PORTAL
Program On Regulation, Therapeutics, And Law

Division of Pharmacoepidemiology and Pharmacoeconomics
Harvard Medical School | Brigham & Women's Hospital

Phone: 617-278-0930
Fax: 617-232-8602
www.PORTALresearch.org

THE INFLATION REDUCTION ACT OF 2022: REDUCING EXCESSIVE SPENDING AND SUPPORTING PATIENT ACCESS TO BRAND-NAME DRUGS WHILE PROMOTING MEANINGFUL INNOVATION

Testimony of:

Aaron S. Kesselheim, M.D., J.D., M.P.H.

Professor of Medicine, Harvard Medical School

Director, Program On Regulation, Therapeutics, And Law (PORTAL)

Division of Pharmacoepidemiology and Pharmacoeconomics

Department of Medicine, Brigham and Women's Hospital

Boston, MA

www.PORTALResearch.org

United States House of Representatives
Oversight and Investigations Subcommittee of the Energy & Commerce Committee
Wednesday, September 20, 2023
Washington, D.C.

Summary of major points

- The Inflation Reduction Act (IRA) for the first time enables the Medicare program to negotiate the prices of the medications it pays for, just as the federal government negotiates prices on virtually all other goods and services it purchases in Medicare and elsewhere in the economy. It will cover drugs for which Medicare spends over $200 million per year that have been at lease 9-13 years on the market; it excludes certain drugs like those approved for only one rare disease indication.
    - Patients pay far more for brand-name prescription drugs in the US—much more than in other comparable countries. This leads to often-unaffordable spending for citizens and for the health care system. Crucially, this makes it difficult for patients – especially seniors on Medicare – to afford their medications, contributing to non-adherence with their prescriptions and negative clinical outcomes.
    - The negotiation that the legislation makes possible is projected to save the country about $100 billion over the next 10 years, which has been paired with limitations on patient out-of-pocket costs in Medicare Part D.
    - Medicare drug price negotiation is expected to increase drug companies' incentives to invest in more meaningful innovation; reducing spending on older drugs that have been sold at high prices for many years will redirect resources into innovative treatments.
- Concerns that the IRA could reduce innovation are overblown.
    - The Congressional Budget Office found that negotiations could lead to as little as 1% fewer new drug approvals over the next 30 years, and the drugs most affected would likely be those offering limited added benefits to patients over existing therapies.
    - There is no evidence the IRA might lead companies to delay launching new cancer drugs, since doing so would reduce the amount of market exclusivity time they would enjoy for the drugs.
    - The IRA provides a specific exclusion related to a small number of drugs covering a single rare disease. However, expanding it to cover any drug with an Orphan Drug Act designation would exempt most blockbuster drugs from negotiation.
    - Manufacturers argue that starting negotiation for small-molecule drugs at 9 years disadvantages them relative to biologic drugs (13 years), but global revenues in the first 9 full years after FDA approval for the current group of small-molecule drugs set for negotiation range from $14-$57 billion; it is unreasonable to expect that for-profit manufacturers would fail to develop a product with the potential for such revenues.
- The IRA's provisions do not run afoul of any Constitutional provisions.
    - The Fifth Amendment Takings Clause is not violated because a taking must be compelled and manufacturers participate in Medicare voluntarily; in addition, private health care companies have no legal right to receive taxpayer dollars or set their own reimbursement rates.
    - The IRA's procedures satisfy the Fifth Amendment Due Process Clause due to the manufacturers' lack of any right to public funds, and the overwhelming public policy imperative to lower excessive drug costs for the American people.
    - First Amendment free speech protections are not violated because the IRA does not implicate any kind of speech or expression at all.
    - The Act is not an unlawful delegation of authority to CMS that would violate the separation of powers, because the IRA provides clear guidance and limits on its authority, including on what drugs to select and what factors to consider in negotiation.
    - The IRA does not unconstitutionally compel participation, because participation in Medicare is voluntary, and offering lucrative payment with conditions is not coercion.

Subcommittee Chairman Griffith, Subcommittee Ranking Member Castor, Committee Chair Rodgers, Committee Ranking Member Pallone, and Members of the Subcommittee:

My name is Aaron Kesselheim. I am an internal medicine physician, lawyer, and a Professor of Medicine at Harvard Medical School, in the Division of Pharmacoepidemiology and Pharmacoeconomics of the Department of Medicine at Brigham and Women's Hospital in Boston, one of the main Harvard teaching hospitals. Within the Division, I lead the Program On Regulation, Therapeutics, And Law (PORTAL), an interdisciplinary research center that studies the intersections between prescription drug affordability and use, laws and regulations related to medications, and the development and cost of drugs. PORTAL is one of the largest non-industry-funded research centers in the country that focuses on pharmaceutical use, law, and economics. In 2020, I was elected to the National Academy of Medicine.

I am honored to have been invited today to talk to you about the Inflation Reduction Act (IRA) of 2022, which initiated a process through which the Centers for Medicare and Medicaid Services (CMS) can for the first time negotiate the prices that Medicare pays for some brand-name drugs, much as the government negotiates the prices of nearly everything else that it pays for. I will start by discussing the design of the IRA's drug price negotiation provisions, why they are needed, and how they will work to lower excessive drug prices for Medicare patients and the federal government. Next, I will address some common concerns that have been expressed about the effect of the IRA on prescription drug innovation and show why they are not valid. Finally, I will discuss why the IRA's provisions do not violate any Constitutional principles.[1]

I. The IRA Filled a Major Policy Gap to Contain the Costs of Unaffordable Drugs by Setting up Medicare Drug Price Negotiation

The US spends far more on prescription drug prices per capita than any other industrialized nation. Total prescription drug spending here jumped from $427 billion in 2015 to $634 billion in 2022.[2] High US drug prices are primarily driven by spending on brand-name drugs, which make up only about 10% of prescriptions, but account for about 80% of spending.[3] These high prices are not indicators of the workings of the free market or a mechanism for innovation to reach patients, but of a system that allows manufacturers to freely set and raise prices while preventing effective competition – an arrangement nearly unprecedented in the world of government purchasing for nearly everything else.

Brand-name prescription drug prices are so high in the US, and much higher than in other comparable countries, because of a confluence of market characteristics. First, we allow drugmakers to set the prices at which the government has to but their products. Then we give

[1] For providing research and drafting support for this statement, I would like to acknowledge the assistance of C. Joseph Ross Daval, J.D., Benjamin N. Rome, M.D., M.P.H., Jerry Avorn, M.D., Olivier J. Wouters, Ph.D., and Alexander C. Egilman.

[2] Tichy EM, Hoffman JM, Tadrous M, Rim MH, Suda KJ, Cuellar S, Clark JS, Newell MK, Schumock GT. National trends in prescription drug expenditures and projections for 2023. American Journal of Health System Pharmacy 2023;80(14):899-913.

[3] Kesselheim AS, Avorn J, Sarpatwari A. The high cost of prescription drugs in the United States: origins and prospects for reform. JAMA 2016;316(8):858-871.

manufacturers long periods of market exclusivity during which they are protected from competition by means of patents and other statutes that prevent FDA approval of direct copies. The system is designed this way because research and development costs for new drugs are high, and it can take several years for adequate testing on new drugs to be completed. Market exclusivity periods are primarily defined by patents, which are government grants of monopoly that allow manufacturers to prevent competitors from copying the drug for 20 years. A drug's key patent on its active ingredient is usually obtained close to the time of discovery; for successful drug products, manufacturers often seek and obtain numerous additional patents on a drug's various formulations, methods of use, and manufacturing processes, even including any simple devices used to administer the drug, such as the injector for the EpiPen, for which the active ingredient is a half-century old, or lifesaving inhaler devices for patients with asthma or COPD, most of which contain drugs that have been off-patent for years. This thicket of dozens or even hundreds of patents can block direct competition for many years past the date of FDA approval. Manufacturers also take numerous additional steps to extend their patent thickets to delay generic entry as long as possible.[4] In addition, other federal statutes provide guaranteed periods of exclusivity by preventing the FDA from approving competing products for a minimum number of years after regulatory approval.[5] Overall, market exclusivity for new drugs lasts a median of about 14-15 years, and 1 in 4 drugs has exclusivity lasting longer than 17 years.[6]

Second, during those market exclusivity periods we allow pharmaceutical manufacturers to charge whatever they want—a condition not seen in any other developed nation. Median new drug launch prices increased from $2,115 per year in 2008 to $180,007 per year in 2021.[7] Higher prices are not necessarily linked to drugs that are more valuable or efficacious for patients. Indeed, during that same period, from 2007 to 2017, fewer than one-third of new drugs approved by the FDA had moderate or greater therapeutic benefits than their competition, according to independent health technology assessment agencies in other countries.[8] At the same time, numerous laws and rules force government or private payors.to cover many high-priced drugs. Prescription drug insurance, such as Medicare Part B and Part D, shields patients from paying the full price of a drug directly, since out-of-pocket costs are typically only a small percentage of the cost. This eliminates brand-name drug companies' catalyst to set "free market" prices.[9] However, patients do end up bearing these costs through rising premiums or taxes which they must pay.

---

[4] Vokinger KN, Kesselheim AS, Avorn J, Sarpatwari A. Strategies that delay market entry of generic drugs. JAMA Internal Medicine 2017;177(11):1665-1669.

[5] Small-molecule drugs, those derived from chemical processes, are protected for at least 5 years; drugs for rare diseases are protected for 7 years; and biologic drugs, those derived from living organisms, are protected for 12 years. Kesselheim AS, Sinha MS, Avorn J. Determinants of market exclusivity for prescription drugs in the United States. JAMA Internal Medicine 2017;177(11):1658-1664.

[6] Rome BN, Lee CC, Kesselheim AS. Market exclusivity length for drugs with new generic or biosimilar competition, 2012-2018. Clinical Pharmacology and Therapeutics 2021;109(2):367-371.

[7] Rome BN, Egilman A, Kesselheim AS. Trends in prescription drug launch prices, 2008-2021. JAMA 2022;327(21):2145-2147.

[8] Hwang TJ, Ross JS, Vokinger KN, Kesselheim AS. Association between FDA and EMA expedited approval programs and therapeutic value of new medicines: retrospective cohort study. BMJ. 2020;371:m3434.

[9] Frank RG and Newhouse JP. Should drug prices be negotiated under Part D of Medicare? And if so, how? Health Affairs 2008;27:33-43.

Medicare Part B pays for virtually all FDA-approved drugs at the level of the average sales price in the private market. Private Medicare Part D plans can negotiate with drug manufacturers, but their leverage is limited because they must cover at least 2 drugs in every class and must cover all drugs in 6 "protected classes," including many mental health and cancer drugs. Before the IRA, many patients with Medicare Part D coverage have had to pay out-of-pocket costs that could total over $10,000 a year;[10] starting in 2025, thanks to the IRA, patients' annual out-of-pocket costs will be capped at $2000.

As a result of our current policies, brand-name manufacturers set drug prices in the US at levels far exceeding prices for the very same drugs made by the same companies for use in other high-income countries around the world, as demonstrated in studies by colleagues in my research group, the Office for the Assistant Secretary for Planning and Evaluation, and others.[11] In addition, manufacturers frequently raise prices each year on existing drugs at rates much higher than the rate of inflation, even when no improvements to them are made.[12] These high prices have important implications for patients. Americans struggle to afford their prescriptions, and 3 in 10 report not taking a medication as prescribed by their doctor because of the cost.[13] Non-adherence to important medications leads to worse patient outcomes, including increased death rates ty.[14] Rising drug costs are passed on to consumers either as out-of-pocket costs or through higher premiums, which makes insurance less affordable. For example, in June of 2021, the FDA approved the monoclonal antibody aducanumab (Aduhelm) for Alzheimer's disease despite no clear evidence that the drug worked. The manufacturer initially priced the drug at $56,000 per year, a price it was estimated could have cost the government $6-29 billion per year.[15] Since this drug would have been covered under Medicare Part B, to plan for this predicted spike in spending, CMS announced the largest-ever annual increase in Medicare premiums, with standard monthly Part B premiums paid by patients increasing from $148.50 to $170.10. When Medicare spending was then averted on this particular drug because the Medicare program later decided

---

[10] Dusetzina SB. Your money or your life – the high cost of cancer drug under Medicare Part D. New England Journal of Medicine 2022;386(23):2164-2167.

[11] Hwang TJ, Jain N, Lauffenburger JC, Vokinger KN, Kesselheim AS. Analysis of proposed Medicare Part B to Part D shift with associated changes in total spending and patient cost-sharing for prescription drugs. JAMA Internal Medicine 2019;179(3):374-380; Mulcahy AW, Whaley CM, Gizaw M, Schwam D, Edenfield N, Becerra-Ornelas AU. International prescription drug price comparisons: current empirical estimates and comparisons with previous studies. ASPE Reports. July 1, 2022. Available at: https://aspe.hhs.gov/reports/international-prescription-drug-price-comparisons

[12] Egilman AC, Kesselheim AS, Rome BN. Estimated Medicare Part B savings from inflationary rebates. JAMA 2023;329(1):89-92.

[13] "About three in ten adults report not taking their medicines as prescribed at some point in the past year because of the cost." Kirzinger A, Montero A, Sparks G, Valdes I, Hamel L. Public opinion on prescription drugs and their prices. Kaiser Family Foundation. August 21, 2023. Available at: https://www.kff.org/health-costs/poll-finding/public-opinion-on-prescription-drugs-and-their-prices/

[14] Gagne JJ, Choudhry NK, Kesselheim AS, Polinski JM, Hutchins D, Matlin OS, Brennan TA, Avorn J, Shrank WH. Comparative effectiveness of generic and brand-name statins on patient outcomes. Annals of Internal Medicine 2014;161:400-407.

[15] Katz J, Kliff S, Sanger-Katz M. New drug could cost the government as much as it spends on NASA. New York Times June 23, 2021. Available at: https://www.nytimes.com/2021/06/22/upshot/alzheimers-aduhelm-medicare-cost.html

not to pay for a drug that did not clearly work outside of its clinical trials, the Part B premium and annual deductible both declined in 2023.[16] This example shows how Medicare spending on high-priced brand-name drugs and patient premiums are closely linked. Even in less dramatic instances, rising drug costs force higher Medicare premiums for virtually all Medicare patients.

High drug prices also have spillover implications for other aspects of health care and social spending, because less public and private spending is available to meet other needs. Medicaid programs, for example, have had to respond to expanding prescription drug costs by cutting coverage for other services and limiting access to medications.[17]

In this context, the IRA offers important relief for the health care system by allowing Medicare to directly negotiate prices for certain drugs, just as it negotiates prices with hospitals, doctors, clinical laboratories, and nearly every other entity that provides goods or services to the Medicare program. Negotiated prices under the IRA will apply only to a limited number of brand-name drugs covered by government-granted monopolies if they have been on the market for at least 9 years (13 years for biologic drugs) and that have cost the Medicare program $200 million or more in a year. Other drugs are exempt from negotiation, such as drugs only approved for a single rare disease. In its negotiations, CMS is required to take into account various characteristics of the drug, such as whether it represents an important therapeutic advance or fulfills an unmet medical need, whether it has recouped its research and development costs, and any federal funding that contributed to its discovery.[18] The legislation imposes upper bounds on the negotiated price for now of no greater than 75% of the non-federal average manufacturer price for drugs 9-16 years after approval; this increases to 40% for drugs greater than 16 years after approval. In exchange, once a negotiated price is finalized, all Part D plans will be required to cover the drug on their formularies.[19] Negotiated prices will be in place until there is actual direct competition from a generic or biosimilar version. The IRA also provides for the possibility of price renegotiation if there are material changes, such as approval of a new indication. The legislation limits the number of drugs that can negotiated to just 20 drugs each year, after a 3-year lead-in period with even lower limits.[20]

The IRA Medicare negotiation provisions offer key improvements to the US drug pricing system. First, negotiation offers the promise of real savings for patients and for the health care system. The Congressional Budget Office estimated that negotiation—even with all of its exceptions and limitations—could provide a savings of approximately $100 billion over 10 years for the federal

---

[16] King R. Medicare Part B premiums to decline slightly in 2023 due to low Aduhelm use. Fierce Healthcare Sept 27,2022. Available from: https://www.fiercehealthcare.com/payers/medicare-part-b-premiums-decline-slight-2023-due-low-aduhelm-use.

[17] Galewitz P. States cut Medicaid drug benefits to save money. Kaiser Health News July 24 2012. Available at: https://khn.org/news/medicaid-cuts-sidebar/

[18] Hwang TJ, Kesselheim AS, Rome BN. New reforms to prescription drug pricing in the US: opportunities and challenges. JAMA 2022;328(11):1041-1042.

[19] Id.

[20] Id.

government.[21] Savings to Medicare will be passed on to seniors with Medicare coverage and the taxpayers who fund the program. In the IRA, Congress used the anticipated savings from negotiation as part of the justification for making prescription drug coverage more generous, such as the $2000 cap on Medicare Part D patient out-of-pocket costs, elimination of out-of-pocket costs for vaccines, and caps on insulin spending at $35 per month.[22] Savings generated from negotiation could be used to provide additional benefits to seniors under Medicare or further reduce out-of-pocket costs.

Second, the Medicare negotiation provision offers the prospect of real improvements to the current incentive system for prescription drug innovation. When brand-name manufacturers can freely set prices for drugs, even those that are "me-too" drugs with limited clinical advantages over what we already have, it reduces the pressure for companies to develop new medications that are really important medical discoveries. By allowing manufacturers to charge high prices indefinitely for ho-hum products for as long as they can keep direct competition off the market, the current system incentivizes brand-name manufacturers to invest substantial resources in developing patent thickets and engaging in other strategies—often called "evergreening"—to maintain revenue streams on their current products, rather than investing in meaningful new innovation. Thus, Medicare drug price negotiation is likely to improve incentives to invest in meaningful innovation. Giving Medicare the opportunity to negotiate prices for prescription drugs based on a drug's clinical benefits compared with therapeutic alternatives will continue to direct more manufacturer effort toward meeting unmet medical needs or providing important clinical benefits, while reducing spending on drugs that lack these characteristics.[23] Brand-name drugs that offer better outcomes to patients will be rewarded with higher prices than their competitors, creating a powerful incentive for manufacturers to invest their resources in bringing to market drugs that will achieve a justified price premium rather than products that won't offer patients any meaningful new health benefits.[24] Similarly, reducing spending via negotiation on drugs that have been sold at high prices for at least 9-13 years will support efforts to redirect resources into making innovative treatments available. In one review of pharmaceutical manufacturers with at least one FDA-approved product from 1985-2001, the most important predictor of new product introductions was the expiration of exclusivity protection on a current product.[25]

---

[21] Congressional Budget Office. Estimated budgetary effects of subtitle I of reconciliation recommendations for prescription drug legislation. Available from: https://www.cbo.gov/system/files?file=2022-07/senSubtitle1_Finance.pdf

[22] The out-of-pocket spending cap in Part D was estimated to cost the government an additional $782 million per year in 2019. Gangopadhyaya A and Garrett B. Capping Medicare beneficiary Part D spending at $2,000. March 2022. Urban Institute. Available from: https://www.rwjf.org/en/insights/our-research/2022/02/capping-medicare-beneficiary-part-d-spending-at-2000.html.

[23] Kesselheim AS, Hwang TJ, Avorn J. Paying for prescription drugs in the new administration. JAMA 2021;325(9):819-820.

[24] Fojo T, Mailankody S, Lo A. Unintended consequences of expensive cancer therapeutics—the pursuit of marginal indications and a me-too mentality that stifles innovation and creativity: the John Conley lecture. JAMA Otolaryngology–Head & Neck Surgery. 2014;140(12):1225-1236.

[25] Graham SJH and Higgins MJ. The impact of patenting on new product introductions in the pharmaceutical industry (April 4, 2007). Available at SSRN: https://ssrn.com/abstract=984628.

II. Addressing Other Concerns about the Effect of the IRA on Prescription Drug Innovation

When any drug pricing reform is introduced, pharmaceutical industry lobbyists argue that it will reduce innovation. But it's vital to recognize that large pharmaceutical manufacturers invest only about 10-20% of their revenues in research and development;[26] that percentage is even lower if we consider only clinically useful innovation. As a result, providing guaranteed high profit margins to such manufacturers whatever they produce, as we do now, doesn't directly translate to substantial investment in innovation. According to one review, 99.4% of new drugs approved 2010–2019 were linked to NIH funding at some point in their development.[27] Research analyses from our group at Harvard Medical School has shown how transformative drug innovation is often based in large part on publicly funded research and development, even though this is rarely reflected in the pricing of the resulting drugs, or in commensurate "payback" to the taxpayers or funding agencies that made them possible.[28] As long as Congress continues funding for the NIH, then we can be assured that the next generation of important new therapeutics will be in the pipeline. If concerns ever arise about insufficient support to bring certain types or classes products through clinical testing and regulatory approval—the roles dominated in the current system by venture capital and private industry funding—the recent production of highly effective Covid-19 vaccines based on about $32 billion in US government funding has shown that public-private partnerships can produce highly promising new treatments.[29] This view is bolstered by experiences in other countries. A recent study done with colleagues at Harvard and internationally found that after Germany implemented price negotiation more aggressive than what Medicare is embarking upon, no drugs that provide important new patient benefits left the German market.[30]

An independent estimate by the Congressional Budget Office (CBO) estimated that the Inflation Reduction Act would lead to just 1% fewer new drug approvals over the next 30 years,[31] in

---

[26] Kesselheim AS, Avorn J, Sarpatwari A. The high cost of prescription drugs in the United States: origins and prospects for reform. JAMA 2016;316(8):858-871.

[27] Cleary EG, Jackson MJ, Zhou EW, Ledley FD. Comparison of research spending on new drug approvals by the National Institutes of Health vs. the pharmaceutical industry, 2010–2019. JAMA Health Forum 2023;4:e230511.

[28] See, e.g., Kesselheim AS, Tan YT, Avorn J. The roles of academia, rare diseases, and repurposing in the development of the most transformative drugs. Health Affairs 2015;34:286-294; Nayak RK, Avorn J, Kesselheim AS. Public support for late-stage new drug discovery; cohort study. BMJ 2019;367:l5766

[29] Lalani HS, Nagar S, Sarpatwari A, Barenie RE, Avorn J, Rome BN, Kesselheim AS. US Public investment in the development of mRNA COVID-19 vaccines: retrospective cohort study. BMJ 2023;380:e073747.

[30] Stern AD, Pietrulla F, Herr A, Kesselheim AS, Sarpatwari A. The impact of price regulation on the availability of new drugs in Germany. Health Affairs 2019;38(7):1182-1187. The oncology drug regorafenib (Stivarga) was withdrawn from the market; it received an early positive assessment, but was later reassessed by the Federal Joint Committee, which failed to confirm its prior positive benefit assessment.

[31] Congressional Budget Office Cost Estimate: Estimate Budgetary Effects of Public Law 117-169 (September 7, 2022).

contrast to industry-funded studies that threatened more catastrophic forecasts.[32] The CBO made no predictions about which types of drugs would be among this 1%, and it is likely that the drugs most affected would be those that offer limited added benefits to patients over existing therapies.

Some specific arguments by the pharmaceutical industry about how the IRA might affect innovation are worth addressing individually.

A. Delaying Launch of Rare Cancer Drugs

Drug company executives and their allies have suggested that the IRA might lead companies to delay the launch of new cancer drugs. Many new cancer therapies are first approved for rare diseases, or as later lines of therapy, before being approved for broader indications over time. Critics have argued that the IRA changes the calculus for cancer drugs and would lead them to delay entry of drugs for rare cancers. For example, in August 2023, the CEO of Roche's Genentech announced that the IRA would lead the company to delay approval for a new ovarian cancer drug (a rare cancer) by approximately 3 years until it also completed trials in prostate cancer (a more common cancer).[33] Why? He argued that the delay would allow Roche 9 years of broader Medicare sales for both ovarian and prostate cancer before negotiated prices take effect, while the prior approval strategy would allow for nine years of Medicare sales for ovarian cancer but only 6 years for prostate cancer.

The notion that a drug company would intentionally withhold an effective cancer drug from the market is ethically appalling, but this particular scenario is also flawed for many economic reasons. First, drug companies will continue to have incentives to test cancer drugs in rare or late-stage cancers before investing in trials to study drugs for more common cancers. For example, one important reason drug companies pursue rare cancer indications for their investigational drugs is to reduce pre-approval spending, since cancer drugs approved for rare diseases can rely on using smaller and less rigorous studies, often based on surrogate measures rather than real clinical endpoints.[34] The IRA does not change this.

Second, the IRA negotiation does not take effect until a drug has been on the market for at least 9-13 years, and decisions like the one that the Roche CEO invoked are often made at least 3-5 years before approval. It is highly unlikely that the prospect of reduced payments 12-18 years in the future would be meaningful enough to strongly affect a manufacturer's decision about how to prioritize testing for its investigational products, especially ones that could help patients with a potentially fatal cancer. This is even more true given that the IRA only affects Medicare payments

[32] Philipson TJ et al. The potentially larger than predicted impact of the IRA on small molecule R&D and patient health (Aug 25, 2023) https://bpb-us-w2.wpmucdn.com/voices.uchicago.edu/dist/d/3128/files/2023/08/Small-Molecule-Paper-Aug-25-2023.pdf ; Gassull D, Bowen H, Schulthess D. IRA's impact on the US biopharma ecosystem, (June 1, 2023) https://vitaltransformation.com/2023/05/iras-impact-on-the-us-biopharma-ecosystem/

[33] Cohrs R. Genentech weighs slow-walking ovarian cancer therapy to make more money under drug pricing reform. STATE. 2023 Aug 10.

[34] Kesselheim AS, Myers JA, Avorn J. Characteristics of clinical trials to support approval of orphan vs nonorphan drugs for cancer. JAMA 2011;305:2320-2326.

– the IRA will have no direct effect on revenue from private payers. A launch delay for Roche's ovarian cancer drug would relinquish revenues from both public and private payers in the US for all indications. Such a move would be even more fiscally disastrous if the ongoing clinical trials for prostate cancer do not show the expected clinical benefits, and so this scare-tactic argument makes no sense.

Third, delaying launch of a drug would reduce the amount of market exclusivity time remaining on the patent that covers the active ingredient once that drug is approved. While drug companies frequently obtain several patents on their drugs, the primary patent is usually the strongest and hardest to overturn in litigation brought by potential generic or biosimilar competitors. Thus, if Roche delayed the launch of their drug by 3 years, the product would likely have fewer years of protection against direct competition from generics or biosimilars, which will lower prices far more than Medicare negotiation. Moreover, investigational cancer drugs with the same mechanism of action are likely being pursued by other companies, so if the Roche CEO delays launch of his company's product, he might find that he ends up entering a market with more competitors that would reduce expected sales of his company's drug.

In summary, leaving aside the embarrassing ethical assumptions that underlie these arguments, it is exceedingly unlikely that the changes in the IRA will lead drug manufacturers to delay the launch of useful newer products. If anything, the addition of a 9-year clock before Medicare negotiation will encourage manufacturers to speed innovation on secondary uses of their products to maximize sales before negotiation takes effect.

B. *Reducing Incentives for Rare Disease Drug Innovation*

The IRA provides a specific exclusion for rare disease drugs: drugs that have a single rare disease indication are not candidates for negotiation. To fall within this exemption, a drug may have been granted only a single designation by the FDA under the Orphan Drug Act as being indicated for a disease affecting fewer than 200,000 patients per year and must be FDA approved for indications that fall only within this designation. Some critics of the IRA have argued that the existence of this exemption reduces manufacturers' incentives to seek subsequent indications for FDA-approved rare disease drugs, since manufacturers would prefer to remain exempt from Medicare price negotiation.

The fears about this criticism are largely overblown and would apply to only a small number of drugs, if at all. In a forthcoming study, my colleagues and I focused on the 282 drugs between 2012 and 2021 that had at least one year of Medicare spending over $200 million. Among these, 95 (34%) had at least one Orphan Drug Act indication. Among those 95, 25 would have been eligible for the exemption outlined by the IRA. Among the remaining 70, 37 were originally approved for a common condition and then subsequently approved for a rare disease. Innovation among this group would not be threatened either, since these drugs are presumably getting a far higher fraction of their revenue from their original, non-rare disease indication. Among the remaining 33, 13 were originally approved for a rare disease indication and then subsequently for a more common indication. As discussed above, the idea that development of these drugs

would be disincentivized by the IRA is economically unsound. That leaves a total of just *20 drugs* over the course of a decade that could be the subject of concern.

There is good reason to believe that subsequent rare disease indications for these drugs still would have been sought. First, among these 20 drugs, 9 were approved for multiple rare disease indications, which together can lead to substantial revenues that would exceed any reduction from Medicare negotiation after 9-13 years. Second, manufacturers might still pursue subsequent rare disease drug indications if they believe that revenues from payors outside of Medicare would make up for any reduction in revenue from Medicare negotiation.

Some have argued that to preserve incentives for developing treatments for rare diseases, *any drug* with an Orphan Drug Act designation should be exempt from Medicare negotiation.[35] This would be costly and ineffective, leading to the exclusion of dozens of drugs, including products that are approved for both common and rare diseases. Such an expansion would also create an easy loophole for companies to avoid negotiation on blockbuster products by pursuing low-cost, low-value Orphan Drug Act-designated indications.[36]

If Congress is open to amending the IRA, a better solution would be to eliminate the Orphan Drug Act sole-indication exemption altogether. The IRA already protects low-revenue drugs by excluding from negotiation any drug with Medicare sales below $200 million. If any drug – including one that treats a rare disease – exceeds this threshold, it is likely to be a blockbuster product that will have made its manufacturer many billions of dollars in revenue by the time of negotiation, so it is unclear what this exemption is protecting. In the previous study of rare disease drugs, we found that for the 10 single rare disease-designated drugs that could become eligible for price negotiation under the IRA in coming years, the actual and projected revenues ranged from $4 billion to $72 billion in the years before drugs would be old enough to face price negotiation under the current IRA framework. In a separate study with colleagues in my research group, we found that drugs initially approved for an Orphan Drug Act-designated condition were just as lucrative for their manufacturers as drugs developed for more common conditions: among 315 drugs marketed from 2008 to 2015, median 5-year net sales were $719 million for Orphan Drug Act-designated drugs and $812 million for other drugs.[37]

C. *Reducing Incentives for Small-Molecule Drug Innovation*

Critics have also expressed concern about the different time periods before Medicare drug price negotiation can begin: 9 years for small-molecule drugs and 13 years for biologic drugs. The argument here is that the shorter protection for small molecule drugs will lead manufacturers to abandon small-molecule drug development in favor of biologic drugs. In one article, an executive

[35] Council for Affordable Health Coverage. How the IRA is impacting rare disease patients. March 1, 2023.
[36] Yin W. R&D policy, agency costs and innovation in personalized medicine. Journal of Health Economics 2009;28(5):950-962.
[37] Tu SS, Nagar S, Kesselheim AS, Lu Z, Rome BN. Five-year sales for newly marketed prescription drugs with and without initial Orphan Drug Act designation. JAMA 2023;329(18):1607-1608.

at Lilly argued that they would not have pursued a small-molecule drug to treat breast cancer without the additional 4 years of protection from negotiation that biologics drugs get.[38]

But this criticism is also flawed for many reasons. Again leaving aside the embarrassing threat that a major drug company would leave a promising drug to treat cancer on the shelf because it wanted to make more money, it is also important to recognize the scope of revenues that the drugs subject to Medicare negotiation will have earned even after 9 years on the market. Among the first 10 drugs selected for price negotiation, 7 were small-molecule drugs (Eliquis, Farxiga, Imbruvica, Januvia, Jardiance, Xarelto, Entresto) and global revenues for these products in the first 9 full years after FDA approval ranged from approximately $15 billion to $57 billion *per drug*.[39] In the case of the Lilly drug specifically cited as being a potential loss to IRA negotiation after 9 years of being on the market, that drug was approved in 2017 and peak global revenue is expected to be around $3 billion per year at the end of 2029. If its market exclusivity continues until 2032 (15 years, which is around the median time) and assuming the IRA results in *zero* Medicare revenue starting in 2027 (which far exceeds what it is designed to do), the change in present value (or potential profits to be realized) in 2017 would decrease from $24 billion to $20 billion. It would be absurd for a pharmaceutical manufacturer to set aside small-molecule drug innovation that could lead to revenues at that level. Furthermore, small molecule drug innovation remains advantageous for many development reasons, including lower cost of production, greater ease in administration (usually oral, while most biologic drugs are injected), and greater simplicity in the supply chain.

III. The Constitutionality of the IRA

In recent months, drug manufacturers and their allies have filed nine lawsuits claiming that the Inflation Reduction Act's Medicare Price Negotiation Plan is unconstitutional.[40] I will now explain why the five main constitutional claims they make fail.

First, manufacturers claim that the IRA violates the Takings Clause of the Fifth Amendment, which prohibits the taking of private property for public use without just compensation. It does not, for two reasons. First, a taking must be compelled. Manufacturers participate in Medicare voluntarily, and can avoid negotiations by divesting their drug to another company or by withdrawing from Medicare and Medicaid participation entirely, as CMS recently clarified,[41]

[38] Skovronsky DM. The IRA's nonsensical distinction between small- and large-molecule drugs. STAT News First Opinion. May 9, 2023. Available from: https://www.statnews.com/2023/05/09/ira-inflation-reduction-act-small-large-molecule-drugs/

[39] Results compiled through 2022 using global revenue data. Entresto only contributed 7.5 years of data and Jardiance 8.5 years. This is a conservative estimate, since the numbers are not adjusted for inflation.

[40] Complaints have been filed by Merck, the Chamber of Commerce, Bristol Myers Squibb, the Pharmaceutical Research and Manufacturers of America (PhRMA), Astellas, Janssen (Johnson & Johnson), Boehringer Ingelheim, AstraZeneca, and Novartis. Georgetown Health Care Litigation Tracker: Inflation Reduction Act. (accessed Sept 18, 2023) https://litigationtracker.law.georgetown.edu/issues/inflation-reduction-act/

[41] CMS Guidance: Medicare Drug Price Negotiation Program: Revised Guidance (June 30, 2023) https://www.cms.gov/newsroom/press-releases/cms-releases-revised-guidance-historic-medicare-drug-price-negotiation-program

without facing a tax or penalty. Second, the Takings Clause protects only legitimate property interests. As courts have long held, private health care entities have no legal right to receive taxpayer dollars, to set their own reimbursement rates, or even to participate in Medicare at all.[42] The same is true for prescription drug manufacturers.

Paying less for something is not the same as physically taking it, as the manufacturers argue.[43] By their reasoning, *any* effort to contain health care costs would constitute a taking by the government. For traditional Medicare coverage, Medicare sets fee-for-service rates from services provided by doctors, and both the Department of Defense and the Department of Veterans Affairs have statutory caps on drug prices, and can negotiate lower prices beyond that level.[44]

The takings claim rings especially hollow given Medicare's pre-IRA payment model for prescription drugs, in which Medicare was explicitly prohibited in all circumstances from negotiating prices and required by law to provide coverage for most new drugs.[45] Manufacturers have been free until now to set prices throughout the full lifecycle of their drugs without any meaningful constraint, and without the considerations that the IRA now requires Medicare to use in negotiations for a small number of drugs near the end of their exclusivity periods, such as a drug's clinical benefit. As a result, American taxpayers spend more on prescription drugs than any other country, and many top-selling Medicare drugs offer no added clinical benefit over existing alternatives, some of which cost less. The Inflation Reduction Act attempts to level the playing field by untying Medicare's hands, so that it can negotiate prices as it does for other goods and services within and outside health care, and just like any other market participant purchasing health services.

Second is a claim that the Act violates the Due Process Clause of the Fifth Amendment. The scope of due process protection depends on the weight of the relevant public and private interests.[46] The negotiation procedures easily pass this test, because whatever value might accrue from maintaining high revenues for drug companies is vastly outweighed by the public policy imperative of ensuring fair drug costs for the American people.

Due Process protects only "life, liberty, or property."[47] Although manufacturers may own and sell the drugs they make, companies do not have a constitutionally protected right to receive taxpayer

---

[42] "[A] long line of cases instructs that no taking occurs where a person or entity voluntarily participates in a regulated program or activity." Baker County Medical Services Inc v. Attorney General, 763 F.3d 1274, 1276 (11th Cir. 2014).

[43] Some complaints allege that the negotiation plan creates a *per se* or "classic" taking, in which the government "directly appropriates private property." Lingle v. Chevron U.S.A., 544 U.S. 528, 539 (2005).

[44] CBO Report. A comparison of brand-name drug prices among selected federal programs (Feb 18, 2021); GAO Report. Prescription drugs: Department of Veterans Affairs paid about half as much as Medicare Part D for selected drugs in 2017. (December 2020).

[45] Sachs R. Delinking Reimbursement. Minn. L. Rev. (2018).

[46] Mathews v Eldridge, 424 U.S. 319 (1976).

[47] Twinamatsiko AJ and Baron ZL. Policy dispute masquerading as Constitutional theory? Due process attacks on Medicare drug negotiation program. (Aug 17, 2023) https://oneill.law.georgetown.edu/policy-dispute-masquerading-as-constitutional-theory-due-process-attacks-on-medicare-drug-negotiation-program/

dollars in the form of Medicare reimbursement. Because they lack a property right to public funds, the Due Process Clause does not shield them from negotiation. Courts have recognized procedural due process rights in the context of certain public benefits, such as social security for those with disabilities.[48] But Medicare is not an entitlement program for drug manufacturers; rather, Medicare's intended beneficiaries are the American people, many of whom cannot afford the cost of drugs at the rates manufacturers have set.

Some drug manufacturers claim there is a substantial public interest in maintaining their current revenues, which produce the highest profit margins of any sector in the US economy,[49] and argue that any decrease in revenue will choke off innovation. These assertions attempt to justify any profit margins and any price, and have little rigorous, independent evidence for support. While it is true that manufacturers spend substantial sums on development, it does not follow that fair prices will reduce the incentive, or impede the means, of developing valuable medicines. For example, as described above, almost all new therapies involve some degree of public support, and many of the most clinically useful medical advances are made with substantial taxpayer support, through financial de-risking, as well as the funding of basic research and even in some cases late-stage clinical trials. The argument that high drug company revenues are *per se* a public good holds no water.

In light of this overwhelming public interest, the negotiation procedures set forth in the Act are more than sufficient to satisfy due process.

Third, opponents of the IRA claim that the Act violates the free speech protections of the First Amendment by compelling them to express a view they do not hold. But participation is not compelled, nor does it implicate any kind of speech or expression at all.

As explained in a recent article in JAMA, manufacturers are simply trying to use the First Amendment as a tool to force Medicare to purchase their products at monopolistic prices.[50] But the government is only trying to act like any rational consumer by negotiating the price—it is not compelling drug firms to communicate anything about their products or their prices.[51] Rather, the IRA initiates a government program focused on regulating conduct, not speech.[52] A negotiation requirement is not a free speech issue and the First Amendment is not a right to have the government keep silent in its dealings with private parties.[53]

Fourth, some manufacturers claim that the Act is an unlawful delegation of authority to CMS, in violation of the separation of powers between the legislative and executive branches. An impermissible delegation could occur ***if*** Congress failed to provide an "intelligible principle" to

[48] Goldberg v. Kelly, 397 U.S. 254 (1970); Mathews v. Eldridge, 424 U.S. 319 (1976).
[49] Ledley FD, McCoy SS, Vaughan G, Cleary EG. Profitability of large pharmaceutical companies compared with other large public companies. JAMA 2020;323(9):834-843.
[50] Tu SS, Tushnet R. Free speech challenges to the Inflation Reduction Act. JAMA 2023 Aug 29.
[51] Id.
[52] Id.
[53] Id.

guide the agency's implementation of the law.[54] But the IRA provides clear guidance and limits on CMS's authority, from defining which drugs are eligible for negotiation to outlining in great detail the negotiation process itself.

Manufacturers have focused on CMS's authority to determine a maximum fair price for a drug, arguing that its discretion is unconstitutionally broad—even though CMS determines prices for many other medical goods and services. In addition, Congress included clear guardrails here as well, capping the maximum price and including a list of statutory factors CMS must consider. The manufacturers objecting to the IRA do not explain how Congress could have further limited CMS's negotiating power without contravening the fundamental purpose of the Act to lower drug costs by empowering Medicare to negotiate fair prices. Thus, the claim about CMS's discretion amounts to a disagreement with Congress's legitimate choice to authorize CMS to negotiate at all, and fails to demonstrate an unconstitutional delegation of authority to a federal agency.

Manufacturers focus as well on how the IRA insulates certain CMS decisions, including the maximum fair price, from judicial review, and has empowered CMS to publish informal guidance, instead of requiring notice-and-comment rules, as it initiates the negotiation process. These features are not unconstitutional, and instead reflect prudent policy judgments made by Congress with an understanding of the practical barriers CMS faces to implement the law.

The use of guidance among agencies is commonplace when implementing complex statutes, and does not preclude accountability. CMS's use of guidance thus far has been deeply participatory, soliciting and responding to the comments it receives, and offering manufacturers and the broader public opportunity to raise objections and make recommendations.

Congress's choice to bar judicial review of the maximum fair price fits with the purpose of the Act to facilitate a negotiation between Medicare and the manufacturer. Granting manufacturers additional leverage via the courts, where judges would be asked to review fact-specific determinations on items such as prescribing practices, distribution data, and research and development costs, would impede that negotiation for little reward. The Supreme Court has recently upheld similar bars to judicial review.[55] It makes sense that in the detail-laden context of drug negotiations, the IRA tasks CMS, rather than courts, with implementing some of its most complicated provisions.

Finally, some drugmakers claim that the Act unconstitutionally compels companies to participate, because it conditions Medicare and Medicaid reimbursement on their participation in price negotiations. This claim confuses a carrot with a stick; an incentive is not a threat. The fact that Medicare reimbursement constitutes such a huge portion of pharmaceutical revenues is all the more reason it should be able to negotiate fair prices.

[54] Whitman v. American Trucking Associations, 531 U.S. 457, 474 (2001).
[55] Thryv, Inc., v. Click-To- Call Techs. 140 S. Ct. 1367 (2020).

The manufacturers claim that they cannot withdraw from participation in Medicare and Medicaid because, in effect, participation is too lucrative for them to refuse. This is not coercion. If they do not want to engage in negotiations, they do not have to participate. If they do, they are subject to the conditions that Congress may impose on any voluntary federal health care program.

Similarly, manufacturers claim that they cannot meaningfully negotiate because at the end of the day they must accept CMS's offer. But that's just how a negotiation works. Given that manufacturers participate in Medicare voluntarily, this argument amounts to a recognition of Medicare's vast untapped purchasing power over prescription drugs—power it has until now been prohibited from leveraging to attain reasonable prices.

Manufacturers focus as well on the excise tax imposed if they seek reimbursement without participating in negotiations. This tax, too, is optional. If the manufacturer prefers not to sell to Medicare at a fair, negotiated price, they do not have to sell at all.

It is not surprising that the arguments in these lawsuits lack merit. The pharmaceutical industry is attempting to accomplish through the courts what it could not through the democratic process—maintaining unreasonably high brand-name drug prices at the expense of patients and the American public.