*, 156 F.3d 384, 393 (2d Cir. 1998). Indeed, for some providers, the IRA threatens their "very existence and financial stability." *Accident, Injury & Rehab., PC v. Azar*, 336 F. Supp. 3d 599, 605 (D.S.C. 2018); Nyquist Decl. ¶ 10. And patients have a protected interest in making choices about their medical care, including being able to continue accessing life-sustaining medicines. *See England v. La. State Bd. of Med. Exam'rs*, 259 F.2d 626, 627 (5th Cir. 1958) (per curiam); *Andrews v. Ballard*, 498 F. Supp. 1038, 1048–51 (S.D. Tex. 1980); Nyquist Decl. ¶ 6;

Spiegel Decl. ¶ 20.

B. The IRA's Procedures Are Constitutionally Insufficient

To determine whether the government has afforded constitutionally adequate procedures under the Due Process Clause, courts balance (1) "the private interest that will be affected by the official action," (2) "the risk of an erroneous deprivation of such interest through the procedures used, and the probable value, if any, of additional or substitute procedural safeguards," and (3) "the Government's interest, including the function involved and the fiscal and administrative burdens that the additional or substitute procedural requirement[s] would entail." *Mathews v. Eldridge*, 424 U.S. 319, 335 (1976). But where the program "provides *no process* whatsoever," the government has "a glaring problem," which "alone" compels the conclusion that it is unconstitutional. *Schepers v. Comm'r*, 691 F.3d 909, 915 (7th Cir. 2012). That is the case here, where the IRA purportedly exempts the Drug Pricing Program from notice-and-comment rulemaking, facially bars administrative and judicial review, and contains no other mechanism for manufacturers, providers, or patients to comment on, or contribute to the agency's decision-making process. Because *no* process cannot constitute *due* process, there is no need for this Court to address the full *Mathews* balancing test. But if this Court were to apply the *Mathews* test in full, the IRA flunks it.

First, the private interests at stake are indisputably weighty. Having a drug selected for "negotiation" under the IRA will have significant economic ramifications for the manufacturer. *See* Garthwaite Decl. ¶¶ 72, 102–03; Bernie Decl. ¶¶ 10, 16–17; Costello Decl. ¶¶ 18–20; Gluck Decl. ¶ 15. Indeed, in some instances, the economic viability of a product may turn *entirely* on HHS's decision whether the product is selected for "negotiation"—or is grouped with other products as one qualifying single source drug. *See* Garthwaite Decl. ¶¶ 72, 102–03; *see also* Gluck Decl. ¶ 15.

The private interests for providers and patients are similarly massive. Providers, including

NICA members, have invested enormous resources building facilities and processes for administering Medicare-reimbursed drugs effectively and efficiently. Nyquist Decl. ¶ 9. For many providers, the effect of IRA price controls on reimbursement rates may make the difference between profit and loss, or even between continuing operations and going out of business. *Id.* ¶ 10. For patients such as those served by NICA members and those represented by GCCA, the decision may be one of life and death. *Id.* ¶ 4. HHS's decisions may determine whether existing products remain available to Medicare and Medicaid beneficiaries and whether future products are brought to market for *any* patients. *Id.* ¶ 10; s*ee also* Spiegel Decl. ¶¶ 14–18.

Second, the risk of erroneous deprivation is high. According to CMS, the IRA leaves many key questions unanswered, allowing the agency to fill in the gaps. Yet CMS also maintains that the Drug Pricing Program is exempt from notice-and-comment rulemaking through 2028, and the statute purportedly bars judicial review of key implementation decisions. *See* 42 U.S.C. § 1320f note; *id.* § 1320f–7. In combination, these features mean that neither regulated entities nor the public have any right to provide views on key determinations before they are made, to have those views taken into account, or to seek judicial review after those decisions become final. Without *any* mechanism for external input or accountability—before or after implementation decisions are made—the risk of misapplying a novel, complex statutory scheme is immense.

Third, the government has no legitimate interest in insulating HHS's decision-making from input by affected parties, or in denying judicial review even for basic statutory-interpretation questions. "The fundamental requirement of due process is the opportunity to be heard at a meaningful time and in a meaningful manner." *FDIC v. Bank of Coushatta*, 930 F.2d 1122, 1130 (5th Cir. 1991) (quotation marks omitted). Yet the IRA affords manufacturers, providers, and patients *no* opportunity to be heard on many of HHS's most consequential implementation

decisions. And this lack of process cannot be justified by any valid governmental interest. The government has identified no emergency requiring suspension of ordinary administrative processes affording input by affected parties and judicial review. Giving interested parties the opportunity to comment on decisions about the law's implementation, and to seek review of statutorily impermissible or irrational choices, would impose only minimal "fiscal and administrative burdens." *Mathews*, 424 U.S. at 335. And such external input would go a long way to reducing "the risk of an erroneous deprivation" of public and private interests. *Id.*

C. Participation in the Drug Pricing Program Is Not Voluntary

The IRA's trampling of the Due Process Clause cannot be excused on the ground that manufacturers' "participation in the Medicare program is voluntary." *Texas Clinical Labs, Inc. v. Shalala*, 1999 WL 1243200, at *4 (N.D. Tex. Dec. 21, 1999). Manufacturers spent billions of dollars developing innovative medicines long before the IRA was enacted, so it cannot be fairly said that manufacturers were "on notice" or "assumed[] the risk" that that pricing would later be decided by government *fiat*. *Id.* at *5. And there is nothing "voluntary" about being forced to choose between acceding to the government's demands on pain of massive penalties or withdrawing from nearly half of the national market for prescription drugs.

The Supreme Court rejected a similar voluntariness argument in *NFIB*. There, the Affordable Care Act attempted to coerce states into expanding their Medicaid programs by "threatening to withhold all of [their] Medicaid grants." 567 U.S. at 575. The Court found that scheme unconstitutional, rejecting the federal government's argument that states "voluntarily and knowingly accept[ed] the terms" of the Medicaid program. *Id.* at 577 (citation omitted). The seven-justice majority explained that, "[i]nstead of simply refusing to grant new funds to States that will not accept the new conditions, Congress … also threatened to withhold those States' existing Medicaid funds." *Id.* at 579–80. The sheer size of the Medicaid program, moreover, made that

threat coercive—"a gun to the head." *Id.* at 581. And Congress "surprise[ed] participating States with post-acceptance or 'retroactive' conditions," which states "could hardly anticipate" when they "developed intricate statutory and administrative regimes over the course of many decades … under existing Medicaid." *Id.* at 581, 584.

Just as the Affordable Care Act threatened to withhold *all* Medicaid funds to coerce states into accepting *new* conditions, the IRA threatens to withhold coverage for *all* of a manufacturer's drugs to coerce price concessions on *one* selected drug in an entirely *new* program. The conditions the IRA places on participation in Medicare and Medicaid thus "take the form of threats to terminate other significant independent grants." *Id.* at 580. Similarly, if withdrawing Medicaid funding was a "gun to the head" of participating states, then withdrawing coverage for all of a manufacturer's products under Medicare and Medicaid is, if anything, even more coercive. *See supra*, at 27; *cf. Doe v. Univ. of Scis.*, 961 F.3d 203, 213 (3d Cir. 2020) (recognizing that "total withdrawal of federal funding" can be "economic dragooning" and "a gun to the head"). And manufacturers "could hardly anticipate" that Congress would pass a draconian new price-control regime when they agreed to participate in Medicare and Medicaid and invested enormous sums to develop innovative medicines years ago. *See* Gluck Decl. ¶¶ 10, 14.

Moreover, as explained, exiting from Medicare and Medicaid does not merely create financial problems for manufacturers; it could devastate providers' and patients' access to the most-frequently prescribed medicines as well. If a manufacturer withdrew from these public insurance programs, their products would lose coverage, and beneficiaries who rely on those products—which frequently will have earned their place as "high-spend" Medicare drugs precisely because there are no satisfactory alternatives—could no longer use federal funding to access their medications. That would be devastating for millions of patients. Leaving patients with no recourse

is directly contrary to manufacturers' core mission, and it could tarnish a manufacturer's reputation in the eyes of patients and providers. *See* Garthwaite Decl. ¶ 88; Bernie Decl. ¶ 16; Costello Decl. ¶ 10; Gluck Decl. ¶ 13. That reputational harm alone could cause further, irreparable long-term financial harm. Manufacturers cannot lightly offer a cutting-edge treatment to millions of patients one day and then take it away the next. Their business relies heavily on the trust of the providers who prescribe their medicines and the patients who take them. *See id.*

In any event, manufacturers could not exit Medicare and Medicaid immediately even if they wanted to. As explained, the Medicare Part D statute delays a manufacturer's ability to terminate its relevant agreements with HHS for 11 to 23 months. *See* 42 U.S.C. §§ 1395w-114a(b)(4)(B)(ii), 1395w-114c(b)(4)(B)(ii), 1395w–153(a)(1). While CMS has represented that it will take administrative action to reduce the delay down to 30 days, *see Revised Guidance* at 120–21, manufacturers have no assurance that the agency will follow through. To begin with, CMS made these representations in the Revised Guidance, which is nonbinding. While the Revised Guidance purports to be "final" on this point, CMS previously issued parts of the Initial Guidance as "final," only to turn around and change them in the Revised Guidance.

Furthermore, CMS's statutory basis for reducing the exit delay is dubious at best and could be subject to serious challenge by providers or patients. The Part D statute contains separate provisions for termination of a manufacturer's Part D agreements—one for termination "[b]y a manufacturer" within 11 to 23 months, and another for termination "[b]y the Secretary [of HHS]" upon 30 days' notice. 42 U.S.C. § 1395w-114a(b)(4)(B)(i), (ii); *id.* § 1395w-114c(b)(4)(B)(i), (ii). The latter provision authorizes termination only "for a knowing and willful violation of the requirements of the agreement or other good cause shown." *Id.* § 1395w-114a(b)(4)(B)(i); *id.* § 1395w-114c(b)(4)(B)(i). In other words, HHS may terminate a manufacturer's agreements only

for serious misconduct. In the Revised Guidance, however, CMS asserts that it will find "good cause" at a manufacturer's request, even if it has committed no misconduct. *See Revised Guidance* at 120–21. CMS thus is seeking to rewrite the statute, transforming the provision governing HHS's termination for misconduct into an end-run around statutory limitations governing termination by a manufacturer. That flouts CMS's duty to "read the words Congress enacted in their context and with a view to their place in the overall statutory scheme." *Turkiye Halk Bankasi A.S. v. United States*, 143 S. Ct. 940, 948 (2023) (quotation marks omitted). Manufacturers accordingly must assume that termination will take up to 23 months, during which time continued participation in Medicare Part D and the IRA's Drug Pricing Program is not voluntary in any sense.

Even if CMS were authorized to reduce the delay for manufacturers to exit Medicare Part D, it remains infeasible for manufacturers to withdraw from Medicare and Medicaid. It is no secret that Medicare and Medicaid make up almost half of the national prescription drug market, which manufacturers cannot simply abandon. CMS's purported reduction is a transparent attempt to bolster the fiction that participation in the IRA's Drug Pricing Program is "voluntary" while ensuring that, in practice, manufacturers still cannot opt out. CMS's dubious assertion of authority simply confirms the agency's willingness to rewrite federal law to suit its own purposes. Finally, though patients are "voluntarily" participating in the market for lifesaving drugs, the IRA denies them procedural due process to participate in decisions that could deprive them of those drugs. *See* Spiegel Decl. ¶¶ 9, 20–22. That is all the more reason the IRA's Drug Pricing Program is unconstitutional.

CONCLUSION

For the foregoing reasons, this Court should grant summary judgment to Plaintiffs, declare the IRA's Drug Pricing Program unconstitutional, and enjoin Defendants from implementing it.

Dated: August 10, 2023 Respectfully submitted,

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Exhibit 01

IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TEXAS
AUSTIN DIVISION

NATIONAL INFUSION CENTER ASSOCIATION, on behalf of itself and its members; GLOBAL COLON CANCER ASSOCIATION, on behalf of itself and its members; and PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA, on behalf of itself and its members, Plaintiffs, vs. XAVIER BECERRA, in his official capacity as Secretary of the U.S. Department of Health and Human Services; the U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; CHIQUITA BROOKS-LASURE, in her official capacity as Administrator of the Centers for Medicare and Medicaid Services; and the CENTER FOR MEDICARE AND MEDICAID SERVICES, Defendants.	CIVIL ACTION NO. 1:23-cv-00707

EXPERT DECLARATION OF PROFESSOR CRAIG GARTHWAITE

August 10, 2023

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I. INTRODUCTION

A. Qualifications

1. I am the Herman R. Smith Research Professor in Hospital and Health Services and a tenured Professor of Strategy at the Kellogg School of Management, Northwestern University. I am also the Director of the Program on Healthcare at Kellogg. I teach courses in the economics of strategy and healthcare strategy and organize Kellogg's healthcare business curriculum. In addition, I am a Research Associate at the National Bureau of Economic Research, and a Faculty Associate at the Institute for Policy Research at Northwestern University.

2. I received a Ph.D. in Economics from the University of Maryland at College Park, a Master's in Public Policy from the Gerald R. Ford School of Public Policy at the University of Michigan, and a B.A. in Political Science from the University of Michigan.

3. Prior to my graduate studies, I was an Economist at Public Sector Consultants in Lansing, MI, and the Director of Research and Chief Economist at the Employment Policies Institute, in Washington, DC.

4. My research focuses on the business of healthcare with a focus on the interaction between private firms and public policies. My recent work has studied pricing and innovation in the biopharmaceutical sector. In this area, I have examined the effect of changes in market size on investments in new product development, the evolving world of precision medicine, the innovation response of United States pharmaceutical firms to increases in demand, and the relationship between health insurance expansions and drug prices. Additionally, I have examined the impact of policies directed at orphan drugs and potential changes to the drug pricing landscape more broadly.[1] Finally, I have examined the demand response of the market to firms receiving new FDA indications for existing medications.[2]

[1] *See e.g.*, Bagley, Nicholas, et al., "The Orphan Drug Act at 35: Observations and an Outlook for the Twenty-First Century," *Innovation Policy and the Economy*, Vol. 19, No. 1, 2019, pp. 97-137, available at https://www.journals.uchicago.edu/doi/full/10.1086/699934. *See also* Chandra, Amitabh, and Craig Garthwaite, "The Economics of Indication-Based Drug Pricing," *The New England Journal of Medicine*, Vol. 377, No. 2, July 13, 2017, pp. 103-106.

[2] *See e.g.*, Berger, Benjamin, et al., "Regulatory Approval and Expanded Market Size," *NBER Working Paper*, June 2021, No. 28889, available at https://www.nber.org/system/files/working_papers/w28889/w28889.pdf.

5. My research has been published in journals such as the Quarterly Journal of Economics, the American Economic Review, the Review of Economics and Statistics, the Journal of Health Economics, the New England Journal of Medicine, the Annals of Internal Medicine, and Health Affairs and has been profiled in media outlets such as the New York Times, the Wall Street Journal, the Washington Post, and Vox. I have testified before the United States Senate, United States House of Representatives, and state legislatures on matters related to healthcare reform, pharmaceutical markets, competition in healthcare markets, and labor economics.[3] I have also testified several times before Congress on matters related to potential healthcare reform focused on controlling drug prices.[4]

6. A copy of my curriculum vitae is attached as **Appendix A** to this report and includes a list of my publications authored in the previous ten years. **Appendix B** includes a list of cases in which I have testified either at deposition or trial within the last four years, and recent testimony before Congress.

B. Assignment

7. I have been asked to describe the economic impact of the Inflation Reduction Act of 2022 with regards to the Medicare Drug Pricing Provision.[5] In particular, I have been asked to evaluate the "negotiation" process required by the Medicare Drug Pricing Provision, and to consider the impact of setting prices for certain selected drugs on innovative behavior by manufacturers and the corresponding potential impacts on current and future patients.

8. In executing my assignment, I have relied on my own training and research, relevant literature, and publicly-available information. A list of the materials that I have relied upon is

[3] *See e.g.*, Garthwaite, Craig Testimony before the House Committee on Oversight and Reform, May 18, 2021, available at https://www.congress.gov/117/meeting/house/112631/witnesses/HHRG-117-GO00-Wstate-GarthwaiteC-20210518.pdf. *See also* Garthwaite, Craig Testimony before the Senate Committee on Commerce, Science, And Transportation's Consumer Protection, Product Safety, and Data Security Subcommittee, May 5, 2022, available at https://www.commerce.senate.gov/services/files/18C46017-860D-4A6A-816D-1290A0B4FBC2.

[4] *See e.g.*, Garthwaite, Craig Testimony before the House Committee on Education and Labor Subcommittee Health, Education, Labor, and Pensions, September 26, 2019, available at https://edworkforce.house.gov/uploadedfiles/craig_garthwaite_-_testimony.pdf. *See also* Garthwaite, Craig Testimony before the Senate Committee on Health, Education, Labor, and Pensions, March 22, 2023, available at https://www.help.senate.gov/imo/media/doc/Senate_Testimony_HELP_Garthwaite.pdf.

[5] I am aware that the Inflation Reduction Act of 2022 has additional provisions that may impact drug prices and patient costs, including a requirement that manufacturers pay rebates if the prices of their drugs increase faster than inflation and limits on Medicare patient out-of-pocket spending, among others. I have not considered or discussed their impacts on patient access in this declaration but reserve the right to do so.

provided in **Appendix C**. I also directed a team of employees from Analysis Group, Inc. ("Analysis Group"), an economics research and consulting group. I am being compensated at an hourly rate of $900. In addition, I receive a portion of the fees paid to Analysis Group for its work. No compensation to me or to Analysis Group is contingent on my findings or on the outcome of this litigation.

9. This declaration summarizes the opinions that I have formed since the Inflation Reduction Act of 2022 was enacted in August 2022, the Centers for Medicare and Medicaid Services ("CMS") Guidance was issued in March 2023 and revised in June 2023, and the Internal Revenue Service ("IRS") Guidance was issued in August 2023. My opinions are based on the research and analyses that I was able to undertake during this period and the information available to me as of the date of this declaration, as well as my own understanding of the Inflation Reduction Act, CMS Guidance, and IRS Guidance. My work in this matter is ongoing, and I may amend or supplement my opinions and declaration, if necessary and appropriate, based on further review of information, research and analyses, or changes to my understanding of the law or its implementation.

II. SUMMARY OF OPINIONS

10. The United States is the undisputed global leader in pharmaceutical innovation, with U.S. firms responsible for $122 billion or 58.9 percent of global research and development ("R&D") spending in 2020 and more than half of the world's new drugs in the last decade. The U.S. market-based approach to setting pharmaceutical prices allows manufacturers and investors to be sufficiently rewarded for drug candidates that do come to market so that they can absorb losses when most drug candidates in development fail. While patients in the U.S. have historically benefited from this approach through the earliest and broadest access to new medications (nearly 80 percent of medicines approved by the FDA in 2021 were available in the U.S. before any other country), fundamental changes to this environment and uncertainty about whether these changes will persist in the future pose an immediate threat to global innovation and access to future treatments in the U.S.

11. In August 2022, the U.S. Congress passed the Inflation Reduction Act of 2022 ("IRA"). The law includes a provision directing the Centers for Medicare and Medicaid Services ("CMS")

to implement a "price negotiation program to lower [Medicare] prices for certain high-priced single source drugs" by setting a so-called maximum fair price ("MFP") that must be offered to all eligible Medicare purchasers and beneficiaries. The statute grants CMS substantial latitude to define certain key terms and processes and to set MFPs, while also imposing extreme penalties on manufacturers who reject the MFPs set by CMS. This combination effectively establishes a *price-setting regime* rather than a *price negotiation process* for covered drugs, which will lead to substantial disruption of the drug development environment that benefits U.S. patients.

12. While the IRA includes some guidelines and broad definitions for identifying MFP-eligible drugs and determining MFPs, it leaves many specifics to CMS' discretion. For example, the IRA states that the MFP cannot exceed the lower of the product's Average Sales Price ("ASP") for a Part B drug or plan-weighted net negotiated price for a Part D drug and an applicable percent of the average non-federal average manufacturer price ("non-FAMP"), but, for most drugs, does not include a floor price. Similarly, while it directs CMS to consider certain factors (e.g., the cost of therapeutic alternatives, comparative effectiveness, unmet medical need), whether and how CMS incorporates these factors in its price calculation is undefined and subject to CMS' sole determination. CMS' Guidance, released on March 15, 2023 and revised on June 30, 2023, sets out CMS' interpretation of certain key terms of the IRA, as well as its intentions for implementing the IRA's directive to "develop and use a consistent methodology and process… that aims to achieve the lowest maximum fair price for each selected drug." Certain definitions reflected there (e.g., for a Qualifying Single Source Drug ("QSSD") subject to MFP-setting and how CMS will measure whether a generic is marketed to determine if competition exists) will expand the statute's price-setting impact on the biopharmaceutical marketplace, manufacturers, and patients.

13. Moreover, the statute imposes extreme penalties on manufacturers who reject CMS' MFP final "offer." Manufacturers will be faced with an untenable choice between: (1) accepting the MFP set by CMS, no matter how low; (2) an excise tax for non-compliance that could escalate from 186 to 1,900 percent of total U.S. revenues from all purchasers for a given product (not just Medicare or government sales); or (3) withdrawing *all products* from coverage under Medicare and Medicaid.

14. Because of the broad latitude the IRA grants CMS alongside the extreme penalties it imposes on manufacturers who reject the MFP set by CMS, Congress has effectively given CMS the unfettered power to set prices for eligible drugs. Indeed, so unconstrained are these prices that CMS could conceivably set a $0 MFP. From an economic perspective, manufacturers (particularly those that sell multiple products), would be better off accepting an offer close to a zero price (or even a negative price, i.e., pay CMS for the right to provide the drug to Medicare participants) than face either of the onerous and financially unsustainable alternatives. Even if such absurd prices were not set by CMS, manufacturers would constantly face the threat that they could be, creating substantial economic uncertainty. This is particularly important in drug development given that manufacturers must make large investment decisions over a decade before potential prices will be set – forcing them to predict the decisions of future CMS leaders operating with broad latitude. Moreover, the statute ostensibly purports to prohibit manufacturers from seeking judicial review on key implementation decisions and once CMS has set its final MFP, no matter how low, or the degree to which it has or has not incorporated fair consideration of the factors it is required to consider. As a result, the process amounts to, as the CEO of one biopharmaceutical company recently described it, "negotiating with a gun to the head."

15. The provisions defined in the IRA, together with uncertainty over how CMS will deploy the latitude in setting prices granted by the IRA, will change economic incentives for manufacturers and in turn, will likely result in consequences that will negatively impact patients. These expected consequences are not limited to MFP-eligible drugs, but instead extend to a wider set of products because of competitive dynamics in the prescription drug and health insurance markets. Foremost among these is reduced drug and indication development that will deny patients access to future treatments, resulting in foregone health outcome improvements. Specifically, the IRA's price-setting provisions and timetable will result, among other things, in:

a. ***Disincentives to invest in and develop post-approval indications***. For drugs that have already received initial FDA approval, certain manufacturers will conclude that post-approval indication development programs are no longer economical because there is not sufficient time during which the drug will be able to earn market-based prices to recoup

those investments before the drug becomes subject to MFP-setting. In other cases, manufacturers and investors will conclude that full drug development programs that anticipate multiple post-approval indications are no longer economical and those drugs will no longer be developed at all.

b. ***Disruptions to established oncology drug development approaches and disincentives to develop additional indications that have the potential to be life-saving.*** Historically, many oncology drugs launch with approval either for a narrow patient population where scientific and clinical proof-of-concept can be most rapidly established, as a later-stage treatment for a single tumor type, or both. Over time, manufacturers often then test and seek approval for the drug as an earlier line of therapy, for concomitant treatment with other medications, or for other tumor types. This development approach prioritizes development of the indications that allow the drug to come to market most rapidly and therefore to become available to patients sooner. Under the IRA, manufacturers will face incentives favoring other approaches, such as delaying or forgoing indications for smaller patient populations, or delaying or forgoing trials that would support use with other frequently administered drugs.

c. ***Reduced incentives to develop drugs that primarily treat older or disabled populations.*** Because the IRA sets MFPs for high Medicare-spend drugs, drugs that are disproportionately reimbursed through Medicare (e.g., those that treat neurodegenerative conditions) will be less appealing innovation targets for manufacturers than those that typically treat younger, non-disabled populations, all else equal.

d. ***Reduced innovation investment for diseases typically treated by small molecule drugs.*** Under the IRA, there are nine years before small molecule drugs and 13 years before biologic drugs may face MFP-setting (with the drug possibly being selected for the MFP-setting process starting at seven and eleven years, respectively). This nine-year period contrasts with the current average period for small molecule drugs between branded drug launch and the market entry of the first substitutable generic drug (the "market exclusivity period") of roughly thirteen years. Because of the difference between the periods of time until IRA price-setting for small molecule and biologic drugs, pharmaceutical manufacturers will face incentives to pursue biologic drugs over small

molecule ones, all other factors equal. This is problematic because small molecule generic drug entry is well-established, assuring cheaper generic drug treatment options for patients and payers, including Medicare and other government programs. In addition, small molecule drugs play a central role in certain therapeutic areas because of their inherent properties (e.g., in mental health and central nervous system conditions due to their ability to cross the blood-brain barrier because of their smaller molecular size), are easier and lower-cost to administer, and more convenient for patients.

e. ***Delayed access to new therapies as non-U.S. markets become relatively more appealing for certain drug launches.*** Manufacturers, in my opinion, will respond to altered incentives for post-approval indication development by changing their launch sequencing approaches in certain circumstances. While launching new drugs in the U.S. first has historically been a well-established strategy, post-IRA, manufacturers in some circumstances are more likely to launch in other geographic markets first to gain experience and sales before "starting the clock" for MFP-setting eligibility in the U.S. This will be particularly true if firms plan to expand a product's initial label over time and/or believe that a launch will be more successful if clinicians have more real-world evidence of efficacy.

f. ***Migration of the MFP payment structure to the commercial market.*** In the event that the IRA's MFP-setting approach migrates from Medicare to the commercially-insured population, consequences to innovation will be further compounded. For example, Colorado has established a State Prescription Drug Affordability Board ("PDAB") with authority to set "upper payment limits" for drugs covered both by public and commercial plans, which has already indicated it will use MFPs (that the IRA requires CMS to publish) as an input to those upper payment limits. Similarly, in Minnesota, products that are selected for an upper payment limit by the PDAB and are subject to an MFP must set the upper payment limit at the MFP. Other PDABs are likely to follow suit, further extending the impact of the IRA on prices and innovation beyond Medicare.

III. BACKGROUND

A. Innovation and Development in the Pharmaceutical Market

1. The drug development process is complex, lengthy, risky, and expensive

16. The process of discovering and developing new drugs is widely understood to be a lengthy, risky, and expensive one. According to the 2021 Congressional Budget Office ("CBO") report on R&D in the pharmaceutical industry:

> "Developing new drugs is a costly and uncertain process, and many potential drugs never make it to market. Only about 12 percent of drugs entering clinical trials are ultimately approved for introduction by the FDA. In recent studies, estimates of the average R&D cost per new drug range from less than $1 billion to more than $2 billion per drug… [t]he development process often takes a decade or more, and during that time the company does not receive a financial return on its investment in developing that drug."[6]

Despite this low success rate, the U.S. biopharmaceutical industry spent more than an estimated $122 billion on R&D in 2020 alone.[7] To maintain this level of investment, the expected return for drugs that do make it to market must be high enough to counterbalance the substantial likelihood of failure. Importantly, firms (including both manufacturers and external investors, such as venture capital and private equity firms) must make judgments about the expected return of a product over a decade before it will actually come to market and begin earning revenues. This requires predicting the market dynamics the product will face at that time prior to making this large fixed and sunk set of initial development investments (i.e., investments that cannot be recovered or repurposed). As the CBO confirms, "[l]ower expected returns would probably mean fewer new drugs, because there would be less incentive for companies to spend on R&D."[8]

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[6] "Research and Development in the Pharmaceutical Industry," *Congressional Budget Office,* April 2021, available at https://www.cbo.gov/publication/57126.

[7] "U.S. Investments in Medical and Health Research and Development 2016-2020," *Research America*, January 2022, available at https://www.researchamerica.org/wp-content/uploads/2022/07/ResearchAmerica-Investment-Report.Final_.January-2022.pdf. Note it is unclear to what degree this estimate comprehensively captures expenditures by external investors (e.g., venture capital, private equity) and it thus may be an underestimate of total U.S. R&D investment.

[8] "Research and Development in the Pharmaceutical Industry," *Congressional Budget Office,* April 2021, Box 3, available at https://www.cbo.gov/publication/57126.

17. The path to a successful new drug is complex and unsure, involving an ecosystem composed of many different types of institutions and firms. Each party plays a role along the complex and uncertain path from early-stage research, to proof-of-concept, to clinical trials in research volunteers, and ultimately, if successful at each stage, to FDA approval and commercialization. The variety of organizations at each step of this process are motivated by different goals and each provides its own unique contribution.

18. While the earliest stages of research are often funded by public actors (e.g., government funders such as the National Institutes of Health, or nonprofit organizations such as universities), reflecting the "public good" nature of basic research, this is only one step in the long path from "bench to bedside." Navigating the rest of this path typically requires a succession of private firms to invest large amounts of fixed and sunk capital with little certainty of a profitable return. Firms are willing to make these investments based on risk-adjusted models of the profitability of their investments — models that are premised on predictions and assumptions about market conditions many years in the future. These private firms, whether early-stage startups or established firms, can only attract and justify the necessary capital for drug development if they expect to generate a return for their investors that is sufficiently attractive compared to other non-pharmaceutical investment options. This is the fundamental economic reality at the center of the drug development process.[9]

19. With the support of venture capital and private equity investors, early-stage biotech firms generate new scientific approaches and drug leads, but are often not ultimately responsible for bringing a drug candidate all the way through clinical testing, regulatory review and approval, and commercialization. Rather, they often seek various forms of economic relationships that reward them for achieving defined milestones and allow them to be acquired by larger, more established, and diversified biopharmaceutical firms (i.e., those with multiple product pipelines).

[9] For further discussion, *see* Garthwaite, Craig Testimony before Senate Committee on Health, Education, Labor, and Pensions, March 22, 2023, available at https://www.help.senate.gov/imo/media/doc/Senate_Testimony_HELP_Garthwaite.pdf.

2. The stages of the drug development process

20. Once early-stage research has identified potential clinical value in a specific molecule or moiety,[10] the drug development process begins. This process involves investments at three stages: pre-clinical research (before human testing begins); clinical testing (human clinical trials and regulatory approval); and post-approval R&D (continued exploration and development of the drug's potential in new patient populations and disease indications). I describe each stage briefly below.

21. **Pre-clinical testing**. Prior to clinical trials in human subjects, potential drug development candidates undergo various pre-clinical tests to determine if the drug candidate is sufficiently promising in terms of pharmacological activity as well as efficacy and safety in relevant animal models to merit further investment and exploration. Many candidates studied during the pre-clinical testing phase are rejected, and never enter clinical trials. Moreover, pre-clinical testing is expensive and time-consuming, with the CBO summarizing that, based on analysis from a 2016 study, "preclinical development accounted for an average of 31 percent of a company's total expenditures on drug R&D, or $474 million per approved new drug," and "takes an average of about 31 months."[11] Candidate drugs that survive the pre-clinical phase are then subjected to extensive clinical testing for safety and efficacy in human research volunteers.

22. **Clinical testing**. Companies file Investigational New Drug ("IND") applications with the FDA detailing planned clinical studies to advance promising drug candidates to human testing.[12] Clinical development typically encompasses three phases: Phase I, Phase II, and Phase III, with research volunteer population sizes that steadily increase from fewer than 100 patients in Phase I trials to Phase III trials that may enroll thousands of patients across many

[10] An active moiety is defined as "the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance." 21 Code of Federal Regulations ("C.F.R.") §314.3, available at https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-314.

[11] "Research and Development in the Pharmaceutical Industry," *Congressional Budget Office,* April 2021, available at https://www.cbo.gov/publication/57126, referencing results from DiMasi, Joseph A., et al., "Innovation in the pharmaceutical industry: New estimates of R&D costs," *Journal of Health Economics*, Vol. 47, May 2016, pp. 20-33.

[12] "Investigational New Drug (IND) Application," *FDA*, available at https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application.

clinical trial sites around the country and the world.[13] The clinical testing phase requires a significant amount of time – averaging 95 months from the start of Phase I trials to the conclusion of Phase III trials.[14] Each phase serves a specific purpose, and they are typically completed sequentially:[15]

- **Phase I** trials (also known as human safety trials) involve a small group of healthy volunteers, usually between 20 and 100 people, who are given the new drug or treatment for the first time. The goal of this phase is to determine the safety of the drug. Drugs with higher levels of expected toxicity are typically tested on people who have the targeted illness.
- **Phase II** trials include a larger group of patients, usually several hundred, who have the condition being treated. The goal of this phase is to evaluate the effectiveness of the treatment and to further assess its safety and identify any side effects.
- **Phase III** trials involve an even larger group of patients, often between 300 and 3,000 people, who have the condition being treated – with the number of patients being dictated in part by the patient population and the statistical power necessary to demonstrate efficacy. The goal of this phase is to confirm the effectiveness of the treatment relative to no treatment, monitor side effects, and compare the new treatment with existing treatments.

23. Traditionally, the FDA has required positive results in two Phase III trials for approval.[16] In addition, **post-approval R&D** may be undertaken to test the development of additional

[13] "What Happens in a Clinical Trial?" *Healthline*, available at https://www.healthline.com/health/clinical-trial-phases. Trial size often varies depending on the treatment area. For example, oncology trials have fewer patients compared to non-oncology specialties. *See* Hirsch, Bradford, et al., "Characteristics of Oncology Clinical Trials," *JAMA Internal Medicine*, Vol. 173, No. 11, June 10, 2013, Table, available at https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/1682358.

[14] "Research and Development in the Pharmaceutical Industry," *Congressional Budget Office,* April 2021, available at https://www.cbo.gov/publication/57126, referencing results from DiMasi, Joseph A., et al., "Innovation in the pharmaceutical industry: New estimates of R&D costs," *Journal of Health Economics*, Vol. 46, May 2016, pp. 20-33.

[15] "Research and Development in the Pharmaceutical Industry," *Congressional Budget Office,* April 2021, available at https://www.cbo.gov/publication/57126; "Step 3: Clinical Research," *FDA*, January 4, 2018, available at https://www.fda.gov/patients/drug-development-process/step-3-clinical-research.

[16] "Development & Approval Process | Drugs," *FDA*, available at https://www.fda.gov/drugs/development-approval-process-drugs.

indications and uses (e.g., potential clinical uses in diseases and patients not originally tested).[17] For example, oncology drugs approved to treat certain cancers may be tested in other tumor types, and immunology drugs may be tested on other conditions responding to the same anti-inflammatory pathways. Typically, as basic safety and efficacy parameters have been established in Phase I and II trials for the same drug, they may not be required (or required to the same extent) for other disease indications, uses, and patient populations.

24. Post-approval R&D may also focus on pharmacovigilance monitoring and long-term safety and side effect issues, which may not have been detected in the clinical trials required for the drug's original approval.[18] For example, long-term follow-up studies in cardiovascular disease may take many years and involve multiple tens of thousands of patients.[19] Indeed, policies increasingly promote or require the use of real-world evidence ("RWE"), with manufacturers investing in such studies to meet regulatory requirements or to further demonstrate the benefits of the therapy.[20] In addition, in certain circumstances, manufacturers may need to fulfill **post-marketing requirements**, such as demonstrations of clinical benefit

[17] I use the term "post-approval R&D" to encompass voluntary R&D activities such as post-marketing commitments that are not required by statute or regulation ("PMCs"), studies by manufacturers to investigate new indications and uses of the drug, and follow-up and monitoring studies for already-approved indications and uses undertaken without an FDA requirement. I distinguish these voluntary activities and investments by manufacturers from mandatory "post-marketing requirements," defined below.

[18] "Research and Development in the Pharmaceutical Industry," *Congressional Budget Office*, April 2021, available at https://www.cbo.gov/publication/57126.

[19] For example, the ALLHAT hypertension and lipid control trial took 8 years to complete. "Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)," *National Heart, Lung, and Blood Institute*, available at https://www.nhlbi.nih.gov/science/antihypertensive-and-lipid-lowering-treatment-prevent-heart-attack-trial-allhat.

[20] For example, the most recent reauthorization of the Prescription Drug User Fee Amendments, PDUFA VII, incorporated as part of the FDA User Fee Reauthorization Act 2022, established a new pilot program "which seeks to identify approaches for generating RWE that meet regulatory requirements in support of labeling for effectiveness (*e.g.,* new indications, populations, dosing information) or for meeting post-approval study requirements." *See* "Advancing Real-World Evidence Program," *FDA*, October 20, 2022, available at https://www.federalregister.gov/documents/2022/10/20/2022-22795/advancing-real-world-evidence-program.

for drugs approved under the accelerated approval pathway, or other safety-related studies required by the FDA.[21]

25. The cost of developing a single successful drug includes the cost of all pre-clinical and clinical trial cash outlays (for both successful and unsuccessful development attempts), as well as capital costs, which reflect the fact that drug development requires locking up these funds for many years. Total costs vary by the magnitude of the clinical trial outlays required, the probability of passing the requirements of each subsequent testing phase, and the length of time necessary to complete each phase — factors which may vary by the disease area, patient population, and other influences. As noted, the overwhelming majority of drug candidates entering pre-human and clinical testing in research volunteers fail, and the costs of development reflect that harsh reality. Estimates of the share of drugs that progress from one phase to the next vary, but one study estimated that "for every 100 drugs entering phase I trials, around 60 advanced to phase II trials, just over 20 entered phase III trials, and only about 12 gained FDA approval."[22] Average R&D costs for approved drugs reflect this high possibility of failure, and a manufacturer's total R&D expenditures also incorporates investments in drugs that fail in pre-human and clinical testing and do not reach the market.[23] Estimates of total development costs vary, but one study estimated an average cost of $2.6 billion (in 2013 dollars) per approved drug based on data on 106 randomly selected drugs

[21] Here, I adopt the FDA's definition of "postmarketing requirements" ("PMRs") as "studies and clinical trials that sponsors are ***required*** to conduct under one or more statutes or regulations" (emphasis in the original). These include studies that are required to be conducted to demonstrate clinical benefit for drugs approved under the accelerated approval pathway, certain required pediatric studies, certain studies for products approved under the Animal Efficacy Rule, and studies required by the FDA to assess a known serious risk related to the use of the drug, signals of a serious risk related to the use of the drug, or to identify an unexpected serious risk when available data indicate the potential for a serious risk. *See* "Postmarketing Requirements and Commitments: Introduction," *FDA*, available at https://www.fda.gov/drugs/guidance-compliance-regulatory-information/postmarket-requirements-and-commitments.

[22] "Research and Development in the Pharmaceutical Industry," *Congressional Budget Office,* April 2021, available at https://www.cbo.gov/publication/57126. *See also* "Step 3: Clinical Research," *FDA*, January 4, 2018, available at https://www.fda.gov/patients/drug-development-process/step-3-clinical-research, which estimates that 70 percent of drugs progress from phase I to phase II, 33 percent of those that enter phase II to phase III, and 25-30 percent of those that begin phase III ultimately go to market.

[23] "Research and Development in the Pharmaceutical Industry," *Congressional Budget Office*, April 2021, available at https://www.cbo.gov/publication/57126.

that initiated development between 1995 and 2007.[24] Including post-approval R&D costs increased the estimate to $2.9 billion.[25]

3. Clinical advances may come from new drugs or from new indications for and uses of approved drugs

26. Clinical advances for patients may come from the discovery, development, and testing of new molecules, or from researching and testing new uses for those molecules among different diseases and patient groups, after they are approved (usually in the form of "post-approval indications").[26] From 2011-2021, 460 new molecular entities ("NMEs") were approved by the FDA.[27] Often, NMEs represent groundbreaking innovations in pharmaceutical research, offering new therapeutic options for patients suffering from various diseases or conditions. At the same time, the process of developing completely new NMEs is risky, time-consuming, and expensive, typically requiring extensive preclinical and clinical studies to ensure safety and efficacy. A manufacturer developing an NME also incurs financial risk due to the relative uncertainty surrounding a product with no real-world data. In addition to the scientific risk, firms are exposed to market risk as competitor products can reduce the revenues of successfully launched drugs. Indeed, it typically takes years for drugs to achieve peak revenues and within this time new molecules, additional indications and uses of competing drugs, or generic versions of existing competitors can be developed and launched, leading to market share pressure and more price competition.[28]

27. New post-approval indications for existing FDA-approved drugs represent an important aspect of drug development and can be of critical clinical importance to patients. My co-authors and I conducted a study of drugs approved by the FDA, and found that between 1995 and 2019, post-approval indications represented approximately 40 percent of all (i.e., total

[24] DiMasi, Joseph A., et al., "Innovation in the pharmaceutical industry: New estimates of R&D costs," *Journal of Health Economics,* Vol. 47, May 2016, pp. 20-33.
[25] DiMasi, Joseph A., et al., "Innovation in the pharmaceutical industry: New estimates of R&D costs," *Journal of Health Economics,* Vol. 47, May 2016, pp. 20-33.
[26] Here I define an "indication" to reflect a separate entry in the "Indications and Usage" section of the FDA label for the approved product. 21 C.F.R. §201.57(c)(2) available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=201.57.
[27] Van Arnum, Patricia, "New Drug Approvals in 2021: The Numbers and Trends," *Value Chain Insights*, January 27, 2022, available at https://www.dcatvci.org/features/new-drug-approvals-in-2021-the-numbers-and-trends/.
[28] Bauer, Hans H., and Marc Fischer, "Product life cycle patterns for pharmaceuticals and their impact on R&D profitability of late mover products," *International Business Review*, Vol. 9, No. 6, December 2000, pp. 703-725.

initial plus post-approval) indications.[29] Another study of 88 new medicines (71 small molecules and 17 biologics) first approved by the FDA between 2010 and 2012 found that post-approval indications (including, for example, new tumor types or new patient populations) are a common feature of drug development; 47, or just over half of the 88 studied drugs, received at least one post-approval indication, and the post-approval indications represented 58 percent of the 209 total indications (including both initial and post-approval indications). Further, many of these post-approval indications were approved years after the initial approval; 53 (44 percent) of them were approved seven or more years after the drug's initial approval. Both small molecule and biologic drugs generated post-approval indications (59 percent of the biologics and 52 percent of the small molecule drugs received at least one post-approval indication).[30] Similarly, another study found that, of the average cost associated with producing a single FDA-approved drug, 25 percent went to post-approval R&D (including additional indications, new dosage forms and strengths, and post-approval monitoring studies).[31]

28. Moreover, because post-approval indications generally can rely on previously completed scientific research and early-phase clinical trials related to safety and some aspects of efficacy, the development of post-approval indications reflects more streamlined pre-clinical and clinical testing, making it a more cost-efficient path for new treatment options than developing a new molecular entity drug. As common biological pathways become better understood, their importance will likely increase.

29. While post-approval indications can be clinically important in many disease states, they are particularly important in oncology. For example, biologic drug Keytruda (pembrolizumab) is an immune checkpoint inhibitor that acts by strengthening the body's immune system T

[29] Berger, Benjamin, et al., "Regulatory Approval and Expanded Market Size," *NBER Working Paper,* June 2021, No. 28889, available at https://www.nber.org/system/files/working_papers/w28889/w28889.pdf.
[30] "Implications of the Inflation Reduction Act Price Setting Provisions on Post-approval Indications for Small Molecule Medicines," *Partnership for Health Analytic Research*, June 2023, available at https://www.pharllc.com/wp-content/uploads/2023/05/Implications-of-the-IRA-on-Post-Approval-Small-Molecules-2006-2012_Final.pdf; Longo, Nicole, "New government price setting policy threatens post-approval research," *PhRMA*, November 10, 2022, available at https://catalyst.phrma.org/new-government-price-setting-policy-threatens-post-approval-research.
[31] DiMasi, Joseph A., et al., "Innovation in the pharmaceutical industry: New estimates of R&D costs," *Journal of Health Economics,* Vol. 47, May 2016, pp. 20-33. Figure references the share of estimated total out-of-pocket R&D cost attributable to post-approval R&D; the corresponding figure when capitalized is 11 percent.

cells' ability to kill some specific cancer cells.[32] It was approved with a single indication in 2014 for certain patients with melanoma,[33] but post-approval clinical trials have shown that the mechanism of action can help many patients with a wide variety of cancers.[34] As I discuss further in Section V.B, Keytruda has subsequently received many additional approvals over the past nine years, for a total of 36 current disease indications across 18 tumor types. While Keytruda may be exceptional in its total number of post-approval indications, Rituxan, which was approved in 1996 for the treatment of non-Hodgkin's lymphoma, provides a similar example; since its initial launch, Rituxan has subsequently been approved for seven additional indications, including three entirely outside of oncology.[35] Several were approved eleven or more years after the drug's initial approval. These approvals are summarized in **Exhibit 2**.

B. Introduction to Medicare and the Current Process for Drug Price Negotiation

30. Before assessing the implications of the IRA Medicare Drug Pricing Provision, I briefly review the different parts of the Medicare program and the benefits Medicare beneficiaries received under each program (which will help frame the impact of the IRA).

1. Medicare program structure

31. Medicare is the U.S. federal health insurance program for people who are 65 or older, certain younger people with disabilities, and people with end-stage renal disease.[36] Medicare is provided through four different parts (A, B, C, and D). Collectively, these four programs provide beneficiaries with inpatient, skilled nursing, hospice, nursing home, at-home health,

[32] "Pembrolizumab (Keytruda)," *Cancer Research UK*, October 8, 2019, available at https://www.cancerresearchuk.org/about-cancer/treatment/drugs/pembrolizumab.
[33] "Keytruda FDA label," *Drugs@FDA*, as of September 4, 2014, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125514lbl.pdf.
[34] "Selected Indications for KEYTRUDA (pembrolizumab)," *Keytruda*, available at https://www.keytrudahcp.com/approved-indications/.
[35] *See* **Exhibit 2**.
[36] "What's Medicare?" *Medicare.gov*, available at https://www.medicare.gov/what-medicare-covers/your-medicare-coverage-choices/whats-medicare.

outpatient care, and prescription drug coverage.[37] In 2021, Medicare benefit payments totaled $829 billion.[38]

32. **Medicare Part A** is administered by CMS and covers inpatient hospital stays, some care in skilled nursing facilities ("SNF") relating to a qualifying inpatient hospital stay, hospice care, limited nursing home care (inpatient-level care in a SNF that is not custodial or long-term care), and some at-home health care.[39]

33. **Medicare Part B** is also administered by CMS and covers medically necessary items and services and certain preventive services. Part B coverage includes physicians' visits, medical supplies, outpatient care, and drugs or biologics that are administered by a physician or other healthcare provider (typically drugs that are infused or injected).[40] By statute, Part B also covers certain types of drugs such as oral anti-cancer, anti-emetic drugs, and certain inhalation drugs.[41]

34. **Medicare Part C**, more commonly known as Medicare Advantage ("MA"), provides an alternative to "original Medicare" coverage through Medicare Part A and Part B. Coverage is provided through plans offered by private health insurance companies that Medicare pays. Most MA plans also include Part D coverage, as well as some additional benefits, such as

[37] "What's Medicare?" *Medicare.gov*, available at https://www.medicare.gov/what-medicare-covers/your-medicare-coverage-choices/whats-medicare.
[38] Cubanski, Juliette, and Tricia Neuman, "What to Know about Medicare Spending and Financing," *Kaiser Family Foundation*, January 19, 2023, available at https://www.kff.org/medicare/issue-brief/what-to-know-about-medicare-spending-and-financing/.
[39] "What Part A covers," *Medicare.gov*, available at https://www.medicare.gov/what-medicare-covers/what-part-a-covers.
[40] "What Part B covers," *Medicare.gov,* available at https://www.medicare.gov/what-medicare-covers/what-part-b-covers; "Prescription drugs (outpatient)," *Medicare.gov*, available at https://www.medicare.gov/coverage/prescription-drugs-outpatient; "Drug coverage under different parts of Medicare," *Centers for Medicare & Medicaid Services,* March 2023, available at https://www.cms.gov/outreach-and-education/outreach/partnerships/downloads/11315-p.pdf.
[41] "Medicare Parts B/D Coverage Issues," *Centers for Medicare & Medicaid Services,* available at https://www.cms.gov/medicare/prescription-drug-coverage/prescriptiondrugcovcontra/downloads/partsbdcoveragesummarytable_041806.pdf.

vision and dental, that original Medicare does not cover.[42] As of 2022, nearly half (48 percent) of Medicare beneficiaries chose to enroll in an MA plan.[43]

35. **Medicare Part D** became available to Medicare beneficiaries in 2006 and helps cover the cost of prescription drugs (i.e., drugs purchased at a pharmacy and that are usually self-administered).[44] Like MA, Medicare Part D is also administered by private health insurance companies and offered through competing plans selected by Medicare beneficiaries. Beneficiaries may choose to enroll in stand-alone Part D prescription drug plans ("PDPs") or MA plans that include Part D coverage (called "MA-PD plans").[45]

2. Current mechanism for Part D and Part B drug reimbursement

36. Reimbursement for drugs administered under Medicare Part D and Medicare Part B is handled differently. Part D is administered by private plan sponsors who are individually responsible for negotiating reimbursement rates with drug manufacturers through a competitive private market process. The prices realized by manufacturers under the Part D program are their list prices less competitive discounts and rebates.[46] In contrast, Part B drugs are acquired and administered by providers, such as hospital outpatient clinics and physicians' offices, and those providers are generally reimbursed by Medicare for those drugs according to a formula that includes the ASP of the drug plus an additional percentage amount. ASP reflects manufacturer net prices to most U.S. commercial ASP-eligible purchasers.[47]

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[42] "Your coverage options," *Medicare.gov*, available at https://www.medicare.gov/health-drug-plans/health-plans/your-coverage-options; "What's a Medicare Advantage Plan," *Medicare.gov*, revised April 2015, available at https://www.medicare.gov/sites/default/files/2018-07/11474.pdf.

[43] Freed, Meredith, et al., "Medicare Advantage in 2022: Enrollment Update and Key Trends," *Kaiser Family Foundation*, August 25, 2022, available at https://www.kff.org/medicare/issue-brief/medicare-advantage-in-2022-enrollment-update-and-key-trends.

[44] "What's Medicare?" *Medicare.gov*, available at https://www.medicare.gov/what-medicare-covers/your-medicare-coverage-choices/whats-medicare; Hoadley, Jack, "Medicare's New Adventure: The Part D Drug Benefit," *The Commonwealth Fund*, March 1, 2006, available at https://www.commonwealthfund.org/publications/fund-reports/2006/mar/medicares-new-adventure-part-d-drug-benefit.

[45] Cubanski, Juliette, and Anthony Damico, "Medicare Part D: A First Look at Medicare Drug Plans in 2023," *Kaiser Family Foundation*, November 10, 2022, available at https://www.kff.org/medicare/issue-brief/medicare-part-d-a-first-look-at-medicare-drug-plans-in-2023/.

[46] Rebates and discounts may be paid directly to plan sponsors, but also to drugs wholesalers (e.g., prompt pay or volume discounts), pharmacies, or PBMs. *See* "Follow the Pill: Understanding the U.S. Commercial Pharmaceutical Supply Chain, *Kaiser Family Foundation*, February 28, 2005, available at https://www.kff.org/other/report/follow-the-pill-understanding-the-u-s/.

[47] SSA, §1847A(c).

37. Because Medicare Part D plans are administered through private health insurance companies, reimbursement to drug manufacturers works much the same way as it does in employer-provided or other commercial health plan coverage. Plan sponsors (or their designated Pharmacy Benefit Manager ("PBM"))[48] negotiate directly with drug manufacturers to determine reimbursement rates (including discounts and rebates).[49] The negotiated price is often conditioned on formulary placement (e.g., the manufacturer's product cannot be on a less favorable formulary tier than a competitor's product) and whether or not there will be access restrictions, such as prior authorization or step therapy requirements.[50] Because formulary placement and access restrictions are the primary ways that insurers orient their beneficiaries towards specific products, manufacturers are willing to offer lower prices for conditions that will increase the demand for their drugs.[51] Part D plan sponsors and manufacturers participate in the negotiation, with manufacturers competing against one another for preferred formulary position and access, and plans in a given geography competing against each other to offer an attractive set of drugs covered and premium amounts to beneficiaries.

38. Under Medicare Part B, CMS reimburses providers who purchase and administer single-source small molecule and originator biologic Part B drugs directly ("buy and bill"),

[48] PBMs are contracted by insurers to act as intermediaries with drug manufacturers. PBMs provide a range of services, including creating and structuring formularies, negotiating rebates for all members with drug manufacturers, and processing claims, among others. *See* "Pharmacy Benefit Managers," *National Association of Insurance Commissioners*, updated June 1, 2023, available at https://content.naic.org/cipr-topics/pharmacy-benefit-managers.

[49] "Prescription Drug Pricing in the Private Sector," *Congressional Budget Office*, January 2007, pp. 1-26, at pp. 2-3, available at https://www.cbo.gov/sites/default/files/110th-congress-2007-2008/reports/01-03-prescriptiondrug.pdf.

[50] "Prescription Drug Pricing in the Private Sector," *Congressional Budget* Office, January 2007, pp. 1-26, at p. 2, available at https://www.cbo.gov/sites/default/files/110th-congress-2007-2008/reports/01-03-prescriptiondrug.pdf; Forrester, Caroline, "Benefits of Prior Authorizations," *Journal of Managed Care Pharmacy*, July 2020, Vol. 26, No. 7, pp. 820-822, at p. 820, available at https://www.jmcp.org/doi/pdf/10.18553/jmcp.2020.26.7.820.

[51] Grabowski, Henry, and C. Daniel Mullins, "Pharmacy Benefit Management, Cost-Effectiveness Analysis and Drug Formulary Decisions," *Social Science & Medicine*, Vol. 45, No. 4, August 1, 1997, pp. 535-544.

generally using a fixed formula of Average Sales Price plus 6 percent ("ASP + 6%").[52,53] In the case of biosimilars, this formula is ASP plus 8 percent (for qualifying products) or 6 percent (for non-qualifying products) of the ASP of the reference biological product.[54] Providers purchase drugs at prices that may vary depending on volume or other discounts available to them or the Group Purchasing Organizations ("GPOs") that represent them.[55,56] Generally, all Part B-eligible drugs (i.e., physician-administered drugs) are covered by Medicare, without the same type of formulary selection and coverage decisions seen for Part D drugs that are applied by private sector plans.[57] Historically, for MA plans, prior authorization was discouraged and step therapy was prohibited. Beginning in 2019, however, MA plans were permitted to apply step therapy requirements in some circumstances (i.e., for new prescriptions or administrations of Part B drugs for beneficiaries not actively receiving the medication).

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[52] ASP is a volume-weighted average actual selling price for a given drug, net of price concessions (such as volume, prompt pay, discounts, chargebacks, and rebates), and excluding certain sales (those excluded from the determination of Medicaid Best Price), calculated with a two-quarter lag. *See* "Average Sales Prices: Manufacturer Reporting and CMS Oversight," *Department of Health and Human Services,* February 2010, p. 2, available at https://oig.hhs.gov/oei/reports/oei-03-08-00480.pdf.

[53] Due to provisions in the Budget Control Act of 2011 and the Balanced Budget and Emergency Deficit Control Act beginning in 2013, "ASP + 6%" effectively became "ASP + 4.3%" for a defined period of years, with suspensions and a 1 percent phase-in during the pandemic. *See* Weidner, Susan, et al., "Observations Regarding the Average Sales Price Reimbursement Methodology," *Evidence-Based Oncology*, June 2021, Vol. 27, No. 4, pp. SP156-SP160, at p. SP156, available at https://www.ajmc.com/view/observations-regarding-the-average-sales-price-reimbursement-methodology; "Medicare Part B Drugs: Trends in Spending and Utilization, 2006-2017," *ASPE Issue Brief*, November 2020, pp. 1-23, at FN 10, available at https://aspe.hhs.gov/sites/default/files/private/pdf/264416/Part-B-Drugs-Trends-Issue-Brief.pdf.

[54] Prior to the IRA, the reimbursement rate for all biosimilars was ASP plus 6 percent of the ASP of the reference biological product. Starting October 1, 2022, the IRA defined a temporary reimbursement rate of ASP plus 8 percent of the ASP of the reference biological product for "qualifying biosimilars" for a 5-year period. A "qualifying biosimilar" is one that maintains a lower ASP than its reference biological product during the 5-year period that began on October 1, 2022. For new qualifying biosimilars first paid under Medicare Part B from October 1, 2022 to December 31, 2027, the 5-year period starts the first day of the calendar quarter that payments are made. "Part B Biosimilar Biological Product Payment," *CMS.gov*, available at https://www.cms.gov/medicare/medicare-fee-for-service-part-b-drugs/mcrpartbdrugavgsalesprice/part-b-biosimilar-biological-product-payment.

[55] "What Is a GPO?" *Healthcare Supply Chain Association*, available at https://supplychainassociation.org/about-us/what-is-gpo/.

[56] O'Brien, Dan, et al., "Group Purchasing Organizations: How GPOs Reduce Healthcare Costs and Why Changing Their Funding Mechanism Would Raise Costs," *Healthcare Supply Chain Association*, pp. 1-40, at p. 21, available at https://supplychainassociation.org/wp-content/uploads/2018/05/Leibowitz_GPO_Report.pdf.

[57] Nall, Rachel, "What is the difference between Medicare Part B and Medicare Part D?" *MedicalNewsToday*, updated March 18, 2021, available at https://www.medicalnewstoday.com/articles/medicare-part-b-vs-part-d#about-medicare.

3. Drug price negotiation within the current Medicare structure

39. The Medicare Part D program was designed to foster competition between plan sponsors and reduce costs.[58] This was reflected, among other things, in a statutory "non-interference clause," which prohibited the Department of Health and Human Services ("HHS") from interfering "with the negotiations between drug manufacturers and pharmacies and PDP sponsors" or from requiring "a particular formulary or institut[ing] a price structure for the reimbursement of covered part D drugs."[59] Because coverage of particular drugs for most classes is not required and Part D relies on negotiation by private firms, Part D plans reflect the preferences for tradeoffs between premium costs and access of members and potential members. As I describe further below, because broader drug coverage appeals to beneficiaries, plans are generally incentivized to include as many treatment options as necessary to attract a sufficient number of customers to their plan at a given premium. However, Part D plans retain the option of not including certain treatments on their formularies (or positioning them on less favorable tiers) if the price offered by a manufacturer for a specific product is judged to be too high given the demand of customers for access to that particular product. In this way, negotiations reflect both the preferences of patients and outside options of manufacturers, i.e., manufacturers have the option to refuse to sell a given drug to a particular plan without forgoing the entire market for all of their products.

40. The role of the private market as a means of negotiating prices under Part D is not an accident or incidental feature of the design of the law. The Medicare Modernization Act ("MMA"), which created the Part D drug benefit, followed years of bipartisan debate about the optimal design of prescription drug coverage in the Medicare program, and the importance of market competition to drive efficient outcomes. For example, discussing a precursor plan in 2000, Rep. Pete Stark stated that:

[58] Lakdawalla, Darius and Wesley Yin, "Insurers' Negotiation Leverage and the External Effects of Medicare Part D," *The Review of Economics and Statistics,* Vol. 97, No. 2, May 1, 2015, pp. 314-331, at Section 2.1, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4414344/pdf/nihms554423.pdf; "Competition and the Cost of Medicare's Prescription Drug Program," *Congressional Budget Office*, July 2014, at Chapter 2, available at https://www.cbo.gov/sites/default/files/113th-congress-2013-2014/reports/45552-PartD.pdf.
[59] Social Security Act ("SSA"), §1860D-11(i)(1)-(2).

> "[We] will have a plan that is absolutely voluntary and that promotes people keeping their current coverage if they like it; that has catastrophic protection; that is simple and is run by private contractors not bureaucrats; and **uses the private market to negotiate prices and not government price controls**."[60] (emphasis added)

41. Similarly, in calling for prescription drug reform, President Bill Clinton remarked, "[w]e desperately need a comprehensive plan to provide a prescription drug benefit that is optional, affordable, accessible to all, **based on competition, not price controls** (emphasis added), to boost seniors bargaining power to get the best possible price…"[61] On signing the MMA into law, a White House press release from President George Bush said, "[p]rivate health plans will compete for seniors' business by providing better coverage at affordable prices-helping to control the costs of Medicare **by using market-place competition, not government price-setting**." (emphasis added).[62]

42. As I describe in Section III.B.2, under the MMA, the government contracts with private insurers to administer drug plans, which negotiate retail drug prices and rebates directly with pharmacies and manufacturers.[63] Part D plan sponsors and manufacturers both carry leverage in the negotiation, driving a competitive process that generally results in lower drug prices as well as a wide range of plan options to beneficiaries. While Part D plans must reflect either a defined standard benefit or a plan of actuarially-equivalent value,[64] they are given substantial latitude to develop unique formularies, placing them in a strong negotiating position with drug manufacturers. Part D plans are required to cover all drugs in six "protected classes,"[65]

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[60] Rep. Stark statement, "Hearing of the House Ways and Means Committee on Medicare and Prescription Drug Coverage," *Federal News Service*, June 13, 2000.
[61] "Remarks by the President at Call to Action for Medicare and Prescription Drug Reform," *White House press release,* May 10, 2000.
[62] "Fact Sheet: Medicare Prescription Drug, Improvement, and Modernization Act of 2003," *White House press release,* December 8, 2003, available at https://georgewbush-whitehouse.archives.gov/news/releases/2003/12/20031208-3.html.
[63] Lakdawalla, Darius and Wesley Yin, "Insurers' Negotiation Leverage and the External Effects of Medicare Part D," *The Review of Economics and Statistics,* Vol. 97, No. 2, May 1, 2015, pp. 314-331, at Section 2.1, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4414344/pdf/nihms554423.pdf.
[64] "What are the Medicare Part D Defined Standard Benefits and Alternatives?" *Medicareful Living*, August 5, 2021, available at https://living.medicareful.com/what-are-the-medicare-part-d-defined-standard-benefits-and-alternatives.
[65] Protected classes include immunosuppressants, antidepressants, antipsychotics, anticonvulsants, antiretrovirals, and antineoplastics. "Medicare Advantage and Part D Drug Pricing Final Rule (CMS-4180-F)," *CMS.gov*, May 16, 2019, available at https://www.cms.gov/newsroom/fact-sheets/medicare-advantage-and-part-d-drug-pricing-final-rule-cms-4180-f.

but are only required to cover two drugs in other classes.[66] As a result, in contrast with MFP-setting, both manufacturers and plan sponsors usually have the option to *walk away* from a negotiation. Plan sponsors may put certain drugs on less favorable tiers, or place access conditions like prior authorization or step therapy for drugs sold by manufacturers who do not offer competitive pricing.[67] Moreover, while a Part D insurer must negotiate manufacturer rebates for Part D enrollees separately from rebates for its commercial plan enrollees, in practice, an insurer with more Part D enrollees may have more negotiating leverage across all transactions.[68]

43. Simultaneously, Part D plan sponsors compete in a crowded marketplace against other plans and must include a broad range of therapies to appeal to beneficiaries. In 2023, the average Medicare beneficiary could choose between 24 PDP stand-alone plans or 35 MA plans for provision of Part D coverage.[69] These plans offer different packages of drug coverage to their members, selected based on net prices (including discounts and rebates) offered by manufacturers, their assessment of the clinical importance of the drugs, and the demands of their members. Medicare's online plan finder allows beneficiaries to easily compare plans available to them across a number of factors, including cost and drug coverage.[70] As a result, plan sponsors have an incentive to include a broad range of products on their formularies to retain and gain new beneficiaries, giving the drug manufacturers some leverage, as well.

44. The Medicare Part D structure has been successful in its objective to foster competition between plan sponsors and reduce costs. For instance, a CBO analysis found that plans' bids

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[66] "What Medicare Part D drug plans cover," *Medicare.gov*, available at https://www.medicare.gov/drug-coverage-part-d/what-medicare-part-d-drug-plans-cover.
[67] *See* Duggan, Mark and Fiona Scott Morgan, "The Effect of Medicare Part D on Pharmaceutical Prices and Utilization," *NBER Working Paper Series*, April 2008, No. 13917, pp. 1-37, available at https://www.nber.org/system/files/working_papers/w13917/w13917.pdf.
[68] Lakdawalla, Darius and Wesley Yin, "Insurers' Negotiation Leverage and the External Effects of Medicare Part D," *The Review of Economics and Statistics,* Vol. 97, No. 2, May 1, 2015, pp. 314-331, at Section 2.1, available at available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4414344/pdf/nihms554423.pdf.
[69] "The Average Medicare Beneficiary Has a Choice of 43 Medicare Advantage Plans and 24 Part D Stand-Alone Plans for Coverage in 2023," *Kaiser Family Foundation Newsroom*, November 10, 2022, available at https://www.kff.org/medicare/press-release/the-average-medicare-beneficiary-has-a-choice-of-43-medicare-advantage-plans-and-24-part-d-stand-alone-plans-for-coverage-in-2023/.
[70] "Explore your Medicare Coverage Options," *Medicare.gov*, available at https://www.medicare.gov/plan-compare/#/?year=2023&lang=en.

were lower when a larger number of plan sponsors competed in a region.[71] Moreover, some have observed that spending on Part D has been below initial projections since the start of the program.[72,73] Similarly, current competition and negotiation in Part D result in substantial rebates, estimated to reduce net costs to Medicare Part D plans on average 42.3 percent (and up to 69 percent) below list prices, after removing patient cost-sharing.[74]

IV. INFLATION REDUCTION ACT (IRA) DRUG PRICING NEGOTIATION PROGRAM

45. The IRA's "Drug Pricing Negotiation Program" aims to lower the prices of high Medicare-spend drugs that do not have generic or biosimilar competition by requiring CMS to set Maximum Fair Prices ("MFPs") for certain Part D and Part B prescription drugs and biologics, starting in 2026. The program will begin with ten drugs covered under Medicare Part D in 2026, followed by increasing numbers of additional drugs in subsequent years.[75] By 2031, 100 drugs will have been selected for MFP-setting across Medicare Part B and Part D, and it has been estimated that the drugs likely to be selected represented almost half of Part B and Part D drug spending in 2020.[76]

46. While the law provides that CMS must "develop and use a consistent methodology and process… that aims to achieve the lowest maximum fair price for each selected drug,"[77] it leaves many terms and processes ambiguous and open for CMS to define, including specifics of how the MFP "negotiation" process will proceed and how required inputs into the MFP will be considered. For example, the IRA defines a maximum ceiling price where the MFP

[71] "Competition and the Cost of Medicare's Prescription Drug Program," *Congressional Budget Office*, July 2014, at p. 2, available at https://www.cbo.gov/sites/default/files/113th-congress-2013-2014/reports/45552-PartD.pdf.
[72] Forecasts for Fiscal Year 2012 start at over $120 billion in 2004 and reduced to $60 billion in 2012, which was just over actual Medicare Part D spending in 2012. *See* Holtz-Eakin, Douglas, and Robert Book, "Competition and the Medicare Part D Program," *American Action Forum*, September 11, 2013, available at https://www.americanactionforum.org/print/?url=https://www.americanactionforum.org/research/competition-and-the-medicare-part-d-program/, Figure on page 6.
[73] "Competition and the Cost of Medicare's Prescription Drug Program," *Congressional Budget Office*, July 2014, at p. 7, available at https://www.cbo.gov/sites/default/files/113th-congress-2013-2014/reports/45552-PartD.pdf.
[74] "Estimate of Medicare Part D Costs After Accounting for Manufacturer Rebates," *QuintilesIMS Institute*, October 2016, available at https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/estimate-of-medicare-part-d-costs-after-accounting-for-manufacturer-rebates.pdf.
[75] SSA, §1192.
[76] "Updated Reconciliation Package Changes Drugs Eligible for Negotiation," *Avalere Health*, July 25, 2022, available at https://avalere.com/insights/updated-reconciliation-package-changes-drugs-eligible-for-negotiation.
[77] SSA, §1194.

cannot exceed a certain amount, but, for most drugs, does not include a floor price. Beginning with this ceiling price, the IRA directs CMS to consider certain other factors, including the cost of therapeutic alternatives, comparative effectiveness, and unmet medical need. How CMS incorporates these factors in its price calculation is undefined in the statute and is subject to CMS determination. If a manufacturer accepts the resulting MFP, it must be offered to all eligible purchasers and Medicare beneficiaries. Failure to do so results in onerous financial consequences that make the supposed "negotiation" more akin to a price-setting regime rather than an actual negotiation.

47. On March 15th, 2023, CMS released an Initial Guidance document, subsequently revised on June 30th, 2023, to clarify its interpretation of the IRA and intentions for implementation.[78] The definitions and intentions included in the guidance exemplify the nearly unlimited discretion the IRA has granted to CMS in regard to implementing the Drug Price Negotiation Program.

48. In this section, I summarize the law and corresponding CMS Guidance, discuss how provisions in the law provide CMS with substantial and unchecked power to define critical elements of the statute, and explain why the process the IRA dictates is more akin to price setting than negotiation.

A. Summary of Drug Price Negotiation Program and CMS Guidance

49. As I discuss in Section III.B, prices for drugs covered by Medicare Part D are currently negotiated directly between manufacturers and Part D plan sponsors or their PBM representatives. Congress sets reimbursement under Part B based on the market prices and average discounts experienced by a broad set of U.S. purchasers – Part B reimbursement to

[78] "Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments," *CMS*, March 15, 2023, available at https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf ("CMS Initial Guidance"); "Medicare Drug Price Negotiation Program: Revised Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026," *CMS*, June 30, 2023, available at https://www.cms.gov/files/document/revised-medicare-drug-price-negotiation-program-guidance-june-2023.pdf ("CMS Guidance").

providers, generally, is set at ASP plus 6 percent.[79] Prior to the passage of the IRA, Congress specifically prohibited the federal government from directly negotiating prices for drugs covered under Medicare Part D through a non-interference clause.[80] The IRA Drug Pricing Negotiation Program amends the previously referenced non-interference clause and now requires the CMS to set prices for certain of the highest-spend Part D drugs (beginning in 2026) and Part B drugs (beginning in 2028).

1. Drugs eligible for pricing program

(a) IRA Statute

50. According to the IRA, drugs subject to MFPs must be Qualifying Single Source Drugs ("QSSDs"), which generally are Part D or Part B-covered brand-name drugs or biologics without generic or biosimilar competitors (and not subject to certain statutory exclusions, discussed below).[81] An increasing number of drugs will become MFP-eligible over the years based on their total Medicare spend, beginning with ten Part D drugs for 2026, followed by another 15 Part D drugs for 2027, 15 Part B or D drugs for 2028, 20 Part B or D drugs for

[79] As noted earlier, due to provisions in the Budget Control Act of 2011 and the Balanced Budget and Emergency Deficit Control Act beginning in 2013, "ASP + 6%" effectively became "ASP + 4.3%" for a defined period of years, with suspensions and a 1 percent phase-in during the pandemic. *See* Weidner, Susan, et al., "Observations Regarding the Average Sales Price Reimbursement Methodology," *Evidence-Based Oncology*, June 2021, Vol. 27, No. 4, pp. SP156-SP160, at p. SP156, available at https://www.ajmc.com/view/observations-regarding-the-average-sales-price-reimbursement-methodology; "Medicare Part B Drugs: Trends in Spending and Utilization, 2006-2017," *ASPE Issue Brief*, November 2020, pp. 1-23, at FN 10, available at https://aspe.hhs.gov/sites/default/files/private/pdf/264416/Part-B-Drugs-Trends-Issue-Brief.pdf. ASP is the average price to all non-federal purchasers in the U.S, including commercial payers, inclusive of discounts and rebates (other than rebates paid under the Medicaid program). *See also* Medicare Prescription Drug, Improvement, and Modernization Act ("MMA") of 2003; SSA, §1847A.

[80] MMA 2003; 42 U.S.C. §1395w-111; SSA, §1860D–11.

[81] For small molecules, a QSSD is a drug (1) that is approved and marketed under section 505(c) of the Federal Food Drug, and Cosmetic Act ("FD&C Act"); (2) for which, as of the selected drug publication date with respect to a given initial price applicability year, at least seven years have elapsed since the date of such approval; and (3) that is not the listed drug for any drug approved and marketed under the Abbreviated New Drug Application under section 505(j) of the FD&C Act. SSA, §1192(e)(1)(A).

For biologics, a QSSD is a product (1) that is licensed and marketed under section 351(a) of the Public Health Service Act ("PHS Act"); (2) for which, as of the selected drug publication date with respect to a given initial price applicability year, at least eleven years have elapsed the date of licensure; and (3) that is not the reference product for any biologic that is licensed and marketed under section 351(k) of the PHS Act. SSA, §1192(e)(1)(B).

For both small molecule drugs and biologics, authorized generics versions will be treated as the same drug as the product approved under 505(c) or licensed under section 351(a) and are not treated as generic or biosimilar competition. SSA, §1192(e)(2)(A).

2029 and every year after.[82] Once a drug becomes subject to an MFP, it will remain so until a certain period of time after it faces a generic or biosimilar competitor, which must also meet CMS' definition of "marketed."[83]

51. The process to identify MFP-eligible drugs for each year will typically begin two years prior, with the exception of those for 2026, for which the process will begin in 2023. The IRA directs CMS to determine Part D "negotiation-eligible drugs," which are (1) the top 50 Medicare-spend QSSDs from Part D (largely small molecule drugs) for which at least seven years have passed since approval, and (2) the top 50 Medicare-spend QSSDs from Part B (largely biologics) for which at least eleven years have passed since licensure (CMS will not develop a list of Part B drugs for the first two years, since these will not be subject to MFPs until 2028).[84] The IRA states that eligible drugs will be selected for the purposes of price-setting based on "total expenditures… during the most recent 12 month period."[85] For Part D products, the IRA specifies that "total expenditures" will be measured based on "the total gross covered prescription drug costs" as defined by the Social Security Act, which in turn depends on CMS' regulatory definition of "gross covered prescription drug costs."[86] For Part B products, the IRA provides that the term "total expenditures" will exclude those expenditures that are "bundled or packaged into the payment of another service,"[87] but does not provide a complete definition of how Part B total expenditures will be calculated. In each year, the designated number of QSSDs with the highest Medicare expenditures that do not meet any of the exclusion criteria will be added to the list of MFP-eligible products.

52. Per the IRA, drugs are not considered QSSDs if they:[88]

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[82] SSA, §1192.
[83] SSA, §1192(c)(1), §1192(d), and §1194(f). The IRA states that a drug will be considered "selected" for price-setting purposes after meeting eligibility criteria to be a QSSD in a year and will remain "selected" for "each subsequent year beginning before the first year that begins at least nine months after the date on which the Secretary determines at least one drug or biological product (A) is approved or licensed… and (B) is marketed pursuant to such approval or licensure." As such, a drug that is already subject to MFP will remain so for at least nine months but up to 21 months after CMS has determined that a generic or biosimilar is marketed. Notably, this period could extend beyond 21 months after a generic or biosimilar actually becomes available based on how CMS elects to determine whether a generic or biosimilar is "marketed," which the IRA left to CMS' discretion.
[84] SSA, §1192(a) and §1192(d).
[85] SSA, §1192(b).
[86] SSA, §1191(c)(5).
[87] SSA, §1191(c)(5).
[88] SSA, §1192(e)(1)(A).

- have a generic or biosimilar approved and marketed; or
- are less than seven years (for small-molecule drugs) or less than eleven years (for biologics) from their FDA-approval or licensure date.

A QSSD can be exempt from the MFP-setting process for several additional reasons:[89]

- if, upon request from a biosimilar sponsor, CMS determines that the reference biologic is highly likely to face biosimilar competition within two years;
- if it has a single orphan designation and all approved indications are within that designation (i.e., no orphan approved indications outside that designation or other orphan designations);
- if it is a plasma-derived product;
- if it had Medicare spend of less than $200 million in 2021;[90] or
- if it is considered a "small biotech drug"[91] (until 2029).

Notably, the IRA does *not* clearly define a number of key elements, including but not limited to how total Medicare expenditures will be measured and how to determine whether a generic/biosimilar is marketed, leaving substantial latitude for CMS to interpret these fundamental elements of the program.

(b) CMS Guidance

53. In its guidance, CMS defines QSSDs as Part D or Part B-covered brand-name drugs or biologics without generic or biosimilar competitors, combining all dosage forms and strengths of the drug/biological product with the same active moiety/ingredient and the same holder of a New Drug Application ("NDA") or Biologics License Application ("BLA"),

[89] SSA, §1192(d)(2), §1192(e)(3) and §11002(f)(1).
[90] This amount will be adjusted using the Consumer Price Index for All Urban Consumers ("CPI-U") for subsequent years.
[91] Small biotech drugs are defined by the IRA as those which account for 1 percent or less of total 2021 Part D or Part B spending and account for 80 percent or more of total 2021 spending under each part on that manufacturer's drugs.

inclusive of products that are marketed under different NDAs/BLAs.[92] Thus, by CMS' definition, a QSSD could incorporate drug or biological products that are branded and sold separately, sometimes across different NDAs or BLAs and trade names.[93] In instances where this occurs, CMS intends to use the earliest date of approval or licensure of the initial FDA application number assigned to the NDA/BLA holder for the active moiety/ingredient to determine if the QSSD meets the MFP eligibility requirements.[94]

54. In its Initial Guidance, CMS stated that it intended to update its interpretation of the regulatory definition of total expenditures described in the IRA (discussed further in Section IV. B below) to "eliminate any potential ambiguity in the regulation text and help to ensure there is a consistent understanding of the term for purposes of both the Part D program and the IRA."[95] In its June 30th, 2023 Guidance, CMS referenced an April 2023 final rule amending the definition of "gross covered prescription drug costs." [96] CMS stated that this definition of "gross covered prescription drug costs" refers to "costs directly related to the dispensing of covered Part D drugs [which] are most logically calculated as the accumulated total of the negotiated prices that are used for purposes of determining payment to the pharmacy or other dispensing entity for covered Part D drugs."[97] CMS clarifies that it will use PDE data to calculate total gross expenditure under Part D and "will not consider any rebates or other price concessions not reflected in the negotiated price of the drug on the PDE to identify and rank negotiation-eligible drugs."[98] Additionally, CMS states that it will use Part B claims data to calculate total allowed charges, inclusive of beneficiary cost-sharing

[92] CMS Guidance §30.1. In its June 30, 2023 Guidance, CMS states that a distinct NDA or BLA does not indicate a distinct QSSD; an active moiety/active ingredient with different dosage forms, strengths, formulations, and licenses is to be considered a single QSSD. CMS bases this interpretation on how it reads Section 1192(d)(3)(B) of the IRA and indicates that "CMS' understanding of the statutory language gives full effect to all relevant provisions of the statute, including sections 1192(e), 1192(d)(3)(B), and 1196(a)(2) of the act; CMS is applying an interpretation of the statute that follows the statutory criteria for the identification of a qualifying single source drug under section 1192(e) of the Act and, consistent with sections 1192(d)(3)(B) and 1196(a)(2) of the Act, effect to the statutory policy that a drug that may be selected for negotiation includes multiple dosage forms and strengths and formulations of that drug." *See* CMS Guidance, p. 11.
[93] While it appears that the 2026 projected list of MFP-eligible drugs will not include any QSSDs encompassing such a scenario, it may occur in future years.
[94] CMS Guidance, §30.1.
[95] CMS Guidance, §30.
[96] CMS Guidance, §30.
[97] CMS Guidance, p. 18.
[98] CMS Guidance, p. 18.

under Part B, to remain consistent with the statutory and regulatory total expenditures definition under Part D which is inclusive of Part D beneficiary cost sharing.[99]

55. With respect to how CMS will measure whether a generic or biosimilar product is marketed, CMS Guidance states that there must be "*bona fide* marketing" (emphasis added) of the generic or biosimilar.[100] CMS indicates that it will review both PDE data and Average Manufacturer Price (AMP) data reported by manufacturers to measure this,[101] but does not provide specific information on what it must see in the PDE or AMP data to determine that bona fide marketing has occurred.[102] Further, CMS indicates that it will take into account the "totality of circumstances" and only allow products to avoid selection or be removed from the selected drug list if they are "subject to meaningful competition,"[103] which it will measure on an ongoing basis once a drug has been selected for MFP.[104] CMS does not provide details on what constitutes "meaningful competition" under the "totality of circumstances."

2. Determining the "maximum fair price"

(a) IRA Statute

56. The IRA states that CMS and each manufacturer of an MFP-eligible drug will enter into a "negotiation"[105] to determine an MFP for all eligible purchasers,[106] which may then be renegotiated if the selected drug is "renegotiation eligible."[107]

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[99] CMS Guidance, p. 17.
[100] CMS Guidance, §30.
[101] CMS Guidance, §30.
[102] While CMS indicates that it will review PDE and AMP data, it leaves open the possibility of using other sources of information, stating that the "determination whether a generic drug or biosimilar is marketed on a bona fide basis will be a *holistic inquiry*" (emphasis added). *See* CMS Guidance, §30.1.
[103] CMS Guidance, p. 74.
[104] CMS Guidance, §90.4.
[105] The use of the "negotiation" or "negotiated price" terminology throughout this report does not imply a finding that the process is a *bona fide* negotiation. *See* Section IV.C.
[106] The IRA defines an MFP-eligible individual with respect to a selected drug as an individual enrolled in a PDP plan under Part D or an MA-PD plan under Part C with coverage provided under the plan for the drug, or an individual who is enrolled under Part B (including those enrolled in an MA plan under Part C) with coverage provided under the plan for the drug. SSA, §1191(c)(1).
[107] A "renegotiation-eligible" drug is defined by the IRA as a selected drug for which: (1) a new indication is added, or (2) there is a change in status to that of an extended-monopoly drug, or (3) there is a change in status to that of a long-monopoly drug, or 4) the Secretary determines that there has been a material change of any of the factors considered during the negotiation process. *See* SSA, §1193(a)(2). *See also* FN 120 for details on the IRA's definition of "monopoly" drugs.

57. The IRA states that the MFP-setting process will begin when CMS publishes the list of drugs selected for a given year by February 1 two years preceding the first year that the MFP is effective.[108] Next, the manufacturer[109] will enter into an "agreement" to participate in the MFP-setting process by February 28, and will submit required information to CMS by March 1.[110] CMS will make an initial MFP "offer" by June 1, giving the manufacturer 30 days to accept or submit a counteroffer. In the event that the manufacturer submits a counteroffer, CMS will send a written response to it, but no timeframe is specified for the CMS response to the counteroffer.[111] The statute does not provide any additional guidance on the course of action for CMS or the manufacturer in the event that the counteroffer is not accepted by CMS, and does not specify a process in which CMS and the manufacturer can discuss or iterate on the offered prices. The MFP-setting process for this initial group of selected drugs will end by November 1.[112] If the manufacturer (defined based on CMS' interpretation of the IRA) chooses to accept CMS' initial or final MFP offer, such Part D drugs will then be covered by all Part D plans at the MFP.

58. The IRA requires CMS to "develop and use a consistent methodology and process… that aims to achieve the lowest maximum fair price for each selected drug,"[113] as well as the ability to specify the process for "renegotiation" of a determined MFP.[114] The IRA states that

[108] For example, a drug selected by February 1, 2025, will face MFP-setting for prices in 2027. Selected drugs for 2026 will follow a different timeline. The list of selected drugs for 2026 will be published no later than September 1, 2023. *See* SSA, §1194.
[109] SSA, §1191(c)(1) cross references SSA, §1847A(c)(6)(A) to define "manufacturer," which in turn refers to SSA, §1927(k)(5) which defines a manufacturer as "any entity which is engaged in—(A) the production, preparation, propagation, compounding, conversion, or processing of prescription drug products, either directly or indirectly by extraction from substances of natural origin, or independently by means of chemical synthesis, or by a combination of extraction and chemical synthesis, or (B) in the packaging, repackaging, labeling, relabeling, or distribution of prescription drug products."
[110] I note that a substantial burden will be placed on manufacturers, who are required to aggregate and submit data as specified by CMS on "Selected Drug Information," "Non-FAMP Data Collection," "Research and Development Costs and Recoupment," "Current Unit Costs of Production and Distribution," "Prior Federal Financial Support," "Patents, Exclusivities, and Approvals," "Market Data, Revenue, and Volume," and "Certification of Submission." In certain cases, manufacturers will be required to obtain and report information on behalf of "Secondary Manufacturers" (*see* FN 121). *See* "Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA)," *CMS*, March 21, 2023, available at https://www.govinfo.gov/content/pkg/FR-2023-03-21/pdf/2023-05784.pdf.
[111] SSA, §1194.
[112] As outlined in **Exhibit 1**, this timeline will be slightly different for drugs included on the 2026 list.
[113] SSA, §1194 (b)(1).
[114] SSA, §1194 (f)(1).

CMS' initial MFP offer to and subsequent discussions with the manufacturer will consider a number of inputs. These factors include but are not limited to:[115]

- the cost of the alternative treatment and comparative effectiveness of the selected drug relative to that alternative;
- the unmet medical needs being addressed by the selected drug;
- R&D costs incurred by the manufacturer and the extent to which these costs have been recouped;
- current costs of production and distribution;
- federal financial support for novel therapeutic discovery and development related to the selected drug; and
- market data, revenue, and sales volume data for the selected drug in the U.S.

59. The IRA does *not* define how to identify these inputs; notably it does not specify how to determine a therapeutic alternative to a selected drug, or how to identify unmet medical need. CMS itself emphasizes that "while the statute requires CMS to provide an initial offer and a justification, it does not specify how CMS should determine an initial offer nor how or to what degree each factor should be considered."[116]

60. The guidance offered by the IRA regarding how the MFP amount should be calculated is limited. The IRA only provides that the MFP amount offered by CMS may not exceed a determined price ceiling, without providing any price floor for most drugs.[117] The price ceiling will be the lower of the product's average net price (Part D drugs) or average sales

[115] SSA, §1194.
[116] CMS Guidance, §60.3.
[117] A temporary price floor is established for small biotech drugs for price applicability years 2029 and 2030. For these drugs, the MFP may not be less than 66 percent of the average non-FAMP, adjusted for inflation. SSA, §1194 (d). This price floor will act as a transition following the small biotech exclusion for price applicability years 2026-2028.

price (Part B drugs),[118] and an applicable percent of the average non-FAMP (with the percentage determined based on the so-called "monopoly" category the drug belongs to).[119,120] This price ceiling is likely to be well below the average commercial prices in the market, as the non-FAMP price metric already incorporates average discounts provided to wholesalers or distributors for commercial distribution.

61. Most notably, while the IRA references a "negotiation" between CMS and manufacturers to determine the MFP for eligible products, it does *not* define how this so-called "negotiation" will take place, leaving substantial latitude for CMS interpretation.

(b) CMS Guidance

62. CMS has provided guidance on how it will identify the manufacturer of each MFP-eligible product, additional dates for the "negotiation" process, and certain details on inputs it will consider for the MFP.

[118] Specifically, the ceiling price cannot exceed the lower of the drug's enrollment-weighted net negotiated price for a Part D drug, or the average sales price for a Part B drug, and a specified percentage of the drug's average non-FAMP. For Part D drugs, this calculation uses the sum of the enrollment-weighted negotiated prices of the drug under each PDP or MA-PD plan, after netting out all price concessions received by the plan or by PBMs on behalf of the plan. For Part B drugs, this calculation uses the average sales price for the drug determined under SSA, §1847A(b)(4). The specified percentage of a drug's average non-FAMP have been set at 75 percent for small-molecule, so-called short-monopoly drugs with more than nine years but less than 12 years since approval, 65 percent for so-called extended-monopoly drugs with between 12 and 16 years since approval or licensure, and 40 percent for so-called long-monopoly drugs with at least 16 years since approval or licensure. For small biotech drugs, starting in 2029, the maximum fair price will be set at 66 percent of the non-FAMP. From 2028 onwards, the MFP can be renegotiated for a drug that becomes a so-called "long-monopoly drug" or "extended-monopoly drug," or if there is a material change in any factors considered during the original price-setting process, including a new indication for the drug. SSA, §1194 (c), §1194(d), and §1194(f).

[119] The non-FAMP is the average price paid to the manufacturer by merchant middlemen (wholesalers and distributors), net of wholesaler discounts and chargebacks relating to non-federal sales. This price does not take into account any prices paid by the federal government or rebates paid by the manufacturer to health plans and PBMs. The non-FAMP was originally formulated as the maximum price for branded drugs that manufacturers can charge the "Big Four" – the Department of Veterans Affairs, the Department of Defense, the Public Health Service, and the Coast Guard. *See* "Prices for Brand-Name Drugs Under Selected Federal Programs," *Congressional Budget Office*, June 2005, available at https://www.cbo.gov/sites/default/files/109th-congress-2005-2006/reports/06-16-prescriptdrug.pdf. Thus, this price was not intended for as large of a patient population as is covered by Medicare.

[120] The IRA defines a so-called "monopoly" for short and long monopoly drugs, which mischaracterizes the competitive environment a drug faces. Specifically, the descriptive term of "monopoly" that the IRA used to classify these drugs is potentially inaccurate and misleading, overlooking the likelihood that branded drugs face competition from therapeutic alternatives during their market exclusivity periods.

63. To the extent that more than one entity meets the statutory definition of manufacturer for a selected drug, CMS intends to designate the entity that holds the NDA(s)/BLA(s) for that drug as the "Primary Manufacturer" for purposes of the price-setting process.[121]

64. Next, the CMS Guidance adds to the dates that the IRA dictates for the price-setting process. CMS will first hold a meeting with manufacturers between the submission of relevant data and the initial offer, which will be restricted to providing context on the original data and adding any newly available data related to alternative treatments.[122] CMS indicates that if neither its initial offer nor the manufacturer's counteroffer is accepted, CMS and the manufacturer can hold up to three possible in-person or virtual meetings before CMS provides its final MFP offer.[123] Specifically, this includes a minimum of one meeting with the manufacturer to discuss CMS' written initial offer, the manufacturer's written counteroffer, and factors considered. After this initial meeting, CMS and the manufacturer each have the option to request one additional meeting. At the conclusion of these meetings, CMS will provide the manufacturer with its final MFP offer, which the manufacturer can choose to accept or reject.[124] **Exhibit 1** summarizes the combined price-setting timeline based on the dates provided in the IRA and in CMS' Guidance.

65. Finally, regarding the factors outlined by the statute for consideration during MFP-setting, CMS has indicated that it will only include pharmaceutical alternatives and that it will consider "data submitted by Primary Manufacturer and the public, FDA-approved indications, indications included in CMS-approved Part D compendia, widely accepted clinical guidelines, and peer-reviewed studies…" as well as "…clinical evidence available through literature searches when a therapeutic alternative has not yet been incorporated into

[121] CMS goes on to state that it intends to refer to any other entity that meets the statutory definition of manufacturer for a drug product included in the selected drug and that either (1) is listed as a manufacturer in an NDA or BLA for the selected drug or (2) markets the selected drug pursuant to an agreement with the Primary Manufacturer as a "Secondary Manufacturer." Secondary Manufacturers would include any manufacturer of any authorized generics and any repacker or relabeler of the selected drug that meet these criteria. CMS Guidance, §40.
[122] CMS Guidance, §60.4. Specifically, the statute states "CMS will invite the Primary Manufacturer for each selected drug to one meeting in Fall 2023 after the data submission deadline. The purpose of this meeting will be for the Primary Manufacturer to provide additional context on its data submission and share new section 1194(e)(2) data, if applicable, as CMS begins reviewing the data and developing an initial offer."
[123] CMS Guidance, §60.4.3. Note that the manufacturer is entitled to two meetings and CMS may request a third.
[124] CMS Guidance, §60.4.3.

nationally recognized, evidence-based guidelines."[125] Moreover, it will consider unmet medical need separately for each indication, and an unmet medical need will be identified "in cases where limited or no treatment options exist."[126]

3. Penalties for refusing the MFP or non-compliance in the MFP-setting process

(a) IRA Statute and IRS Guidance

66. Per the IRA, in the event that a manufacturer chooses not to comply with the MFP-setting process or does not agree to the final MFP, it will be subject to an excise tax. This tax will be levied if a manufacturer fails to enter into the initial "agreement" to participate in the price-setting process in a timely manner, fails to "agree" to the MFP on time, or fails to submit the required information within the stipulated timeframe.[127] While the IRA dictates the tax is calculated based on an "applicable percentage" that starts at 65 percent and escalates by 10 percentage points every 90 days until it reaches 95 percent from the 271st day onward, the tax is calculated as the ratio of "(1) such tax, divided by (2) **the sum of such tax and the price for which so sold** [*sic*] [emphasis added]," which results in a tax rate that is actually much higher.[128] For example, the first day a manufacturer is subject to the excise tax (at a 65 percent rate), the tax would be approximately $1.86 for each dollar of revenue (i.e., $1.86 is equal to 65 percent of $2.86 – the sum of the $1.86 tax and the $1.00 in revenue), or 186 percent of the product's revenue. As such, the excise tax would start at 186 percent and increase every 90 days until it reaches *1,900 percent* from the 271st day onward (e.g., if annual drug net revenues are $1 billion, the excise tax on day 272 would reach $19 billion on an annualized basis, at which point $19 billion would equal 95 percent of the sum of $1 billion plus $19 billion).[129] Alternatively, if a manufacturer does not wish to pay the tax, it

[125] CMS Guidance, §60.3.1.
[126] CMS Guidance, §60.3.3.2.
[127] "Tax Provisions in the Inflation Reduction Act of 2022 (H.R. 5376)," *Congressional Research Service*, August 10, 2023, pp. 4 and 29, available at https://crsreports.congress.gov/product/pdf/R/R47202.
[128] 26 U.S.C. §5000D.
[129] *See e.g.,* "Description of the Revenue Provisions of H.R.3, the "lower drug costs now act of 2019," *Joint Committee on Taxation*, October 18, 2019, available at https://www.congress.gov/116/meeting/house/110137/documents/HMKP-116-WM00-20191022-SD006.pdf; York, Erica, "Lawmakers' Tax Rate to Help Pay for Reconciliation is 1,900 percent," *Tax Foundation*, August 31, 2021, available at https://taxfoundation.org/hr3-tax-pay-for-reconciliation/.

can choose to withdraw *all* of its drugs from coverage under the Medicare and Medicaid programs.[130,131]

67. On August 4th, 2023, the Treasury Department and the IRS issued a brief guidance document for drug manufacturers, producers, and importers with general information on how they intend to implement this tax, including the scope of taxable sales, how the tax will be charged in relation to price, and procedural rules.[132] This document supports the conclusion that the tax escalates from 186 percent to 1,900 percent of a drug's revenues.[133] The guidance also notes that the tax will be imposed on "taxpayer sales of designated drugs dispensed, furnished or administered to individuals under the terms of Medicare."[134] It is not clear what the IRS means by "under the terms of Medicare."

68. Manufacturers could also face significant civil monetary penalties if they are found to violate parts of the price-setting process. For example, manufacturers are subject to penalties of $1 million per day if they fail to comply with the terms required by CMS under the "agreement" required under section 1193 of the Social Security Act.[135] Moreover, if manufacturers fail to offer the finally-determined MFP to a Medicare beneficiary or to that beneficiary's provider

[130] 26 U.S.C. §5000D(c) gives manufacturers the option to "suspend" the excise tax. Under this subsection, the excise tax is suspended beginning on the first day that: 1) a manufacturers gives notice to CMS that it is terminating all of its "applicable agreements" (i.e., Coverage Gap Discount Program ("CGDP") Agreement, Manufacturer Discount Program ("MDP") Agreement, and Medicaid National Drug Rebate Agreement), and 2) none of the manufacturer's Part D drugs are covered under a CGDP or MDP Agreement.

[131] Also, although a manufacturer could theoretically try to avoid Part B coverage by not entering into a Medicaid rebate agreement, CMS as a practical matter may continue to provide reimbursement in error for drugs taken by covered patients when claims are submitted by participating Part B providers, even if the manufacturer does not have a current rebate agreement in place.

[132] "Treasury and IRS issue guidance relating to section 5000D of the Internal Revenue Code," *IRS.gov*, available at https://www.irs.gov/newsroom/treasury-and-irs-issue-guidance-relating-to-section-5000d-of-the-internal-revenue-code.

[133] Specifically, the document states that "when the §5000D tax is separately charged on the invoice or records pertaining to the sale of a designated drug by the manufacturer, the tax is not part of the price of the designated drug." It also states that if the manufacturer does not make a separate charge for the tax while invoicing sales, it will be presumed that the tax is included in the amount charged for the drug, and thus the tax due to the IRS will be computed on and deducted from this amount. The document provides the following example. If the manufacturer charges a purchaser $100 for a drug during the first 90 days of the statutory period but does not separately make a charge for the tax, $65 will be allocated to the tax, while the remaining $35 will be allocated to the price of the drug. *Note:* A tax of $65 on a drug with a price of $35 equals a taxation rate of $65/$35, or 186%. "Section 5000D Excise Tax on Sales of Designated Drugs; Reporting and Payment of the Tax," *IRS.gov*, Section 3; pp. 3-4, available at https://www.irs.gov/pub/irs-drop/n-23-52.pdf.

[134] "Section 5000D Excise Tax on Sales of Designated Drugs; Reporting and Payment of the Tax," *IRS.gov*, Section 3; p. 3, available at https://www.irs.gov/pub/irs-drop/n-23-52.pdf.

[135] SSA, §1197(b).

or dispenser, they are subject to significant civil monetary penalties equal to ten times the difference between the price charged (calculated on a net basis) and the MFP. The statute gives CMS the ability to define what instances constitute a failure to offer the finally-determined MFP to a beneficiary or provider. Additionally, if a manufacturer knowingly submits false information under the procedures for the small biotech exception or the biosimilar delay, it is subject to a $100 million penalty for each item of false information provided.

(b) CMS Guidance

69. The IRA gives the Secretary jurisdiction over the civil monetary penalties by granting CMS the responsibility of identifying and monitoring non-compliance by a manufacturer and establishing a mechanism through which violations shall be reported. The CMS Guidance addresses how CMS will enforce these penalties,[136] and states that the IRS will administer the tax and the Treasury Department will issue additional guidance relating to the excise tax.[137]

70. I have included in **Appendix D** the drugs likely to be subject to MFP in 2026 based on the IRA criteria and CMS Guidance.

B. The IRA gives CMS substantial latitude to define critical elements of the statute

71. The IRA provides CMS with substantial latitude to define critical elements of the law at its discretion. This freedom allows for additional impact on both biopharmaceutical manufacturers and patients as a result of CMS decisions, beyond (and sometimes at odds with) what the IRA specifies. As discussed in Section IV.A, based on the discretion provided in the IRA, CMS has adopted certain definitions and communicated certain implementation processes that it plans to follow. In particular, CMS' Guidance further interprets (1) the definition of QSSD, (2) how total Medicare expenditure will be quantified in selecting the drugs that will be subject to price-setting in a given year, (3) how CMS will determine whether a generic or biosimilar is marketed, and (4) the specifics of the MFP "negotiation"

[136] CMS Guidance, §100.
[137] CMS Guidance, §90.3.

process. While CMS has provided these additional elements of interpretation, other ambiguous aspects of the IRA remain undefined, leading to substantial uncertainty. Most notably, neither the IRA nor the CMS Guidance provide sufficient information on how CMS will enforce the requirement that MFPs be made available to all eligible parties and not to ineligible parties, or whether it will be permissible for Medicare Part D plans nevertheless to put formulary restrictions on products facing MFPs.

72. First, CMS has interpreted the IRA definition of QSSD to include "all drugs with the same active moiety or active ingredient."[138] This interpretation groups multiple drugs or biological products (regardless of dosage form, strength, or route of administration) under a single QSSD, even if they are approved under separate NDAs/BLAs, marketed as different drugs, or used to treat different conditions.[139,140] This interpretation has a number of implications for innovation investments. Specifically:

a. CMS has indicated that it will use the earliest NDA/BLA approval date for that active moiety or active ingredient to "start the clock" on when a QSSD will be MFP-eligible.[141] For example, if a manufacturer produces two drugs with the same active moiety that have differing routes of administration, are marketed as two separate drugs, and have been approved for different indications, for the purposes of price-setting under the IRA, both of them will be treated as the same QSSD. Moreover, the earlier of the two approval dates will be used by CMS to determine when the QSSD will be MFP-eligible. Manufacturers are less likely to develop innovative products with valuable patient benefit if they will be considered the same QSSD as an existing

[138] Elsewhere, an active moiety is defined as "the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance." 21 C.F.R. § 314.3, available at https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-314.
[139] CMS Guidance, p. 12 and §30.1.
[140] CMS's interpretation of the IRA is based on its understanding of SSA, §1192(d)(3)(B) (which directs CMS to "use data that is aggregated across dosage forms and strengths of the drug, including new formulations of the drug, such as an extended release formulation, and not based on the specific formulation or package size or package type of the drug"). Others, including those submitting comments to CMS (*see* CMS Guidance, p. 11) have interpreted the statute differently and do not believe that the language in SSA, §1192(d)(3)(B) is relevant for the identification of QSSD (which is defined separately in SSA, §1192(e)). In this declaration I discuss the innovation implications based on CMS's interpretation of the QSSD definition but note that there would be other innovation implications based on this alternative interpretation.
[141] CMS Guidance, p. 13 and §30.1.

product and will thus be subject to price controls ahead of when they would be expected to face generic or biosimilar competition.

b. Under the CMS definition of QSSD, manufacturers would be disincentivized to engage in additional clinical trials for new indications of their products if they face immediate price controls. For example, Eli Lilly and Boehringer Ingelheim are running clinical trials for Jardiance, their SGLT2 inhibitor that has already been approved for glycemic control and reduction in the risk of cardiovascular death and hospitalization, for a potential new indication in adults with chronic kidney disease.[142,143] Manufacturers are less likely to continue investing in such additional clinical trials if their drugs will be subject to price controls based on the CMS' definition of a QSSD.

c. A further implication of including all dosages and new formulations in the definition of a QSSD is reduced incentives to develop new formulations. Examples of new formulations that provide important patient benefits are newer extended-release/long-acting antipsychotic formulations for individuals living with schizophrenia to prevent relapse and rehospitalization, and to address negative consequences of poor adherence associated with the disease.[144] As I discuss in Section V.A, this definition

[142] Jardiance has already been tested and approved for a chronic kidney disease indication in the EU. "Jardiance FDA label," *Drugs@FDA*, as of June 20, 2023, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/204629s042lbl.pdf; "US FDA accepts supplemental New Drug Application for Jardiance® for adults with chronic kidney disease," *Eli Lilly Investors*, January 20, 2023, available at https://investor.lilly.com/news-releases/news-release-details/us-fda-accepts-supplemental-new-drug-application-jardiancer-0; "Jardiance® (empagliflozin) approved in the EU for the treatment of adults with chronic kidney disease," *BioSpace*, July 25, 2023, available at https://www.biospace.com/article/releases/jardiance-empagliflozin-approved-in-the-eu-for-the-treatment-of-adults-with-chronic-kidney-disease/.

[143] Eli Lilly is also running additional clinical trials on Mounjaro, its tirzepatide drug that has already been approved for type 2 diabetes, for a new weight loss indication. *See* Liu, Angus, "In heavyweight obesity fight, Eli Lilly launches Mounjaro head-to-head trial against Novo Nordisk's Wegovy," *FiercePharma*, April 21, 2023, available at https://www.fiercepharma.com/pharma/heavyweight-obesity-fight-lilly-launches-mounjaro-head-head-trial-against-novos-wegovy. Note that while weight-loss medications are not currently covered by Medicare, it is possible that this may change in the future. For instance, the Treat and Reduce Obesity Act would allow Medicare coverage of weight-loss medications. Moreover, recent modeling suggests that covering new obesity treatments may be an attractive option for policymakers, in that it may contribute to substantial cost offsets for Medicare over time. *See, e.g.,* Young, Kerry D., "Will ICER Review Aid Bid for Medicare to Pay for Obesity Drugs?" *MedScape*, November 21, 2022, available at https://www.medscape.com/viewarticle/984386; "Medicare Coverage of Weight Loss Drugs Could Significantly Reduce Costs," *USC Schaffer*, April 18, 2023, available at https://healthpolicy.usc.edu/article/medicare-coverage-of-weight-loss-drugs-could-significantly-reduce-costs/.

[144] Siegel, Steven J., "Extended Release Drug Delivery Strategies in Psychiatry," *Psychiatry (Edgmont)*, Vol. 2, No. 6, June 2005, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3000189.

will have substantial impacts on indication sequencing decisions and other investments in innovation in the biopharmaceutical industry.

73. Second, the IRA states that MFP-eligible Part D drugs will be selected based on "total expenditures" under Part D, defining these expenditures to include "total gross covered prescription drug costs (as defined in section 1860D-15(b)(3) of the Social Security Act)."[145] The definition of these costs under the Social Security Act depends on CMS' broader regulatory definition of "costs incurred under a Part D plan,"[146] which could be subject to change, introducing substantial ambiguity in how these costs will be determined in the future. For example, at the time the IRA was enacted, CMS' regulations defined "gross covered prescription drug costs" to be *net* of direct and indirect remuneration, including manufacturer rebates and discounts.[147] However, after the IRA was enacted, CMS revised this regulatory definition to *remove* the language that indicated that such costs are net of such direct and indirect remuneration.[148] Since the IRA depends on CMS' cost definition, which is a broader regulatory definition used for a variety of different reimbursement purposes, it may be subject to change periodically. This definition and the corresponding exclusion or inclusion of direct and indirect remuneration will play an important role in determining which Part D QSSDs will be selected for MFP-setting.

74. Third, the IRA stipulates that drugs facing approved and "marketed" generic or biosimilar competition are ineligible for selection or will no longer be subject to the MFP. CMS has taken the position that it may define the term "marketed" to mean "bona fide" marketing. While CMS has indicated that it will review PDE and AMP data to determine whether a drug has been marketed,[149] it has not indicated what share of prescriptions or total payments it must see in the PDE or AMP data to determine that there has been "bona fide marketing" of

[145] SSA, §1191(c)(5) and §1860D-15(b)(3).
[146] SSA, §1860D-15(b)(3).
[147] 42 C.F.R. §423.308, available at https://www.ecfr.gov/current/title-42/chapter-IV/subchapter-B/part-423/subpart-G/section-423.308.
[148] "Medicare Program; Contract Year 2024 Policy and Technical Changes to the Medicare Advantage Program, Medicare Prescription Drug Benefit Program, Medicare Cost Plan Program, and Programs of All-Inclusive Care for the Elderly," *CMS*, April 12, 2023, available at https://www.federalregister.gov/documents/2023/04/12/2023-07115/medicare-program-contract-year-2024-policy-and-technical-changes-to-the-medicare-advantage-program.
[149] CMS Guidance, §30.

the generic or biosimilar, nor what will happen if that share changes over time.[150] Moreover, CMS has indicated that it "will not set a single specific numeric threshold for meaningful generic drug or biosimilar competition,"[151] and has left open the possibility of utilizing other sources of information to determine whether marketing of a generic product is "bona fide," stating that the decision will be based on a "totality-of-the-circumstances inquiry that will not necessarily turn on any one source of data."[152] Under this definition, the agency appears to believe that it could require that a generic or biosimilar hold any share of sales or prescriptions in order to determine that it is marketed, and this threshold will have an important and far-reaching impact. After CMS determines that there is "bona fide marketing" of a generic or biosimilar, the Guidance states that CMS will "monitor whether robust and meaningful competition exists in the market" and could feasibly place a drug back on the selected drug list if it deems that there is not "meaningful competition."[153]

75. For small molecule drugs, this would be especially pertinent when a single QSSD includes multiple products, only one of which is generic. For example, if a manufacturer develops a new extended-release formulation of one of its drugs, both the original formulation and the extended-release formulation might be considered the same QSSD. If a generic is available for the original formulation but not the extended-release formulation, the generic's share of total QSSD sales would appear smaller, even if it presented a viable, less expensive therapeutic option for patients and puts downward pressure on the price of the extended-release formulation. Given the ambiguity around what total payment or prescription share threshold or other criteria CMS will require to determine whether there is "bona fide marketing" of a generic, it is unclear whether in this example both the original formulation and extended-release formulation products would collectively be subject to MFP-setting.

76. The lack of clarity is likely to be similarly meaningful for biologics; while small molecule generic uptake is generally rapid and straightforward, this is not yet the case for biosimilars, where uptake can be affected by a number of factors that would impact a determination of whether such a threshold was met. Moreover, because biosimilar uptake thus far has been

[150] CMS Guidance, §30.1.
[151] CMS Guidance, p. 75.
[152] CMS Guidance, §70.
[153] CMS Guidance, § 90.4.

slower and less predictable than small molecule generic uptake,[154] it is even possible that a biosimilar's share of sales will change over time, fluctuating above and below whatever threshold CMS sets to determine that a biosimilar is marketed.

77. Fourth, the IRA directs CMS to "develop and use a consistent methodology and process… that aims to achieve the lowest maximum fair price for each selected drug,"[155] but it does not clarify the specifics of the MFP "negotiation" process, nor whether CMS is permitted to change its methodology over time. Specifically:

a. The IRA provides high-level guidance on a number of dimensions CMS must consider, such as the cost of therapeutic alternatives, comparative effectiveness relative to these alternatives, and whether the product addresses unmet medical need, but it leaves these terms open for CMS to define. For example, with regard to the determination of therapeutic alternatives, the statute does not require the clinical indication(s) to be the same as those of the MFP-eligible product. Because there is no defined approach to determine the relevant market, the law gives CMS substantial latitude to identify relevant therapeutic alternatives, which could include very inexpensive products that may occasionally be used to treat the same condition(s) as the selected drug but do not truly represent an appropriate clinical alternative for most patients. Moreover, CMS has not explained how it will address circumstances where an MFP-eligible product is indicated to treat more than one condition and if (or how) the indications of multiple products, and the use across those indications and products, will be weighted to calculate initial and subsequent MFP offers. For example, a drug like Dupixent is indicated to treat multiple conditions (i.e., asthma, eczema, and eosinophilic esophagitis); each of these conditions has different therapeutic alternatives that would (in theory) serve as inputs to the MFP calculation. While CMS may determine that Dupixent faces competition from very inexpensive topical over-the-counter corticosteroids for the treatment of eczema,[156] these

[154] Kozlowski, Steven, et al., "Uptake and Competition Among Biosimilar Biological Products in the US Medicare Fee-for-Service Population," *Journal of General Internal Medicine*, Vol. 37, No. 16, June 1, 2022, pp. 4292-4294, available at https://link.springer.com/article/10.1007/s11606-022-07670-7.
[155] SSA, §1194(b)(1).
[156] "Available Eczema Treatments," *National Eczema Association*, available at https://nationaleczema.org/eczema/treatment/.

are not a viable alternative to treat asthma.[157] The freedom the IRA provides to CMS to determine and apply multi-market calculations could have substantial impacts on the MFPs it offers to manufacturers.

b. The IRA imposes a price ceiling for the MFP-setting process, but it does not include a price floor for most drugs.[158] Moreover, the IRA sets out a directive to push prices as low as possible during the price-setting process. Ultimately, if desired, CMS could set the MFP at $0. From an economic perspective, manufacturers (particularly those that sell multiple products), would be better off accepting an offer close to a zero price (or even a negative price– i.e., pay CMS for the right to provide the drug to Medicare participants– with the IRS calculating the excise tax as above 100 percent of U.S. revenues for the MFP drug) than face either of the onerous and financially unsustainable alternatives. Even if such absurd prices were not set by CMS, the threat that they could be illustrates the extreme power that the statute vests in CMS, and the uncertainty it introduces into investors' economic calculations. The statute purports to prohibit manufacturers from seeking judicial review once CMS has set its final MFP, no matter how low or the degree to which it has or has not incorporated fair consideration of the factors it is required to consider, or the input of manufacturers or others.

c. The IRA does not specify the extent of CMS' engagement with manufacturers through each step of the "negotiation" process. CMS' Guidance states that they will meet with manufacturers once between the submission of relevant data and the initial offer. However, this meeting is restricted to providing context on the original data and adding any additional relevant data from the statute.[159] The provisions of the IRA leave no room for manufacturer input on topics such as potential evidence sources and therapeutic comparator choice in the period after MFP-eligible drug selection but prior to initiation of the price-setting process. The IRA also does not require CMS to be transparent in its

[157] *See, e.g.*, "Asthma," *Mayo Clinic*, available at https://www.mayoclinic.org/diseases-conditions/asthma/diagnosis-treatment/drc-20369660.
[158] There is a temporary price floor for small biotech drugs. See SSA, §1194(d).
[159] CMS Guidance, §60.4. Specifically, the statute states "CMS will invite the Primary Manufacturer for each selected drug to one meeting in Fall 2023 after the data submission deadline. The purpose of this meeting will be for the Primary Manufacturer to provide additional context on its data submission and share new section 1194(e)(2) data, if applicable, as CMS begins reviewing the data and developing an initial offer."

decision-making and the analyses considered in price-setting and does not specify whether manufacturers will have an opportunity to correct errors and assumptions and provide important context during the process. Moreover, the IRA does not outline a "renegotiation" process, leaving it up to CMS to formulate a course of action to control whether a previously determined MFP will be subject to a "renegotiation" process in subsequent years (either raising or lowering the MFP). This lack of specificity in the law effectively gives CMS unrestrained power over determining the steps involved in the price-setting process, forcing the manufacturer to accept the hand it is dealt.

d. Finally, the IRA does not specify whether CMS is permitted to adjust its "consistent methodology" over time. As I discuss in Section III.A.1, making the decision to invest in pharmaceutical development now requires forecasting returns well into the future. Given the freedom that the IRA has granted CMS, firms are being forced to make decisions today based on a very uncertain future regulatory environment. This uncertainty, combined with the unprecedented power granted to CMS under the statute, in my opinion will exacerbate the consequences I discuss in Section V.

78. Beyond the key issues that are left for CMS' interpretation, the statute leaves open how CMS will enforce the requirement that manufacturers make MFPs available to eligible parties, while preventing MFPs from being offered to ineligible entities. Specifically, as I describe in Section III.B.2, under a "buy and bill" approach, Part B drugs are purchased by outpatient clinics, physicians' offices, or other eligible providers directly from manufacturers or wholesalers.[160] Currently, clinics or other purchasers may be eligible for discounted prices from manufacturers, and are subsequently reimbursed at ASP + 6% for Medicare claims.[161] Under the IRA, purchasers will only be reimbursed at MFP + 6% for MFP-eligible drugs

[160] Ginsburg, Paul B., et al., "The use of vendors in Medicare Part B drug payment," *Brookings*, August 2, 2019, available at https://www.brookings.edu/blog/usc-brookings-schaeffer-on-health-policy/2019/08/02/the-use-of-vendors-in-medicare-part-b-drug-payment/.

[161] "Report to Congress on Medicaid and CHIP," *Medicaid and CHIP Payment and Access Commission*, March 15, 2023, available at https://www.macpac.gov/wp-content/uploads/2023/03/MACPAC_March-2023-Report-WEB-Full-Booklet_508.pdf. As discussed earlier, "ASP + 6%" effectively became "ASP + 4.3%" for a defined period of years, with suspensions and a 1 percent phase-in during part of the federal Public Health Emergency for COVID-19. *See* Weidner, Susan, et al., "Observations Regarding the Average Sales Price Reimbursement Methodology," *Evidence-Based Oncology*, June 2021, Vol. 27, No. 4, pp. SP156-SP160, at p. SP156, available at https://www.ajmc.com/view/observations-regarding-the-average-sales-price-reimbursement-methodology.

provided to Medicare patients, and manufacturers are required to effectively sell these units to these purchasers at or below the MFP. But it is not always known which patient (e.g., a Medicare patient in a Medicare Advantage plan or a commercially-insured patient in a plan offered by the same insurer) is associated with each unit. As such, there must be an after-the-fact reconciliation between the manufacturer and the purchaser to ensure the correct price paid for each unit corresponds to the type of patient who receives it.

79. Not only is this operationally complex, but significant issues have arisen with similar programs. For example, the 340B pricing program "allows eligible healthcare clinics and hospitals… to purchase outpatient drugs at a 20-50% discount."[162] Under this program, there have been claims of drug price diversion (i.e., ineligible individuals receiving discounted prices),[163] duplicate discounts (i.e., the same prescription erroneously getting discounted under multiple discount programs, for instance 340B and Medicaid),[164] and a lack of audits, transparency, and enforcement activity.[165] The accuracy and propriety of discounts claimed by covered entities under the 340B program remains a controversial topic and the subject of

[162] Mulligan, Karen, "The 340B Drug Pricing Program: Background, Ongoing Challenges and Recent Developments," *USC Schaeffer*, October 2021, pp. 1-18, at p. 1, available at https://healthpolicy.usc.edu/wp-content/uploads/2022/07/USC_Schaeffer_340BDrugPricingProgram_WhitePaper.pdf.

[163] Mulligan, Karen, "The 340B Drug Pricing Program: Background, Ongoing Challenges and Recent Developments," *USC Schaeffer*, October 2021, pp. 1-18, at p. 9, available at https://healthpolicy.usc.edu/wp-content/uploads/2022/07/USC_Schaeffer_340BDrugPricingProgram_WhitePaper.pdf ("Although contract pharmacies increase the distribution of 340B discounted drugs, they also increase the complexity of identifying 340B prescriptions because they simultaneously serve patients of covered entities and non-340B providers. Consequently, contract pharmacies increase the risk of drug diversion, which occurs when 340B drugs are provided to a non-340B eligible patient. To prevent diversion, contract pharmacies must correctly identify which patients and prescriptions are 340B eligible… However, drug diversion still occurs.")

[164] Mulligan, Karen, "The 340B Drug Pricing Program: Background, Ongoing Challenges and Recent Developments," *USC Schaeffer*, October 2021, pp. 1-18, at pp. 7-8, available at https://healthpolicy.usc.edu/wp-content/uploads/2022/07/USC_Schaeffer_340BDrugPricingProgram_WhitePaper.pdf.

[165] Mulligan, Karen, "The 340B Drug Pricing Program: Background, Ongoing Challenges and Recent Developments," October 2021, pp. 1-18, at p. 7, available at https://healthpolicy.usc.edu/wp-content/uploads/2022/07/USC_Schaeffer_340BDrugPricingProgram_WhitePaper.pdf ("The 340B program has been examined regularly by the Government Accountability Office (GAO) and the Department of Health and Human Services Office of Inspector General (OIG), and their reports have highlighted several issues with the program, including limited oversight, lack of transparency, concerns stemming from DSH hospitals and contract pharmacies, and duplicate discounts.").

ongoing litigation.[166] While there is an IRA 340B nonduplication provision that prohibits applying both 340B and MFP discounts in a duplicated manner to the same units of a selected drug and CMS mentions that they will work with the Health Resources and Services Administration "to help to ensure that the MFP is made available to 340B covered entities where appropriate and that there is no duplication with the 340B ceiling price," CMS does not provide specific details on how this complexity will be managed and monitored or how access to the MFP will be limited only to eligible parties.[167]

80. In addition, the IRA does not explicitly prevent Part D plans from placing drugs subject to MFP on less favorable formulary tiers or imposing utilization management requirements. While the CMS Guidance states that CMS intends to use its formulary review process to ensure that this does not occur, it does not clarify how it intends to enforce these requirements across a large and diverse set of Part D plans.[168] The lack of clarity on whether CMS will adequately protect drugs subject to MFP from these circumstance may cause manufacturers to have to negotiate additional rebates on top of the MFP with Part D plans and PBMs to ensure favorable formulary access.

C. The Drug Price "Negotiation" Program is Actually a Price-Setting Program

81. The most basic definition of negotiate is "to arrange for or bring about through conference, discussion, **and compromise**" (emphasis added).[169] From an economic perspective, this means coming to an agreement that is superior to either party's best alternative option to a negotiated agreement ("BATNA"). If either party's BATNA represents a better outcome for

[166] Mulligan, Karen, "The 340B Drug Pricing Program: Background, Ongoing Challenges and Recent Developments," *USC Schaeffer*, October 14, 2021, pp.1-18, at p. 1, available at https://healthpolicy.usc.edu/wp-content/uploads/2022/07/USC_Schaeffer_340BDrugPricingProgram_WhitePaper.pdf; "The Federal 340B Drug Pricing Program: What It Is, and Why It's Facing Legal Challenges," *The Commonwealth Fund*, September 8, 2022, available at https://www.commonwealthfund.org/publications/explainer/2022/sep/federal-340b-drug-pricing-program-what-it-is-why-its-facing-legal-challenges.

[167] It is possible that this uncertainty will further expose manufacturers to enforcement actions under the IRA (in the form of the civil monetary penalties equal to 10 times the difference between the price the manufacturer actually makes available and the MFP, multiplied by the total number of units sold) for failing to ensure access to the determined MFP to an eligible Medicare beneficiary or dispenser. SSA, §1197(a).

[168] As of 2023, there were 801 stand-alone Part D plans being offered to Medicare beneficiaries, with at least 2,557 more Medicare Advantage plans that provide Part D coverage. *See* "An Overview of the Medicare Part D Prescription Drug Benefit," *Kaiser Family Foundation,* October 19, 2022, available at https://www.kff.org/medicare/fact-sheet/an-overview-of-the-medicare-part-d-prescription-drug-benefit/.

[169] "negotiate," *Merriam-Webster.com*, available at https://www.merriam-webster.com/dictionary/negotiate.

that party, the negotiation will come to an impasse and that party will exit the negotiation. In order for compromise to occur within a negotiation, each party must have a realistic option to walk away if the conditions offered by the counterparty are not acceptable. When the rules of negotiation are such that one party's BATNA is not actually a feasible alternative, a more powerful opposing party can effectively demand whatever outcome it chooses. Under such circumstances, the "negotiation" is effectively reduced to a process more akin to price-setting by the party with the greater power, or "negotiation with a gun to your head," as a biopharmaceutical CEO recently described it.[170]

82. Others have recognized this distinction between price negotiation amongst parties confronting a "zone of possible agreement"[171]—even where parties have differing levels of bargaining power—and price-setting imposed by one party. For instance, the World Health Organization distinguishes between three distinct processes by which prices may be determined in healthcare: individual negotiations between providers and payers; negotiation between associations of providers and payers; and unilateral administrative price setting.[172] Similarly, in a review of potential design considerations in approaches to "government regulated or negotiated drug prices," the authors distinguish between three alternative approaches: "unilateral HHS authority to set prices"; "HHS sets prices through notice and comment rulemaking"; and an "independent arbitrator sets prices."[173] The first of these potential approaches ("unilateral HHS authority to set prices") closely approximates the design reflected in the IRA. In this approach:

> The Secretary would have the discretion to consider, as appropriate, the information and positions exchanged during the initial negotiation stage, as well as any expert analysis HHS might choose to consider. HHS would have broad discretion, including whether to establish procedures for public comment by stakeholders such as manufacturers, beneficiary organizations, insurers and

[170] Constantino, Annika K., "Pfizer CEO Says Medicare will likely face legal action over drug price negotiations," *CNBC*, May 11, 2023, available at https://cnb.cx/3M0M3Pk.
[171] "What is the Zone of Possible Agreement?" *Harvard Law School Program on Negotiation*, available at https://www.pon.harvard.edu/tag/zone-of-possible-agreement/.
[172] Barber, Sarah L., et al., "Price setting and price regulation in health care: lessons for advancing universal health coverage," *World Health Organization*, 2019, p. 29, available at https://apps.who.int/iris/bitstream/handle/10665/325547/9789241515924-eng.pdf?sequence=1&isAllowed=y.
[173] Ginsburg, Paul B., and Steven M. Lieberman, "Government regulated or negotiated drug prices: Key design considerations," *Brookings*, August 30, 2021, available at https://www.brookings.edu/essay/government-regulated-or-negotiated-drug-prices-key-design-considerations/.

> employers. In addition, the legislation could provide guidance to HHS, potentially limiting its discretion by specifying factors which might argue for a higher or lower price within the permitted range.[174]

83. In this section I examine what the BATNAs look like for manufacturers and CMS under the IRA to demonstrate why the law is not structured to facilitate a true negotiation. As I describe in more detail in Section IV.A, the "negotiation" process dictated by the provisions of the IRA begins with an initial MFP offered by CMS to the manufacturer ("initial offer"), which will be based on its determination of the therapeutic alternative(s) and the perceived benefits of the MFP-eligible product relative to such alternative(s). This initial offer may not exceed a specified ceiling specifically defined in the IRA.[175] If the manufacturer declines CMS' initial offer, it may submit a counteroffer within 30 days (per the IRA). If CMS declines the counteroffer, per the CMS Guidance, CMS and the manufacturer may hold up to three meetings to discuss the inputs to and calculation of the MFP. Following these meetings, CMS will submit a final written price determination to the manufacturer ("final offer"), which the manufacturer can choose to accept or decline.[176]

84. While the process outlined in the IRA incorporates some limited opportunities for the manufacturer to provide feedback to CMS on the MFP calculation, there is no requirement for CMS to offer this or for CMS to incorporate this information into its decision-making process. If CMS chooses to ignore this feedback in its final MFP determination, the manufacturer is left with no practical recourse. Specifically, as described in more detail in Section IV.A and summarized below, the IRA provides manufacturers with only two options if they reject CMS' final MFP offer: (1) face an excise tax for non-compliance that could escalate from 186 to 1,900 percent of total U.S. revenues from all purchasers for a given product (not just Medicare or government sales), or (2) withdraw *all products* from Medicare

[174] Ginsburg, Paul B., and Steven M. Lieberman, "Government regulated or negotiated drug prices: Key design considerations," *Brookings*, August 30, 2021, available at https://www.brookings.edu/essay/government-regulated-or-negotiated-drug-prices-key-design-considerations/.
[175] CMS Guidance, §60.1 and §60.2.
[176] CMS Guidance, §60.4.

and Medicaid coverage.[177] The consequence of either of these options would be catastrophic for almost any manufacturer.

85. Under the first option (accept the excise tax), manufacturers would be charged an escalating excise tax penalty until they opt to accept CMS' MFP *or* they successfully withdraw all products from Medicare and Medicaid coverage. As I discussed in Section IV.A.3(a), recent IRS guidance confirms an escalating tax rate ranging from 186 to 1,900 percent of the drug's total U.S. revenues, which is also supported by the Congressional Research Service ("CRS") and CBO.[178] The magnitude of this penalty makes it unfeasible for manufacturers to reject CMS' final MFP price determination, as the tax itself could rapidly deplete revenues. For example, if the MFP-eligible drug accounts for approximately 13 percent or more of its manufacturer's total net revenues, applying the excise tax over a full year (beginning at 186 percent and escalating to 1,900 percent by day 272) would result in an excise tax liability of 100 percent of the manufacturer's total net revenues.

86. Under the second option (withdraw from Medicare and Medicaid), manufacturers would be forced to withdraw *all products* from Medicare and Medicaid coverage. Not only does this give extra weight to the MFP-setting by tying its consequences to other products that are not

[177] 26 U.S.C. §5000D(c). It is also notable that having a manufacturer withdraw all products from Medicare and Medicaid coverage could *increase* Medicare spending, as a result of their withdrawing low-cost small molecule generic or biosimilar alternatives to higher cost drugs that are included in their drug portfolio. Besides the direct effects of replacing a lower-cost drug with a higher-cost drug, the price of other products covered by Medicare may increase as a result of the reduced competition. Of the ten products listed in **Appendix D**, four are produced by manufacturers who also produce at least one biosimilar. This number is likely to grow over time as the biosimilar market expands.

[178] According to the CRS report, "the excise tax would range from 185.71% to 1,900% of the selected drug's price depending on the duration of noncompliance." It goes on to elaborate that, because the statute defines the applicable tax rate as the ratio of the tax to the tax plus price, this simplifies to a higher de facto tax rate than the stated applicable rate under the statute. "Tax Provisions in the Inflation Reduction Act of 2022 (H.R. 5376)," *Congressional Research Service*, p. 6, available at https://crsreports.congress.gov/product/pdf/R/R47202; the CBO report specifies that it "expects that drug manufacturers will comply with the negotiation process because the costs of not doing so are greater than the revenue loss from lower, negotiated prices." "How CBO Estimated the Budgetary Impact of Key Prescription Drug Provisions in the 2022 Reconciliation Act," *Congressional Budget Office*, February 2023, p. 10, available at https://www.cbo.gov/system/files/2023-02/58850-IRA-Drug-Provs.pdf

covered by the negotiation process,[179] but also has serious financial and reputational ramifications.

87. First, Medicare and Medicaid constitute a substantial portion of drug sales in the U.S. and for many manufacturers. A 2023 Kaiser Family Foundation study estimated that, as of 2021, Medicare accounted for 32 percent of U.S. retail prescription drug sales.[180] A similar summary stated that, as of 2017, Medicare accounted for 30 percent of retail prescription drug sales and Medicaid accounted for an additional 10 percent.[181] Moreover, reimbursement from Medicare and Medicaid is unlikely to be the only foregone revenue that manufacturers experience by exercising this option. As I discuss in Section III.B, Medicare predominantly insures patients over 65 years old and certain younger people with disabilities. If patients need to begin long-term treatment in the years leading up to Medicare eligibility, physicians may be less likely to select a drug for their patients for which they will lose coverage once they rely on Medicare. As a result, choosing to withdraw from Medicare and Medicaid could lead to spillover effects in the commercial market associated with additional lost revenues.

88. Second, withdrawing all products from Medicare and Medicaid raises broader ethical concerns for manufacturers and could lead to costly reputational damage. These two programs insure millions of older and financially needy patients.[182] Withdrawing all products from coverage would eliminate access to many safe and effective medications, including those not subject to MFP-setting. Not only would this be devastating for millions of patients,

[179] In its June 30, 2023 Guidance, CMS clarified that it will find "good cause" to expedite Part D termination in 30 days if withdrawal from Medicare and Medicaid coverage is the option a manufacturer elects to take, enabling them to "avoid incurring excise tax liability…" Despite this update, the remaining options presented to manufactures under the IRA are still highly coercive and amount to a price-setting process rather than a negotiation. *See* CMS Guidance, p. 33, §40.1, and §40.6.

[180] Cubanski, Juliette and Tricia Neuman, "What to Know about Medicare Spending and Financing," *Kaiser Family Foundation*, January 19, 2023, available at https://www.kff.org/medicare/issue-brief/what-to-know-about-medicare-spending-and-financing/.

[181] Cubanski, Juliette, and Matthew Rae, "How Does Prescription Drug Spending and Use Compare Across Large Employer Plans, Medicare Part D, and Medicaid?" *Kaiser Family Foundation*, May 20, 2019, available at https://www.kff.org/medicare/issue-brief/how-does-prescription-drug-spending-and-use-compare-across-large-employer-plans-medicare-part-d-and-medicaid/.

[182] As of 2022, 65.0 million people are enrolled in Parts A and B of Medicare, and 88.5 million people are enrolled in Medicaid & CHIP. There is some overlap in these numbers as 12.5 million people are jointly enrolled in Medicare and Medicaid. *See* "CMS Fast Facts," *CMS*, March 2023, available at https://data.cms.gov/sites/default/files/2023-03/CMSFastFactsMar2023.pdf; Peña, Maria T., et al., "A Profile of Medicare-Medicaid Enrollees (Dual Eligibles)," *Kaiser Family Foundation*, January 31, 2023, available at https://www.kff.org/medicare/issue-brief/a-profile-of-medicare-medicaid-enrollees-dual-eligibles/.

but this decision would harm manufacturers' reputations, which could lead to further financial repercussions. Indeed, a recent study found that "[health care professionals] worldwide want the peace of mind that they are prescribing treatments from brands they respect… and… [o]utside a medication's functional characteristics… corporate reputation is the No. 1 factor that influences an HCP's decision to prescribe or recommend a therapy."[183] Ultimately, forgoing Medicare and Medicaid reimbursements would substantially reduce manufacturer revenues and has the potential for costly reputational damage. As a result, similar to paying the excise tax, withdrawal from these programs is unlikely to be an option that most manufacturers could meaningfully consider.

89. The issue of an unrealistic BATNA for manufacturers is exacerbated by the fact that CMS is directed by the IRA to "develop a methodology and process… that aims to achieve the lowest maximum fair price for each selected drug," without defined limits;[184] the law specifies an upper limit on the MFP (a price ceiling), but for most drugs the law does not include a lower limit (a price floor), any standards for reasonableness, or judicial review in the event that manufacturers disagree with the accuracy of the basis for CMS' final price-setting amount. As I discuss in Section IV.A.2(a), the IRA does not define how CMS must (1) determine the therapeutic alternatives, nor (2) the specifics of valuing the perceived benefits of the negotiated product relative to the chosen therapeutic alternative. These ambiguous provisions give CMS significant latitude to select an "alternative" that is substantially less expensive than the negotiated product but is not actually viewed as a true alternative by prescribers in most cases, and to undervalue the perceived benefits of the negotiated product, both of which could be used to drive down the MFP. This could especially be the case when the set of potential alternative products includes generic drugs.

90. Overall, CMS faces little risk of manufacturers rejecting the final MFP amount no matter how low it is. Indeed, the CBO explicitly stated that it "expects that drug manufacturers will comply with the negotiation process because the costs of not doing so are greater than the

[183] "Health Reputation: More than Medicine," *WE Communications*, 2023, at pp. 1-2, available at https://www.we-worldwide.com/media/k02kcyrr/we-brands-in-motion-2023-healthy-reputation.pdf.
[184] SSA, §1194(b).

revenue loss from lower, negotiated prices,"[185] and an identical earlier excise tax provision was assumed by the Joint Committee on Taxation to generate zero revenues, consistent with the reason that no manufacturer could realistically afford to be subject to and pay it for any extended length of time.[186]

V. THE IRA WILL REDUCE PHARMACEUTICAL INNOVATION AND DELAY PATIENT ACCESS TO NOVEL THERAPIES

91. The United States has historically been a global leader in pharmaceutical innovation, with $122 billion or 58.9 percent of global R&D spending in 2020.[187] A market-based approach to pharmaceutical pricing in the U.S. has resulted in patients in the U.S. benefiting from the earliest and broadest access to new medications, with nearly 80 percent of medicines approved by the FDA in 2021 being available in the U.S. before any other country.[188]

92. As I discussed in Section III.A, drug development (after early-stage scientific research) is typically funded by private investors. For smaller biotech firms, this investment comes from external sources, such as venture capital or private equity. For larger, more established manufacturers, it can come from either external sources or through reinvestment of revenues into the R&D pipeline.[189] Any substantial reductions in expected return on investment ("ROI") will change investment decisions, reducing innovation in the pharmaceutical space. In a recent analysis evaluating the impact of proposed legislation to control drug prices, the CBO found that a reduction in expected returns on R&D for future drugs would "reduce the

[185] "How CBO Estimated the Budgetary Impact of Key Prescription Drug Provisions in the 2022 Reconciliation Act," *Congressional Budget Office*, February 2023, p. 10, available at https://www.cbo.gov/system/files/2023-02/58850-IRA-Drug-Provs.pdf.
[186] "Re: Effects of Drug Price Negotiation Stemming From Title 1 of H.R. 3, the Lower Drug Costs Now Act of 2019, on Spending and Revenues Related to Part D of Medicare," *Congressional Budget Office*, October 11, 2019, p. 8, available at https://www.cbo.gov/system/files/2019-10/hr3ltr.pdf.
[187] "Total global pharmaceutical R&D spending 2014-2028," *Statista,* October 2022; "U.S. Investments in Medical and Health Research and Development 2016-2020," *Research America*, January 2022, available at https://www.researchamerica.org/wp-content/uploads/2022/07/ResearchAmerica-Investment-Report.Final_.January-2022.pdf (I calculate the U.S. share of total global spending on pharmaceutical R&D by dividing $122 billion by $207 billion).
[188] "Advancing Health Through Innovation: New Drug Therapy Approvals 2021," *FDA*, January 2022, available at https://www.fda.gov/media/155227/download.
[189] "Research and Development in the Pharmaceutical Industry," *Congressional Budget Office,* April 2021, available at https://www.cbo.gov/publication/57126.

introduction of new drugs."[190] Furthermore, the CBO report cites several studies that find a relationship between market size for pharmaceutical products and innovation, including an increase in new drug approvals when the market expands.[191]

93. For both smaller biotech firms and larger established manufacturers, the goal of investors is ROI, whether through a profitable "exit" (that is, the sale of rights to a newly developed drug or company) or future revenue.

94. A profitable "exit" typically happens in the form of an acquisition of the rights to a drug or the purchase of its owner, though some early-stage biotechnology firms may go public through an initial public stock offering. A trend toward going public has reversed in recent years given existing market conditions, but may rebound in the future.[192] However, even many of these firms with early-stage IPOs are also subsequently acquired by larger firms with the assets to further develop and commercialize the product. This private venture capital or private equity funding is highly mobile and has no particular commitment to the pharmaceutical industry; it is simply in search of the highest returns on behalf of investors, such as large pension funds. If potential returns from biotech investments fall, investors will redirect their funds from the pharmaceutical sector towards the next best option. The financial terms of these eventual exits are dictated by the expected revenues of the product in the market and thus would be affected by aggressive price regulation and other factors that decrease average expected returns.

95. Likewise, established biopharmaceutical firms are influenced by expected returns when they make economic decisions regarding the acquisition of drug candidates and startup firms, and the further development of those drug candidates and launched drugs. Changes in the

[190] "Re: Effects of Drug Price Negotiation Stemming From Title 1 of H.R. 3, the Lower Drug Costs Now Act of 2019, on Spending and Revenues Related to Part D of Medicare," *Congressional Budget Office*, October 11, 2019, p. 2, available at https://www.cbo.gov/system/files/2019-10/hr3ltr.pdf.
[191] Dubois, Pierre, et al., "Market Size and Pharmaceutical Innovation," *RAND Journal of Economics*, Vol. 46, No. 4, October 26, 2015, pp. 844-871; Blume-Kohout, Margaret E. and Neeraj Sood, "Market Size and Innovation: Effects of Medicare Part D on Pharmaceutical Research and Development," *Journal of Public Economics*, Vol. 97, January 2013, pp. 327-336; Acemoglu, Daron and Joshua Linn, "Market Size in Innovation: Theory and Evidence From the Pharmaceutical Industry," *Quarterly Journal of Economics*, Vol. 119, No. 3, August 2004, pp. 1049-1090. While the size of effect varies across study, each one establishes that changing the expected market size for pharmaceutical products changes R&D investment and subsequently the number of new drugs entering the market.
[192] "Biotech's post-IPO boom: rebounding from a 2022 Low?" *Pharmaceutical Technology*, March 23, 2023, available at https://www.pharmaceutical-technology.com/comment/biotech-post-ipo-boom/.

economic "rules of the game" and expected returns to their investments influence their decisions about the deployment of their resources.

96. With its exclusive focus on lowering Medicare drug prices, the IRA ignores the impact of reduced drug revenues and the corresponding consequence of lower expected ROI for future drug development. The CBO estimates that "net prices for selected drugs will decrease by roughly 50 percent, on average, as a result of negotiation."[193] Because Medicare accounts for approximately 30 percent of prescription drug spending in the U.S.,[194] imposing MFPs will have a meaningful impact on revenues.

97. The scientific risk associated with drug development on investment decisions is compounded by the long timelines associated with bringing a drug to market. The average clinical and approval phase times for new molecular entities from 2005-2009 was between seven and eight years, depending on whether the drug received priority status or not.[195] With MFPs for the first group of drugs set to come into effect in 2026, some drugs that are currently being developed will have to take into account potentially reduced revenues due to the IRA.

98. The IRA's impact on prices and corresponding investment decisions in my opinion will result in several consequences related to drug development, some of which will disproportionately impact certain patient populations (e.g., cancer patients and patients with conditions that disproportionately impact older individuals). Moreover, because of competitive dynamics, these consequences are unlikely to be limited to the drugs or manufacturers of drugs ultimately subject to MFP-setting. Most drugs face competition from branded alternatives even before generic formulations of their own molecules are available. If one drug in a category experiences a stark reduction in price due to the imposition of an MFP, alternative branded products will need to reduce their prices to effectively compete, as well. As a result, these consequences will extend to: (1) drugs in disease categories with any

[193] "How CBO Estimated the Budgetary Impact of Key Prescription Drug Provisions in the 2022 Reconciliation Act," *Congressional Budget Office*, February 2023, p. 10, available at https://www.cbo.gov/system/files/2023-02/58850-IRA-Drug-Provs.pdf.
[194] Cubanski, Juliette, and Tricia Neuman, "What to Know about Medicare Spending and Financing," *Kaiser Family Foundation*, January 19, 2023, available at https://www.kff.org/medicare/issue-brief/what-to-know-about-medicare-spending-and-financing/.
[195] Kaitin, Kenneth I., and Joseph A. DiMasi, "Pharmaceutical Innovation in the 21st Century: New Drug Approvals in the First Decade, 2000-2009," *Clinical Pharmacology & Therapeutics*, Vol. 89, No. 2, February 2011, pp. 183-188, at p. 185.

MFP-eligible alternatives, (2) products already on-market whose manufacturers are weighing investment in additional indications and face uncertain or changed prospects in the disease category, (3) products in development facing similar uncertain revenue prospects years in the future, and (4) potential early-stage prospects, especially those in disease categories with existing generic products that could be considered therapeutic alternatives. Ultimately, this could encompass almost all products, directly or indirectly. Because the IRA changes the "rules of the game" and adds new elements of financial risk to investment calculations, it will affect the full landscape of products and investors.

A. Distortions and disruptions to established indication sequencing approaches will impact patient access to new therapies

99. The optimal strategy for a manufacturer facing the risky proposition of developing a new drug is often to launch with a single indication where the scientific path is clearest and the clinical data supporting efficacy and safety is the strongest. After the drug has launched, the manufacturer will pursue subsequent indications over time. Because the IRA creates a new, shorter period to earn market-based returns for drugs that fall under the MFP-setting provisions and does not allow for exceptions or extensions related to new indications,[196] manufacturers have an incentive to pause, terminate, or adjust their development and launch approaches, with potential impact on future treatment availability.

100. Currently, manufacturers consider an array of factors when determining whether to pursue development of a drug in a specific therapeutic area. These factors include the duration, cost and probability of technical success during development, peak net sales from the drug's initial indication(s), the potential for additional follow-on indications, and the drug's commercial sales lifetime prior to generic or biosimilar entry, which is affected by factors such as patent protection and statutory exclusivity provisions (including, for example, for orphan diseases and pediatric indications). Each of these factors affects the ROI a drug is expected to produce. The IRA's new "price-setting" has the effect of (1) creating a new point in time after which it will be uneconomic to invest in additional post-approval indications, and (2) discouraging pursuit of certain indications, such as those that are likely to include

[196] SSA, §1192(e).

alternative treatments that are generic or otherwise relatively inexpensive (e.g., they are of an older treatment generation or part of a different classes of medications that could be considered therapeutic alternatives (based on the IRA's vague definition) once the drug becomes MFP-eligible).

101. Because the IRA shortens the length of time MFP-eligible drugs can earn market-based returns, it skews incentives away from a strategy of an initial launch with a narrower indication, followed by additional approvals later. For example, biologic Dupixent was initially approved in 2017 for the treatment of atopic dermatitis (eczema).[197] Since then, it has received 4 subsequent indications for different conditions,[198] and Sanofi just released Phase III trial results for the treatment of chronic obstructive pulmonary disease ("COPD") – a condition that has not seen a new approved therapy in more than a decade.[199] With a shorter period to earn market-based returns, the incentive to undergo the COPD trial nearly seven years after Dupixent's initial launch would be significantly diminished. Instead of the incremental approval approach seen with Dupixent (and other drugs), manufacturers are likely to consider different strategies, such as delaying launch in order to include a broader set of indications from the outset, subject to patent considerations. Such a strategy would result in increased development complexity, higher pre-launch costs, and delays for some indications that would otherwise be ready to be launched and be available to U.S. patients sooner.

102. In other instances, manufacturers are likely to conclude that a given post-approval development program is no longer economical because there is not sufficient time to earn market-based returns before the drug becomes MFP-eligible, or because an additional indication could, on the margin, actually cause a drug that would not otherwise be MFP-eligible to become MFP-eligible as a result of those incremental sales.

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[197] "FDA Approves First Treatment for Eosinophilic Esophagitis, a Chronic Immune Disorder," *FDA,* May 20, 2022, available at https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-eosinophilic-esophagitis-chronic-immune-disorder.

[198] "Dupixent FDA label," *Drugs@FDA*, as of October 17, 2022, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761055s046lbl.pdf.

[199] Dunleavy, Kevin, "With Dupixent leading the way, Sanofi's taking on the 'big players' in respiratory diseases: exec," *FiercePharma*, May 22, 2023, available at https://www.fiercepharma.com/pharma/dupixent-leading-way-copd-sanofi-set-play-big-boys-and-girls-respiratory-diseases.

103. It is even possible that manufacturers will conclude that a certain full drug development program, including initial and post-approval indications, is no longer economical and will pass on an opportunity to invest in, acquire, or develop the drug. Such decisions would lead to valuable new treatments being lost, not only as a result of new drugs not being developed but also by preventing the positive spillover effect that scientific advances can have on other, future products' development. A recent example of the ripple effect of new scientific advances is the development of COVID-19 vaccines, which boosted the research on how the mRNA vaccine technology can be applied to other diseases, including HIV and cancer, among other conditions.[200]

104. Additionally, as I discussed in Section IV.B, the IRA's lack of specific requirements that CMS must follow to identify therapeutic alternatives could have negative impacts on therapeutic advances. For example, in my view, manufacturers will be less likely to seek approval for indications where the therapeutic alternative is expected to include a generic drug if and when the drug becomes MFP-eligible, even if the drug presents a significant therapeutic advancement relative to competitive products. One example is Auvelity, a drug developed by Axsome Therapeutics that was approved by the FDA in August 2022 for the treatment of major depressive disorder ("MDD").[201] Auvelity is the "first and only rapid-acting oral medicine approved for the treatment of MDD," an important therapeutic advancement that was recognized by the FDA when it granted breakthrough therapy designation for Auvelity for the treatment of MDD in March 2019, and subsequently

[200] *See e.g.*, "mRNA Vaccine Technology: A Promising Idea for Fighting HIV," *National Institutes of Health*, February 20, 2023, available at https://covid19.nih.gov/news-and-stories/mrna-vaccine-technology-promising-idea-fighting-hiv.
[201] "Auvelity FDA label," *Drugs@FDA*, as of August 18, 2022, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215430Orig1s000Correctedlbl.pdf; "Auvelity FDA Approval Letter," *Drugs@FDA*, as of August 18, 2022, available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/215430Orig1s000Correctedltr.pdf.

evaluated the NDA under priority review.[202,203] Notably, Axsome Therapeutics developed Auvelity for the treatment of MDD in the context of a therapeutic area where the standard of care include selective serotonin reuptake inhibitors ("SSRIs") and serotonin and norepinephrine reuptake inhibitors ("SNRIs"), both of which have many generic options.[204] Drugs such as Auvelity will be less likely to be developed in the first place if their expected therapeutic alternatives for the purpose of MFP setting have generic versions. While generic availability of competing products is a factor that manufacturers like Axsome Therapeutics consider in the current environment, they rely on the market's ability to recognize and reward clinical benefit and product differentiation, which CMS may not choose to do in its unilateral identification of a therapeutic alternative.

105. Finally, in my view, the IRA's timeline for the imposition of MFP-setting will affect incentives for the collection of safety and efficacy data in real world settings, which can involve lengthy follow-up studies and can be vital for determining long-term viability, efficacy, and cost-effectiveness of a drug and to inform clinician decisions about optimal prescribing for a given patient. Some lengthy post-approval clinical trials will become economically unviable with the shortened periods of market-based pricing. For example, the Health Outcomes and Reduced Incidence with Zoledronic Acid Once Yearly-Pivotal Fracture Trial (HORIZON) and extensions followed participants for up to nine years and helped shed light on the long-term effectiveness zoledronic acid treatment for osteoporosis.[205]

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[202] "Axsome Therapeutics Announces FDA Approval of AUVELITY™, the First and Only Oral NMDA Receptor Antagonist for the Treatment of Major Depressive Disorder in Adults," *Axsome Therapeutics Press Release*, August 19, 2022, available at https://www.multivu.com/players/English/9034852-axsome-therapeutics-announces-fda-approval-auvelity/.

[203] The FDA Breakthrough Therapy designation "is a process designed to expedite the development and review of drugs that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s)." "Breakthrough Therapy," *FDA*, available at https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy. The FDA Priority Review designation is intended to "direct overall attention and resources to the evaluation of applications for drugs that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications." "Priority Review," *FDA*, available at https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review.

[204] "Practice Guideline for the Treatment of Patients with Major Depressive Disorder," *Psychiatry Online*, October 2010, available at https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf.

[205] Black, Dennis M., et al., "The effect of 6 versus 9 years of zoledronic acid treatment in osteoporosis: a randomized second extension to the HORIZON-Pivotal Fracture Trial (PFT)," *Journal of Bone and Mineral Research,* Vol. 30, No. 5, December 26, 2014, pp. 934-944, available at https://asbmr.onlinelibrary.wiley.com/doi/10.1002/jbmr.2442.

B. Established oncology drug development approaches will be disrupted

106. The IRA's disruption to indication sequencing investment decisions is likely to be particularly problematic for oncology drugs. Many oncology drugs launch with approval as a later-stage treatment for a single diagnosis and, over time, seek approval as an earlier line of therapy, for concomitant treatment with other medications, and for other tumor types or diagnoses.[206]

107. For example, the biologic Keytruda was originally approved in 2014 for a single indication to treat certain patients with melanoma, but post-approval clinical trials have shown that the mechanism can help many patients with a wide variety of cancers. Keytruda has subsequently received additional disease approvals over the past nine years, with a current total of 36 disease indications across 18 tumor types.[207] Details of the timing and description for each additional indication are available in **Exhibit 3**. Moreover, company leadership recently indicated that the IRA would directly undermine the ability to develop additional indications, stating that, "If you look at our drug Keytruda … we are less than halfway through the development program. I don't know if in the future you will be able to do that, where you keep investing in the follow-on indications, and that concerns me."[208]

108. Even with relatively costly development and slower launch-to-peak-sales curves, oncology products have historically been appealing to investors due in part to the possibility of additional post-approval indications and growing sales from these indications. A development strategy that had the manufacturer prioritizing development of the indication(s) that would allow the drug to come to market most rapidly, and therefore would be available to patients sooner, was often favored. With the IRA, manufacturers will face incentives to re-

[206] "Implications of the Inflation Reduction Act Price Setting Provisions on Post-approval Indications for Small Molecule Medicines," *Partnership for Health Analytic Research*, June 2023, available at https://www.pharllc.com/wp-content/uploads/2023/05/Implications-of-the-IRA-on-Post-Approval-Small-Molecules-2006-2012_Final.pdf.

[207] Keytruda holds indications to treat patients with certain types of bladder cancer, breast cancer, cervical cancer, colorectal cancer, diffuse large B-cell lymphoma, esophageal cancer, gastric cancer, head and neck cancer, hepatocellular (liver) cancer, Hodgkin's lymphoma, Merkel cell carcinoma, non-small cell lung cancer, renal cell cancer, squamous cell carcinoma, solid tumors, and uterine (endometrial) cancer. "Keytruda FDA label," *Drugs@FDA,* as of April 3, 2023, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125514s136lbl.pdf.

[208] Merrill, Jessica, "US Pricing Reform Puts Cancer Drug Innovation At Risk, Drug Leaders Warn," *Scrip*, November 2, 2022.

think this approach, either delaying or forgoing indications for smaller patient populations and disease indications, compared with the current approach. This, in turn, will also reduce their ability to rely on valuable real-world evidence accumulated through clinical practice in the design and implementation of future clinical trials. A recent concrete example is the statement by Genentech CEO that the company faces difficult decisions about how best to sequence research on an oral cancer molecule that could help patients with diseases like ovarian cancer with smaller populations, or with prostate cancer with larger populations: "It's a cancer drug that we think has best-in-class potential. We believe it has potential in breast cancer, ovarian cancer, and prostate cancer. Normally, we would develop it in a fast market approach for ovarian cancer. That's the shortest path to patients … but that is a much smaller indication than prostate cancer, which would take three years longer. So the dilemma we're facing right now is, do we go with the initial indication being prostate cancer and then hold off on the development and the approval of ovarian because the clock will be started with prostate?… We face a lot of difficult decisions to make squaring the science and the societal patient unmet need together with the business case. It's frustrating that this is an artifact of government legislation, which is creating a disincentive for us to do the right thing for patients."[209]

109. Moreover, as noted, the negative consequences for manufacturer revenues related to the IRA are not limited to the drugs that end up on the selected drug list. Oncology drugs commonly have indications across multiple types of cancer. When a drug with multiple indications becomes subject to an MFP, alternative treatments for every indication will compete for formulary placement and coverage with a product with a much lower price. This could drive down the price and corresponding expected returns of those alternative products as well, creating a dynamic that discourages further innovation in any treatment area that has (or expects to have) an MFP-eligible product. This reduction in expected market-based returns extends beyond MFP-eligible drugs and is likely to lead to fewer future options for patients.

110. There is some early evidence that manufacturers are already canceling or pausing development of cancer drugs. For example, Eli Lilly's CEO recently cited the IRA as a

[209] Cohrs, Rachel, "Genentech weighs slow-walking ovarian cancer therapy to make more money under drug pricing reform," *STAT*, August 10, 2023.

reason for abandoning the development of a BCL2 inhibitor for the treatment of blood cancer. A spokesperson indicated, "[t]he IRA changes many dynamics for small molecules in oncology and when we integrated those changes with this program and its competitive landscape, the program's future investment no longer met our threshold."[210] The CEO of BMS also confirmed that the IRA has led them to review their portfolio when he said "I do expect that we will cancel some programs, whether that is, you know, a full-on indication for an existing medicine or a new medicine. We are undergoing a review of our portfolio now," noting that "[t]he biggest impact of IRA is actually in oncology. It's in cancer therapy."[211]

C. IRA pricing provisions will disincentivize innovation of drugs that typically treat older or disabled populations

111. Because the IRA focuses its price-setting activity on high Medicare-spend drugs, drugs that are disproportionately reimbursed through Medicare will be less appealing innovation investment targets for manufacturers than those that typically treat younger, non-disabled populations, all else equal. Because Medicare beneficiaries are predominantly age 65+ or disabled, the populations typically identified as most in need of therapeutic options will likely lose future treatments due to changes in resource distribution for development and innovation.[212]

112. For example, drug therapy innovation in the Alzheimer's space, which has a history of substantial R&D cost yielding little medical benefit, would be further challenged by reducing incentives that target the 65+ population, where one in nine people suffer from Alzheimer's disease.[213] From 1995 to 2021, cumulative private clinical R&D funding for Alzheimer's disease was estimated to be $42.5 billion overall and $24 billion incurred during Phase III.[214]

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[210] Gelman, Max, "Updated: Eli Lilly blames Biden's IRA for cancer drug discontinuation as the new pharma playbook takes shape," *EndPoints News*, November 1, 2022.
[211] Smyth, Jamie, "Bristol Myers Squibb warns US price reforms will dent drug development," *Financial Times*, November 20, 2022.
[212] Tarazi, Wafa, et al., "Medicare Beneficiary Enrollment Trends and Demographic Characteristics," *Office of the Assistant Secretary for Planning and Evaluation*, March 2, 2022, pp. 1-13, at p. 5, available at https://aspe.hhs.gov/reports/medicare-enrollment.
[213] "Alzheimer's Facts and Figures Report," *Alzheimer's Association*, available at https://www.alz.org/alzheimers-dementia/facts-figures.
[214] Cummings, Jeffrey L., et al., "The costs of developing treatments for Alzheimer's disease: A retrospective exploration," *Alzheimer's Dementia*, Vol. 18, No. 3, March 2022, pp. 469-477, at pp. 471-472, available at https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.12450.

Still, only a small number of drugs for symptomatic treatment have been approved by the FDA.[215] Similarly, ophthalmic conditions such as geographic atrophy (a chronic, progressive degeneration of the macula) disproportionately impact senior populations and have very few therapeutic options.[216] The disincentives created by the IRA to invest in research for diseases primarily affecting the 65+ population will only exacerbate an already-difficult pathway for treatments of diseases such as Alzheimer's and geographic atrophy.

113. Indeed, there is historical evidence that changes to profitability due to government policy have influenced the level and mix of investment in innovation for drugs targeting the Medicare population. For example, the introduction of Medicare Part D was found to spur drug research and innovation targeting illnesses that predominantly affect seniors.[217] A separate analysis found that a 1 percent increase in potential market size, proxied by long-run demographic aging in the United States, led to a 4-6 percent increase in the entry of non-generic drugs and new molecular entities.[218] Conversely, price-setting in the Medicare program in my opinion will disincentivize clinical research and development for products aimed at the elderly.

D. Disincentives to invest in small molecule drugs

114. Under the IRA, there are seven years before small molecule drugs and eleven years before biologic drugs can be considered for inclusion in the price-setting process, and generally nine years and thirteen years, respectively, before an MFP applies.[219] Because of the difference between the eligibility periods for small molecules and biologics, and because nine years is below the current average period of market exclusivity for small molecule drugs,[220] this will

[215] "Medications for Alzheimer's Disease," *Stanford HealthCare*, available at https://stanfordhealthcare.org/medical-conditions/brain-and-nerves/alzheimers-disease/treatments/medications.html.
[216] Harrison, Wendy, and Joe Wheat, "Sizing Up Geographic Atrophy," *Review of Optometry*, June 15, 2020, available at https://www.reviewofoptometry.com/article/sizing-up-geographic-atrophy.
[217] Dranove, David, et al., "Does consumer demand pull scientifically novel drug innovation?" *RAND Journal of Economics*, Vol. 53, No. 3, August 18, 2022, pp. 590-638. *See also* Blume-Kohout, Margaret E. and Neeraj Sood, "Market Size and Innovation: Effects of Medicare Part D on Pharmaceutical Research and Development," *Journal of Public Economics*, Vol. 97, January 2013, pp. 327-336.
[218] Acemoglu, Daron and Joshua Linn, "Market Size in Innovation: Theory and Evidence From the Pharmaceutical Industry," *Quarterly Journal of Economics*, Vol. 119, No. 3, August 2004, pp. 1049-1090.
[219] SSA, §1192(e).
[220] Grabowski, Henry, et al., "Continuing trends in U.S. brand-name and generic drug competition," *Journal of Medical Economics,* Vol. 24, No. 1, August 2, 2021, pp. 908-917, at p. 911, available at https://www.tandfonline.com/doi/full/10.1080/13696998.2021.1952795.

further incentivize pharmaceutical manufacturers to pursue biologic drugs over small molecule ones, all other factors equal.

115. A further shift towards biologics comes with potential downsides:

a. Small molecule generic drugs tend to be cheaper to develop than biosimilars of biologics,[221] and demonstrating "sameness" for purposes of generic drug approval is, from a scientific and regulatory procedure perspective, much simpler than demonstrating biosimilarity.[222] As a result, once the patent term and statutory exclusivity ends, the share of the referenced brand drugs fall rapidly, reaching just 18 percent one year after first generic entry for drugs with sales of at least $250 million the year before generic entry (in 2019 dollars), and 23 percent for all drugs.[223] The current statutory framework for small molecule generic entry has resulted in the percentage of retail prescriptions being dispensed as a generic drug reaching over 90 percent.[224] Once available, generic drugs offer patients a cheaper option for equivalent treatment. This pattern is not yet as established with biosimilars, and the IRA is likely to reduce incentives for biosimilar entry by lowering biologic reference prices and therefore the corresponding returns on investment for biosimilar products.[225]

b. Due to their chemical structure, small molecule drugs are typically administered orally, resulting in benefits for patients who are therefore able to avoid trips to

[221] Grabowski, Henry, et al., "Regulatory and Cost Barriers are Likely to Limit Biosimilar Development and Expected Savings in the Near Future," *Health Affairs,* Vol. 33, No. 6, June 2014, pp. 1048-1057.
[222] Blackstone, Erwin A., and Joseph P. Fuhr, "The Economics of Biosimilars," *American Health & Drug Benefits*, Vol. 6, No. 8, September/October 2013, pp. 469-478, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4031732/.
[223] Grabowski, Henry, et al., "Continuing trends in U.S. brand-name and generic drug competition," *Journal of Medical Economics,* Vol. 24, No. 1, August 2, 2021, pp. 908-917, at p. 911, available at https://www.tandfonline.com/doi/full/10.1080/13696998.2021.1952795.
[224] "The Use of Medicines in the U.S.," *IQVIA*, May 2021, available at https://www.iqvia.com/insights/the-iqvia-institute/reports/the-use-of-medicines-in-the-us.
[225] Indeed, the IRA recognizes this undesirable outcome by allowing biosimilar manufacturers to request a delay in the addition of their reference products for MFP-eligibility (*see* SSA, §1198). But this delay will only be effective if the reference product has not yet become subject to an MFP. For example, if Keytruda is subject to an MFP beginning in 2028 without any biosimilar manufacturer filing for delay, once a biosimilar manufacturer *is* ready to launch, its price will be anchored to Keytruda's MFP rather than its pre-MFP market price. As a result, the IRA will likely lead to an overall decrease in biosimilar entry, reducing competition for certain products.

doctors' offices or infusion centers, which pose significant obstacles to receiving regular treatment (particularly in rural areas).[226]

c. Because the IRA establishes a beneficiary out-of-pocket maximum for Part D but not Part B,[227] a shift towards drugs more often covered by Part B is likely to be more expensive for patients who do not have supplemental insurance (i.e., Medigap, employer-sponsored retiree health coverage, or Medicaid), who account for nearly 1 in 5 Medicare beneficiaries.[228]

116. Certain therapeutic areas where small molecules account for a large portion of drug treatments will likely be disproportionately affected by a shift away from small molecule drug development. This is the case, for example, of mental health and central nervous system (CNS) conditions for which small molecules account for the vast majority of drug treatments.[229] Pharmaceutical companies that specialize in these treatment areas in my opinion will be disproportionately affected by the IRA incentives favoring biologics, and in some cases may even exit the therapeutic area or cease to exist, resulting in reduced development of drugs in essential therapeutic areas.

E. The "U.S. launch first" strategy will likely no longer be a foregone conclusion

117. Various analyses have confirmed that initial launch sequencing decisions are influenced by drug pricing regime, and therefore there is a relationship between price regulation regime and how quickly patients in a given country have access to new drug therapies:

a. In a study of the launch experience of 85 new chemical entity drugs in 25 industrialized countries launched between 1994 and 1998, only 55 percent of potential country-

[226] Mócsai, Attila, et al., "What is the future of targeted therapy in rheumatology: biologics or small molecules?" *BMC Medicine*, Vol. 12, No. 43, March 13, 2014, pp. 1-9, at p. 7, available at https://bmcmedicine.biomedcentral.com/articles/10.1186/1741-7015-12-43.
[227] SSA, §1860D-2(b); Werble, Cole, "Medicare Part B," *Health Affairs Health Policy Brief*, August 10, 2017, available at https://www.healthaffairs.org/do/10.1377/hpb20171008.000171/.
[228] Koma, Wyatt, et al., "A Snapshot of Sources of Coverage Among Medicare Beneficiaries in 2018," *Kaiser Family Foundation*, March 23, 2021, available at https://www.kff.org/medicare/issue-brief/a-snapshot-of-sources-of-coverage-among-medicare-beneficiaries-in-2018/.
[229] Brazil, Rachel, "A barrier to progress: getting drugs to the brain," *The Pharmaceutical Journal*, May 15, 2017, ("[Taking] small molecules and [making] them more liquid soluble…[has] given us 95% of the drugs that we use for the central nervous system.").

compound launches occurred, and many launches involved months or years of delay. [230] In the sample, the U.S. led with 73 launches, i.e., more than 85 percent of the 85 new chemical entity drugs covered in the study. Most other countries had far fewer launched products and those that were launched had longer average launch lags: "The results indicate that countries with lower expected prices or smaller expected market size have fewer launches and longer launch delays, controlling for per capita income and other country and firm characteristics."[231]

b. An analysis of launch experience in 15 countries from 1992 to 2003 for drugs in 12 major therapeutic classes found that "launch timing and prices of new drugs are related to a country's average prices of established products in a class. Thus, to the extent that price regulation reduces price levels, such regulation directly contributes to launch delay in the regulating country."[232]

c. In an analysis of the timing of launches of 642 new drugs in 76 countries between 1983 and 2002, Cockburn, Lanjouw and Schankerman also found "countries that adopt strong pharmaceutical price controls experience significantly longer launch lags for new drugs. We estimate that introducing price controls increases launch lags by about 25 percent, and with instrumental variables the estimate rises to more than 80 percent."[233]

118. Because of the approach taken in the U.S., where manufacturers set market-based prices at launch, manufacturers typically adopt a "U.S. launch first" approach to global drug launch sequencing, leading to U.S. patients having the fastest and broadest access to newly developed therapies. For example, a 2019 report by IQVIA, a health data analytics company, found that patients in the United States had the broadest access to oncology drugs launched

[230] Danzon, Patricia. M., et al., "The Impact of Price Regulation on the Launch Delay of New Drugs — Evidence from Twenty-Five Major Markets in the 1990s," *Health Economics*, Vol. 14, No. 3, March 2005, pp. 269-292, available at https://repository.upenn.edu/entities/publication/7d075784-9731-468c-96b1-4586b00d3918.
[231] Danzon, Patricia M., et al., "The Impact of Price Regulation on the Launch Delay of New Drugs — Evidence from Twenty-Five Major Markets in the 1990s," *Health Economics*, Vol. 14, No. 3, March 2005, pp. 269-292, available at https://repository.upenn.edu/entities/publication/7d075784-9731-468c-96b1-4586b00d3918.
[232] Danzon, Patricia M., and Andrew J. Epstein, "Effects of Regulation on Drug Launch and Pricing in Interdependent Markets," *Advances in Health Economics and Health Services Research*, Vol. 23, 2012, pp. 35-71, available at https://faculty.wharton.upenn.edu/wp-content/uploads/2018/12/Effects-of-regulation-on-drug-launches.pdf.
[233] Cockburn, Iain M., et al., "Patents and the Global Diffusion of New Drugs," *American Economic Review*, Vol. 106, No. 1, January 2016, pp. 136-164.

in 2013-2017, with 96 percent of drugs being available by 2018.[234] Additionally, the U.S. had the quickest access of all studied countries with access to 94 percent of all oncology drugs launched within two years.[235] On the other hand, patients in the United Kingdom had access to only 76 percent of drugs overall and 70 percent within two years of first global launch.[236]

119. As I discuss in Section V.A, manufacturers will likely respond to altered incentives for post-approval indication development by reconsidering and changing their launch sequencing approaches. While historically, launching new drugs first in the U.S. has been a well-established commercialization strategy, in some cases post-IRA, certain manufacturers will likely opt to launch in places such as the European Union or Japan first in order to avoid "starting the IRA clock" and preserving the time prior to MFP eligibility. Although 76 percent of novel medicines in 2021 were first approved in the U.S.,[237] product launches in Europe often take place close in time.[238] Moreover, despite its regulatory challenges (e.g., longer review times by the European Medicines Agency and price negotiation at the national level),[239] Europe remains an important market for manufacturers as it accounts for over 20 percent of the global pharmaceutical market.[240] Given these realities, the IRA's regulations in my opinion will incentivize producers to more carefully consider launching in Europe first before exposing themselves to an MFP after some years on the U.S. market. This will be particularly appealing if manufacturers think that they need to build out evidence of efficacy;

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[234] "Global Oncology Trends 2019: Therapeutics, Clinical Development and Health System Implications," *IQVIA*, May 2019, Exhibit 24, available at https://intelligencepharma.files.wordpress.com/2019/05/global-oncology-trends-2019-report.pdf.
[235] "Global Oncology Trends 2019: Therapeutics, Clinical Development and Health System Implications," *IQVIA*, May 2019, Exhibit 24, available at https://intelligencepharma.files.wordpress.com/2019/05/global-oncology-trends-2019-report.pdf.
[236] "Global Oncology Trends 2019: Therapeutics, Clinical Development and Health System Implications," *IQVIA*, May 2019, Exhibit 24, available at https://intelligencepharma.files.wordpress.com/2019/05/global-oncology-trends-2019-report.pdf.
[237] "Advancing Health Through Innovation: New Drug Therapy Approvals 2021," *FDA*, January 2022, available at https://www.fda.gov/media/155227/download.
[238] Heskett, Clay, et al., "First Biopharma Product Launch in Europe: What It Takes to Succeed," *L.E.K. Consulting*, available at https://www.lek.com/sites/default/files/insights/pdf-attachments/2044-First-Biopharma-Product-Launch-in-Europe-What-It-Take.pdf.
[239] Joppi, Roberta, et al., "Food and Drug Administration vs European Medicines Agency: Review times and clinical evidence on novel drugs at the time of approval," *British Journal of Clinical Pharmacology*, Vol. 86, No. 1, December 16, 2019, pp. 170-174, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6983504/.
[240] Ronte, Hanno, et al., "Deciding on the right path: how biotechs should expand in(to) Europe," *Deloitte Insights*, January 25, 2022, available at https://www2.deloitte.com/xe/en/insights/industry/life-sciences/expanding-into-european-biotech-industry.html.

launching in Europe would allow them to earn revenue while gaining market acceptance, potentially avoiding a ramp-up period while "on the clock" in the U.S. This strategy would leave patients in the U.S. waiting for treatments that would have otherwise been available.

120. Manufacturers will also be more likely to consider some launch approaches where the cost of getting to market is lower. In China, while drug prices are lower, the costs associated with completing clinical trials are also much lower and the insured population served is very large (and expanding), making it an appealing market to develop proof-of-concept for various indications before identifying the optimal indication(s) to pursue in the U.S.[241]

F. Migration of the MFP payment structure to the commercially insured population would compound disincentives for innovation

121. The IRA's MFP itself will likely migrate from Medicare to the commercially insured population (i.e., "spill over" from Medicare to the commercial market). In some cases, this will be statutorily imposed by State Prescription Drug Affordability Boards ("PDABs").[242] Additionally, certain commercial insurers are expected to try to reflect MFPs into their own negotiation process with manufacturers.[243] Any migration into the commercially insured population will further compound the aforementioned consequences to innovation.

122. PDABs are independent bodies established in several states that analyze prescription drug costs and, to varying degrees, regulate drug prices.[244] There are currently seven states with

[241] "China's Latest Approach to Drug Development and Approvals," *AAPS Newsmagazine*, March 2021, available at https://www.aapsnewsmagazine.org/aapsnewsmagazine/articles/2021/mar21/elearning-mar21.
[242] For example, recent legislation enables the Minnesota PDAB to set upper payment limits on all sales of select pharmaceutical products in the state; if the product is subject to a Medicare MFP, the upper payment limit must be equal to the MFP. *See* Minnesota Statutes, §62J.88-92.
[243] According to the CMS Guidance "the Negotiation Program does not regulate payment rates by payers outside of the Medicare program (e.g., in the commercial markets)." But the Guidance goes on to note that, "CMS will publish the MFP for each selected drug, as required by law. The MFP for each selected drug could be published by pharmaceutical pricing database companies and could be used by other payers for reimbursement and other purposes. Payers will continue to have discretion to consider Medicare payment rates among other considerations in establishing their own payment policies." *See* CMS Guidance, p. 40.
[244] Clark, Bobby, and Marlene Sneha P., "Can State Rx Drug Affordability Boards Address High-Cost Prices?" *Commonwealth Fund*, October 11, 2011, available at https://www.commonwealthfund.org/blog/2022/can-state-prescription-drug-affordability-boards-address-high-cost-drug-prices.

PDABs and several others with pending legislation to establish such boards.[245] Certain PDABs, such as those in Maine and New Hampshire, are not allowed to set upper payment limits for the private sector and only have jurisdiction over public health plans.[246] Others, however, have the authority to set upper payment limits not only for public plans but also commercial plans.[247] For example, Washington, Colorado, Maryland, and Minnesota PDABs have the authority to set upper payment limits for many commercially insured consumers in the state, and Oregon is set to follow pending additional legislative approval.[248] Minnesota's PDAB has already been required to set upper payment limits at the Medicare MFP for drugs subject to the Medicare MFP.[249] Additionally, Colorado has stated its intention to utilize Medicare's MFP as a reference for setting upper payment limits,[250] and it will be a strong policy consideration for other state PDABs moving forward, further extending the reach of the IRA beyond Medicare.[251]

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[245] PDABs currently exist in Colorado, Maryland, Minnesota, Oregon, Washington, Maine, and New Hampshire. *See* "2023 State Legislative Action to Lower Pharmaceutical Costs," *National Academy for State Health Policy*, updated July 7, 2023, available at https://nashp.org/2023-state-legislative-action-to-lower-pharmaceutical-costs/; "2022 RxTracker," *National Academy for State Health Policy*, available at https://eadn-wc03-8290287.nxedge.io/wp-content/uploads/2023/01/Rx-Tracker-2022-Archive.pdf; "Comparison of State Prescription Drug Affordability Review Initiatives," *National Academy for State Health Policy*, March 31, 2022, available at https://nashp.org/comparison-of-state-prescription-drug-affordability-review-initiatives/.

[246] "Comparison of State Prescription Drug Affordability Review Initiatives," *National Academy for State Health Policy*, March 31, 2022, available at https://nashp.org/comparison-of-state-prescription-drug-affordability-review-initiatives/.

[247] "Comparison of State Prescription Drug Affordability Review Initiatives," *National Academy for State Health Policy*, March 31, 2022, available at https://nashp.org/comparison-of-state-prescription-drug-affordability-review-initiatives/.

[248] "Comparison of State Prescription Drug Affordability Review Initiatives," *National Academy for State Health Policy*, March 31, 2022, available at https://nashp.org/comparison-of-state-prescription-drug-affordability-review-initiatives/; *See also* "2023 State Legislative Action to Lower Pharmaceutical Costs," *National Academy for State Health Policy*, updated July 7, 2023, available at https://nashp.org/2023-state-legislative-action-to-lower-pharmaceutical-costs/.

[249] Minnesota Statutes, §62J.88-92.

[250] 3 Colo. Code Regs. §702-9-4.1, available at https://casetext.com/regulation/colorado-administrative-code/department-700-department-of-regulatory-agencies/division-702-division-of-insurance/rule-3-ccr-702-9-prescription-drug-affordability-board/part-3-ccr-702-9-4-upper-payment-limits/section-3-ccr-702-9-41-upper-payment-limit-methodology.

[251] For example, the National Academy for State Health Policy, a nonpartisan policy development organization, has already proposed model legislation for states to utilize new rates set by CMS under the IRA for public and commercial plans. Reck, Jennifer, and Drew Gattine, "New NASHP Model Legislation Supports State Efforts to Lower Drug Costs by Leveraging Medicare Negotiations," *National Academy for State Health Policy*, November 11, 2022, available at https://nashp.org/new-nashp-model-legislation-supports-state-efforts-to-lower-drug-costs-by-leveraging-medicare-negotiations/.

123. While commercial insurers will likely not have the same leverage to force price reductions on manufacturers during formulary negotiations, Medicare payment structures have spilled over to the commercial market in the past. For example, after the MMA established the ASP-based system for Medicare, a substantial portion of commercial payers adjusted their reimbursement and payment approaches from other benchmarks (e.g., Wholesale Acquisition Cost (WAC) or Average Wholesale Price (AWP) to one based on ASP over time.[252] Similarly, a 2017 study examining how Medicare influences private insurers' payments found that changes to Medicare physician reimbursements led to changes in private reimbursement rates as well. Specifically, the authors found that the relationship between the two was almost one-to-one — i.e., that a one dollar change in Medicare prices led to a one dollar change in private prices.[253] Another study examined the impact of Medicare regulatory spillovers in the context of physicians' choices regarding surgery setting and stated, "[o]ur work consequently reveals the long reach of Medicare rulemaking and its ability to shape physician behavior and healthcare delivery beyond the statutory scope of the regulation."[254] Finally, in comments published with their Guidance, CMS suggests that commercial payors may rely on published MFPs "in establishing their own payment policies."[255] Ultimately, even assuming CMS is able to limit unintentional spillover of MFPs into the commercial market (i.e., commercial payors being erroneously provided with the MFP), past history suggests that may commercial payors will attempt to replicate the Medicare payment methodology and will rely on the publicly available MFPs to do so.

[252] Mullen, Patrick, "The Arrival of Average Sales Price," *Biotechnology Healthcare*, Vol. 4, No. 3, June 2007, pp. 48-53, at pp. 49-50, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3541838/; Alwardt, Sarah, et al., "IRA Question of the Week_ How Will Negotiation Affect Reimbursement," *Avalere Health*, March 23, 2023, available at https://avalere.com/insights/ira-question-of-the-week-how-will-negotiation-affect-reimbursement.
[253] Clemens, Jeffrey, and Joshua D. Gottlieb, "In the Shadow of a Giant: Medicare's Influence on Private Physician Payments," *Journal of Political Economy*, Vol. 125, No. 1, 2017, pp. 1-39, available at https://www.journals.uchicago.edu/doi/full/10.1086/689772.
[254] Geruso, Michael, and Michael R. Richards, "Trading spaces: Medicare's regulatory spillovers on treatment setting for non-Medicare patients," *Journal of Health Economics*, Vol. 84, July 2022, pp. 1-31, at p. 8.
[255] CMS Guidance, p. 40. Moreover, the Guidance also notes that "Medicare already establishes and publishes payment rates for drugs under Part B using the Average Sales Price (ASP) methodology that may be used by other payers (such as state Medicaid programs), and Medicaid also publishes various pharmaceutical pricing benchmarks, such as the National Average Drug Acquisition Cost (NADAC) file and Federal Upper Limits (FULs) for multiple source drugs, that may be used by other payers."

G. The "small biotech drugs" exclusion could lead to counterproductive reductions in drug development efficiency and increased risk of clinical trial failures

124. As I noted earlier, acquisition of smaller, start-up companies in the pharmaceutical industry is a common route from discovery and early-stage development to commercial launch.[256] Larger pharmaceutical manufacturers frequently acquire early-stage drugs outright or rights to develop and market them to usher them successfully through the late clinical trial process, regulatory review, and/or marketing introduction. These larger manufacturers may have experience, organizational depth, and resources that increase the chance of success in later-phase clinical trials and regulatory approval, and with lower costs.[257] For example, an analysis of a data set containing information on over 1,900 compounds under development in the U.S. by over 900 firms between 1988 and 2000 showed that "(p)roducts developed in an alliance tend to have a higher probability of success, at least for the more complex phase 2 and phase 3 trials, and particularly if the licensee is a large firm," and the authors concluded that "(o)ur results confirm that alliances with large firms increase the probability of success in clinical trials for drugs originated by small firms."[258]

125. As another indicator, a recent IQVIA report found that emerging biopharma companies received complete response letters (CRLs), which detail outstanding deficiencies which must be corrected in a submission package, at a 38 percent higher rate than other biopharma companies (12.7 percent of the time, as opposed to 9.2 percent of the time), and that they were deficient more frequently for clinical reasons that might require additional clinical trials.[259]

126. If drugs are able to avoid inclusion on the selected drug list because they are owned by smaller biotech companies, on the margin, this will likely provide an incentive to delay an

[256] "Emerging Biopharma's Contribution to Innovation," *IQVIA*, June 2022, available at https://www.iqvia.com/insights/the-iqvia-institute/reports/emerging-biopharma-contribution-to-innovation.
[257] "Emerging Biopharma's Contribution to Innovation," *IQVIA*, June 2022, available at https://www.iqvia.com/insights/the-iqvia-institute/reports/emerging-biopharma-contribution-to-innovation.
[258] Danzon, Patricia M., et al., "Productivity in Pharmaceutical-Biotechnology R&D: the Role of Experience and Alliances," *Journal of Health Economics*, Vol. 24, No. 2, March 2005, pp. 317-339.
[259] Emerging biopharma companies were defined as those with less than $500 million in annual sales and less than $200 million in R&D spending per year, *see* "Emerging Biopharma's Contribution to Innovation," *IQVIA*, June 2022, available at https://www.iqvia.com/insights/the-iqvia-institute/reports/emerging-biopharma-contribution-to-innovation.

otherwise attractive sale to or milestone-based agreement with a larger manufacturer, which could reduce efficiency through the clinical trial process and may even result in some drugs failing clinical trials that would otherwise have been successful. While the "small biotech" exclusion from the selected drug list is currently scheduled to end after 2028, it may affect plans for some smaller companies with ongoing clinical trial programs and presents uncertainty around whether the exception will be extended in the future.

H. The "orphan drug" exclusion will deter manufacturers from seeking incremental indications on drugs with a single orphan designation

127. The IRA excludes from MFP-setting drugs that have a single orphan designation and approved indication(s) only within that single designated rare disease or condition.[260] Because this exclusion does not extend to drugs indicated to treat more than one disease (even if those two diseases combined have fewer than 200,000 patients – the threshold for an orphan designation),[261] manufacturers will be disincentivized from seeking any incremental approvals for drugs that currently hold a single orphan designation.

128. As I discuss in Section III.A.3, clinical advances made through seeking new indications for existing drugs can provide a more efficient route to expanding treatment options for patients. This is especially valuable for patients with rare diseases and a small patient population that can benefit from pre-established safety of an already-approved treatment. Under CMS's interpretation of the IRA, any drug that has an orphan designation will no longer be exempted from MFP-setting if it is approved for any indication outside of the single orphan-designated disease.[262] Creating a disincentive to invest in subsequent orphan indications will further limit treatment development for patients who already have limited options. It also discourages the efficiency gains that can be made by approving a drug for a new disease type after it has already undergone a costly discovery and development process.

129. For example, small molecule drug Amvuttra, which holds an orphan designation and is currently only indicated to treat adults with polyneuropathy caused by hATTR

[260] SSA, §1192(c)(3)(A).
[261] "Orphan Products: Hope for People With Rare Diseases," *FDA*, March 1, 2018, available at https://www.fda.gov/drugs/information-consumers-and-patients-drugs/orphan-products-hope-people-rare-diseases.
[262] SSA §1192(e)(3)(A).

amyloidosis,[263] was in a Phase III clinical trial for the treatment of Stargardt disease – another rare disease for which there are no treatment options.[264] But the manufacturer recently announced the decision to abandon this trial while they "evaluate the impact of the Inflation Reduction Act on therapies being developed from orphan disease."[265] Decisions such as these – which could adversely affect patients with great unmet need – are likely to become more common under the IRA.

VI. CONCLUSION

130. The IRA establishes what is effectively a price-setting regime for critically important Medicare drugs — with the potential for far-reaching effects across nearly all drugs, therapeutic categories, and patient populations. As a result of the IRA's system of extreme penalties, manufacturers will have no economically viable alternative to acquiescing to almost any price set by CMS, no matter how unrelated this price might be to product value. As a result of the changes in incentives for investment in drug innovation, the IRA will have substantial impact on current and future patients, forgoing access to some future medical innovations in favor of lower prices for today's drugs, thereby also forgoing the health benefits of those unknown future innovations.

Craig Garthwaite
August 10, 2023

[263] "Amvuttra FDA label," *Drugs@FDA*, as of June 13, 2022, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215515s000lbl.pdf.
[264] "Stargardt Disease," *National Eye Institute,* updated September 29, 2021, available at https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/stargardt-disease ("There's no treatment for Stargardt disease, but vision rehabilitation can help people make the most of their remaining vision").
[265] "Alnylam Pharmaceuticals, Inc. (ALNY) Q3 2022 Earnings Call Transcript," *Seeking Alpha*, October 27, 2022.

APPENDIX A
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APPOINTMENTS

Kellogg School of Management, Northwestern University
Professor of Strategy, 2020 - Present
Herman R. Smith Research Professor in Hospital and Health Services, 2017-Present
Director, Program on Healthcare at Kellogg, 2016 - Present
Associate Professor of Strategy (with tenure), 2016 – 2020
Assistant Professor of Strategy, 2010 - 2016
Senior Lecturer and Donald P. Jacobs Scholar in Management and Strategy, 2009 - 2010

National Bureau of Economic Research
Research Associate, 2016-Present
Faculty Research Fellow, 2011-2016

Institute for Policy Research, Northwestern University
Faculty Associate, 2015 - Present

EDUCATION

Ph.D. Economics, University of Maryland at College Park, 2009
M.A. Economics, University of Maryland at College Park, 2008
M.P.P Gerald R. Ford School of Public Policy at the University of Michigan, 2001
B.A. Political Science, cum laude, University of Michigan, 2000

PUBLIC SERVICE

Member, Aspen Economic Strategy Group (2021 – Present)

Member, Congressional Budget Office Panel of Healthcare Advisers (2020 – Present)

Member, Congressional Budget Office Technical Review Panel for the Health Insurance Simulation Model (2018-2020)

Member, Health Affairs Council on Spending and Value (2018-2023)

Testimony, United States House of Representatives, 2018
- House Judiciary Committee, Subcommittee on Regulatory Reform, Commercial and Antitrust Law: "Competition in the Pharmaceutical Supply Chain: The Proposed Merger of CVS Health and Aetna"

Testimony, United States House of Representatives, 2019
- House Judiciary Committee, Subcommittee on Regulatory Reform, Commercial and Antitrust Law: "Diagnosing the Problem: Exploring the Effects of Consolidation and Anticompetitive Conduct in Health Care Markets"

Testimony, United States Senate, 2019

- Senate Judiciary Committee, Subcommittee on Antirust, Competition Policy, and Consumer Rights: "Your Doctor/Pharmacist/Insurer Will See You Now: Competitive Implications of Vertical Consolidation in the Healthcare Industry"

Testimony, United States House of Representatives, 2019

- House Education and Labor Committee, Subcommittee on Health, Education, Labor and Pensions: "Making Health Care More Affordable: Lowering Drug Prices and Increasing Transparency"

Testimony, United States House of Representatives, 2021

- House Oversight and Reform Committee "Unsustainable Drug Prices (Part III)"

Testimony, United States Senate, 2022

- Senate Committee on Commerce, Science, and Transportation's Consumer Protection, Product Safety, and Data Security Subcommittee: "Ensuring Fairness and Transparency in the Market for Prescription Drugs"

Testimony, United States Senate, 2023

- Senate Committee on Health, Education, Labor, and Pensions: "Taxpayers paid billions for it: So why is Moderna considering quadrupling the price of the COVID vaccine?"

ACADEMIC PUBLICATIONS

"The Impact of Early Discharge Laws on the Health of Newborns," (with William Evans and Heng Wei), *Journal of Health Economics,* 2008, 27(4): 843-870.

"The Economic Benefits of Pharmaceutical Innovations: The Case of Cox-2 Inhibitors," *American Economic Journal: Applied Economics,* 2012, 4(3): 116-137.

"Empirical Evidence on the Value of Pharmaceuticals," (with Mark Duggan), in *The [Oxford] Handbook of the Economics of the Biopharmaceutical Industry*: Oxford University Press: Oxford, 2012: 463-492.

"The Doctor Might See You Now: The Supply Side Effects of Public Health Insurance Expansions." *American Economic Journal: Economic Policy* 2012, 4(3): 190-217.

"Heterogeneity in the Benefits of Greater Treatment Intensity" (with William Evans), *The Review of Economics and Statistics,* 2012, 94(3): 635-649.

"Can Celebrity Endorsements Affect Political Outcomes: Evidence from the 2008 US Democratic Presidential Primary," (with Tim Moore), *The Journal of Law, Economics, and Organizations,* 2013, 29(2): 355-384.

"Demand Spillovers, Combative Advertising, and Celebrity Endorsements," *American*

Economic Journal: Applied Economics, 2014, 6(2): 76-104.

"Giving Mom a Break: The Effect of Higher EITC Payments on Maternal Health" (with William Evans), *American Economic Journal: Economic Policy,* 2014, 6(2): 258-290.

"Public Health Insurance, Labor Supply, and Employment Lock," (with Tal Gross and Matthew Notowidigdo), *Quarterly Journal of Economics*, 2014, 129(2): 653-696.

"Health Spending Slowdown Is Mostly Due to Economic Factors, Not Structural Change in the Health Care Sector" (with David Dranove and Christopher Ody), *Health Affairs,* 2014, 33(8): 1399-1406.

"The Economic Downturn and its Lingering Effects Reduced Medicare Spending Growth by $4 Billion In 2009–12," (with David Dranove and Christopher Ody), *Health Affairs*, 2015, 34(8): 1368-1375.

"Investment Subsidies and the Adoption of Electronic Medical Records in Hospitals." (with David Dranove, Chris Ody, and Bingyang Li), *Journal of Health Economics,* 2015, 44: 309-19.

"The Market Impacts of Product Patents in Developing Countries," (with Mark Duggan and Aparajita Goyal), A*merican Economic Review*, 2016, 106(1): 99-135

"The Black/White Educational Gap, Stalled Progress, and the Long Term Consequences of the Emergence of Crack Markets," (with William Evans and Timothy J. Moore), *The Review of Economics and Statistics*, 2016, 98(5): 832-847.

"Affordable Care Act's Medicaid Expansion Led to Substantial Decreases in Uncompensated Care but Levels and Many Hospitals Remain High," (with David Dranove and Christopher Ody), *Health Affairs,* 2016, 35(8): 1471-1479.

"How do Hospitals Respond to Negative Financial Shocks? The Impact of the 2008 Stock Market Crash (with David Dranove and Christopher Ody)," *The RAND Journal of Economics*, 2017, 48(2): 485–525.

"Insurance Expansion and Hospital Emergency Department Access: Evidence from the Affordable Care Act," (with John Graves, Tal Gross, and Matthew Notowidigdo), *Annals of Internal Medicine,* Feb 7 2017, 166(3):172-179

"Success and Failure in the Insurance Exchanges (with John Graves)," *New England Journal of Medicine,* March 9, 2017, 376(10):907-910

"The Economics of Indication Based Pricing (with Amitabh Chandra)," *New England Journal of Medicine,* July 2017, 377(2):103-106.

"Hospitals as Insurers of Last Resort," (with Tal Gross and Matthew Notowidigdo), *American Economic Journal: Applied Economics,* 2018, 10(1): 1-39.

"The CVS–Aetna Merger: Another Large Bet on the Changing U.S. Health Care Landscape," (with Austin Frakt), *Annals of Internal Medicine,* January 9, 2018.

"The Orphan Drug Act at 35: Observations and an Outlook for the Twenty-First Century," (with Nicholas Bagley, Benjamin Berger, Amitabh Chandra, and Ariel D. Stern) in *Innovation Policy and the Economy*, 2018, Volume 19, pages 97-137, National Bureau of Economic Research, Inc.

"Characterizing the Drug Development Pipeline for Precision Medicine, (with Chandra, Amitabh, Garthwaite, Craig and Stern, Ariel Dora Stern), *Economic Dimensions of Personalized and Precision Medicine,* 2018, National Bureau of Economic Research, Inc.

"It's Time to Reform the Orphan Drug Act," (with Nicholas Bagley, Amitabh Chandra, and Ariel D. Stern), *NEJM Catalyst*, Dec 19, 2018.

"Economic Principles for Medicare Reform (with Amitabh Chandra)," *ANNALS of the American Academy of Political and Social Science,* 2019, 686(1): 63-92.

"All Medicaid Expansions Are Not Created Equal: The Geography and Targeting of the Affordable Care Act," *Brookings Papers on Economic Activity,* Fall 2019 (with John Graves, Tal Gross, Zeynal Karaca, Victoria Marone, and Matthew Notowidigdo)

"The Economics of Medicare for All," book chapter in *Maintaining the Strength of American Capitalism* published by the *Aspen Economic Strategy Group*, eds. Melissa Kearney and Amy Ganz, December 2019.

"Insurance access and demand response: Price and welfare implications," (with David Dranove and David Besanko), *Journal of Health Economics,* 2020, 73.

"The Economics of Medical Procedure Innovation," (with David Dranove, Christopher Heard, and Bingxiao Wu), *Journal of Health Economics,* January 2022, Vol. 81.

Guns and Violence: The Enduring Impact of Crack Cocaine Markets on Young Black Males, (with Bill Evans and Timothy J. Moore), *Journal of Public Economics,* February 2022, vol. 206.

"Endogenous Quality Investments in the US Hospital Market," (with Chris Ody and Amanda Starc), *Journal of Health Economics,* July 2022, 84:10236.

"Does consumer demand pull scientifically novel drug innovation?," (with David Dranove and Manuel Hermosilla), *RAND Journal of Economics*, August 18 2022, Vol. 53 Issue 3.

"The Returns to Medical Inventions," (with David Dranove and Binxiao Wu), *The Journal of Law & Economics*, November 2022, Vol 65 Num. S2.

"Expected Profits and The Scientific Novelty of Innovation," NBER Working Paper #27093, (with David Dranove and Manuel Hermosilla), forthcoming, *RAND Journal of Economics*

WORKING PAPERS

"Regulatory Approval and Expanded Market Size," NBER Working Paper #28889 (with Amitabh Chandra and Benjamin Berger)

"Who Profits From Amateurism: Rent-Sharing in Modern College Sports," NBER Working Paper #27734 (with Jordan Keener Matthew J. Notowidigdo Nicole F. Ozminkowski), *revise and resubmit, American Economic Journal: Applied Economics*

"The Impact of Private Contracting on Healthcare for the Old and Sick: Evidence from California's Medicaid Program" (with Mark Duggan and Adelina Wang)

"Reinsuring the Insurers of Last Resort" (with Chris Ody and David Dranove)

"The Opportunities and Limitations of Monopsony Power in Healthcare: Evidence from the United States and Canada," July 2019 (with Jillian Chown, David Dranove, and Jordan Keener)

"Artificial Intelligence, the Evolution of the Healthcare Value Chain, and the Future of the Physician," NBER Working Paper #30607 (with David Dranove)

OTHER PUBLICATIONS

The Impact of the ACA's Medicaid Expansion on Hospitals' Uncompensated Care Burden and the Potential Effects of Repeal (with David Dranove and Christopher Ody), *Commonwealth Fund Issue Brief*, May 2017.

"A Floor and Trade Proposal for Hospital Charity Care," The Hamilton Project working paper.

CASES

Wildcat Physical Therapy (with Dylan Duffy), 2019

Evaluating Vertical Integration at AB-Inbev Across the Globe (with Sarit Markovich, Eugenio Gomez A Latorre, and Andrea Meyer), 2018, Kellogg 5-118-002)

Consumer Cost Sharing in Health Insurance (with Chris Ody), 2018

Quality Provision in the Nursing Home Industry (with Chris Ody), 2017

Renal Care in the United States, 2020

Sovaldi: Pricing a Breakthrough Drug (with Meghan Busse), 2015

The Global Aircraft Manufacturing Industry, 2002-2011 (with Jen Brown), 2012. Kellogg Case #5-312-505.

Starbucks: A Story of Growth, (with Jen Brown and Meghan Busse), 2011. Kellogg Case #5-211-259.

PERMANENT WORKING PAPERS

Pharmaceutical Profits and the Social Value of Innovation, NBER Working Paper #20212, (with David Dranove and Manuel Hermosilla)

"The Effect of In-Utero Conditions on Long Term Health: Evidence from the 1918 Spanish Flu Pandemic," April 2008 (First Draft, July 2007).

TEACHING

Core Business Strategy (STRT 431), Kellogg School of Management, 2009-Present
Foundations of Strategy, Kellogg-HKUST EMBA, 2016-Present
Strategy Frameworks Kellogg EMBA, 2017-Present
Healthcare Strategy (STRT 443), Kellogg School of Management, 2017-Present
Healthcare Strategy (STRTX 945), Kellogg School of Management EMBA, 2017-Present
Value Creation and Capture in Biopharmaceuticals (HCAK 960), 2022 - Present

HONORS AND AWARDS

Sidney J. Levy Teaching Award for Electives, 2021
Kellogg Chairs' Core Course Teaching Award, 2019
Lavengood Professor of the Year Finalist, 2019
Lavengood Professor of the Year Finalist, 2018
Kellogg Faculty Impact Award, Healthcare Strategy, 2018
Sidney J. Levy Teaching Award for Electives, 2017
Poets and Quants 40 Best Under 40 Professors, 2015
Kellogg Faculty Impact Teaching Award, Business Strategy, 2012
Kellogg Faculty Impact Teaching Award, Business Strategy, 2012
Kellogg Chairs' Core Course Teaching Award, 2011
International Institute of Public Finance (IIPF) Young Economists Award, 2011
Kellogg Faculty Impact Teaching Award, Business Strategy, 2010
University of Maryland Third Year Paper Fellowship

INVITED PRESENTATIONS

2008: University of Notre Dame
2009: Chicago Booth Graduate School of Business
2010: University of Wisconsin-Madison, Dartmouth College, University of Notre Dame
2011: AEA Annual Meeting, University of Illinois-Chicago, Olin Business School at Washington University, Harris School of Public Policy at the University of Chicago, Indiana University SPEA, National Tax Association Annual Meeting, AcademyHealth Research Insights Meeting
2012: AEA Annual Meeting (Presenter and Discussant), Society of Labor Economists Annual Meeting, NBER Summer Institute, University of Illinois Urbana-Champaign, University of California-Davis, Columbia University

2013: University of Chicago Health Economics Workshop, University of British Columbia, University of California-San Diego, University of Kentucky, Texas A&M University, Wharton School of the University of Pennsylvania, University of Maryland, Brookings Institution, UC-Davis Poverty Center
2014: AEA Annual Meeting, Northwestern Law School, RAND Corporation, Rice University/University of Houston, HDMS User Forum, Bates/White Life Science Conference, Vanderbilt University, University of Michigan RWJF Scholars, Northwestern University Economics Department
2015: AEA Annual Meeting, Stanford University, University of California-Irvine, MIT/BU Health Economics Seminar, Syracuse University, NBER Summer Institute, UT-Austin, University of Maryland
2016: Harris School of Public Policy at the University of Chicago, Owen School of Management, Vanderbilt University.
2017: National Tax Association Annual Meeting
2018: University of Georgia, Auburn University, Harvard University, Boston University, American Enterprise Institute, University of Southern California
2019: American Medical Association, Ohio State University, University of Louisville, Emory University, Aspen Ideas Festival, Aspen Economic Strategy Group, University of Utah, Aspen Ideas Festival, Aspen Ideas Health Festival, Aspen Economic Strategy Group
2020: Harris School of Public Policy at the University of Chicago
2022: The Wharton School

ACADEMIC ACTIVITIES

Co-Editor, *Journal of Public Economics*, (2016 – 2020)

Reviewer: *American Economic Review, Quarterly Journal of Economics; Journal of Political Economy; Econometrica; Review of Economic Studies; New England Journal of Medicine, The Journal of Public Economics; American Economic Journal: Economic Policy; Health Affairs; The Review of Economics and Statistics; The Journal of Industrial Economics; The Journal of Health Economics; The Journal of Human Resources; Journal of Policy Analysis and Management; International Journal of Industrial Organization; Health Economics; Social Science and Medicine; Economic Inquiry*

PAST EMPLOYMENT

Employment Policies Institute, Washington, DC
Director of Research and Chief Economist, 2003-2005
Public Sector Consultants, Lansing, MI
Economist, 2002-2003

OUTSIDE ACTIVITIES

Affiliated Consultant, Analysis Group (2018-Present)
Consultant for Wal-Mart Inc. (2019-2020)
Eli Lilly Advisory Board (2020)
Janssen Advisory Board (2021 - Present)

Speaking engagements for Allergan, Alexion, Digestive Health Professionals Association National Pharmaceutical Council, Wisconsin Association of Health Plans, Great American Insurance.

APPENDIX B
EXPERT CONSULTING AND TESTIMONY

1. (Presentation) Marshfield Clinic Zoning Appeal, Oneida County Planning and Development committee, Oneida County, WI, December 14, 2017 (on behalf of appellant).

2. (Deposition testimony) *In Re*: United States of America ex rel. Frank M. Rembert and Michael R. Paradise vs. Bozeman Health Deaconess Hospital D/B/A Bozeman Health and Deaconess-Intercity Imaging, LLC. D/B/A Advanced Medical Imaging, United States District Court, District of Montana, Butte Division, Case No. 2:15-cv-00080-SHE, December 11, 2015 (on behalf of Relators).

3. (Testimony) Before the House Judiciary Committee, Subcommittee on Regulatory Reform, Commercial and Antitrust Law, February 27, 2018.

4. (Testimony) Before the House Judiciary Committee, Subcommittee on Regulatory Reform, Commercial and Antitrust Law, March 7, 2019.

5. (Declaration) *In Re*: Merck, et al. v. United States Department of Health and Human Services, et al., United States District Court for the District of Columbia, Case 1:19-cv-01738, June 14, 2019 (on behalf of Plaintiffs).

6. (Declaration) *In Re*: Biotechnology Innovation Organization, et al. v. Alex Azar in his official capacity as Secretary of the United States Department of Health and Human Services, et al., United States District Court for the District of Northern California, Civil Case No: 20-cv-08603, December 11, 2020 (on behalf of Plaintiffs).

7. (Deposition testimony) *In Re*: National Prescription Opiate Litigation, United States District Court, Northern District of Ohio, Eastern Division, MDL No. 2804 Case No 17-MD-2804, June 7, 2019 and July 14, 2021 (on behalf of Defendant CVS).

8. (Testimony) Before the Senate Judiciary Committee, Subcommittee on Antirust, Competition Policy, and Consumer Rights, June 12, 2019.

9. (Testimony) Before the United States House of Representatives, House Education and Labor Committee, Subcommittee on Health, Education, Labor and Pensions, September 26, 2019.

10. (Testimony) Before the House Oversight and Reform Committee, May 18, 2021.

11. (Deposition testimony) State of Florida, Office of the Attorney General, Department of Legal Affairs v. Purdue Pharma L.P. et al., in the Circuit Court of the Sixth Judicial Circuit in for Pasco County, Florida, Case No. 2018-CA-001438, December 13, 2021 (on behalf of Defendant CVS).

12. (Testimony) Before the Senate Committee on Commerce, Science, and Transportation's Consumer Protection, Product Safety, and Data Security Subcommittee, May 5, 2022.

13. (Testimony) Before the Senate Committee on Health, Education, Labor, and Pensions, March 22, 2023.

APPENDIX C
MATERIALS RELIED UPON

Books and Articles

Acemoglu, Daron and Joshua Linn, "Market Size in Innovation: Theory and Evidence From the Pharmaceutical Industry," *Quarterly Journal of Economics*, Vol. 119, No. 3, August 2004, pp. 1049-1090.

Bagley, Nicholas, et al., "The Orphan Drug Act at 35: Observations and an Outlook for the Twenty-First Century," *Innovation Policy and the Economy*, Vol. 19, No. 1, 2019, pp. 97-137, available at https://www.journals.uchicago.edu/doi/full/10.1086/699934.

Bauer, Hans H., and Marc Fischer, "Product life cycle patterns for pharmaceuticals and their impact on R&D profitability of late mover products," *International Business Review*, Vol. 9, No. 6, December 2000, pp. 703-725.

Berger, Benjamin, et al., "Regulatory Approval and Expanded Market Size," *NBER Working Paper*, June 2021, No. 28889, available at https://www.nber.org/system/files/working_papers/w28889/w28889.pdf.

Black, Dennis M., et al., "The effect of 6 versus 9 years of zoledronic acid treatment in osteoporosis: a randomized second extension to the HORIZON-Pivotal Fracture Trial (PFT)," *Journal of Bone and Mineral Research,* Vol. 30, No. 5, December 26, 2014, pp. 934-944, available at https://asbmr.onlinelibrary.wiley.com/doi/10.1002/jbmr.2442.

Blackstone, Erwin A., and Joseph P. Fuhr, "The Economics of Biosimilars," *American Health & Drug Benefits*, Vol. 6, No. 8, September/October 2013, pp. 469-478, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4031732/.

Blume-Kohout, Margaret E. and Neeraj Sood, "Market Size and Innovation: Effects of Medicare Part D on Pharmaceutical Research and Development," *Journal of Public Economics*, Vol. 97, January 2013, pp. 327-336.

Chandra, Amitabh, and Craig Garthwaite, "The Economics of Indication-Based Drug Pricing," *The New England Journal of Medicine*, Vol. 377, No. 2, July 13, 2017, pp. 103-106.

Clemens, Jeffrey, and Joshua D. Gottlieb, "In the Shadow of a Giant: Medicare's Influence on Private Physician Payments," *Journal of Political Economy*, Vol. 125, No. 1, 2017, pp. 1-39, available at https://www.journals.uchicago.edu/doi/full/10.1086/689772.

Cockburn, Iain M., et al., "Patents and the Global Diffusion of New Drugs," *American Economic Review*, Vol. 106, No. 1, January 2016, pp. 136-164.

Cummings, Jeffrey L., et al., "The costs of developing treatments for Alzheimer's disease: A retrospective exploration," *Alzheimer's Dementia*, Vol. 18, No. 3, March 2022, pp. 469-477, available at https://pubmed.ncbi.nlm.nih.gov/34581499/.

Danzon, Patricia M., and Andrew J. Epstein, "Effects of Regulation on Drug Launch and Pricing in Interdependent Markets," *Advances in Health Economics and Health Services Research*, Vol. 23, 2012, pp. 35-71, available at https://faculty.wharton.upenn.edu/wp-content/uploads/2018/12/Effects-of-regulation-on-drug-launches.pdf.

Danzon, Patricia M., et al., "Productivity in Pharmaceutical-Biotechnology R&D: the Role of Experience and Alliances," *Journal of Health Economics*, Vol. 24, No. 2, March 2005, pp. 317-339.

Danzon, Patricia M., et al., "The Impact of Price Regulation on the Launch Delay of New Drugs — Evidence from Twenty-Five Major Markets in the 1990s," *Health Economics*, Vol. 14, No. 3, March 2005, pp. 269-292, available at https://repository.upenn.edu/entities/publication/7d075784-9731-468c-96b1-4586b00d3918.

DiMasi, Joseph A., et al., "Innovation in the pharmaceutical industry: New estimates of R&D costs," *Journal of Health Economics,* Vol. 47, May 2016, pp. 20-33.

Dranove, David, et al., "Does consumer demand pull scientifically novel drug innovation?" *RAND Journal of Economics*, Vol. 53, No. 3, August 18, 2022, pp. 590-638.

Dubois, Pierre, et al., "Market Size and Pharmaceutical Innovation," *RAND Journal of Economics*, Vol. 46, No. 4, October 26, 2015, pp. 844-871.

Duggan, Mark and Fiona Scott Morgan, "The Effect of Medicare Part D on Pharmaceutical Prices and Utilization," *NBER Working Paper Series*, April 2008, No. 13917, pp. 1-37, available at https://www.nber.org/system/files/working_papers/w13917/w13917.pdf.

Forrester, Caroline, "Benefits of Prior Authorizations," *Journal of Managed Care Pharmacy*, July 2020, Vol. 26, No. 7, pp. 820-822.

Geruso, Michael, and Michael R. Richards, "Trading spaces: Medicare's regulatory spillovers on treatment setting for non-Medicare patients," *Journal of Health Economics*, Vol. 84, July 2022, pp. 1-31.

Grabowski, Henry, and C. Daniel Mullins, "Pharmacy Benefit Management, Cost-Effectiveness Analysis and Drug Formulary Decisions," *Social Science & Medicine*, Vol. 45, No. 4, August 1, 1997, pp. 535-544.

Grabowski, Henry, et al., "Continuing trends in U.S. brand-name and generic drug competition," *Journal of Medical Economics,* Vol. 24, No. 1, August 2, 2021, pp. 908-917, available at https://www.tandfonline.com/doi/full/10.1080/13696998.2021.1952795.

Grabowski, Henry, et al., "Regulatory and Cost Barriers are Likely to Limit Biosimilar Development and Expected Savings in the Near Future," *Health Affairs,* Vol. 33, No. 6, June 2014, pp. 1048-1057.

Heskett, Clay, et al., "First Biopharma Product Launch in Europe: What It Takes to Succeed," *L.E.K. Consulting*, available at https://www.lek.com/sites/default/files/insights/pdf-attachments/2044-First-Biopharma-Product-Launch-in-Europe-What-It-Take.pdf.

Hirsch, Bradford, et al., "Characteristics of Oncology Clinical Trials," *JAMA Internal Medicine*, Vol. 173, No. 11, June 10, 2013, Table, available at https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/1682358.

Holtz-Eakin, Douglas, and Robert Book, "Competition and the Medicare Part D Program," *American Action Forum*, September 11, 2013, available at https://www.americanactionforum.org/print/?url=https://www.americanactionforum.org/research/competition-and-the-medicare-part-d-program/.

Joppi, Roberta, et al., "Food and Drug Administration vs European Medicines Agency: Review times and clinical evidence on novel drugs at the time of approval," *British Journal of Clinical Pharmacology*, Vol. 86, No. 1, December 16, 2019, pp. 170-174, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6983504/.

Kaitin, Kenneth I., and Joseph A. DiMasi, "Pharmaceutical Innovation in the 21st Century: New Drug Approvals in the First Decade, 2000-2009," *Clinical Pharmacology & Therapeutics*, Vol. 89, No. 2, February 2011, pp. 183-188.

Kozlowski, Steven, et al., "Uptake and Competition Among Biosimilar Biological Products in the US Medicare Fee-for-Service Population," *Journal of General Internal Medicine*, Vol. 37, No. 16, June 1, 2022, pp. 4292-4294, available at https://link.springer.com/article/10.1007/s11606-022-07670-7.

Lakdawalla, Darius and Wesley Yin, "Insurers' Negotiation Leverage and the External Effects of Medicare Part D," *The Review of Economics and Statistics,* Vol. 97, No. 2, May 1, 2015, pp. 314-331, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4414344/pdf/nihms554423.pdf.

Longo, Nicole, "New government price setting policy threatens post-approval research," *PhRMA*, November 10, 2022, available at https://catalyst.phrma.org/new-government-price-setting-policy-threatens-post-approval-research.

Mócsai, Attila, et al., "What is the future of targeted therapy in rheumatology: biologics or small molecules?" *BMC Medicine*, Vol. 12, No. 43, March 13, 2014, pp. 1-9, available at https://bmcmedicine.biomedcentral.com/articles/10.1186/1741-7015-12-43.

Mullen, Patrick, "The Arrival of Average Sales Price," *Biotechnology Healthcare*, Vol. 4, No. 3, June 2007, pp. 48-53, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3541838/.

Siegel, Steven J., "Extended Release Drug Delivery Strategies in Psychiatry," Psychiatry (Edgmont), Vol. 2, No. 6, June 2005, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3000189.

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Weidner, Susan, et al., "Observations Regarding the Average Sales Price Reimbursement Methodology," *Evidence-Based Oncology*, June 2021, Vol. 27, No. 4, pp. SP156-SP160, available at https://www.ajmc.com/view/observations-regarding-the-average-sales-price-reimbursement-methodology.

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Legislation

Code of Federal Regulations, available at https://www.ecfr.gov/.

Colorado Administrative Code, available at https://casetext.com/regulation/colorado-administrative-code.

Medicare Prescription Drug, Improvement, and Modernization Act of 2003, available at https://www.congress.gov/bill/108th-congress/house-bill/1.

Minnesota Statutes, available at https://www.revisor.mn.gov/statutes/.

Social Security Act, available at https://www.ssa.gov/OP_Home/ssact/ssact-toc.htm.

"Text - H.R.5376 - 117th Congress (2021-2022): Inflation Reduction Act of 2022," *Library of Congress*, August 16, 2022, available at https://www.congress.gov/bill/117th-congress/housebill/5376/text.

United States Code, available at https://www.law.cornell.edu/uscode/text.

Other Documents and Webpages

"2022 RxTracker," *National Academy for State Health Policy*, available at https://eadn-wc03-8290287.nxedge.io/wp-content/uploads/2023/01/Rx-Tracker-2022-Archive.pdf.

"2023 State Legislative Action to Lower Pharmaceutical Costs," *National Academy for State Health Policy*, updated July 7, 2023, available at https://nashp.org/2023-state-legislative-action-to-lower-pharmaceutical-costs/.

"Advancing Health Through Innovation: New Drug Therapy Approvals 2021," *FDA*, January 2022, available at https://www.fda.gov/media/155227/download.

"Advancing Real-World Evidence Program," *FDA*, October 20, 2022, available at https://www.federalregister.gov/documents/2022/10/20/2022-22795/advancing-real-world-evidence-program.

"Alnylam Pharmaceuticals, Inc. (ALNY) Q3 2022 Earnings Call Transcript," *Seeking Alpha*, October 27, 2022.

Alwardt, Sarah, et al., "IRA Question of the Week_ How Will Negotiation Affect Reimbursement," *Avalere Health*, March 23, 2023, available at https://avalere.com/insights/ira-question-of-the-week-how-will-negotiation-affect-reimbursement.

"Alzheimer's Facts and Figures Report," *Alzheimer's Association*, available at https://www.alz.org/alzheimers-dementia/facts-figures.

"Amjevita (Adalimumab-Atto), First Biosimilar to Humira, Now Available in the United States," *Amgen Press Release*, January 31, 2023, available at https://www.prnewswire.com/news-releases/amjevita-adalimumab-atto-first-biosimilar-to-humira-now-available-in-the-united-states-301734177.html.

"Amvuttra FDA label," *Drugs@FDA*, as of June 13, 2022, available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215515s000lbl.pdf.

"An Overview of the Medicare Part D Prescription Drug Benefit," *Kaiser Family Foundation,* October 19, 2022, available at https://www.kff.org/medicare/fact-sheet/an-overview-of-the-medicare-part-d-prescription-drug-benefit/.

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APPENDIX D

1. CMS has indicated that it will release the list of MFP-eligible drugs for Initial Price Applicability Year ("IPAY") 2026 in September 2023.[1] Based on the IRA and the CMS Initial Guidance released on March 15, 2023, I have created a list of the drugs that I predict will be included on that list.

2. To create this list, I first examined 50 branded drugs with the highest Medicare Part D spending in 2021, grouped by active moiety using CMS's Medicare Part D Dashboard Data.[2] Next, in line with CMS's guidance for identifying QSSDs, I excluded drugs and biologics that have a generic or biosimilar already available, biologics that are likely to face biosimilar competition within two years, small molecule drugs that will not have been approved for at least seven years as of September 1, 2023, biologics that will not have been approved for at least 11 years as of that date, certain orphan drugs and plasma-derived products, products with Medicare spending of less than $200 million in 2021, and products manufactured by firms that would be considered eligible for the "small biotech" exception.[3]

3. The drug with the highest Medicare Part D spending in 2021 is Eliquis, with total expenditures near $12.6 billion. The next highest drug, Xarelto, had a total Part D spend of less than half that amount, at just over $5.2 billion. The list excludes certain products for having not been on the market for the length of time required by CMS (i.e., seven or eleven years, depending on whether the product is small molecule or biologic).[4] The list also excludes certain products due to the existence of currently-marketed biosimilars and generics.[5]

[1] SSA Section 1191(d)(1).
[2] In the Medicare Part D Dashboard Data, I assume unique combinations of "Gnrc_Name" and "Mftr_Name" are brands. I then manually review the top 20 branded drugs to further aggregate by active moiety.
[3] See Section IV.A.1.(a) for further discussion on MFP exclusion criteria.
[4] Trulicity, Ozempic/Rybelsus, Trelegy Ellipta, and Biktarvy.
[5] Revlimid, Humira, Humalog, Symbicort, and Spiriva are excluded for having currently-marketed generics and biosimilars that were launched after the 2021 Part D data was compiled by CMS. Invega, Invega Sustena, Invega Trinza, and Invega Hafyera are also excluded because, based on CMS' definition of QSSD in its Initial Guidance, they will be aggregated together because they have the same active moiety, and there is generic competition available for Invega. See **Appendix D** table below.

4. A number of researchers and organizations have also produced alternative and overlapping predictions of the list of MFP-eligible drugs for IPAY 2026, although they were produced prior to the issuance of the CMS guidance.[6]

[6] See, e.g., Johnson, Micah et. al, "Which Drug Prices Will Medicare Negotiate First? A Physicians' [*sic*] Perspective," Health Affairs Forefront, September 30, 2022, available at https://www.healthaffairs.org/content/forefront/which-drug-prices-medicare-negotiate-first-physicians-perspective; Dickson, Sean, and Inmaculada Hernandez, "Drugs likely subject to Medicare negotiation, 2026-2028," *Journal of Managed Care & Specialty Pharmacy*, Vol. 29, No. 3, March 2023, pp. 229-235, available at https://www.jmcp.org/doi/full/10.18553/jmcp.2023.29.3.229; and Dunleavy, Kevin, "Pfizer, BMS' Eliquis tops list of drugs destined for Medicare price negotiations in 2026: Moody's," Fierce Pharma, March 30, 2023, available at https://www.fiercepharma.com/pharma/pfizer-bmss-eliquis-tops-list-drugs-destined-medicare-negotiations-2026-moodys.

Appendix D
MFP Price-Setting Drugs for Initial Price Applicability Year 2026
Based on 2021 Medicare Part D Spending Data

Rank	Brand Name[A]	Active Moiety(s)[A]	Medicare Part D 2021 Gross Expenditures[A]	Exclusion Reason
1	Eliquis	Apixaban	$12,575,145,852	
Excluded	Revlimid	Lenalidomide	$5,893,547,689	Generic available as of March 7, 2022.[B]
2	Xarelto	Rivaroxaban	$5,225,547,772	
Excluded	Humira	Adalimumab	$4,731,995,450	Biosimilar available.[C]
Excluded	Trulicity	Dulaglutide	$4,702,174,724	Biologic will not have been approved for at least 11 years.[D]
Excluded	Lantus/Lantus Solostar/Toujeo Max Solostar/Toujeo Solostar	Insulin Glargine,Hum.Rec.Anlog	$4,616,087,398	Biosimilar available.[E]
3	Januvia	Sitagliptin Phosphate	$4,059,534,112	
4	Jardiance	Empagliflozin	$3,735,773,560	
5	Imbruvica	Ibrutinib	$3,150,225,810	
Excluded	Ozempic/Rybelsus	Semaglutide	$3,076,258,172	Small molecule will not have been approved for at least 7 years.[D]
6	Novolog	Insulin Aspart	$2,454,080,766	
7	Xtandi	Enzalutamide	$2,411,262,130	
Excluded	Trelegy Ellipta	Fluticasone/Umeclidin/Vilanter	$2,393,151,303	Small molecule will not have been approved for at least 7 years.[D]
8	Enbrel	Etanercept	$2,357,376,342	
Excluded	Biktarvy	Bictegrav/Emtricit/Tenofov Ala	$2,198,270,149	Small molecule will not have been approved for at least 7 years.[D]
Excluded	Symbicort	Budesonide/Formoterol Fumarate	$2,129,136,756	Generic available as of July 31, 2023.[F]
Excluded	Invega/Invega Sustenna/Trinza/Hafyera	Paliperidone / Palipderidone Palmitate	$2,028,454,625	Generic available for Invega as of September 24, 2015.[G]
9	Myrbetriq	Mirabegron	$1,989,099,248	
Excluded	Humalog	Insulin Lispro	$1,958,818,139	Biosimilar available.[H]
Excluded	Spiriva	Tiotropium Bromide	$1,892,750,964	Generic available as of June 23, 2023.[I]
10	Ibrance	Palbociclib	$1,891,416,132	

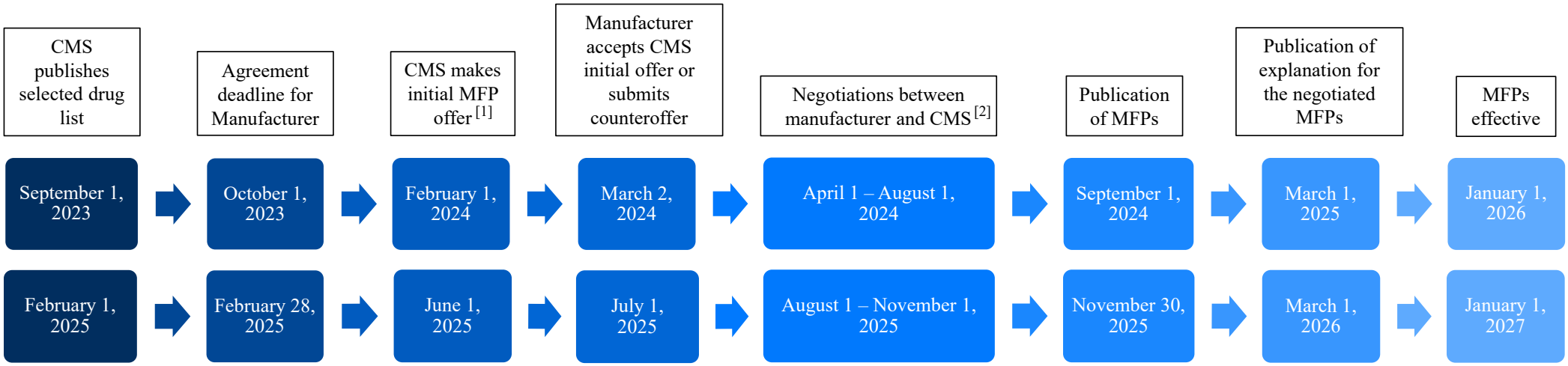
Notes:

[1] To arrive at the MFP Price-Setting Drugs for IPAY 2026, I first compile the top 50 branded drugs by Medicare Part D spending in 2021 and further aggregate by active moiety. I then assesses whether each drug is biologic or small molecule, whether or not it is plasma-derived, whether or not it derives from a small biotechnology manufacturer, whether or not it is an orphan drug, its time since approval as of September 1, 2023 when the IPAY 2026 list is announced, and the existence of biosimilars or generics on the market. Drugs that are not anticipated to meet selection criteria are then excluded from consideration.
[2] Final data to be used by CMS to compile the list of drugs for IPAY 2026 is as of 12 months ending May 31, 2023.

Sources:

[A] CMS Medicare Part D Dashboard Data.
[B] International Myeloma Foundation, "First Generic Revlimid (lenalidomide) Launched," April 14, 2022, available at https://www.myeloma.org/blog/first-generic-revlimid-lenalidomide-launched.
[C] Amgen Press Release, "Amjevita (Adalimumab-Atto), First Biosimilar to Humira, Now Available in the United States," January 31, 2023, available at https://www.prnewswire.com/news-releases/amjevita-adalimumab-atto-first-biosimilar-to-humira-now-available-in-the-united-states-301734177.html.
[D] U.S. Food & Drug Administration, "Drugs@FDA: FDA-Approved Drugs," available at https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm.
[E] Jeremias, Skylar, "Lilly Launches Rezvoglar in the US," *AJMC* , April 1, 2023, available at https://www.centerforbiosimilars.com/view/lilly-launches-rezvoglar-in-the-us.
[F] PR Newswire, "Viatris Announces Launch of Breyna (budesonide and formoterol fumarate dihydrate) Inhalation Aerosol, the First FDA-Approved Generic Version of Symbicort for People with Asthma and Chronic Obstructive Pulmonary Disease, in Partnership with Kindeva," July 31, 2023, available at https://www.prnewswire.com/news-releases/viatris-announces-launch-of-breyna-budesonide-and-formoterol-fumarate-dihydrate-inhalation-aerosol-the-first-fda-approved-generic-version-of-symbicort-for-people-with-asthma-and-chronic-obstructive-pulmonary-disease-in-partn-301888925.html
[G] Vermes, Krystal, "Generic Invega Now Available," *Pharmacy Times* , September 2015, available at https://www.pharmacytimes.com/view/generic-invega-now-available.
[H] AJMC, "Sanofi Launches Follow-On Insulin Lispro, Admelog," April 9, 2018, available at https://www.centerforbiosimilars.com/view/sanofi-launches-followon-insulin-lispro-admelog.
[I] Healio, "FDA approves generic tiotropium bromide inhalation powder," June 23, 2023, available at https://www.healio.com/news/pulmonology/20230623/fda-approves-generic-tiotropium-bromide-inhalation-powder.

Exhibit 1
Negotiation Timeline between CMS and Primary Manufacturer
For Initial Price Applicability Year 2026 and Initial Price Applicability Years 2027 and Beyond



Notes:
[1] During Fall 2023, CMS will meet with the manufacturer of each selected drug to review data submissions, subject to the manufacturer's interest in such meeting. CMS will use these data submissions to develop an initial offer for each selected drug. During this time period, CMS will also hold listening sessions with patients, consumer groups, and other interested parties to obtain input on selected drugs. The CMS Guidance does not indicate whether these meetings will be held in subsequent years.
[2] If the Primary Manufacturer's written counteroffer is not accepted by CMS, CMS will allow for up to three possible in-person or virtual negotiation meetings between the Primary Manufacturer and CMS. For the initial price applicability year 2026, CMS has provided the following deadlines for the negotiation period: April 1, 2024 is the deadline for CMS to respond to the Manufacturer's counteroffer and the latest date for the first CMS-Manufacturer negotiation meeting to be scheduled if CMS declines the counteroffer; June 28, 2024 is the date by which negotiation meetings between CMS and the Manufacturer must be complete; July 15, 2024 is the deadline for CMS to make a final MFP offer if an MFP was not agreed to during negotiations; July 31, 2024 is the deadline for the Manufacturer to accept or reject CMS final offer. CMS will provide additional information in the future regarding deadlines for the negotiation period for initial price applicability years 2027 and beyond.

Sources:
[A] CMS Guidance, June 30th 2023, available at https://www.cms.gov/files/document/revised-medicare-drug-price-negotiation-program-guidance-june-2023.pdf
[B] "Text - H.R.5376 - 117th Congress (2021-2022): Inflation Reduction Act of 2022." Congress.gov, *Library of Congress*, 16 August 2022, https://www.congress.gov/bill/117th-congress/house-bill/5376/text.

Exhibit 2
Rituxan Follow-on Indication Timing[1]

Disease type	Indication Description	Category	Date	Years from original approval
Non-Hodgkin's Lymphoma	Single agent, relapsed or refractory, low grade or follicular, CD20-positive B-cell NHL	Original approval	11/26/1997	0
Non-Hodgkin's Lymphoma	Previously untreated in combination with (cyclophosphamide, doxorubicin, vincristine, and prednisone) (CHOP) or other anthracycline-based chemotherapy regimens	Line of treatment expansion/addition	2/10/2006	8
Non-Hodgkin's Lymphoma[2]	Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy	Line of treatment expansion/addition	9/29/2006	8
Non-Hodgkin's Lymphoma	Non-progressing (including stable disease), low-grade, CD20- positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy	Line of treatment expansion/addition	9/29/2006	8
Rheumatoid Arthritis	In combination with methotrexate in adult patients with moderately-to severely-active RA who have inadequate response to one or more TNF antagonist therapies	New disease type	2/28/2006	8
Chronic Lymphocytic Leukemia	Adult patients, previously untreated and previously treated CD20-positive CLL in combination with fludarabine and cyclophosphamide (FC)	New disease type	2/18/2010	12
Granulomatosis with Polyangiitis and Microscopic Polyangiitis[3]	Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) in adult and pediatric patients 2 years of age and older in combination with glucocorticoids	New disease type	4/19/2011	13
Pemphigus Vulgaris	Moderate to severe Pemphigus Vulgaris (PV) in adult patients	New disease type	6/7/2018	20
Several diseases covered	Pediatric patients 6 months and older, previously untreated, advanced stage, CD20-positive, diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL), Burkitt-like lymphoma (BLL) or mature B-cell acute leukemia (B-AL) in combination with chemotherapy	New population and disease type	12/2/2021	24

Notes:
[1] The "Disease type" column is taken directly from the version of Rituxan's label posted on 12/17/2023. The "Indication description" column summarizes the information provided in the Indications and Usage section of that label. The "Date" column references the first time the new indication was shown. In cases where indications are modified, the modifications are documented in notes below. Small modifications to wording (e.g., adding "single agent" when it was implied) are not explicitly documented.
[2] Indication was modified on 1/28/2011 to make patients achieving a complete or partial response to rituximab in combination with chemotherapy eligible for single-agent maintenance therapy.
[3] Indication was modified on 9/27/2019 to include pediatric patients 2 years of age and older.

Source:
[A] *Drugs@FDA: FDA-Approved Drugs* , https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=125514, accessed on 4/28/2023.

Exhibit 3

Keytruda Follow-on Indication Timing[1]

Disease type	Indication Description	Category	Date	Years from original approval
Melanoma[2]	Unresectable or metastatic melanoma	Original approval	9/4/2014	0
Melanoma[3]	Adjuvant treatment of adult and pediatric with Stage IIB, IIC, or III melanoma folowing complete resection	New disease subtype	2/15/2019	5
Non-Small Cell Lung Cancer[4]	Single agent, metastatic NSCLC whose tumors express PD-L1, with disease progression on or after platinum-based chemotherapy	New disease type	10/2/2015	1
Non-Small Cell Lung Cancer	Single agent, first-line, NSCLC expressing PD-L1 with no EGFR or ALK genomic aberrations and is metastatic	New population	10/24/2016	2
Non-Small Cell Lung Cancer[5]	Combination therapy, first-line, metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor abberations	New disease subtype	5/10/2017	3
Non-Small Cell Lung Cancer	Combination therapy, first-line, metastatic squamous NSCLC	New disease subtype	10/30/2018	4
Non-Small Cell Lung Cancer	Single agent, first-line, NSCLC expressing PD-L1 with no EGFR or ALK genomic aberrations and is Stage III, not candidates for surgical resection or definitive chemoradiation	New disease subtype	6/10/2019	5
Non-Small Cell Lung Cancer	Single agent, adjuvant treatment following resection and chemotherapy for adult patients with Stage IB, II, or IIIA NSCLC	New disease subtype	1/26/2023	9
Head and Neck Squamous Cell Cancer	Single agent, recurrent or metastatic HNSCC with disease progression on or after chemotherapy	New disease type	8/5/2016	2
Head and Neck Squamous Cell Cancer	Single agent, first-line, metastatic or unresectable, recurrent HNSCC whose tumors express PD-L1	Line of treatment expansion/addition	6/10/2019	5
Head and Neck Squamous Cell Cancer	Combination therapy, first-line, metastatic or unresectable, recurrent HNSCC	Line of treatment expansion/addition	6/10/2019	5
Classical Hodgkin Lymphoma[6]	Adult patients with relapsed or refactory cHL	New disease type	3/14/2017	3
Classical Hodgkin Lymphoma	Pediatric patients with refactory cHL, or cHL that has relapsed after 2 or more lines of therapy	Line of treatment expansion/new population	10/14/2020	6
Urothelial Carcinoma[7]	Combination therapy, adult patients with locally advanced or metastatic urothelial carcinoma and not eligble for cisplatin-containing chemotherapy	New disease type	5/18/2017	3
Urothelial Carcinoma	Single agent, locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12-months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy	New population	5/18/2017	3
Urothelial Carcinoma	Single agent with Bacillus Calmette-Guerin (BCG)-unresponsive, high risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy	New disease subtype	1/8/2020	5
Urothelial Carcinoma	Single agent, locally advanced or metastatic urothelial carcinoma who are not eligble for any platinum-containing chemotherapy	New population	8/31/2021	7
Microsatellite Instability-High or Mismatch Repair Deficient Cancer	Adult and pediatric patients with unresectable or metastatic MSI-H or dMMR solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options	New disease type	5/23/2017	3
Gastric Cancer[8]	Combination therapy, first-line, with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma	New disease type	9/22/2017	3
Cervical Cancer	Single agent, with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1	New disease type	6/12/2018	4
Cervical Cancer	Combination therapy, with persistent, recurrent, or metastatic cervical cancer whose tumors express PD-L1	Line of treatment expansion/addition	10/13/2021	7
Primary Mediastinal Large B-Cell Lymphoma	Adult and pediatric patients with refractory PMBCL or have relapsed after 2 or more prior lines of therapy	New disease type	6/13/2018	4
Hepatocellular Carcinoma	Previously treated with sorafenib	New disease type	11/9/2018	4

Exhibit 3
Keytruda Follow-on Indication Timing[1]

Disease type	Indication Description	Category	Date	Years from original approval
Merkel Cell Carcinoma	Adult and pediatric patients with recurent locally advanced or metastatic Merkel cell carcinoma	New disease type	12/19/2018	4
Esophageal Cancer[9]	Locally advanced or metastatic esophageal or GEJ (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation in combination therapy	New disease type	7/30/2019	5
Esophageal Cancer	Locally advanced or metastatic esophageal or GEJ (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation as a single agent after one or more prior lines of systemic therapy for patients with tumors of squamous cell histology that express PD-L1	Line of treatment expansion/addition	3/22/2021	7
Renal Cell Carcinoma	Combination with axitinib, first-line, adult patients with advanced RCC	New disease type	4/19/2019	5
Renal Cell Carcinoma	Combination with lenvatinib, first-line, adult patients with advanced RCC	Line of treatment expansion/addition	8/10/2021	7
Renal Cell Carcinoma	Adjuvant treatment with RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions	New population	11/17/2021	7
Endometrial Cancer	Combination therapy, advanced endometrial carcinoma that is mismatch repair proficient (pMMR) or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation	New disease type	9/17/2019	5
Endometrial Cancer	Single agent, advanced endometrial carcinoma that is MSI-H or dMMR, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation	New population	3/21/2022	8
Tumor Mutational Burden-High Cancer	Adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) solid tumors, that have progressed following prior treatment and who have no satisfactory alternative treatment options	New disease type	6/16/2020	6
Cutaneous Squamous Cell Carcinoma	Recurrent or metastatic cSCC or locally advanced cSCC that is not curable by surgery or radiation	New disease type	6/24/2020	6
Deficient Colorectal Cancer[10]	Unresectable or metastatic MSI-H or dMMR colorectal cancer	New disease type	6/29/2020	6
Triple-Negative Breast Cancer	Combination therapy, locally recurrent or unresectable or metastatic TNBC whose tumors express PD-L1	New disease type	11/13/2020	6
Triple-Negative Breast Cancer	High-risk early-stage TNBC in combination as neoadjuvant treatment, and continued as single agent as adjuvant treatment after surgery	New disease subtype	7/26/2021	7

Notes:
[1] The "Disease type" column is taken directly from the version of Keytruda's label posted on 4/3/2023. The "Indication description" column summarizes the information provided in the Indications and Usage section of that label. The "Date" column references the first time the new indication was shown. In cases where indications are modified, the modifications are documented in notes below. In cases where indication were removed on a label before 4/3/2023, they are not shown in this exhibit. Small modifications to wording (e.g., adding "single agent" when it was implied) are not explicitly documented.
[2] Indication was modified on 12/18/2015 to no longer include disease progression on another ipilimumab.
[3] Indication was modified on 12/3/2021 to specify stage of disease and remove age restriction.
[4] Indication also includes instructions for patients with EGFR or ALK genomic tumor abberations to have disease progression on an FDA-approved therapy prior to receiving Keytruda.
[5] Indication was modified on 8/20/2018 by changing the chemotherapy combination from carboplatin to platinum chemotherapy.
[6] Indication was modified on 10/14/2020 by dropping the line of therapy requirement for adults and moving the requirement from at least 3 prior lines to at least 2 prior lines for pediatric patients.
[7] Indication was modified starting on 6/19/2018 by adding a genetic marker and ending on 4/3/2023 with changing to combination therapy.
[8] Indication was modified starting on 5/5/2/2021 by adding a combination therapy indication and ending on 2/4/2022 with a drop of the single agent therapy indication.
[9] Indication was modified on 3/22/2021 by adding gastroesophageal junction (GEJ) carcinoma that is not amenable to surgical resection or definitive chemotherapy for patients with tumors of squamous cell histology.
[10] The indication for Microsatellite Instability-High Cancer originally included a line for colorectal cancer, but it was given its own broader definition includding Mismatch Repair Deficient Cancer and a change in line of treatment specification.

Source:
[A] *Drugs@FDA: FDA-Approved Drugs* , https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=125514, accessed on 4/21/2023.

Exhibit 02

IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TEXAS
AUSTIN DIVISION

NATIONAL INFUSION CENTER ASSOCATION, on behalf of itself and its members; GLOBAL COLON CANCER ASSOCIATION, on behalf of itself and its members; and PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA, on behalf of itself and its members *Plaintiffs,* v. XAVIER BECERRA, IN HIS OFFICIAL CAPACITY AS SECRETARY OF THE U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; THE U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; CHIQUITA BROOKS-LASURE, IN HER OFFICIAL CAPACITY AS ADMINISTRATOR OF THE CENTERS FOR MEDICARE AND MEDICAID SERVICES; AND THE CENTERS FOR MEDICARE AND MEDICAID SERVICES, *Defendants.*	Civil Action No. 1:23-cv-00707

DECLARATION OF ADAM GLUCK
IN SUPPORT OF PLAINTIFF'S MOTION FOR SUMMARY JUDGMENT

I, Adam Gluck, declare as follows:

1. I am an employee of Sanofi, a global pharmaceutical company. I have worked at Sanofi US (Sanofi) for over six years, holding various roles within the company during my tenure. Presently, I serve as Senior Vice President and Head, U.S. and Specialty Care Corporate Affairs, where I lead Sanofi's corporate affairs efforts and align business strategy with reimbursement, government affairs, patient advocacy, communications and other key teams across a range of therapeutic areas including those addressing inflammatory diseases. As part of my responsibilities, I assess the impact that the Inflation Reduction Act of 2022 (IRA) will have on Sanofi's existing

and future pharmaceutical business. I also have expertise in the operation of the Medicare program, a program that has facilitated access to life-enhancing therapies and other treatment and services for many persons in the U.S. I regularly engage with Centers for Medicare & Medicaid Services (CMS) and other federal agency personnel on issues related to coverage and reimbursement of therapies under the Medicare program.

2. Sanofi is a leading global biopharmaceutical company operating in over 100 countries with its U.S. headquarters located in New Jersey. The company is dedicated to improving the lives of people everywhere through innovative biopharmaceuticals that prevent, treat, and cure illness and disease. To achieve this, we apply breakthrough science, unique technologies, dedicated research and development, manufacturing, and commercialization to transform the practice of medicine. Sanofi manufactures and markets various drugs that are covered by Medicare Part D and Medicare Part B. Sanofi operates at the forefront of science, at times on its own and in other instances through collaboration with other innovator companies through strategic partnerships and alliances to bring cutting-edge medicine to patients. Our pipeline of therapies is broad – it spans diverse therapeutic areas from oncology to immunology and inflammation, multiple sclerosis, neurology, rare disease, and rare blood disorders. Indeed, as of April 27, 2023, Sanofi's research and development pipeline includes 78 clinical-stage projects, 24 of which are in phase 3 or have been submitted to regulatory authorities for approval. These projects consist of examination of new molecular entities and existing therapeutics with potential additional indications or formulations. Through collaborative and individual efforts, Sanofi helps fuel the scientific innovation ecosystem that is so unique – and instrumental to patients' well-being – in the U.S.

3. Sanofi is an active member of Pharmaceutical Research and Manufacturers of America (PhRMA).

4. I understand that, on August 16, 2022, the IRA was signed into law. The IRA provides, in relevant part, for a Medicare price negotiation program, through which the U.S. Department of Health and Human Services (HHS) will establish a so-called "maximum fair price" (MFP) for particular single-source brand-name drugs or biologic products that HHS identifies as among the 50 Medicare Part D and 50 Medicare Part B drugs with the highest total Medicare expenditures. Starting in 2023, HHS will select 10 Medicare Part D products for negotiation, with corresponding MFPs going into effect in 2026. The number of products subject to mandated MFPs will increase each year, starting with 10 Part D products in 2026, and extending to an additional 15 Part D products in 2027, an additional 15 Part D or Part B products in 2028, and an additional 20 Part D or Part B products in 2029 and subsequent years. To be subject to the MFP, at least nine years (for small-molecule drugs) or 13 years (for biological products) must have elapsed from the product's Food and Drug Administration (FDA) approval or licensure date and there must be no generic or biosimilar on the market. While the MFP becomes effective for products based on these number of years since approval, products are selected for negotiation about two years prior to the applicability of the MFP, and HHS publishes the MFP more than one calendar year before its effective date.

5. Only limited groups of drugs are categorically exempt from IRA negotiation. For instance, the statute exempts from negotiation any orphan drug, which the IRA defines as "a drug… designated as a drug for only one rare disease or condition… and for which the only approved indication (or indications) is for such disease or condition." The statute specifies a product ceiling price (i.e., the MFP), but no price floor. Instead, HHS is directed to consider a

range of confidential, proprietary manufacturer information (including research and development costs, unit costs of production and distribution, and revenue and sales data), as well as evidence about "therapeutic alternatives", to inform the price offer. Once the MFP is established, pharmaceutical manufacturers must "provide access to [the MFP]" to eligible Medicare enrollees, as well as hospitals, physicians, and other providers in connection with Medicare utilization of the product. The U.S. government, in turn, will use the MFP as the basis for Medicare reimbursement of the relevant product. Part D sponsors generally must include on their formularies Part D products that are subject to an MFP.

6. While the IRA describes this program as a price "negotiation" to agree upon a maximum "fair" price, the program is far from mutually- or voluntarily-negotiated, or fair, in its design. The statute establishes a rigid "negotiation" process that, from the outset, is bounded by a capped MFP that varies within increasingly restrictive (i.e., lower) caps as more time has elapsed since FDA approval of the product. A manufacturer that does not comply with the negotiation provision as established by the IRA—by failing to timely enter into a "negotiated" agreement, agree to the maximum "fair" price, or submit required data to the Secretary—is subject to enormous penalties and so-called "excise taxes." These include (i) civil monetary penalties of up to 10 times the amount charged in excess of the MFP, for each unit of product, and (ii) an escalating "excise tax" calculated using a statutory "applicable percentage" starting at 65 percent of prior year sales, increasing to 95 percent after 270 days of noncompliance. The "excise tax" can equal up to 1,900 percent of the relevant product's price for each unit sold during the period of noncompliance. It continues to apply until (i) the manufacturer comes into compliance, (ii) there is the launch of a generic or biosimilar, and/or (iii) the manufacturer's termination of its Medicaid Drug Rebate Program, Medicare Part D Coverage Gap Discount Program, and Medicare Part D

Manufacturer Discount Program agreements with respect to all of the manufacturer's products across its entire portfolio. Confronted with the prospect of such enormous "excise taxes" for failure to comply with the government's ordained MFP, companies like Sanofi have no meaningful option other than to concede to application of the MFP.

7. Beyond this, the price negotiation program is being implemented absent ordinary processes that apply to agency action, with substantial, seemingly-unfettered, authority delegated to HHS to make critical program implementation decisions. Indeed, HHS has already started implementing the IRA in ways that pose significant harm to Sanofi, patients, caregivers, and others. For instance, on March 15, 2023, CMS issued a memorandum relating to the implementation of the first year of the IRA negotiation program. *See* "Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 - 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments" ("Initial Memorandum"). In issuing the Initial Memorandum, CMS made clear that, in the instances in which the agency was soliciting public comment, it was doing so "voluntar[il]y." Various guidance on the selection of drugs for mandatory price negotiation was issued as a "final [agency position], without a comment solicitation." In multiple instances in the Initial Memorandum, CMS demonstrated the extent to which it intends to exercise expansive authority to implement the price negotiation program in ways that will harm pharmaceutical innovation, patients, and the overall health system. For instance, the agency said it intends to define a "qualifying single source drug", for purposes of the negotiation program, by aggregating all products held by a manufacturer under separate Food and Drug Administration (FDA) approvals if the products contain the same active ingredient or active moiety – a position that runs contrary to the Medicare program's longstanding practice of granting a unique pricing and reimbursement profile to products with distinct NDAs or

BLAs. CMS also failed to provide clear, coherent criteria for determining when a generic or biosimilar is marketed for purposes of exempting the relevant brand product from IRA selection, opting instead to adopt a vague standard that the generic or biosimilar must be marketed in a "bona fide" manner. Further, the agency chose to interpret "total expenditures," for purposes of determining top-spend Part D products subject to negotiation, based on gross rather than net costs, without any meaningful explanation for this decision. And the agency said it will determine an "initial offer" (presumably an amount below the MFP) based on highly subjective, non-scientifically-rigorous criteria regarding cost-effectiveness and cost of alleged comparator products. The agency specified no floor for the "initial offer," nor did it outline a principled set of boundaries on (i) eligible therapeutic comparators or (ii) evidence that may inform the "initial offer." If manufacturers are aggrieved by, and disagree with, the initial offer they are given only cursory process to set forth their objection and a counter-offer. Even then, under a strict confidentiality policy, manufacturers are restricted from accessing material information about the initial offer or its basis, thereby limiting their ability to meaningfully review and voice their objections. And HHS's intended interpretation of the orphan drug exclusion, including the agency's independent addition of criteria in order to qualify for the exclusion, raises concerns. Specifically, CMS decided to require that all dosage forms and strengths and different formulations of the qualifying single source drug must satisfy various criteria in order for the orphan drug exclusion to apply to any dosage form or strength of a product. CMS foreclosed public comments on all such agency decisions around drug selection. Sanofi therefore has no opportunity to engage with the agency regarding these concerns and anticipated harms. In these ways and others, HHS has already demonstrated that it views itself as having unbounded freedom to implement the IRA as it chooses, absent judicial or other legal review, or public engagement or transparency.

8. On June 30, 2023, CMS released a second guidance memorandum with further instruction for the first year of the IRA negotiation program. *See* "Medicare Drug Price Negotiation Program: Revised Guidance, Implementation of Sections 1191 - 1198 of the Social Security Act for Initial Price Applicability Year 2026" ("Revised Memorandum"). Rather than tempering its expansive use of authority in the wake of "many constructive, thoughtful, and helpful comments", the agency instead doubled down. CMS largely reiterated its prior guidance, including around the definition of a "qualifying single source drug", its use of a holistic bona-fide marketing standard to identify biosimilars, and its expansive interpretation of the orphan drug exclusion. The agency also failed to alleviate concerns regarding the lack of insight into the process CMS will use, or the information it will rely on, to determine the initial offer.

9. Based on my review of the IRA, Sanofi anticipates that it will be adversely impacted by the IRA negotiation program, raising constitutional concerns on multiple levels. Single-source brand drugs that have the potential to benefit patients across an array of indications, in particular, will be adversely impacted by the IRA. This is because incentives to run additional clinical trials on new indications will be drastically reduced if price cuts or fines are imposed before the full clinical potential of such drugs is realized. Sanofi has several such single-source brand name drugs that provide a clear example of the harmful impact of the agency's decisions on Sanofi. Based on current sales and guidance from CMS, Sanofi anticipates that at least one of these drugs may be among the products selected by HHS for MFP negotiation in the upcoming years. These drugs are first-in-class therapies without biosimilar alternatives. I believe that HHS is likely to select at least one of Sanofi's drugs for MFP negotiation in the next few years, with the MFP going into effect shortly thereafter.

10. For years, Sanofi has made considerable investments in development efforts related to multiple distinct indications for several drugs that significantly benefit patients. These drugs could generate many new regulatory submissions across indications and age groups. Sanofi has made significant investments in prospective new indications for patients with serious diseases that currently have inadequate or even no treatment options. These investments in clinical trials were undertaken at great risk given that many trials for other investigational treatments have failed to demonstrate significant clinical outcomes for vulnerable patient populations. Our willingness to take a calculated risks to improve patient care has led to the positive results from clinical trials in several instances. In some cases, these trial results represent significant achievements in an environment in which no new treatment approaches have been approved in more than a decade. However, this substantial investment in pursuing such indications is at risk of significant erosion in value if these later indications are ultimately approved by FDA and then, as CMS unilaterally determined will be the case for the first year of the program, is aggregated with longer-standing, already-approved, separate indications and therefore is selected for negotiation and subject to the MFP. If HHS selects one of Sanofi's drugs with a suite of indications (including newly approved indications) for mandatory MFP negotiation, as expected, the forced price reductions would significantly undermine the company's return on its development investments – returns that the company reasonably anticipated when it first decided to pursue these investments many years ago.

11. In some instances, Sanofi's price for its drugs was established based on a sustainable, fair and reasonable pricing approach that an independent, evidence-based organization, the Institute for Clinical and Economic Review (ICER), recognized as cost-effective. Often these products have also been subject to very limited price increases, consistent with Sanofi's publicly communicated pricing principles. Based on the statutory formula and cap on the

calculation of MFP, and what CMS has indicated about its process for formulating "initial offer[s]," Sanofi expects that the MFP imposed on its drugs, especially single-source drugs with multiple indications, will not be a fair or reasonable price, nor will it be consistent with the equitable, market-based pricing that Sanofi has long expected since the company first invested in these drugs. Sanofi makes sizeable investments in research and development across its portfolio. In 2022 alone, expenditures on research and development amounted to €6,706 million, reflecting 15.6% of Sanofi's net sales. The company's research and development expenses include investments in the development of various pipeline products and prospective new indications for existing products, some of which may never receive approval. The company has long undertaken these collective investments – either on its own or through thoughtful collaborations with other innovators – under the expectation that it will be able to obtain sufficient financial returns on products that receive approval and are commercialized. Sanofi has decades of experience as a pharmaceutical manufacturer and, therefore, ample experience with arms-length, free market-based price negotiations with customers and other counterparties. Sanofi has invested in the development of existing and prospective future therapies in reasonable expectation of returns under a continued, free market-based, level playing field with fair, independently-determined prices for its products.

12. Absent the IRA's coerced MFP negotiation, Sanofi would not (i) voluntarily enter into pricing negotiations with HHS for many if not most of its drugs, (ii) voluntarily agree to provide prices at the significant discounts mandated by the IRA, or (iii) voluntarily agree that the prices imposed by HHS are "fair." Instead, the IRA imposes on a manufacturer the sweeping obligation to provide access to a government-determined MFP across a range of supply chain transactions with customers and payors. Sanofi is further compelled to disclose to HHS

confidential, proprietary information, at threat of sizeable fines, as part of the "negotiation" process. The manufacturer and HHS do not "negotiate" the MFP on equal footing, and, instead, the MFP supersedes all free-market negotiations and serves as a compelled, government-established price cap. The MFP overrides the otherwise-applicable commercial market price for a product, instead authorizing the government to obtain the product for a mere fraction of its fair commercial market price. Such a price cap is unprecedented in our company's history of negotiating prices with health plans in connection with the Medicare program. This MFP price cap is not reflective of commercial market prices and is not a "fair" price to which Sanofi would voluntarily agree—in the absence of punitive consequences for non-compliance.

13. Sanofi will be compelled to participate in the IRA-prescribed negotiation process, and concede to the coerced MFP, for its drugs for at least the following two reasons. *First*, the statutorily-prescribed civil monetary penalties and "excise taxes" for failure to adhere to the negotiations and concede to the MFP are enormously punitive and will have serious adverse consequences for Sanofi, if they are imposed. Sanofi cannot pay an excise tax up to 1,900 percent of the relevant product's price for each unit sold for even a short duration of time without suffering significant, adverse financial harm and eroding the pipeline for research and development of future treatments to the detriment of patients. Instead, the penalties that the statute envisions leave Sanofi with no business choice other than to accept the coerced MFP price cap. *Second*, the statutory provision under which excise taxes cease to continue to apply (i.e., if a manufacturer discontinues its participation in the Medicaid Drug Rebate Program, the Medicare Part D Coverage Gap Discount Program, and the Medicare Part D Manufacturer Discount Program across the manufacturer's entire portfolio of products) provide illusory relief. Terminating these agreements means that Sanofi could no longer receive reimbursement for its entire portfolio of drug products

in the Medicaid, Medicare Part B, and Medicare Part D programs, which together account for roughly half of all prescription drug expenditures in the U.S. As a business matter, Sanofi derives billions of dollars every year from participation in these programs. Sanofi cannot afford to forego that revenue without significant detrimental consequences to its business. More fundamentally, Sanofi is committed to providing access to our medicines to the vulnerable populations that Medicare and Medicaid serve. Sanofi takes its commitment to patients seriously; in fact, it is the foremost consideration for everything the business does. If Sanofi no longer participated in these programs, millions of Medicaid and Medicare patients would be deprived of access to needed Sanofi therapies across multiple key therapeutic areas. This would be of enormous detriment to patients and the broader health care system, both of which would be deprived of scientific breakthroughs that stand to improve lives. Exiting the Medicare and Medicaid programs is thus anathema to Sanofi's mission and does not provide relief in mitigating the IRA's significant penalties for failing to concede to the negotiations and MFP.

14. As with all of its portfolio and pipeline future therapies, Sanofi has invested in the development of new indications with the reasonable expectation of returns under a continued, free market-based, level playing field with fair, independently-determined prices for its products. Yet, based on the statutory formula and cap on the calculation of MFP, Sanofi expects that the MFP for its drugs, and particularly for new indications, will not be fair or reasonable, nor will it be consistent with the equitable, market-based pricing that Sanofi has long expected since the company first invested in the development of many of these drugs.

15. The myriad harms of the IRA illuminate broader harms that Sanofi will confront across its entire portfolio of already-launched and prospective future therapies. In response to these harms, Sanofi will need to take concerted steps such as reevaluating the value of continuing

to pursue, and ultimately launching, new indications for approved drugs and other prospective therapies, given the challenge the company may confront in recouping substantial research and development investments. For certain therapies or indications, the company may need to address the prospect of launching at a financial loss. In order to avoid this consequence, Sanofi may reconsider – and perhaps ultimately abandon – clinical areas of pursuit, including prospective collaborations with other innovator companies, a detriment to the broader pharmaceutical innovation ecosystem. Sanofi would have no meaningful relief from these harms, given the magnitude of the "excise tax" that it would need to pay to avoid the MFP – a substantial amount that would bear no relationship to any alleged "harm" or "wrong" on the part of Sanofi.

16. Beyond these harms to Sanofi, there would be striking detriment to patients – patients who might benefit from newly-launched indications that address unique disease states, and patients who would benefit from other unpursued treatments for life-threatening conditions. For certain disease states in which Sanofi is a leading developer of pharmaceutical treatments – including but not limited to immunology and inflammation, diabetes, rare blood disorders, cardiovascular disease, oncology, multiple sclerosis and neurology – there could be substantial harm to Medicare patients, and the caregivers and families who support them. Patient quality of life, and livelihood itself in some instances, could be compromised – all due to a misguided drug price negotiation program being implemented without any reasonable or lawful constraints. Indeed, for some patients it could mean the difference between life and death.

17. Sanofi faces numerous additional harms from the price negotiation program, including in non-Medicare markets. For instance, because the list of drugs subject to negotiation will be published and publicly known (as will the MFP), Sanofi believes that the drug selection decisions and MFP publication will influence market dynamics and pricing outside the Medicare

program. This will compound the above-mentioned harms and further prevent Sanofi from pursuing the research and development of future therapeutics, on its own and through collaborations. Additionally, Sanofi expects that certain competitor Part D products will be selected for MFP negotiation, and therefore will generally be subject to guaranteed formulary coverage across all Part D plans. As Part D plan sponsors are only required to cover at least two products per therapeutic class (with the exception of defined "protected classes"), Sanofi reasonably anticipates it will be harmed when these competitor products are selected for MFP negotiation as Sanofi may either (i) lose formulary coverage for its competitive product, or (ii) be forced to offer artificially larger rebates/discounts to pharmacy benefit managers (PBMs). In either instance, Sanofi would be financially harmed, and patients could face meaningful disruption to their care without lower out-of-pocket costs. Relatedly, as PBMs may no longer receive rebates (or, if they do, may receive significantly reduced rebate amounts) in connection with MFP-negotiated products, Sanofi reasonably anticipates that PBMs will demand greater rebates/discounts and price concessions in negotiations for other products across Medicare and commercial market segments. And, for Part B-selected products, the price negotiation program may leave providers financially underwater. For Part B-selected products, reimbursement will be tied to the lower MFP price, regardless of whether the provider acquired the product at the traditional market-based price, potentially creating incentives for them to choose products on which they can recoup their costs, rather than products that are the most clinically efficacious for a given patient.

18. Beyond this, the process for implementing the IRA raises significant constitutional concerns and has already caused harm to Sanofi. The price negotiation program violates Sanofi's Fifth Amendment's Due Process right to be free from government deprivation of property without

constitutionally sufficient procedures. Sanofi has multiple property interests at stake, including its patent rights related to its drug products and its rights to recoup from its investments at market-based rates that are free from arbitrary and unlawful government constraints. The procedures that the government has set forth to respond to such deprivations are legally inadequate. HHS is implementing the price negotiation program absent notice-and-comment rulemaking and without even accepting comments on pivotal program elements such as the selection of drugs subject to negotiation. Sanofi therefore lacks processes through which to participate in, object to, and have transparency regarding the design and implementation of a program that dramatically implicates its property interests. The IRA statute further precludes judicial and administrative review of key agency decisions, leaving HHS with seemingly limitless authority to claim private property absent procedural protections. Sanofi has significant concerns about CMS's unilateral decisions – absent the benefit of any public comment or input. Sanofi has a strong interest in commenting on agency decisions and implementation. Yet, the process CMS has put forward for engagement around key decisions does not provide an adequate or meaningful opportunity for the company to engage with CMS. This is the case notwithstanding the fact that the agency's implementation decisions are critical to the business and its property interests and will have significant financial and other consequences for Sanofi and the patient populations Sanofi works to serve.

19. In sum, based on my review of the IRA, I am substantially certain that HHS will select one of Sanofi's drugs for price negotiation in the early years of the program. Based on the existing scheme and penalties and "excise taxes" contemplated by the IRA, Sanofi will be compelled to participate in the price negotiation program. The resulting "negotiated" prices will not be "fair" and will harm Sanofi. Various other components of the IRA will significantly, and adversely, impact Sanofi across the company's broader portfolio of products and across Sanofi's strategic collaborations with other innovators. Indeed, the very economic viability of certain products – including prospective new products or indications that Sanofi might launch on its own or through cooperative collaboration with others – will turn on whether the products are subject to negotiation. HHS will wield impermissible power to make decisions that could be financially crippling for the company. Sanofi is being deprived of constitutionally-afforded due process in safeguarding its most vital property interests – the fruits of years of research and development investments. Alongside these wrongs to Sanofi are significant harms to Medicare and other patients – innocent bystanders to HHS's impermissible action who stand to lose the best of science and innovation, including the potential miracle of cures.

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

Executed this 10th day of August, 2023.

Adam Gluck
Senior Vice President and Head,
U.S. and Specialty Corporate Affairs
Sanofi US
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Washington DC 20004
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Exhibit 03

IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TEXAS
AUSTIN DIVISION

NATIONAL INFUSION CENTER ASSOCATION, on behalf of itself and its members; GLOBAL COLON CANCER ASSOCATION, on behalf of itself and its members; and PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA, on behalf of itself and its members, Plaintiffs, vs. XAVIER BECERRA, in his official capacity as Secretary of the U.S. Department of Health and Human Services; the U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; CHIQUITA BROOKS-LASURE, in her official capacity as Administrator of the Centers for Medicare and Medicaid Services; and the CENTERS FOR MEDICARE AND MEDICAID SERVICES, Defendants.	Civil Action No. 1:23-cv-00707

DECLARATION OF BRIAN NYQUIST

I, Brian James Nyquist, declare and state as follows:

1. I am over eighteen (18) years of age, am of sound mind, and have never been convicted of a felony. I am fully capable and competent to testify to and have personal knowledge of the matters stated in this declaration. Every statement of fact contained herein is true and correct to the best of my knowledge.

2. I am the chief executive officer of the National Infusion Center Association ("NICA"), a nonprofit trade association. NICA is the nation's voice for non-hospital, community-based infusion providers. I also serve as Board Treasurer for the Infusion Access Foundation, a

nonprofit organization dedicated to ensuring that patients have access to consistent, high-quality provider-administered medication preparations in a safe environment. I earned my Bachelor's Degree in Human Biology from the University of Texas, and my Master's Degree in Public Health from Texas A&M University. I have previously served as a policy analyst at the Texas House of Representatives' Committee on Public Health. My graduate studies focused on health policy and management.

3. "Infusion" or "infusion therapy" refers to the delivery of medications directly into the veins of a patient. Infusion therapies typically are used when oral medications are insufficient, inappropriate, or unavailable. Many of the newest and most effective treatments are therapeutic biological products (or "biologics") derived from living cells. Biologics cannot be taken orally in pill form, as they will not remain molecularly stable and effective after exposure to the digestive system. Thus, they must be administered directly into the blood stream intravenously via infusion therapy or indirectly via injection therapy.

4. Biologics are critical treatments for many chronic diseases. They reduce healthcare consumption by decreasing the use of opioid-based pain medications, optimizing health outcomes, and maximizing quality of life. Most importantly, biologics minimize the physical, emotional, and economic burdens of disease. Innovative drugs and biologics save patients' lives.

5. Certain biologics therapies must be administered and supervised by a medical provider, and patients needing those treatments traditionally have two options for receiving them: infusion centers or hospitals. Infusion centers are non-hospital locations, such as specialist physicians' offices or freestanding ambulatory centers, where drug treatments can be administered by an appropriate provider. Hospitals also offer these therapies, but hospital administration is typically more expensive and takes longer than administration at an infusion center.

6. Millions of patients rely on biologics to treat a variety of complex, chronic conditions. Many of the newest infusible medications are used to treat autoimmune conditions, which are diseases in which the body's immune system turns on itself, attacking healthy cells mistaking them as foreign cells. Examples of autoimmune disorders include inflammatory bowel diseases, including Crohn's disease and ulcerative colitis; rheumatoid arthritis; multiple sclerosis; psoriasis; psoriatic arthritis; and lupus. Infusion therapy is also used to treat other conditions, such as resistant infections, many types of cancer, migraines, osteoporosis, osteoarthritis, and hemophilia.

7. In general, patients receiving infusion therapies require such treatment because (1) their condition is unresponsive to, or difficult to treat with, conventional treatment modalities; (2) the patient has exhausted conventional treatment options; or (3) the patient's condition is so aggressive and severe that, in their physician's medical opinion, a therapeutic biologic is necessary.

8. Medicare patients represent a high proportion of patients in the majority of infusion centers; and for some infusion centers, Medicare patients are the vast majority of the patients that provider serves.

9. NICA's members are in the business of extending and improving patients' lives by providing them with new and innovative drugs and biologics. However, providers administering these innovative treatments are only able to continue operating because they have built business operations around obtaining reimbursement for those treatments at market prices. Market-based reimbursement is the foundation of how providers serve the needs of their patients and keep their doors open.

10. Most of NICA's infusion-center members are small businesses struggling to survive. NICA's members fear that the IRA's arbitrary and capricious changes to payment and reimbursement for certain drugs will throw their financial stability into peril. Some of NICA's members will either be forced to stop treating Medicare patients or close their doors entirely. And if NICA members stop providing drug and biologic therapies, patients nationwide will suffer from their inability to quickly, easily, and/or cheaply get the medications on which they rely to live their lives.

11. All Americans deserve access to affordable, high-quality care in a safe environment. But the IRA, especially given its rushed implementation and the agency's attempts to make decisions without oversight or input from interested parties, will disrupt that access to devastating effect.

12. Pursuant to 28 U.S.C. § 1746 and other appliable law, I declare under penalty of perjury that the foregoing is true and correct, and within my personal knowledge.

Executed in Austin, Travis County, Texas, on the 10th day of August, 2023.

DocuSigned by:
Brian Nyquist
0B99D3761108488...

Brian J. Nyquist

Exhibit 04

UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF TEXAS
AUSTIN DIVISION

NATIONAL INFUSION CENTER ASSOCATION, on behalf of itself and its members; GLOBAL COLON CANCER ASSOCIATION, on behalf of itself and its members; and PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA, on behalf of itself and its members,

Plaintiffs,

v.

XAVIER BECERRA, in his official capacity as Secretary of the U.S. Department of Health and Human Services; the U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; CHIQUITA BROOKS-LASURE, in her official capacity as Administrator of the Centers for Medicare and Medicaid Services; and the CENTERS FOR MEDICARE AND MEDICAID SERVICES,

Defendants.

Civil Action No. 1:23-cv-00707

DECLARATION OF ANDREW SPIEGEL IN SUPPORT OF MOTION FOR SUMMARY JUDGMENT

I, Andrew Spiegel, declare pursuant to 28 U.S.C. § 1746 as follows:

1. I am an adult and if called to testify in this matter could and would testify as set forth herein. The information in this declaration is true to the best of my knowledge, information and belief.

2. I am the Executive Director of the Global Colon Cancer Association (GCCA), a plaintiff in this action.

3. I have been an advocate for patients and caregivers in the fight against colorectal cancer for nearly 25 years. In 1998, my own mother was diagnosed with metastatic colon cancer, and passed away nine months later from the disease. Since that time, I have dedicated myself personally and professionally to this cause.

4. In 1999, I co-founded and subsequently became the Chief Executive Officer of

the Colon Cancer Alliance, now known as the Colorectal Cancer Alliance, the first not-for-profit organization in the United States founded by survivors, caregivers and friends to educate the public about colorectal cancer and provide support to those affected by the disease.

5. In 2011, through cooperation between the Colorectal Cancer Alliance and its European counterpart EuropaColon, I co-founded the GCCA and became its Executive Director. The GCCA is a global community in which people around the world can unite and battle colorectal cancers with one unified voice. The GCCA advocates for patient-centered policy around the globe to ensure increased awareness and screening, access to quality medical treatments and help our member organizations innovate and leverage the full potential of effectuating change. The GCCA also supports the creation of new local patient advocacy groups in developing countries that have no colorectal cancer organizations.

6. I am Board Chair of the World Patients Alliance and former Board Member of the International Alliance of Patients' Organizations. I previously served on the Stand Up to Cancer Advocate Advisory Council. I co-founded and serve on the steering committee of the Alliance for Safe Biologic Medicines; am on the Board and am past Chair of the Digestive Disease National Coalition (DDNC). In 2012, I received the David Jagelman Award for Patient Advocacy from the American Society of Colon and Rectal Surgeons. In March 2013, I was nominated as Exact Sciences' first Hero of the Month. In August 2014, I received the C- Change Together, Hidden Hero Award. In 2019, I received the Lifetime Achievement Award from the Digestive Disease National Coalition.

7. Because of these advocacy and education efforts I am knowledgeable about the needs of patients and caregivers in the screening, diagnosis and treatment of colorectal cancers, and cancer in general. This includes the role and importance of pharmaceutical products in the treatment of colorectal cancers and cancer in general. As the head of a global organization, I have observed the differences in availability and access to these products in different countries around the world, and the way that this impacts treatments for patients in each country.

8. I submit this declaration in support of the Plaintiffs' Motion for Summary Judgment in this action.

I. THE DRUG PRICING PROGRAM HARMS PATIENTS

9. The "Drug Price Negotiation Program" (Drug Pricing Program or Program), enacted as part of the Inflation Reduction Act of 2022, Pub. L. 117-169 (IRA or the Act), will harm patients by jeopardizing their access to the medications that they need to live. In the long term, patients will be harmed if the pricing scheme eliminates manufacturers' incentives to invest in new and innovative medicines to treat cancer and rare disease. Finally, HHS has developed the Drug Price "Negotiation" Program without affording patients—who depend on pharmaceutical access and innovation to save, extend, and improve their lives—the opportunity to comment on key elements of the Program and purportedly without opportunity for patients to obtain judicial or administrative review of HHS decisions that deprive patients of life-altering and life-saving medicines.

A. Access to Pharmaceuticals is Critical for Cancer Treatment

10. Pharmaceutical products are an indispensable component of the treatment of colon and other cancers. Some patients with Stage II colon cancer are treated surgically, then provided a course of adjuvant chemotherapy after their procedure if they are at high risk of remission. For patients with more advanced Stage III or IV colon cancer, chemotherapy, biological and immune therapies are an indispensable component of the standard of care.

11. Patients living with cancer or other serious disease depend upon access to medications to live.

12. The circumstance is the same for many other different types of cancers, each of which physicians treat with life-saving pharmaceutical products.

13. Overall cancer survival rates have improved dramatically in the past decades, thanks to early screening and to the development, clinical testing, regulatory approval and marketing of new pharmaceutical products.

B. The Drug Pricing Program Will Disrupt Patients' Access to Needed Treatments, Thereby Worsening Patient Outcomes

14. Research and development into treatments for cancers and rare diseases is costly, lengthy, and risky. Even as development costs are rising more steeply, potential returns on

investment are becoming smaller and more uncertain.[1]

15. The Drug Pricing Program compels manufacturers to acquiesce to prices dictated by the government or to face a potential excise tax reaching as high as 1,900% of a manufacturer's total U.S. revenues for a drug. Because the Program sets no pricing floor, except for a very limited exception, drug manufacturers could face having to sell drugs at prices that no longer justify the enormous research and development costs needed to identify and test drugs to bring them to market.

16. The Program threatens to force manufacturers to exit the Medicare and Medicaid markets, thereby threatening access to drugs for millions of patients who depend on Medicare and/or Medicaid.

17. The Program threatens to deter manufacturers from undertaking the critical research and development required to bring new pharmaceuticals to market.

18. Patients do not voluntarily elect to need the drugs that would be subject to the Program – or the drugs whose development will be foregone because it is no longer economically rational for manufacturers to invest in the necessary research and trials.

19. Patients in the United States have benefitted from these new products even more so than patients in other countries because these new products are available here widely and quickly. Nearly 90% of new medicines launched since 2011 are available in the United States.[2] Germany comes in a distant second at 63% of new medicines available, followed by 59% for the United Kingdom, 50% for France, and only 46% for Canada. I have observed personally during my interactions with patient advocates in other countries, that the quick access to new treatments is a significant advantage to United States patients. I have observed that GCCA's members in countries with price controls have reduced access compared to our members that work in countries without those controls.

C. HHS Has Deprived Patients and Other Stakeholders of the Opportunity to

[1] *See* Research and Development in the Pharmaceutical Industry, Congressional Budget Office 16–17 (Apr. 2021), https://www.cbo.gov/publication/57126; U.S. Dep't of Health & Human Servs. & U.S. Food & Drug Admin., Paving the Way for Personalized Medicine 4 (Oct. 2013), https://bit.ly/3Vfj0un.
[2] See PhRMA, The United States vs. Other Countries: Availability of New Medicines Varies (Nov. 2020), https://onphr.ma/36oGV3V.

Comment on the Price-Setting Process and Operates to Insulate the Process from Judicial or Administrative Review

20. In addition to these harms, the Drug Pricing Program deprives patients of their interest in being able to continue accessing the drugs they depend on to live.

21. The IRA describes the rate-setting process as a "negotiation," but this process involves no negotiation. The Act does not require HHS to undertake notice-and-comment rulemaking, or even to solicit external input at all, in the price-setting process.[3] The arbitrary and unlawful price-setting scheme threatens to drive providers out of business, which directly impacts patients' ability to access needed drugs.

22. The text of the IRA purports to foreclose administrative and judicial review of the decisions undergirding the Drug Pricing Program. As a result, patients, providers, and manufacturers—all of whom are most affected by these decisions—have no recourse to challenge government actions that directly affect them.

* * *

I declare under penalty of perjury that the foregoing is true and correct.

Executed on August _10__, 2023.

Andrew Spiegel

[3] *See* Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 - 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments, issued March 15, 2023 by HHS CMS, available online at https://www.cms.gov!files/documentlmedicare-drUg-Pricenegotiation-program-initial-guidance.pdf.

Exhibit 05

IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TEXAS
AUSTIN DIVISION

NATIONAL INFUSION CENTER ASSOCATION, on behalf of itself and its members; GLOBAL COLON CANCER ASSOCATION, on behalf of itself and its members; and PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA, on behalf of itself and its members, Plaintiffs, vs. XAVIER BECERRA, in his official capacity as Secretary of the U.S. Department of Health and Human Services; the U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; CHIQUITA BROOKS-LASURE, in her official capacity as Administrator of the Centers for Medicare and Medicaid Services; and the CENTERS FOR MEDICARE AND MEDICAID SERVICES, Defendants.	**DECLARATION OF KRISTEN BERNIE** Civil Action No. 1:23-cv-00707

I, Kristen Bernie, declare pursuant to 28 U.S.C. § 1746 as follows:

BACKGROUND OF DECLARANT

1. I am an adult and if called to testify in this matter would testify as set forth herein. The information in this declaration is true to the best of my knowledge, information, and belief. It is based on my personal knowledge and experience, including through records kept in the course of PhRMA's regularly conducted activities. I submit this declaration in support of PhRMA's motion for summary judgment.

2. PhRMA is a non-profit corporation comprising the country's leading research-based pharmaceutical and biotechnology companies, each of whom is devoted to discovering and

developing new medications that allow people to live longer, healthier, and more productive lives. Over the last decade, PhRMA member companies have more than doubled their annual investment in the search for new treatments and cures, including nearly $101 billion in 2022 alone. PhRMA, *2023 PhRMA Annual Membership Survey* at 3 (July 26, 2023), http://bitly.ws/Rgpj. PhRMA serves as the pharmaceutical industry's principal policy advocate, representing its members' interests in matters before Congress, the Executive Branch, state regulatory agencies and legislatures, and the courts. PhRMA is committed to advancing public policies that foster continued medical innovation and educating the public about the drug development and discovery process. A list of PhRMA's current members is available at https://phrma.org.

3. PhRMA members manufacture many of the most innovative and widely prescribed medicines in America, which are recognized as the standard of care for the conditions they treat. Many medicines manufactured by PhRMA members are widely used by patients covered under Medicare Part B and Part D. PhRMA members manufacture many medicines that, because of their success and widespread use, are the among the most frequently reimbursed medicines under those programs.

4. Since May 2018, I have worked in the Policy and Research Department at PhRMA and I currently serve as a Vice President for Policy and Research at PhRMA. As part of this role, I oversee and perform work related to assessing the impact of legislation and regulation on the federal budget and the pharmaceutical industry. This work includes overseeing and preparing estimates of federal costs or savings from changes in policy, as well as estimates to changes in industry revenues. My work extends across markets, including assessments for Medicare Part B and Part D, Medicaid, the 340B Drug Pricing Program, and the commercial market.

5. For the Inflation Reduction Act (IRA) specifically, my work has focused on the provisions establishing the "Drug Price Negotiation Program" under Medicare (Drug Pricing Program or Program) and the provisions establishing inflation-based rebates for Medicare Part B and Part D. My work has included projecting which medicines will be eligible for selection under the Drug Pricing Program, as well as overseeing work on this topic. I also oversaw the preparation of an industry impact analysis covering the major drug-pricing provisions of the IRA.

6. Prior to joining PhRMA, I spent four months as a Principal Analyst at the Congressional Budget Office (CBO), a nonpartisan federal agency that produces independent analyses on budgetary and economic issues for Congress. Prior to that, I spent nearly nine years in the National Economics and Statistics Group at PricewaterhouseCoopers. I hold a Master of Public Policy degree from the University of Chicago's Harris School of Public Policy and a Bachelor of Arts degree in Economics from Wellesley College.

THE IRA'S DRUG PRICING PROGRAM

7. Signed into law on August 16, 2022, the IRA establishes a Drug Pricing Program under Medicare. Under that Program, the U.S. Department of Health and Human Services (HHS) will establish a "maximum fair price" (MFP) for certain qualifying single-source drugs or biologic products that HHS identifies as among the 50 Part D and 50 Part B drugs with the highest total Medicare expenditures. A qualifying single source drug generally is one that (1) is marketed under a new drug application or a biologics license application, (2) has been approved by FDA for at least seven years for drugs or 11 years for biologic products, and (3) is not the reference drug for a marketed generic drug or biosimilar product. Beginning in 2023, HHS must rank qualifying single-source drugs based on total expenditures under Medicare (first in Part D and then in future years both Part B and Part D) during a defined 12-month period, with drugs having the highest

total expenditures during that period ranked the highest. Once eligible drugs have been ranked, the IRA directs HHS to select an increasing number of the highest-ranked drugs for the Program each year. HHS will select 10 Part D drugs in 2023, with MFPs taking effect in 2026; 15 Part D drugs in 2025, with MFPs taking effect in 2027; 15 Part D and Part B drugs in 2026, with MFPs taking effect in 2028; and 20 Part D and Part B drugs in 2027 and each year thereafter, with MFPs taking effect in 2029 and each year thereafter. This process is cumulative—once selected, a drug remains selected until HHS determines that it no longer constitutes a qualifying single source drug.

8. Once innovative drugs are ranked and selected under the Drug Pricing Program, the IRA directs HHS to "enter into agreements" with manufacturers to "negotiate" the MFP. While the IRA describes this process as a "negotiation" to agree upon a maximum "fair" price, it does not look anything like an ordinary commercial negotiation. Under the IRA, manufacturers must provide HHS with a substantial quantity of closely guarded proprietary and trade secret information, including the manufacturer's R&D costs, market data for the drug, and costs of production and distribution. Failure to produce the required information subjects manufacturers to a penalty of $1 million for each day of noncompliance, as well as a staggering, escalating excise tax. In an ordinary negotiation, parties can choose, without penalty, the offers they are willing to make. The IRA also requires HHS to demand deep minimum discounts, which increase as the time since FDA approval of the product increases. And for most drugs there is no price floor, allowing HHS to insist on prices well below the statutory ceiling.

9. Once HHS has imposed an MFP for a selected drug, HHS will publish it more than one calendar year before its effective date. The statute then provides that manufacturers must provide "access to" the MFP to a wide variety of individuals and entities participating in Medicare. These include all eligible individuals who are administered or dispensed selected drugs under

Medicare Parts B and D; all "pharmacies, mail order services, and other dispensers" that dispense selected drugs to Medicare beneficiaries; and all "hospitals, physicians, and other providers of services and suppliers" that furnish or administer selected drugs to Medicare beneficiaries. If manufacturers fail to provide the required access to the MFP, they are subject to a civil monetary penalty of ten times the difference between the price actually charged and the MFP, multiplied by the total number of units sold.

10. Participation in the "negotiations" under the IRA's Drug Pricing Program is not voluntary. If manufacturers do not enter into an agreement to "negotiate" an MFP or "agree" to an MFP by the statutory deadline, then they are subject to an excise tax, which, as the Congressional Research Service has explained, starts at approximately 186% of total sales from the drug and increases every 90 days until it reaches 1900% of total sales from the drug. *See* Cong. Rsch. Serv., *Tax Provisions in the Inflation Reduction Act of 2022 (H.R. 5376)* 4 tbl. 2 (2022), http://bitly.ws/Rgx6. *See also* IRS, *Section 5000D Excise Tax on Sales of Designated Drugs; Reporting and Payment of the Tax (Notice 2023-52)* § 3.01 (Aug. 4, 2023), http://bitly.ws/Rosp. To put this in context, if a manufacturer had monthly sales (exclusive of the excise tax amount) of $1 million on a selected drug, the manufacturer's maximum liability under the excise tax would total $19 million each month, an unsustainable financial liability. The excise tax continues to apply until (1) the manufacturer comes into compliance, (2) HHS determines that a generic or biosimilar has been approved and "marketed," or (3) the manufacturer notices the termination of its agreement under the Medicaid Drug Rebate Program, and terminates its Medicare Part D Coverage Gap Discount Program and Medicare Part D Manufacturer Discount Program agreements with respect to all of its medicines.

11. Accordingly, a manufacturer's only alternative to complying with the MFP imposed by HHS or paying the excise tax is to exit from Medicare and Medicaid altogether. This is not a feasible alternative for PhRMA's members. The federal government is by far the largest payor in the healthcare market, with Medicare and Medicaid accounting for almost half of annual nationwide spending on retail prescription drugs. *See* Cong. Budget Off., *Prescription Drugs: Spending, Use, and Prices* 8 (2022), http://bitly.ws/RorX. In addition, exiting Medicare and Medicaid would leave patients covered by those programs without access to *any* of the manufacturer's drugs, disrupting patients' medical care and resulting in fewer available treatment options for Medicare beneficiaries. And even if a manufacturer wanted to exit from Medicare and Medicaid, the Part D statute delays a manufacturer's exit for 11-to-23 months. While the Centers for Medicare & Medicaid Services (CMS) has stated in guidance that it will reduce that delay down to 30 days, I am not aware that the agency has ever used that procedural mechanism to expedite a manufacturer's exit from Part D, and it is my understanding that any attempt to do so could be subject to challenge.

12. The IRA also severely limits manufacturers' ability to participate in the implementation process, in two ways. First, the statute provides that HHS "shall implement this section, including the amendments made by this section, for 2026, 2027, and 2028, by program instruction or other forms of program guidance." In guidance, CMS has read that language as exempting the Drug Pricing Program from any requirement to undergo notice-and-comment rulemaking through 2028. Second, the statute provides that "[t]here shall be no administrative or judicial review" of a number of HHS's key determinations, including "[t]he selection of drugs," "the determination of negotiation-eligible drugs," "the determination of qualifying single source

drugs," and "[t]he determination of a [MFP] under [the Act]." On its face, that language appears to limit the ability of manufacturers to challenge key HHS implementation decisions.

THE IRA WILL HARM PHRMA'S MEMBERS

13. Medicare expenditure data is not yet publicly available to allow outside analysts to determine which 10 drugs will be selected for the first round of pricing "negotiations" in September 2023, and uncertainty surrounding how CMS will apply its bona fide marketing standard for generic and biosimilar competitors adds additional ambiguity. Based on the most recent data that are publicly available, however, it is a virtual certainty that medicines manufactured by PhRMA members will be selected for the first list.

14. In my role at PhRMA, I oversaw a project to assess which medicines are most likely to be selected for the first list. The project relied on the following sources: CMS's dashboard for Part D spending by drug for 2021 (the latest year available), publicly available information from the FDA (including the Orange Book and Purple Book), and Medi-Span (a private prescription drug data service). Absent public information on the date of generic market entry, the analysis assumed that a generic would enter the market the later of (1) the latest regulatory exclusivity date listed in the Orange Book or (2) 30-months after the earliest patent expiration date. For biologics, absent public information on the date of biosimilar market entry, the analysis treated the market entry date as unknown. It further assumed that a generic or biosimilar would be "marketed" for purposes of the IRA if the generic or biosimilar were available for sale in the United States. The resulting analysis showed that, of the 10 medicines projected to be selected for the Drug Pricing Program in 2023, nine are manufactured by PhRMA members.

15. In addition, I have reviewed CMS's dashboard for Part D spending by drug, and of the 30 medicines with the highest Part D expenditures in 2021, 24 (80 percent) are manufactured

by PhRMA members. For that reason, I am extremely confident that the first selected drug list will include at least one medicine manufactured by a member of PhRMA. Indeed, I am unable to imagine a reasonable scenario in which the vast majority of the drugs included on each of the first three annual lists of selected drugs under the Drug Pricing Program are not manufactured by members of PhRMA.

16. I understand that being subject to the IRA's Drug Pricing Program will substantially and imminently harm pharmaceutical manufacturers and, in turn, the patients and the public that rely on their lifesaving and life-extending medicines.

17. CBO, for example, estimates that "net prices for selected drugs will decrease by roughly 50 percent, on average, as a result of negotiation" under the IRA's Drug Pricing Program. CBO, *How CBO Estimated the Budgetary Impact of Key Prescription Drug Price Provisions in the 2022 Reconciliation Act* at 10 (Feb. 2023), https://bit.ly/3YfFTAx. In other words, all else equal, manufacturers of selected drugs under the Drug Pricing Program will be paid on average only half of what they are today.

18. I also oversaw a project to analyze the impact of the IRA's Drug Pricing Program on pharmaceutical manufacturers. Using assumptions that generated similar federal budget impacts as estimated by CBO in its final budgetary impact assessment of the IRA, CBO, *Estimated Budgetary Effects of Public Law 117-169, to Provide for Reconciliation Pursuant to Title II of S. Con. Res. 14* (Sep. 7, 2022), http://bitly.ws/Rgqh, the analysis projected that the Drug Pricing Program will cost pharmaceutical manufacturers approximately $160 billion in lost revenue over a ten-year period. The analysis also projected that the industry cost could be as high as approximately $320 billion over a ten-year period if assumed impacts were doubled (for example, if Medicare spending

fell more than implied under CBO's estimate because CMS set lower MFPs or if spillover effects impacted markets beyond Medicare).

I declare under penalty of perjury that the foregoing is true and correct.

Executed on August 10, 2023.

Kristen Bernie

Kristen Bernie

Exhibit 06

IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TEXAS
AUSTIN DIVISION

NATIONAL INFUSION CENTER ASSOCATION, on behalf of itself and its members; GLOBAL COLON CANCER ASSOCATION, on behalf of itself and its members; and PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA, on behalf of itself and its members, Plaintiffs, vs. XAVIER BECERRA, in his official capacity as Secretary of the U.S. Department of Health and Human Services; the U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; CHIQUITA BROOKS-LASURE, in her official capacity as Administrator of the Centers for Medicare and Medicaid Services; and the CENTERS FOR MEDICARE AND MEDICAID SERVICES, Defendants.	Civil Action No. 1:23-cv-00707

DECLARATION OF PATRICK COSTELLO
IN SUPPORT OF PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT

I, Patrick Costello, declare pursuant to 28 U.S.C. § 1746 as follows:

1. I am an adult and if called to testify in this matter could and would testify as set forth herein. The information in this declaration is true to the best of my knowledge, information and belief. It is based on my personal knowledge and experience and in part informed by input from others at Amgen Inc. ("Amgen") with relevant personal knowledge and through records kept in the course of Amgen's regularly conducted business activities.

2. Since June 2021, I have served as the Executive Director and head of United States Value and Access Insights and Analytics for Amgen. I am responsible for understanding many aspects of Amgen's drug pricing and accessibility in the United States, such as strategy, pricing decisions, and the impact of price on various areas of Amgen's United States business.

Prior to June 2021, I held various roles of increasing responsibility in Amgen's finance and commercial organizations.

3. Amgen is a member of Pharmaceutical Researchers and Manufacturers of America ("PhRMA"), one of the plaintiffs in this action. I submit this declaration in support of the Plaintiffs' Motion for Summary Judgment.

I. AMGEN'S MISSION TO SERVE PATIENTS AND COMMITMENT TO INNOVATION

4. Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses. We currently offer for sale across the United States a number of life-saving and life-enhancing drugs. Many are biologics, meaning they are made within living cells. To take three examples:

a. *Enbrel*® (Etanercept): Approved in 1998, Enbrel® was the first biologic medicine approved as a treatment for moderate to severely active rheumatoid arthritis, a disease that, left unaddressed, can have devastating effects such as bone erosion and joint deformity. Today, Enbrel® faces intense competition from several different medicines[1] and is available not only to treat certain rheumatoid arthritis patients, but also certain patients with chronic moderate-to-severe plaque psoriasis and patients with active psoriatic arthritis.[2]

b. *Repatha*® (Evolocumab): In 2015, Repatha® became the first cardiovascular drug of its kind—a "PCSK9 inhibitor"—to be approved in the world.[3] In the United

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1 *See* https://www.hopkinsarthritis.org/arthritis-info/rheumatoid-arthritis/ra-treatment/ (last visited August 8, 2023).

2 *See* https://www.enbrel.com/ (last visited August 4, 2023).

3 *See* Amgen News, available online at: https://wwwext.amgen.com/media/news-releases/2015/07/european-commission-approves-amgens-new-cholesterollowering-medication-repatha-evolocumab-the-first-pcsk9-inhibitor-to-be-approved-in-the-world-for-treatment-of-high-cholesterol/ (last visited August 8, 2023).

States, Repatha® is currently approved to, among other things, reduce the risk in certain patients of myocardial infarction, stroke, and coronary revascularization; and to reduce low-density lipoprotein cholesterol ("bad cholesterol") in certain patients with heterozygous familial hypercholesterolemia, an inherited genetic disorder that causes dangerously high cholesterol levels.[4]

c. TEZSPIRE® (Tezepelumab-ekko) is a first-in-class biologic approved as an add-on maintenance treatment for patients aged 12 and over with severe asthma.[5] Severe asthma is debilitating: Patients experience frequent symptoms and exacerbations, and significant limitations on lung function, meaningfully impacting quality of life. Many had an inadequate response to previously-available biologics and oral corticosteroids and thus have not been able to achieve asthma control.[6] For these patients, TEZSPIRE® represents an important and much-needed new treatment option. And earlier this year, the US Food and Drug Administration (FDA) approved the TEZSPIRE® self-administered, prefilled, single-use pen. This allows patients to administer TEZSPIRE® at home, improving accessibility and creating more treatment options.[7]

5. Amgen also discovers and develops small molecule medications such as LUMAKRAS® (Sotorasib), a KRAS G12C inhibitor. After being granted Priority Review by the

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[4] *See* https://www.repatha.com/ (last visited August 4, 2023) and https://medlineplus.gov/ency/article/000392.htm (last visited August 8, 2023).

[5] *See* https://www.tezspire.com/ (last visited August 4, 2023); https://wwwext.amgen.com/newsroom/press-releases/2023/02/tezspire-approved-for-self-administration-in-the-u-s--with-a-new-pre-filled-pen (last visited August 8, 2023). Amgen is in a collaboration with AstraZeneca for the development and commercialization of TEZSPIRE®.

[6] *See* https://wwwext.amgen.com/newsroom/press-releases/2023/02/tezspire-approved-for-self-administration-in-the-u-s--with-a-new-pre-filled-pen (last visited August 8, 2023).

[7] *See* https://investors.amgen.com/news-releases/news-release-details/tezspirer-approved-self-administration-us-new-pre-filled-pen (last visited August 8, 2023).

FDA[8], LUMAKRAS® was approved for treating certain patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer.[9] The approval of LUMAKRAS® is especially meaningful given that, nearly 40 years ago, KRAS was identified as a fundamental driver of many human cancers, but science could not yet determine how to target the protein—its smooth surface did not appear to have anything for a targeted therapy to "latch" onto. This led some scientists to declare KRAS "undruggable."[10] The approval of LUMAKRAS® represents an important new option for patients in the treatment of this common but previously elusive mutation that has challenged researchers for almost half a century.[11]

6. Amgen's work is not finished once a drug is approved, however, as we continue to dedicate significant investment and effort to investigating whether our therapies may serve additional patients with different needs. For example, just last week Amgen announced that the global Phase 3 CodeBreaK 300 study evaluating LUMAKRAS® combined with Vectibix®[12] versus current standard of care in certain patients with KRAS G12C-mutated colorectal cancer

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8 *See* https://wwwext.amgen.com/newsroom/press-releases/2021/02/fda-grants-sotorasib-priority-review-designation-for-the-treatment-of-patients-with-kras-g12c-mutated-locally-advanced-or-metastatic-non-small-cell-lung-cancer (last visited August 8, 2023).

9 *See* https://wwwext.amgen.com/newsroom/press-releases/2021/05/fda-approves-lumakras-sotorasib-the-first-and-only-targeted-treatment-for-patients-with-kras-g12cmutated-locally-advanced-or-metastatic-nonsmall-cell-lung-cancer (last visited August 8, 2023).

10 *See* Megan B. Ryan, et al, *Therapeutic strategies to target RAS-mutant cancers*, 15 *Nature Rev. Clin Oncol.* 709-720 (2018) ("Five decades after its discovery, and despite many focused drug development efforts, RAS is still widely considered an undruggable target.").

11 *See* https://www.amgen.com/newsroom/press-releases/2021/05/fda-approves-lumakras-sotorasib-the-first-and-only-targeted-treatment-for-patients-with-kras-g12cmutated-locally-advanced-or-metastatic-nonsmall-cell-lung-cancer#:~:text=Press%20Releases-,FDA%20Approves%20LUMAKRAS%E2%84%A2%20(Sotorasib)%2C%20The%20First%20And%20Only,Non%2DSmall%20Cell%20Lung%20Cancer (last visited August 4, 2023).

12 Vectibix® (Panitumumab) is another drug Amgen offers in the United States. Vectibix® is approved for, among other things, for the treatment of certain types of metastatic colorectal cancer. *See* https://www.vectibix.com/ (last visited August 8, 2023).

met its primary endpoint of progression-free survival.[13] Amgen is excited and hopeful about what these data may mean for patients.

7. Another example of Amgen's continued dedication to innovation is Blincyto® (Blinatumomab). Since its approval in 2014 to treat a specific type of acute lymphoblastic leukemia (ALL), studies on Blincyto® have demonstrated, among other things, significantly prolonged survival compared with chemotherapy in certain children with ALL[14] and superior overall survival when added to consolidation chemotherapy, compared with standard of care, in certain adult patients whose ALL is newly diagnosed.[15] More recently, in June 2023, the FDA approved Blincyto® for the treatment of certain adult and pediatric patients with CD19-positive B-cell precursor acute lymphoblastic leukemia (B-ALL).[16]

8. In addition to researching new uses for drugs that are already approved, Amgen dedicates substantial effort and investment to its pipeline in the hopes of discovering new therapies that may change and enhance lives in the future. As examples, Amgen is currently investigating Tarlatamab for certain types of prostate and small cell lung cancers;

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[13] *See* https://investors.amgen.com/news-releases/news-release-details/amgen-reports-second-quarter-financial-results ("The global Phase 3 CodeBreaK 300 study evaluating LUMAKRAS combined with Vectibix vs current standard of care in chemorefractory metastatic KRAS G12C mutated colorectal cancer (CRC) met its primary endpoint of progression-free survival (PFS) for both the 240 mg and 960 mg doses of LUMAKRAS.") (last visited August 8, 2023).

[14] *See* https://wwwext.amgen.com/newsroom/press-releases/2021/03/blincyto-blinatumomab-demonstrated-significantly-prolonged-eventfree-survival-compared-with-consolidation-chemotherapy-in-pediatric-patients-with-relapsed-acute-lymphoblastic-leukemia (last visited August 8, 2023).

[15] *See* https://wwwext.amgen.com/newsroom/press-releases/2022/12/blincyto-blinatumomab-added-to-consolidation-chemotherapy-significantly-improves-survival-in-adult-patients-with-measurable-residual-diseasenegative-blineage-acute-lymphoblastic-leukemia-ball (last visited August 8, 2023).

[16] *See* https://www.amgen.com/newsroom/press-releases/2023/06/fda-grants-full-approval-for-blincyto-blinatumomab-to-treat-minimal-residual-diseasepositive-bcell-precursor-acute-lymphoblastic-leukemia (last visited August 4, 2023).

Bemarituzumab for certain non-small cell lung cancers and gastric and gastroesophageal junction cancers; and AMG 193 for certain solid tumors.[17]

9. Amgen also is researching potential therapies in areas beyond oncology. For instance, Amgen is investigating Olpasiran, a small interfering RNA (siRNA) that lowers lipoprotein(a), also known as Lp(a), for the treatment of atherosclerotic cardiovascular disease; Maridebart cafraglutide (formerly AMG 133) for the treatment of obesity; and Rocatinlimab (AMG 451) as a treatment for severe atopic dermatitis.[18]

10. Finally, in addition to offering innovative medications, Amgen currently offers for sale five biosimilar medications in the United States, including Amjevita™[19], an approved biosimilar to Humira® (an anti-inflammation drug marketed by AbbVie, on which the Centers for Medicare and Medicaid Services ("CMS") spent over $4 billion in 2021, under Medicare Part D).[20] We are also currently researching additional biosimilar candidates, which we hope may one day provide even more enhanced patient access and choice. These include biosimilars to Stelara® (on which CMS spent over $1.5 billion in 2021, under Medicare Part D[21]), Eylea® (CMS spent over $3.4 billion in 2021, under Medicare Part B[22]), and Soliris® (CMS spent over $640 million in 2021, under Medicare Part B).[23]

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17 *See* https://www.amgenpipeline.com/ (last visited August 8, 2023).

18 *See id.*

19 *See* https://www.amjevita.com/ (last visited August 8, 2023).

20 *See* Medicare Part D Drugs Drug Dashboard, available online at https://portal.cms.gov/MSTR2021/servlet/mstrWeb?evt=2048001&src=mstrWeb.2048001&documentID=203D830811E7EBD800000080EF356F31&visMode=0&currentViewMedia=1&ru=1&share=1&hiddensections=header,path,dockTop,dockLeft,footer&Server=v343069p&Port=0&Project=OIPDA-BI_Prod& (last visited April 23, 2023).

21 *See id.*

22 *See* Medicare Part B Drug Dashboard, available online at https://portal.cms.gov/MSTR2021/servlet/mstrWeb?evt=2048001&src=mstrWeb.2048001&documentID=AEC7511A11E817EF2FBA0080EFC5E3D8&visMode=0&currentViewMedia=1&Server=v343069p&Project=OIPDA-BI_Prod&Port=0&connmode=8&ru=1&share=1&hiddensections=header,path,dockTop,dockLeft,footer (last visited April 23, 2023).

23 *See id*; https://www.amgenpipeline.com/ (last visited August 8, 2023).

II. THE INFLATION REDUCTION ACT (IRA)

11. On August 16, 2022, the IRA was signed into law. I understand that the IRA provides, in relevant part, for a Medicare price "negotiation" program ("Price Program"). It is my understanding that under the Price Program, the Department of Health and Human Services ("HHS") will establish a so-called "Maximum Fair Price" for particular single-source brand-name drugs or biologic products that HHS identifies as among the 50 Medicare Part D and 50 Medicare Part B drugs with the highest total Medicare expenditures. Under the Price Program, beginning in 2023 HHS must rank single-source "negotiation-eligible drugs" based upon total expenditures under Medicare (first in Part D and then in both Part B and Part D) over a previous twelve-month period. The drugs involving the highest total expenditures during the period at issue are to be ranked the highest. Once such drugs have been ranked, the IRA directs HHS to select an increasing number of the highest-ranked drugs for the Price Program. Part D drugs will be selected for the Price Program starting in 2023, with the first set of affected prices taking effect in 2026; Part B drugs may be selected beginning in 2026, with prices taking effect in 2028.

12. Though the IRA describes this process as a "negotiation" to agree upon a price, it is not a negotiation at all. The IRA empowers the government to mandate a price and in so doing imposes a significant minimum discount that increases as more time has elapsed since FDA approval of a drug. The IRA enables the government to set upper limits, but no lower limits, for so-called negotiated fair prices, so that the government can insist on a very low price well below the statutory ceiling. And once HHS "offers" a price to a manufacturer, the law limits manufacturers' ability to base counteroffers on anything other than factors that are included in the law itself. These statutory factors leave out key considerations, including the impact of an imposed price on innovation.

13. It is my understanding that if a manufacturer does not comply with the process established by the IRA—for example by failing to timely enter into a so-called "agreement" on a price, or failing to submit required data to HHS—then staggering penalties may be imposed. These include an escalating excise "tax" of 186% of total revenues from the drug; this "tax" would increase every 90 days until it reaches 1900% of total revenues. This punitive tax applies until (i) a manufacturer comes into compliance, (ii) there is the launch of a generic or biosimilar, and/or (iii) the manufacturer terminates relevant agreements under the Medicaid Drug Rebate Program, Medicare Part D Coverage Gap Discount Program, and Medicare Part D Manufacturer Discount Program with respect to all of its products.

14. The IRA does not expressly provide for the right to be heard with respect to HHS's implementation of the process described above. To the contrary, HHS has stated that the law directs HHS "to implement the [Price] Program for 2026, 2027, and 2028 by program instruction or other forms of program guidance."[24]

15. On March 15, 2023, CMS issued a memorandum entitled, "Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments" ("Guidance").[25] The Guidance describes how CMS intends to implement the Price Program, including for initial price applicability year 2026.

16. Troublingly, however, CMS issued Section 30 of the Guidance "as final, without a comment solicitation."[26] According to CMS, public comment on Section 30 would be

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[24] *See* Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments, issued March 15, 2023 by HHS CMS, available online at https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf (last visited August 8, 2023).

[25] *Id.*

[26] *Id.*

"impracticable, unnecessary and contrary to the public interest." Though Amgen has significant concerns about Section 30—including as one example the manner in which CMS plans to implement the Special Rule that permits it to delay selection of a reference biologic for price setting for up to two years under certain circumstances—in reliance on CMS's statement that Section 30 was already final, Amgen did not submit comments thereon.

17. CMS stated that it would "voluntarily" accept comments on the remainder Guidance and, accordingly, on April 14, 2023, Amgen submitted comments on other sections. Unfortunately, CMS's revised guidance, issued June 30, 2023, did not adequately address Amgen's concerns.

III. THE IRA'S IMPACT ON AMGEN

18. Amgen has already begun to consider the impact of the IRA in decisions it makes about investment, including with respect to research into new therapies. While we remain true to our commitment of focusing on innovation and discovering and developing first-in-class and best-in-class therapeutics, we are mindful of the serious disincentives the IRA creates for innovation and believe that ultimately patients will pay the price. For example, in late 2022, after the IRA was passed, Amgen made the decision to stop work on one of its early pipeline candidates, after concluding that, in light of the IRA, it would no longer be feasible for Amgen to pursue in the United States. Amgen's decision unfortunately means that the IRA has already begun to negatively impact future patient and provider choice among medicines.

19. The IRA will also have an impact in the future. In 2021, Enbrel® was among the 30 drugs with the highest total expenditures under Medicare Part D.[27] Enbrel® is still under

[27] *See* Medicare Part D Drug Dashboard, available online at https://portal.cms.gov/MSTR2021/servlet/mstrWeb?evt=2048001&src=mstrWeb.2048001&documentID=203D830811E7EBD800000080EF356F31&visMode=0&currentViewMedia=1&ru=1&share=1&hiddensections=header,path,dockTop,dockLeft,footer&Server=v343069p&Port=0&Project=OIPDA-BI_Prod& (last visited April 23, 2023).

patent protection in the United States and though it faces competition from other biologics, no approved biosimilars are available. Based on this, I believe that HHS is likely to select Enbrel® for the Price Program potentially as early as 2023, with the Maximum Fair Price for Enbrel® going into effect as early as 2026.

20. Under the IRA, the minimum discounts are 25% to 60% off baseline prices initially calculated for the Veterans Administration healthcare system. Absent a legal compulsion to do so, Amgen would not agree to these prices, let alone say that they are "fair." Indeed, absent the punitive excise tax imposed by the IRA, Amgen would not participate in the Price Program, as doing so would cause Amgen harm and stymie innovation. But even putting aside the excise tax, Amgen has no practical ability to withdraw from the "negotiation" process the IRA creates. The United States is the largest market for Amgen's drugs, and Medicare patients account for a significant percentage of Amgen's U.S. sales. Amgen thus could not simply refuse to participate in the IRA without suffering a dramatically negative impact on its business. Moreover, withdrawal from Medicare would need to be for all Amgen products, and exiting the program is thus neither practical nor consistent with Amgen's commitment to patients. If Enbrel® is selected, Amgen's only realistic choice will be to participate.

I declare under penalty of perjury that the foregoing is true and correct. Executed on August 8, 2023.

Patrick Costello