The Inflation Reduction Act's Prescription Drug Price Setting Provision: A Year Later

By Richard H. Bagger

Following enactment of federal government prescription drug price setting (under the misnomer of "negotiation") in August 2022, several possible unintended consequences that could harm future medical innovation were predicted. Now, just over a year later, it is becoming increasing clear that the unintended consequences warned of a year ago are indeed starting to be seen in reality.

But first, a quick recap. The Inflation Reduction Act (IRA), which is comprised of several unrelated provisions, established federal government price setting for a discrete number of prescription medicines in Medicare, starting in Part D and then expanding to Part B, and increasing each year.

The price setting provision is described by the law's proponents as "negotiation," which is a complete misnomer. Biopharmaceutical companies already negotiate in Medicare Part D, with the health plans and pharmacy benefit managers (PBMs) that actually provide the benefit. For example, the three largest PBMs (CVS Caremark, Express Scripts and OptumRx) each negotiate on behalf of more people than are covered by the entire Medicare Part D program. They already get the best deals.

That is why the Congressional Budget Office (CBO) originally concluded that legislation to allow the government to negotiate prescription drug prices in Medicare Part D would not save the government any money. The price setting provisions of the IRA only "scored" as saving the government money because the "hammers" in the law – an annual excise tax of up to 95% of a medication's total sales (not just Medicare Part D) and the possibility an entire company's product portfolio could be barred from Medicare and Medicaid -- make the government price "an offer that you can't refuse."

Given that prices established under the IRA have a ceiling but no floor, investors have begun to consider the risk of a medication being selected for government price setting after seven years for small molecule drugs and after eleven years for biologics as a loss of exclusivity type event, potentially similar in economic impact to patent expiration.

This is where the specific design of the IRA's price setting provision is leading to unintended consequences -- forecast a year or more ago and starting to become reality now -- that endanger future medical innovation in completely unintended ways.

Unintended Consequence	**What is Already Happening**
Small molecule drugs are subject to "negotiation" earlier than biologics. Small molecule drugs could lose 50% of the economic value of their patent life through being subject to	• A survey from the Pharmaceutical Research and Manufacturers of America indicated that 63% of its member companies are expecting to shift R&D

government price setting on average five years before patent expiration. Risk that this will disincentivize small molecule development.	investment focus away from small molecules as a result of IRA.[1] • Eli Lilly announced it is canceling work on a BCL2 inhibitor drug that had been undergoing studies for certain blood cancers due to the small-molecule penalty.[2] The company stated, "small molecule medicines are unfairly disadvantaged by the law" and that small-molecule treatments represent 40% of Lilly's overall portfolio.[3] • Congress could address this unintended consequence by making both small molecule drugs and biologics subject to being selected for the government price setting process at the same time, eleven years after FDA approval.
With a shorter commercial life, the IRA disincentivizes the development of new indications/formulations because the financial hurdle for additional indications won't be met. This is especially true for cancer drugs, given the nature of cancer drug development.	• Novartis CEO Vas Narasimhan told *Barron's* that the company has dropped some early-stage cancer drugs from its pipeline because of IRA.[4] • Genentech CEO Alexander Hardy stated that, because the countdown to Medicare negotiations starts at a drug's first approval, drugmakers now have to make tough choices about return on investment and speedy patient access to new therapies. In some cases, the specific application that could get a medicine to patients the quickest isn't necessarily the indication with the largest patient pool. "Now we're trying to figure out how to make a return with a nine-year clock."[5] He warned that the company may slow research for ovarian cancer treatments targeting small populations to make sure drugs treating diseases for larger patient populations would be released first.[6]

[1] Nicole Longo, *WTAS: Inflation Reduction Act Already Impacting R&D Decisions*, PHRMA (Jan. 17, 2023), https://phrma.org/en/Blog/WTAS-Inflation-Reduction-Act-already-impacting-RD-decisions.
[2] *The Inflation Reduction Act's Impact on Drug Discovery and Development*, ELI LILLY (Dec. 8, 2022), https://www.lilly.com/news/stories/inflation-reduction-act-impact-on-drug-discovery-and-development.
[3] *The Inflation Reduction Act's Impact on Drug Discovery and Development*, ELI LILLY (Dec. 8, 2022), https://www.lilly.com/news/stories/inflation-reduction-act-impact-on-drug-discovery-and-development.
[4] Josh Nathan-Kazis, *Novartis CEO: Some Cancer Drugs Dropped From Pipeline Because of Medicare Price Negotiations*, BARRONS (May 19, 2023), https://www.barrons.com/articles/novartis-stock-price-ceo-cancer-drug-medicare-e9b0fcb7.
[5] Zoey Becker, *Genentech CEO Alexander Hardy Warns of "Unintended Consequences" From the Inflation Reduction Act*, FIERCE PHARMA (July 6, 2023), https://www.fiercepharma.com/pharma/genentech-ceo-alexander-hardy-unintended-consequences-inflation-reduction-act.
[6] Rachel Cohrs, *Genentech Weighs Slow-Walking Ovarian Cancer Therapy To Make More Money Under Drug Pricing Reform*, STAT NEWS (Aug. 10, 2023), https://www.statnews.com/2023/08/10/genentech-drug-price-cancer/.

	• AstraZeneca stated that if the IRA had been in place, "significant disincentives would have existed" to pursue the late-line ovarian cancer indication for Lynparza, a small-molecule drug.[7] • Richard Pops, CEO of biopharma Alkermes, stated that the IRA could considerably change how drugs are rolled out across indications: "There will never be another Keytruda. You cannot think about bringing a drug to the market and then building indications over a decade as you expand the potential utility in different cohorts of patients."[8]
Under the IRA, the orphan drug exemption will be lost if orphan drugs are approved for a second indication of any kind, including a second orphan indication. Investment in additional indications for rare conditions could be at risk.	• Alnylam Pharmaceuticals announced it was suspending the development of a treatment for Stargardt disease, a rare eye disorder.[9] The company's drug is currently marketed as treating only amyloidosis and is therefore exempt from Medicare price setting. If Alnylam proceeded with research into treating Stargardt, it would lose its orphan drug exemption from price setting even though the second indication is also for an orphan condition.[10] • AstraZeneca stated that the IRA would have deterred the continued development of SOLIRIS, a drug which has received approval to treat four rare diseases, beyond its initial indication.[11]

[7] *AstraZeneca Urges Re-examination of Unintended Consequences of Inflation Reduction Act on American Cancer and Rare Disease Patients*, ASTRAZENECA (Aug. 25, 2023), https://www.astrazeneca-us.com/media/press-releases/2023/astrazeneca-urges-reexamination-of-unintended-consequences-of-inflation-reduction-act-on-american-cancer-and-rare-disease-patients-08232023.html ("If the IRA had been in place, significant disincentives would have existed for pursuing the late-line ovarian cancer approval in the US, an indication which has benefited patients in great need of this unique medicine for their rare condition.").

[8] Sophie Fessl, *How the IRA Will Affect Drug Development*, BIOSPACE (Apr. 6, 2023), https://www.biospace.com/article/how-the-ira-will-affect-drug-development/.

[9] *Alnylam Pharmaceuticals Reports third Quarter 2022 Financial Results and Highlights Recent Period Activity*, ALNYLAM (Oct. 27, 2022), https://investors.alnylam.com/press-release?id=27046 ("The Company also announces today that it is considering options for the best path toward advancing an RNAi therapeutic for the treatment of Stargardt Disease. At this time, it will not initiate a Phase 3 study of vutrisiran in Stargardt Disease in late 2022, as previously guided, as it continues to evaluate the impact of the Inflation Reduction Act.").

[10] Joe Grogan, *The Inflation Reduction Act is Already Killing Potential Cures*, WALL STREET J. (Nov. 3, 2022), https://www.wsj.com/articles/the-inflation-reduction-act-killing-potential-cures-pharmaceutical-companies-treatment-patients-drugs-prescriptions-ira-manufacturers-11667508291.

[11] *AstraZeneca Urges Re-examination of Unintended Consequences of Inflation Reduction Act on American Cancer and Rare Disease Patients*, ASTRAZENECA (Aug. 25, 2023), https://www.astrazeneca-us.com/media/press-releases/2023/astrazeneca-urges-reexamination-of-unintended-consequences-of-inflation-reduction-act-on-american-cancer-and-rare-disease-patients-08232023.html (stating the IRA "would have deterred the continued development of this life-changing medicine for patients with rare diseases beyond its initial indication").

	• "The [IRA] may lead pharmaceutical manufacturers to develop more single-indication orphan drugs . . . rather than follow-on indications."[12] • The bipartisan ORPHAN Cures Act introduced in September 2023 last month would expand the orphan exemption to include multiple orphan indications.[13]
The IRA will reduce incentives for generic drugs. If selection for price setting becomes a loss of exclusivity event, years before patent expiration, generic drug manufacturers' ability to recoup their investment will be dramatically reduced.	• The IRA will "replace competition – the only proven way to provide patients relief from high brand drug prices – with a flawed framework for government price setting that will chill the development of, and reduce patient access to, lower-cost generic and biosimilar medicines."[14] • Potential that price setting for biologics will impact investment decisions being made now for potential biosimilars, which require hundreds of millions and years to develop; decisions made years before CMS will decide whether to select the biologic of government price setting.[15]
Price setting in Medicare could lead to investment in research for diseases with younger populations being prioritized over research in diseases predominantly for elderly patients.	• Novartis noted the IRA is "leading to companies . . . deprioritizing pills for the elderly, which is not going to be the right thing in the long run for public health."[16]

The consequences of these impacts on the incentives for investment in biopharmaceutical research and development are significant. While the CBO predicted that a dozen drugs would be lost by 2039 as a result of the financial disincentives created by the IRA,[17] only four months after the IRA's enactment, the consulting firm Horizon Government Affairs found that at least 24

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[12] James D. Chambers et al., *Follow-On Indications for Orphan Drugs Related to the Inflation Reduction Act*, JAMA NETWORK OPEN (Aug. 15, 2023).
[13] *ORPHAN Cures Act*, H.R. 5539, 118th Cong. (as introduced, Sep. 18, 2023).
[14] Dan Leonard, *AAM Statement on Senate Passage of Inflation Reduction Act*, ASS'N FOR ACCESSIBLE MED. (Aug. 7, 2022), https://accessiblemeds.org/resources/press-releases/aam-statement-senate-passage-inflation-reduction-act#:~:text=The%20Senate%20has%20chosen%20to,cost%20generic%20and%20biosimilar%20medicines..
[15] Peter Pitts, *Biden Claims He's Lowering Drug Costs. If Only That Were True*, DAILY CALLER (Oct. 17, 2023), https://dailycaller.com/2023/10/17/pitts-biden-humira-biologic-biosimilar-drug-prices/ ("to fully take advantage of the pause, biosimilar manufacturers would somehow have to correctly predict whether CMS will choose a given biologic for price controls, whether their biosimilar will be ready for launch before the price-setting takes effect and whether CMS will grant their request for a delay – all years in advance, before they even start investing in research and development").
[16] Hannah Kuchler & Jamie Smyth, *Novartis Boss Warns US Drug Pricing Reform Poses Risk to Public Health*, FINANCIAL TIMES (July 25, 2023), https://www.ft.com/content/46584130-85df-4e63-b197-3ea26bab6809.
[17] *Estimated Budgetary Effects of Subtitle I of Reconciliation Recommendations for Prescription Drug Legislation*, CONGRESSIONAL BUDGET OFFICE (July 8, 2022) (revised July 13, 2022), https://www.cbo.gov/system/files/2022-07/senSubtitle1_Finance.pdf.

companies had announced plans to curtail drug development.[18] Furthermore, a study funded by Gilead revealed that the IRA could result in 79 fewer small molecule drugs and 188 fewer new indications.[19] This comes at a major cost to patient health and the economy: University of Chicago Economist Tomas J. Phillipson recently co-authored a report that predicts reduced innovation in new drugs due to the IRA will lead to health losses valued at $18 trillion by 2031.[20]

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[18] *ICYMI: Biden's Drug Price Controls Kill Innovation and Drive-Up Long-Term Costs*, HOUSE BUDGET COMMITTEE (June 1, 2023), https://budget.house.gov/press-release/icymi-bidens-drug-price-controls-kill-innovation-and-drive-up-long-term-costs.

[19] Tomas J. Philipson et al., *The Potentially Larger Than Predicted Impact of the IRA on Small Molecule R&D and Patient Health*, U. Chi. (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 (finding that the lower investment in R&D could translate into "79 fewer small molecule drugs or 188 indications, and 116.0 million life years lost over the next 20 years").

[20] Tomas J. Philipson, *The Deadly Side Effects of Drug Price Controls*, WALL STREET J. (Apr. 5, 2023), https://www.wsj.com/articles/medicare-drug-price-controls-will-make-america-sicker-research-innovation-negotiations-private-insurers-b503b4ba (citing Tomas J. Philipson & Troy Durie, *Issue Brief: The Impact of HR 5376 on Biopharmaceutical Innovation and Patient Health*, U. CHI. (Nov. 29, 2021)).