nature biotechnology

Perspective

https://doi.org/10.1038/s41587-023-02096-w

Medicare price negotiation and pharmaceutical innovation following the Inflation Reduction Act

In the format provided by the authors and unedited

SUPPLEMENTARY INFORMATION

Supplementary Table 1
Drugs with Negotiated Price in Effect in 2022, Simulated Based on IRA Negotiation Criteria

Active Moiety / Active Ingredient	Brand Name	NDA/ BLA	Earliest FDA Approval	Company	Therapeutic Class (ATC2)
Abatacept	Orencia	BLA	12/23/2005	BMS	Immunomodulatory
Adalimumab	Humira	BLA	12/31/2002	AbbVie	Immunomodulatory
Albuterol	Ventolin	NDA	5/1/1981	GSK	Respiratory
Apixaban+	Eliquis	NDA	12/28/2012	BMS, Pfizer	Anti-thrombotic
Arformoterol	Brovana	NDA	10/6/2006	Sumitomo	Respiratory
Beclomethasone	Qvar	NDA	9/15/2000	Teva	Respiratory
Bendamustine*	Belrapzo Bendeka Treanda	NDA	3/20/2008	Teva	Anti-neoplastic
Bortezomib	Velcade	NDA	5/13/2003	Takeda	Anti-Neoplastic
Brimonidine, Timolol	Combigan	NDA	10/30/2007	AbbVie	Opthamological
Budesonide, Formoterol	Symbicort	NDA	7/21/2006	AstraZeneca	Respiratory
Cabozantinib*+	Cabometyx Cometriq	NDA	11/29/2012	Exelixis	Anti-neoplastic
Certolizumab+	Cimzia	BLA	4/22/2008	UCB	Immunomodulatory
Cetuximab	Erbitux	BLA	2/12/2004	Eli Lilly	Anti-neoplastic
Corticotropin	Acthar	NDA	4/29/1952	Mallinckrodt	Hormonal
Cyclosporine	Restasis	NDA	12/23/2002	AbbVie	Opthamological
Dabigatran	Pradaxa	NDA	10/19/2010	Boehringer	Anti-thrombotic
Darbepoetin Alfa	Aranesp	BLA	9/17/2001	Amgen	Blood
Darunavir	Prezista	NDA	6/23/2006	JNJ	Anti-viral
Dasatinib	Sprycel	NDA	6/28/2006	BMS	Anti-neoplastic
Dexlansoprazole	Dexilant	NDA	1/30/2009	Takeda	Acid-related disorder
Dextromethorphan, Quinidine	Nuedexta	NDA	10/29/2010	Otsuka	Nervous System
Dronedarone	Multaq	NDA	7/1/2009	Sanofi	Cardiovascular
Eculizumab	Soliris	BLA	3/16/2007	AstraZeneca	Immunomodulatory
Eltrombopag	Promacta	NDA	11/20/2008	Novartis	Anti-hemorrhagic
Enzalutamide+	Xtandi	NDA	8/31/2012	Astellas, Pfizer	Anti-neoplastic
Estrogens (Conj.)	Premarin	NDA	5/8/1942	Pfizer	Hormonal
Etanercept	Enbrel	BLA	11/2/1998	Amgen	Immunomodulatory
Exenatide*	Bydureon Byetta	NDA	4/28/2005	AstraZeneca	Diabetes
Fingolimod	Gilenya	NDA	9/21/2010	Novartis	Immunomodulatory
Insulin Aspart	Novolog	BLA	6/7/2000	Novo Nordisk	Diabetes
Insulin Detemir	Levemir	BLA	6/16/2005	Novo Nordisk	Diabetes
Insulin Lispro	Humalog	BLA	6/14/1996	Eli Lilly	Diabetes
Insulin NPh Human	Humulin	BLA	10/28/1982	Eli Lilly	Diabetes
Insulin NPh Human	Novolin	BLA	6/25/1991	Novo Nordisk	Diabetes
Interferon Beta-1a	Avonex	BLA	5/17/1996	Biogen	Immunomodulatory
Interferon Beta-1a	Rebif	BLA	3/7/2002	Merck KGaA	Immunomodulatory

Ipratropium, Albuterol	Combivent Respimat	NDA	10/24/1996	Boehringer	Respiratory
Lacosamide	Vimpat	NDA	10/28/2008	UCB	Anti-epileptic
Lanreotide	Somatuline Depot	NDA	8/30/2007	Ipsen	Hormonal
Lenalidomide	Revlimid	NDA	12/27/2005	BMS	Immunomodulatory
Leuprolide	Eligard	NDA	1/23/2002	Tolman	Anti-neoplastic
Linaclotide+	Linzess	NDA	8/30/2012	AbbVie	Constipation
Linagliptin	Tradjenta	NDA	5/2/2011	Boehringer	Diabetes
Liraglutide	Victoza	NDA	1/25/2010	Novo Nordisk	Diabetes
Lubiprostone	Amitiza	NDA	1/31/2006	Mallinckrodt	Constipation
Lurasidone	Latuda	NDA	10/28/2010	Sumitomo	Psycholeptic
Mirabegron+	Myrbetriq	NDA	6/28/2012	Astellas	Urological
Mometasone, Formoterol	Dulera	NDA	6/22/2010	Organon	Respiratory
Natalizumab	Tysabri	BLA	11/23/2004	Biogen	Immunomodulatory
Nebivolol	Bystolic	NDA	12/17/2007	AbbVie	Anti-hypertensive
Omalizumab	Xolair	BLA	6/20/2003	Roche	Respiratory
Onabotulinumtoxina	Botox	BLA	12/9/1989	AbbVie	Muscle relaxant
Oxycodone	Oxycontin	NDA	4/5/2010	Purdue	Analgesic
Paclitaxel	Abraxane	NDA	1/7/2005	BMS	Anti-neoplastic
Pazopanib	Votrient	NDA	10/19/2009	Novartis	Anti-neoplastic
Pemetrexed	Alimta	NDA	2/4/2004	Eli Lilly	Anti-neoplastic
Pneumococ 23	Pneumovax	BLA	6/30/1983	Merck	Vaccine
Raltegravir	Isentress	NDA	10/12/2007	Merck	Anti-viral
Ranibizumab	Lucentis	BLA	6/30/2006	Novartis, Roche	Opthamological
Rifaximin	Xifaxan	NDA	5/25/2004	Bausch	Anti-diarrheal
Rivaroxaban	Xarelto	NDA	7/1/2011	JNJ	Anti-thrombotic
Romiplostim+	NPlate	BLA	8/22/2008	Amgen	Anti-hematologic
Ruxolitinib*	Jakafi Opzelura	NDA	11/16/2011	Incyte	Dermatological
Saxagliptin	Onglyza	NDA	7/31/2009	AstraZeneca	Diabetes
Sitagliptin	Januvia	NDA	10/16/2006	Merck	Diabetes
Sitagliptin, Metformin	Janumet	NDA	3/30/2007	Merck	Diabetes
Sorafenib	Nexavar	NDA	12/20/2005	Bayer	Anti-neoplastic
Sunitinib	Sutent	NDA	1/26/2006	Pfizer	Anti-neoplastic
Teriflunomide+	Aubagio	NDA	9/12/2012	Sanofi	Immunomodulatory
Teriparatide	Forteo	NDA	11/26/2002	Eli Lilly	Hormonal
Ticagrelor	Brilinta	NDA	7/20/2011	AstraZeneca	Anti-thrombotic
Tiotropium*	Spiriva	NDA	1/30/2004	Boehringer	Respiratory
Tofacitinib+	Xeljanz	NDA	11/6/2012	Pfizer	Immunomodulatory
Varenicline	Chantix	NDA	5/10/2006	Pfizer	Nervous system

* The IRA consolidates Medicare spending across dosages and formulations of an active moiety/ingredient marketed by the same company, including across NDAs/BLAs. In these instances, a single “drug” for IRA purposes was marketed under more than one brand name.

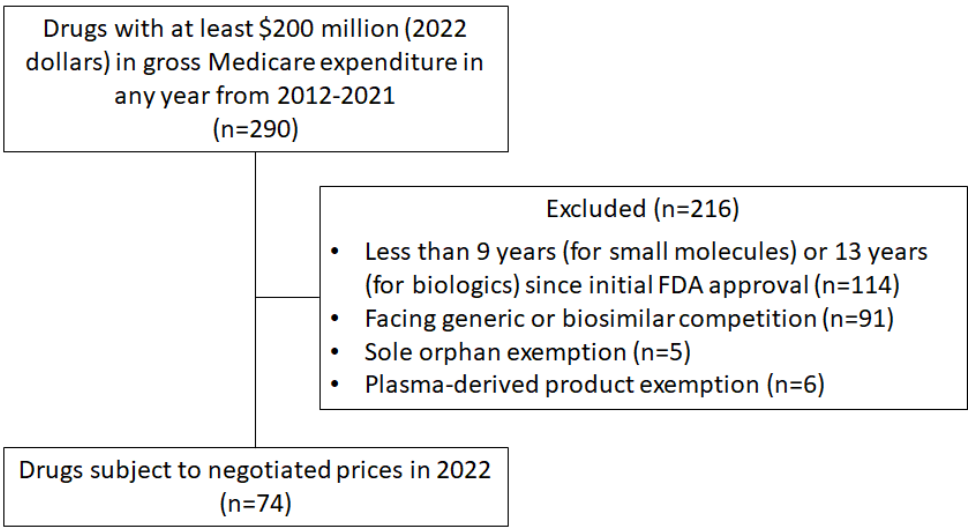
+ Drugs with a Medicare negotiated price in effect for the first time in 2022.

Supplementary Methods

We conducted a cross-sectional study identifying prescription drugs with Medicare spending of >$200 million in any year from 2012 through 2021. Unlike previous studies that estimated prescription drug selection in the negotiation program's first few years,[1,2,3] we estimated drug selection in a mature state, i.e., once the law is operating at a pace in which drugs are selected for negotiation as soon as they are first eligible.

Our analysis applied the IRA's statutory criteria and the Medicare price negotiation guidance released by the Centers for Medicare and Medicaid Services (CMS) in March 2023 and revised in June 2023.[4,5] A STROBE consort diagram of our primary cohort, composed of drugs with a negotiated price in effect in 2022 in our retrospective analysis, is provided in Supplementary Figure 1.

Supplementary Figure 1
STROBE Consort Diagram for Prescription Drugs with Negotiated Prices in 2022, Simulated Based on IRA Selection and Negotiation Criteria



IRA Prescription Drug Negotiation Eligibility Requirements

Medicare drug price negotiation is a multiyear process. A prescription drug must first be found eligible for negotiation. Eligible drugs must (a) have annual Medicare spending exceeding $200 million and (b) have been approved by the U.S. Food and Drug Administration at least 7 years (for small molecules) or 11 years (for biologics) prior to selection. Exemptions from negotiation apply to drugs (c) that are reference products for marketed generic or biosimilar drugs; (d) approved solely for the treatment of a single rare disease; (e) derived from human plasma; and (f) meeting a narrowly defined "small biotechnology" exemption. A delay in selection is permitted (g) for biologics where biosimilar entry is imminent. We applied each of these requirements, following the CMS guidance.

***(a) Medicare Expenditure*.** In each year for which data was available (2012-2021), we identified drugs with annual combined Medicare Part B and Medicare Part D spending above the minimum spending threshold of $200 million in 2022 dollars. Notably, Part B spending for IRA purposes is based on average sales price, which at least partially incorporates rebates and discounts; whereas Part D spending is based solely on gross expenditure, which approximates list price.

The IRA provides a broader definition for what constitutes a single "drug" than in other contexts, such as FDA approval or CMS spending reports. The statute requires CMS to aggregate all dosages and formulations of a drug into a single drug entity and to aggregate spending at the level of that entity, but grants CMS discretion on how to implement this requirement.[6] CMS plans to aggregate spending for all products made by the same company and comprised of the same active moieties (for small molecules) or active ingredients (for biologics), inclusive of products marketed under different FDA applications as well as authorized generics.[7] To identify active moieties and ingredients, we used Drugs@FDA and the FDA's Structure Product Labeling database.[8,9] Per the CMS guidance, we treated a fixed-dose combination as a distinct drug, separate from other drugs containing its active moieties/ingredients.

We used annual Medicare Part B and Part D data from the CMS Medicare Drug Dashboards to calculate Medicare drug spending.[10,11] We reviewed spending on a calendar year basis because publicly available data are reported from January 1-December 31, a slight deviation from the November 1-October 31 basis that will be used by CMS in implementing IRA negotiation.

As specified in the IRA, we adjusted for inflation using the consumer price index for all urban consumers (CPI-U).[12,13] All values are expressed in 2022 dollars.

***(b) Time Since FDA Approval*.** Among prescription drugs with annual Medicare spending over $200 million, we applied the IRA's exclusion of drugs without at least seven years since FDA approval for small molecules, or 11 years for biologics, as of the February 1 selection date in each year.[14,15] We used Drugs@FDA to identify the approval date of the first NDA or BLA for any version of the drug.[16] In some cases, the earliest approval for a drug can be earlier in time than the launch of the most recent dosage/formulation of the drug from which the applicable revenues are derived. We treated flu vaccines, whose composition changes annually, as receiving a new FDA approval with each year's version, essentially exempting them from selection for negotiation.

(c) Generic/Biosimilar Competition. We excluded prescription drugs facing generic or biosimilar competition. We identified generic or biosimilar versions of drugs in our cohort using the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book) and the List of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations (Purple Book). [17,18] We determined when generic and biosimilar versions were first marketed using public Medicaid data.[19,20,21]

***(d) Sole Orphan Exemption*.** We used the FDA Orphan Drug Product designation database and Drugs@FDA to determine if prescription drugs met the statutory requirements for the sole orphan exemption: drugs must have no more than one designation under the Orphan Drug Act (ODA) and all approved indications for that drug must be within that designation.[22]

***(e) Plasma-Derived Product Exemption*.** We identified plasma-derived products using the FDA Approved Blood Products Website.[23,24]

***(f) Small Biotech Exemption*.** The IRA provides a temporary exclusion (applying only during the first three years that the IRA is implemented following congressional passage) for any otherwise eligible drug that makes up more than 80% of the revenue of a "small biotech" company but accounts for less than 1% of Medicare drug spending.[25] Because we were seeking to describe a mature state of price negotiation rather than model the ramp up years, we did not to apply the temporary exclusion.

***(g) Special Biosimilar Entry Delay Rule*.** The selection of a biologic for negotiation can be delayed up to two-years if the Secretary of Health and Human Services, at the request of a biosimilar manufacturer, determines that a biosimilar will "imminently" be marketed.[26] We assumed that in all applicable instances a delay would be requested and granted, but there were no such instances in our data set.

IRA Prescription Drug Negotiation Selection Process

After determining which drugs are negotiation-eligible in any year, CMS will select the drugs that will be negotiated, starting from the qualifying drug with the highest Medicare expenditure that year and working down to the qualifying drug with the lowest expenditure or, if there are more than 20 qualifying drugs, until an annual cap of 20 drugs is reached.[27] A two-year period of negotiation takes place between selection of a drug and implementation of a negotiated price (i.e., before a negotiated price can be implemented at least 9 years or 13 years must have elapsed since initial FDA approval for small molecules and biologics, respectively). Once a drug has a negotiated price in effect, it remains under negotiation until a generic or biosimilar is marketed.

In our retrospective study, we identified drugs that became newly eligible for negotiation each year based on annual Medicare spending between 2012 and 2021. To further our objective of capturing the full effects of IRA price negotiation in a mature, maximally-impactful state, we did not apply the statutory maximum of 20 selected drugs per year. Rather, we placed all drugs meeting the eligibility criteria in each year under negotiation and did not remove them from negotiation until they ceased to be eligible.

Our final IRA cohort of 74 drugs for the primary analysis consists entirely of drugs that met the criteria for selection in any year, starting in 2012, and that continued to be eligible for negotiation during calendar year 2022.

Primary Analysis: IRA Revenue

Our revenue analysis consisted of three parts: (a) identifying U.S. revenues for the products in our cohort, (b) estimating the Medicare share of those revenues, and (c) identifying total global revenues for companies with affected drugs and for the global biopharmaceutical industry.

***(a) Product-Specific U.S. Revenues*.** We obtained product-level U.S. revenue data from SSR Health for all drugs that would have had negotiated prices in effect in 2022.[28] SSR's methodology relies on reports of net revenue based on public financial reporting and reflects price concessions across all payers. SSR's data has been used in studies of drug sales and gross-to-net trends.[29,30,31] For a handful of drugs, SSR did not have revenue data available, requiring us to use estimates from other sources. Data acquisition for those special cases is described in Supplementary Table 2.

***(b) Medicare Share of U.S. Prescription Drug Revenues*.** Following previous studies, we estimated the Medicare share of U.S. revenue for each drug using the Medical Expenditure Panel Survey (MEPS), a publicly available dataset prepared by the Agency for Healthcare Research and Quality (AHRQ).[32,33,34] AHRQ conducts a U.S. survey of a representative sample of the civilian non-institutionalized population regarding prescription drug use, demographic characteristics, and insurance coverage. We calculated the weighted Medicare share for each drug by using personal-level identifiers to link drug utilization data from the MEPS Prescribed Medicine Events File with the demographic and insurance data in the MEPS Full Year Consolidated Data File. We obtained three years of data for each drug and a sample size of at least 100 individuals for each drug class. Like earlier work, we used RxNorm to map each drug's National Drug Code (NDC) to the World Health Organization's Anatomical Therapeutic Chemical classification scheme (ATC) (this defines "Therapeutic Class" in Supplementary Table 1).[35,36]

We calculated the average Medicare market share by therapeutic area for each ATC2 code, defined as the number of people taking the drug divided by the total number of people taking the drug. We then applied the ATC2-level market share estimate to the U.S. revenues for each drug in our cohort (Supplementary Table 3).

For two drugs, leuprolide acetate (Eligard) and oxycodone (Oxycontin), there was no U.S. sales data available as a basis for applying the MEPS analysis. For these drugs, we used the gross Medicare spending for these two drugs (i.e., did not adjust for rebates or discounts), resulting in an overstatement of Medicare revenues for these drugs.

Supplementary Table 2
U.S. Prescription Drug Revenue Data Acquired Outside the SSR Database

Active Moiety / Active Ingredient	Company	Data Acquisition
Albuterol (Ventolin)	GSK	Company report (SSR reports data for this product, but does not include revenues from authorized generics, which the IRA consolidates with branded revenues)
Beclomethasone (Qvar)	Teva	Obtained 2022 total sales data from IQVIA[37] and applied a 44% rebate based on reported class rebate range[38,39]
Dabigatran (Pradaxa)	Boehringer Ingelheim	Obtained 2022 total sales data from IQVIA[40]
Insulin lispro (Humalog)	Eli Lilly	Company report (SSR reports data for this product, but does not include revenues from authorized generics, which the IRA consolidates with branded revenues)
Inteferon beta 1A (Rebif)	Merck KGaA	Company report
Iprotropium/albuterol (Combivent Respimat)	Boehringer Ingelheim	Obtained 2022 total sales data from IQVIA[41] and applied a 44% rebate based on reported class rebate range [42,43]
Lanreotide acetate (Somatuline Depot)	Ipsen	Company report
Nebivolol (Bystolic)	AbbVie	Obtained 2022 total sales data from IQVIA[44] and applied the most recent SSR rebate percentage to calculated net revenues
Pazopanib (Votrient)	Novartis	Obtained 2022 Wall Street consensus sales data from Visible Alpha[45]
Sitagliptin/metformin (Janumet)	Merck	Company report
Sorafenib (Nexavar)	Bayer	Company report
Tiotropium bromide (Spiriva)	Boehringer Ingelheim	Obtained 2022 total sales data from IQVIA[46] and applied a 44% rebate based on reported class rebate range[47,48]

Supplementary Table 3
Medicare Market Share of Prescription Drugs Included in the Simulation (by ATC2 Code)

ATC2 Code	Description	Medicare Share
Alimentary Tract and Metabolism		
A02	Acid-related disorders	54%
A06	Constipation	49%
A07	Anti-diarrheal	49%
A10	Diabetes	54%
Blood and Blood Forming Orans		
B01	Anti-thrombotic	75%
B02	Anti-hemorrhagic	9%
B03	Blood (other)	13%
Cardiovascular System		
C01	Cardiac therapy	47%
C07	Anti-hypertensive	65%
Dermatological		
D11	Dermatological (dermatitis, excluding corticosteroids)	60%
Genitourinary System and Sex Hormones		
G03	Hormonal	23%
G04	Urological	74%
Systemic Hormonal Preparations Excluding Sex Hormones and Insulin		
H01/H05*	Hormonal	55%
Anti-Infectives for Systemic Use		
J05	Anti-viral	21%
J07*	Vaccines	26%
Anti-Neoplastic and Immunomodulating Agents		
L01/L02**	Anti-neoplastic	60%
L03/L04*	Immunomodulatory	34%
Musculo-Skeletal System		
M03	Muscle relaxants	43%
Nervous System		
N02	Analgesic	53%
N03	Anti-epileptic	26%
N05	Psycholeptic	46%
N07	Nervous system (other)	33%
Respiratory System		
R03	Respiratory (obstructive airway diseases)	49%
Sensory Organs		
S01	Opthalmologicals	58%

* ATC2 level sample size was inadequate for this code, as a result ATC2 levels were combined

** L02 anti-cancer drugs were treated as L01 (anti-neoplastic) rather than L02 (endocrine therapy) because average Medicare penetration for L02 drugs reflects uncommon uses for Medicare patients

***(c) Global Prescription Drug Revenues*.** For each pharmaceutical company with a drug with a negotiated price in effect, we obtained publicly posted financial statements to determine total global pharmaceutical revenue. For some companies, this consisted of total revenue. For companies with revenues arising from multiple segments (e.g., consumer products or medical devices), we only included revenues from the segment with prescription drug sales. Links to the relevant sources are provided in Supplementary Table 4.

For two companies, Tolmar and Knoa (formerly Purdue), no public financial information was available. To estimate their global revenues, we scaled up gross Medicare revenues using the MEPS approach described above to estimate global revenues.

Supplementary Table 4
Sources for 2022 Pharmaceutical Company Financial Data

Company	Link to Data Source
AbbVie	https://www.sec.gov/cgi-bin/viewer?action=view&cik=1551152&accession_number=0001551152-23-000011&xbrl_type=v#
Amgen	https://www.sec.gov/cgi-bin/viewer?action=view&cik=318154&accession_number=0000318154-23-000017&xbrl_type=v#
Astellas	https://www.astellas.com/system/files/4q2022_sup_en_isoy1krd92.pdf
AstraZeneca	https://www.sec.gov/cgi-bin/viewer?action=view&cik=901832&accession_number=0001104659-23-023818&xbrl_type=v#
Bausch	https://www.sec.gov/Archives/edgar/data/885590/000114036123017061/ny20007033x3_ars.pdf
Bayer	https://www.bayer.com/sites/default/files/2023-02/Bayer-Annual-Report-2022.pdf
Biogen	https://www.sec.gov/cgi-bin/viewer?action=view&cik=875045&accession_number=0000875045-23-000009&xbrl_type=v#
Bristol-Myers Squibb	https://www.sec.gov/cgi-bin/viewer?action=view&cik=14272&accession_number=0000014272-23-000046&xbrl_type=v#
Boehringer	https://annualreport.boehringer-ingelheim.com/2022/downloads/en/BOE_AR22_Summary-Report_EN_safe.pdf
Eli Lilly	https://www.sec.gov/cgi-bin/viewer?action=view&cik=59478&accession_number=0000059478-23-000082&xbrl_type=v#
Exelixis	https://www.sec.gov/cgi-bin/viewer?action=view&cik=939767&accession_number=0000939767-23-000019&xbrl_type=v#
GSK	https://www.gsk.com/media/9974/20-f-2022.pdf
Incyte	https://www.sec.gov/cgi-bin/viewer?action=view&cik=879169&accession_number=0000879169-23-000008&xbrl_type=v#
Ipsen	https://www.ipsen.com/websites/ipsen_com_v2/wp-content/uploads/2023/02/19134321/fy-2022-results-announcement.pdf

Johnson & Johnson	https://www.sec.gov/cgi-bin/viewer?action=view&cik=200406&accession_number=0000200406-23-000016&xbrl_type=v#
Mallinckrodt	https://www.sec.gov/cgi-bin/viewer?action=view&cik=1567892&accession_number=0001567892-23-000014&xbrl_type=v#
Merck (U.S.)	https://www.sec.gov/cgi-bin/viewer?action=view&cik=310158&accession_number=0001628280-23-005061&xbrl_type=v#
Merck KGaA	https://www.emdgroup.com/content/dam/web/corporate/non-images/investors/reports-and-financials/earnings-materials/2022-q4/us/2022-Q4-Report-NA.pdf
Novartis	https://www.sec.gov/cgi-bin/viewer?action=view&cik=1114448&accession_number=0001370368-23-000006&xbrl_type=v#
Novo Nordisk	https://www.sec.gov/cgi-bin/viewer?action=view&cik=353278&accession_number=0001628280-23-001868&xbrl_type=v#
Organon	https://www.sec.gov/cgi-bin/viewer?action=view&cik=1821825&accession_number=0001821825-23-000003&xbrl_type=v#
Otsuka	https://ssl4.eir-parts.net/doc/4578/ir_material_for_fiscal_ym3/130951/00.pdf
Pfizer	https://s28.q4cdn.com/781576035/files/doc_financials/2023/q1/Q1-2023-PFE-Product-Revenues.xlsx
Purdue	No data available
Roche	https://assets.roche.com/imported/01_230202_IR_FY22_EN.pdf
Sanofi	https://www.sec.gov/cgi-bin/viewer?action=view&cik=1121404&accession_number=0001121404-23-000008&xbrl_type=v#
Sumitomo	https://www.sumitomo-pharma.com/ir/assets/pdf/ebr20230515.2.pdf
Takeda	https://assets-dam.takeda.com/raw/upload/v1683867001/legacy-dotcom/siteassets/system/investors/report/quarterlyannouncements/fy2022/qr2022_q4_qfr_en.pdf
Teva	https://www.sec.gov/cgi-bin/viewer?action=view&cik=818686&accession_number=0001193125-23-031250&xbrl_type=v#
Tolmar	No data available
UCB	https://www.ucb.com/sites/default/files/2023-02/2022_FY-Results_Excel_0.xlsx

Secondary Analysis: Top 250 Prescription Drugs Cohort

We used the SSR data described above to identify the top 250 drugs by 2022 net U.S. sales revenue**.** SSR covers more than 90% of branded drug sales from over 100 pharmaceutical companies, but because its methodology relies on public financial reports it does not include data for drugs marketed by privately held companies, which were not included in the top 250 analysis.

A Note of the Potential Change in the Number of New Drug Approvals

Our analysis does not include an estimate of expected, IRA-related changes in the number of annual new drugs approved by the FDA. There are several reasons we have not done so. First, the number of drugs approved in any given year is not a good proxy for improvements in public health. Second, as discussed in the article, the relationship between changes in R&D spending and the number of drugs developed is not fixed. Third, there have been estimates that between one-third and two-thirds of R&D spending is on the development of new indications or new formulations of previously approved drugs. It is unknown how the IRA might alter the share of a company's R&D spending dedicated to new drugs versus the continued development of existing drugs. Fourth, it is unclear what fraction of drugs being pursued is on the margin (i.e., would not be pursued because of an IRA-related NPV reduction). Finally, there is a non-trivial possibility that Medicare price negotiation results in an increase in the number of new drugs that do not add incremental value relative to what would been developed outside the IRA.

Several strategies have been suggested by which firms might avoid negotiation by advancing essentially identical compounds that qualify as distinct active moieties and to advance them on different timelines in different indications. Similarly, if some firms abandon the continued development of an existing drug because there is not enough value remaining post-price negotiation, other firms may seek to develop their own versions of very similar compounds for the undeveloped indications. Another possibility is that firms will repackage two or more existing drugs from individual doses into fixed dose combinations, which would also have the effect of restarting the negotiation clock. The net effect of these kinds of responses might be an increase in the number of new drugs and no increase in health outcomes.

Illustrative Small Molecule Prescription Drug Revenue Curves

We derived our small molecule revenue curves on an analysis of the revenue trajectories of new small molecule drugs approved by the FDA in 2010 published by Jefferies.[49] We selected a 10.5% discount rate to match the discount rate used in the development cost estimates by Grabowski et al and Wouters et al that we referenced later in our discussion.[50,51]

Analysis

We completed all analyses in Microsoft Excel version 16 and Stata version 17.

REFERENCES FOR SUPPLEMENTARY METHODS

[1] Rome BN, Nagar S, Egilman AC, Wang J, Feldman WB, Kesselheim AS. Simulated Medicare Drug Price Negotiation Under the Inflation Reduction Act of 2022. *JAMA Health Forum.* 2023;4(1):e225218.
[2] Dickson S, Hernandez I. Drugs Likely Subject to Medicare Negotiation, 2026-2028. Journal of Managed Care Specialty Pharmaceutical. 2023 Mar;29(3):229-235.
[3] Reitsma MB, Dusetzina SB, Ballreich JM, Trujillo AJ, Mello MM. Examining Opportunities to Increase Savings From Medicare Price Negotiations. *JAMA Internal Medicine.* Published online April 17, 2023.
[4] Centers for Medicare & Medicaid Services. Medicare Drug Price Negotiation Program: Initial Guidance, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments. March 15, 2023. Accessed April 10, 2023. https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf
[5] Centers for Medicare & Medicaid Services. Medicare Drug Price Negotiation Program: Revised Guidance, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments. June 30, 2023. Accessed July 1, 2023. https://www.cms.gov/files/document/revised-medicare-drug-price-negotiation-program-guidance-june-2023.pdf
[6] Inflation Reduction Act, Sec. 1192(d)(3)(B)
[7] Centers for Medicare and Medicaid Services. 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. March 15, 2023.
[8] U.S. Food and Drug Administration. Drugs@FDA: FDA-approved drugs. Accessed March 20, 2023. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm
[9] U.S. Food and Drug Administration. Online Label Repository. Accessed March 20, 2023. https://labels.fda.gov/
[10] U.S. Centers for Medicare and Medicaid Services. Medicare Part B spending by drug. Accessed March 20, 2023. https://data.cms.gov/summary-statistics-on-use-and-payments/medicare-medicaid-spending-by-drug/medicare-part-b-spending-by-drug
[11] U.S. Centers for Medicare and Medicaid Services. Medicare Part D spending by drug. Accessed March 20, 2023. https://data.cms.gov/summary-statistics-on-use-and-payments/medicare-medicaid-spending-by-drug/medicare-part-d-spending-by-drug
[12] https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Information-on-Prescription-Drugs
[13] U.S. Department of Labor CPI Inflation Calculator. Accessed March 20, 2023. https://www.bls.gov/data/inflation_calculator.htm
[14] Inflation Reduction Act, Sec. 1192(e)(1).
[15] Inflation Reduction Act, Sec. 1191(b)(3).
[16] U.S. Food and Drug Administration. Drugs@FDA: FDA-approved drugs. Accessed March 20, 2023. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm
[17] U.S. Food and Drug Administration Orange Book: Approved Drug Products With Therapeutic Equivalence Evaluations. Accessed March 20, 2023. https://www.accessdata.fda.gov/scripts/cder/ob/default.cfm.
[18] U.S. Food and Drug Administration. Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations. Accessed March 20, 2023. https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/purple-book-lists-licensed-biological-products-reference-product-exclusivity-and-biosimilarity-or.
[19] Centers for Medicare & Medicaid Services. Drug Products in the Medicaid Drug Rebate Program. Accessed April 12, 2021. https://data.medicaid.gov/dataset/0ad65fe5-3ad3-5d79-a3f9-7893ded7963a
[20] https://www.medicaid.gov/medicaid/prescription-drugs/state-drug-utilization-data/index.html

[21] 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.
[22] U.S. Food and Drug Administration. Search Orphan Drug Designations and Approvals. Accessed March 20, 2023. https://www.accessdata.fda.gov/scripts/opdlisting/oopd/
[23] U.S. Food and Drug Administration. Approved Blood Products. Accessed March 20, 2023. https://www.fda.gov/vaccines-blood-biologics/blood-blood-products/approved-blood-products
[24] U.S. Food and Drug Administration. Online Label Repository. Accessed March 20, 2023. https://labels.fda.gov/
[25] Inflation Reduction Act, Sec. 1192(a)(3) and 1192(d)(2).
[26] Inflation Reduction Act, Sec. 1192(f).
[27] Inflation Reduction Act, Sec. 1192(d)(3)(A).
[28] SSR Health. U.S. Brand Price Tool. Updated March 22, 2020. Accessed April 7, 2021. http://www.ssrhealth.com/us-brand-rx-net-price-tool.
[29] Hernandez I, San-Juan-Rodriguez A, Good CB, Gellad WF. Changes in List Prices, Net Prices, and Discounts for Branded Drugs in the US, 2007-2018. JAMA. 2020 Mar 3;323(9):854-862.
[30] Dusetzina SB, Bach PB. Prescription Drugs-List Price, Net Price, and the Rebate Caught in the Middle. JAMA. 2019 Apr 23;321(16):1563-1564.
[31] Kakani P, Chernew M, Chandra A. The Contribution of Price Growth to Pharmaceutical Revenue Growth in the United States: Evidence from Medicines Sold in Retail Pharmacies*. Journal of Health Politics, Policy, and Law.* 2022 December 1; 47 (6): 629–648.
[32] Duggan M, Morton FS. The Effect of Medicare Part D on Pharmaceutical Prices and Utilization. American Economic Review. 2010 Mar;100(1):590-607.
[33] Yeung K, Dusetzina SB, Basu A. Association of Branded Prescription Drug Rebate Size and Patient Out-of-Pocket Costs in a Nationally Representative Sample, 2007-2018. JAMA Network Open. 2021 Jun 1;4(6):e2113393.
[34] Ippolito BN, Levy JF. The Influence of Medicare Part D on the List Pricing of Brand Drugs. Health Services Research. 2023 Feb 3.
[35] Kakani P, Chernew M, Chandra A. The Contribution of Price Growth to Pharmaceutical Revenue Growth in the United States: Evidence from Medicines Sold in Retail Pharmacies. J Health Polit Policy Law. 2022 Dec 1;47(6):629-648.
[36] Kesselheim AS, Wang B, Franklin JM, Darrow JJ. Trends in utilization of FDA expedited drug development and approval programs, 1987-2014: cohort study. BMJ. 2015 Sep 23;351:h4633.
[37] IQVIA. National Sales Perspective (NSP) database. 2022. Proprietary data source. Accessed June 10, 2023.
[38] Feldman WB, Gagne JJ, Kesselheim AS. Trends in Medicare Part D Inhaler Spending: 2012-2018. Annals of the American Thoracic Society. 2021 Mar;18(3):548-550.
[39] Medicare Payment Advisory Committee, June 2023 Report to Congress. June 15, 2023.
[40] IQVIA. National Sales Perspective (NSP) database. 2022. Proprietary data source. Accessed June 10, 2023.
[41] IQVIA. National Sales Perspective (NSP) database. 2022. Proprietary data source. Accessed June 10, 2023.
[42] Feldman WB, Gagne JJ, Kesselheim AS. Trends in Medicare Part D Inhaler Spending: 2012-2018. Annals of the American Thoracic Society. 2021 Mar;18(3):548-550.
[43] Medicare Payment Advisory Committee, June 2023 Report to Congress. June 15, 2023.
[44] IQVIA. National Sales Perspective (NSP) database. 2022. Proprietary data source. Accessed June 10, 2023.
[45] Visible Alpha. Consensus Estimates for Investment Research. Proprietary data source. Accessed June 10, 2023. https://visiblealpha.com.
[46] IQVIA. National Sales Perspective (NSP) database. 2022. Proprietary data source. Accessed June 10, 2023.
[47] Feldman WB, Gagne JJ, Kesselheim AS. Trends in Medicare Part D Inhaler Spending: 2012-2018. Annals of the American Thoracic Society. 2021 Mar;18(3):548-550.
[48] Medicare Payment Advisory Committee, June 2023 Report to Congress. June 15, 2023.
[49] Jefferies. The Drug Pricing Handbook – Everything You Need to Know. September 15, 2022.
[50] DiMasi JA, Grabowski HG, Hansen RW. Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs. Journal of Health Economics. 2016 May;47:20-33.
[51] Wouters OJ, McKee M, Luyten J. Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018. JAMA. 2020 Mar 3;323(9):844-853.