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The impact of health technology made simple

IRA's Impact on the US Biopharma Ecosystem

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Executive Summary

- Vital Transformation (VT) modeled and estimated the impacts of the Inflation Reduction Act's (IRA) pricing provisions for a cohort of the top 200 Part B and D drugs by CMS spend, resulting in 92 drugs impacted by IRA in the next 10 years, which are produced, collectively, by 41 biopharmaceutical companies.
- Had the IRA been in place beginning in 2014, we estimate the reductions in revenue on the impacted drugs to be up to 40%. Because of this, between 24 and 49 therapies currently available today would most likely not have come to market and therefore not available for patients and their providers.
- Looking forward, we estimate that because of the IRA pricing provisions, the substantial reduction in revenue will significantly narrow investment opportunities. Conservatively, as many as 139 drugs over the next 10 years are at risk of not being developed at all.
- Both biologics and small molecule drugs are impacted, with an average reduction in revenue per therapy of $4.9 billion and $4 billion respectively.
- IRA provides a negotiation exemption for orphan drugs that treat only one rare disease. This disincentivizes investments in orphan drugs and areas of high unmet patient need as the broader indications will provide a superior return on investment, as much as $500 million over three years.
- Based on two impact scenarios, we estimate a loss of between 66,800 - 135,900 direct and 342,000 - 676,000 indirect jobs in the U.S. biopharma ecosystem.

Study Objectives:

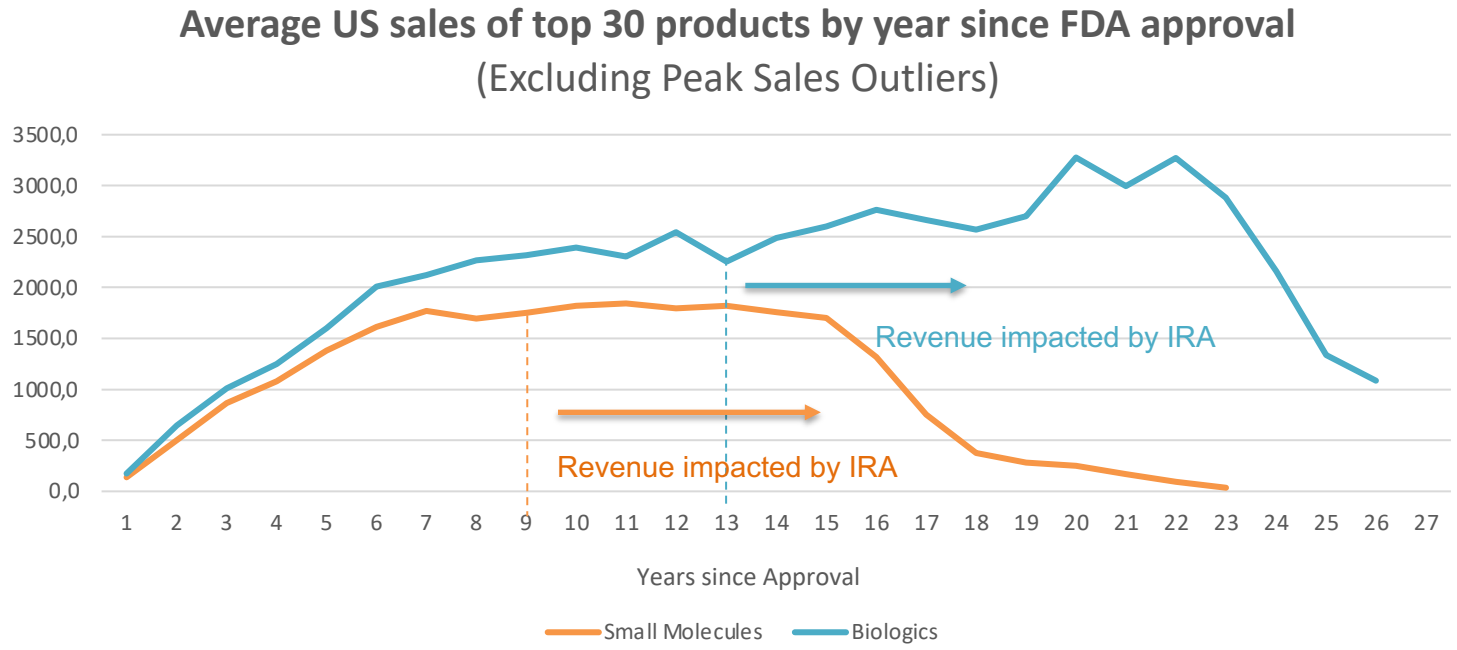
- Model the impact of the Inflation Reduction Act (IRA) on the biopharmaceutical industry:
  - We assume that the, “Maximum Fair Price”, or ceiling price, is a best-case scenario for the cohort of drugs price controlled each year.
  - We compare the projected global revenues from 2026 through 2035 at average market growth rates which are far below the current rate of inflation, to the revised revenues after the implementation of IRA.
  - All revenues are adjusted to 2023 USD (CPI-U).
  - We segment results by small molecules, biologics, indications, and orphan status.
- We model IRA’s impacts for the entire commercial market:
  - IRA states clearly that the “Maximum Fair Price”, or ceiling price, will be “announced”; there is no provision for “announced” price reductions to be confidential, inviting political pressures to apply reductions to commercial prices.
  - We assume a two year delay for the impacts of the IRA to impact commercial pricing.
- We calculated the impact of IRA on the investment ecosystem, drug development, and orphan therapies, jobs, and future patient access under the above scenarios.
  - We use a retrospective cohort analysis to determine the impacts of IRA at the asset level if the law had impacted firm level decisions from 2014.

Overview: Modeling the IRA

- Baseline US revenue and CMS spend per product from 2023 to 2040 were modeled by separating pre- and post-generic revenue profiles of the 30 largest selling products over 10 years.
- All values were adjusted to 2023 constant dollars.
- ‘Negotiated price" impacts begin in 2026 for single source small molecules and in 2028 for single source large molecules.
- We used SEC filings to determine the prevalence, by disease group, of those over 65 versus rest of population to assign revenues per drug as arising from either the commercial or Medicare market.
- For small molecules, the “negotiated ceiling price" was based upon the following criteria:
    - Short Monopoly: 9-11 years after approval, 75% of Non-Federal Average Manufacturers Price (non-FAMP),
    - Extended Monopoly: 12-15 years after approval, 65% of non-FAMP,
    - Long Monopoly: 16+ years, 40% of non-FAMP.
- For large molecules, the “negotiated ceiling price" was based upon the following criteria:
    - Short Monopoly: 13 -15 years after approval, 75% of Non-Federal Average Manufacturers Price (non-FAMP),
    - Extended Monopoly: 16-18 years after approval, 65% of non-FAMP,
    - Long Monopoly: 19+ years, 40% of non-FAMP.

IRA's Impact on Drug Discovery

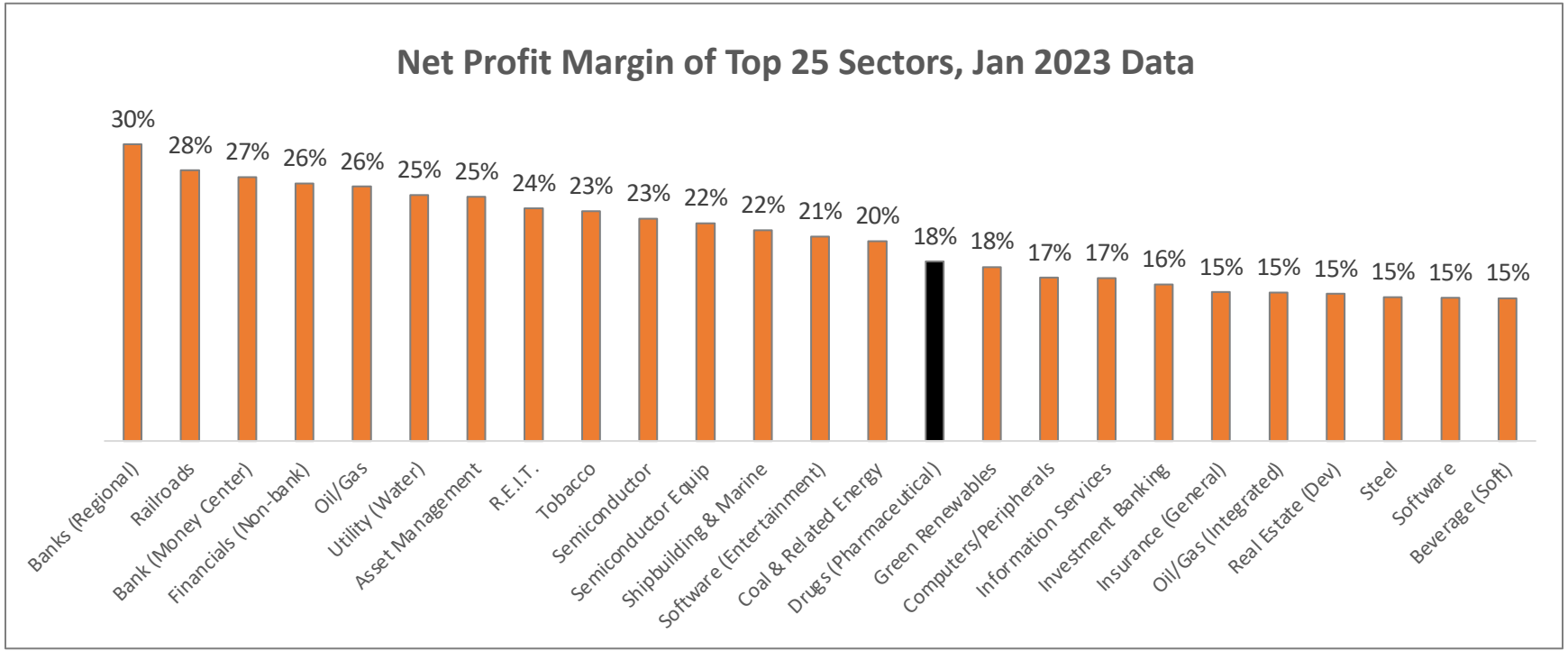
To estimate future revenues of drugs approved by FDA, we modeled the performance of the top selling 30 drugs over the last 10 years from market entry through to generic competition.



Arrows indicate where IRA will put revenues at risk for negotiation after years 9 & 13

Despite the political rhetoric, the Pharma sector is not overly profitable

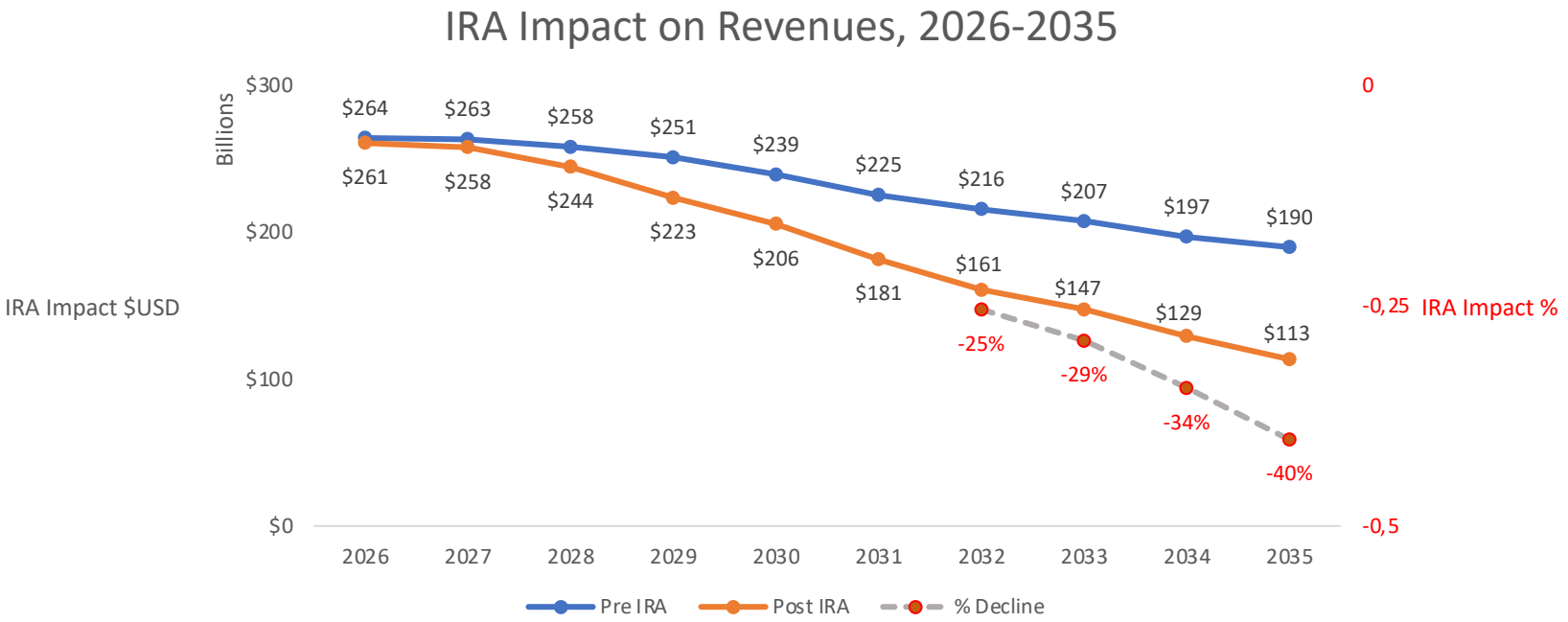
Biotechnology is excluded as it is ranked 92nd



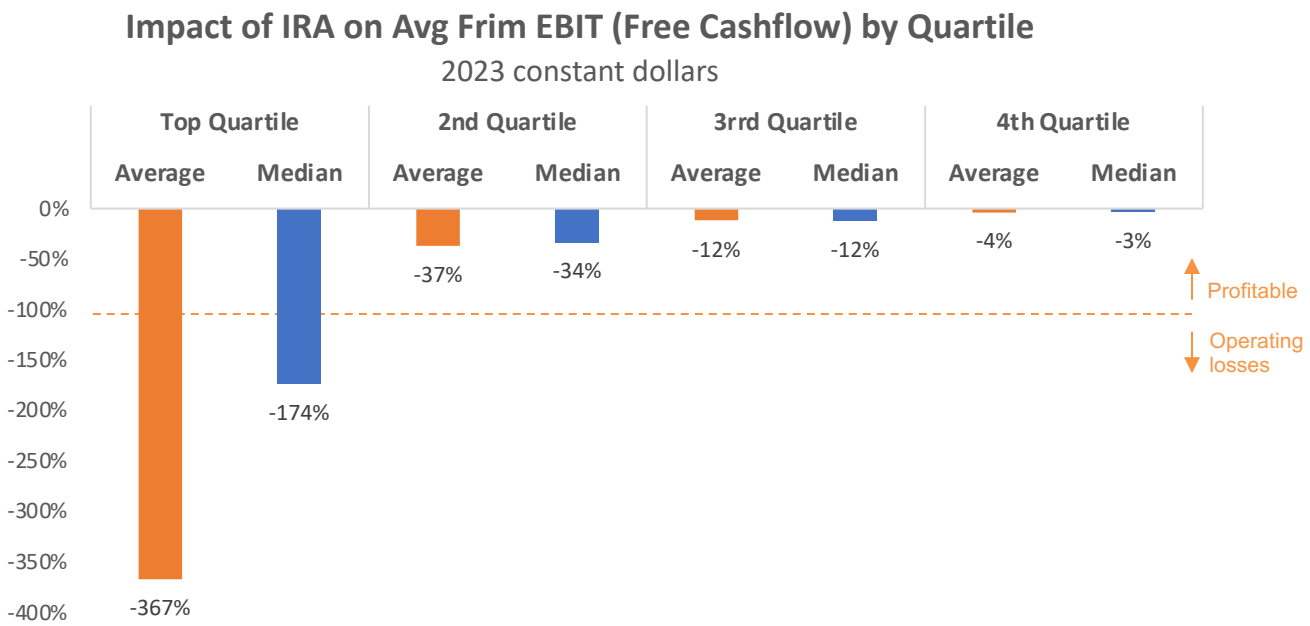
Source: https://pages.stern.nyu.edu/~adamodar/New_Home_Page/datafile/margin.html

IRA has a substantial impact on biopharma sector revenues

41 firms, 92 Therapies



IRA's impact on available cash for investments/pipelines 2026 - 2035



EBIT = earnings before interest expense and taxes, i.e., year end net cash available to a firm

- IRA reduces the ability of companies to reinvest their free cash flow into their future pipelines.
- Over the period from 2018-2022, the 25% most impacted companies see revenue reductions in annual earnings (EBIT) exceeding -350% .
- IRA primarily impacts the most successful and innovative therapies, which fund a majority of the R&D in the biopharma ecosystem.
- It's worth noting that even a 12% drop in EBIT will have substantial negative impacts at the firm level, requiring major cuts in personnel and operations..

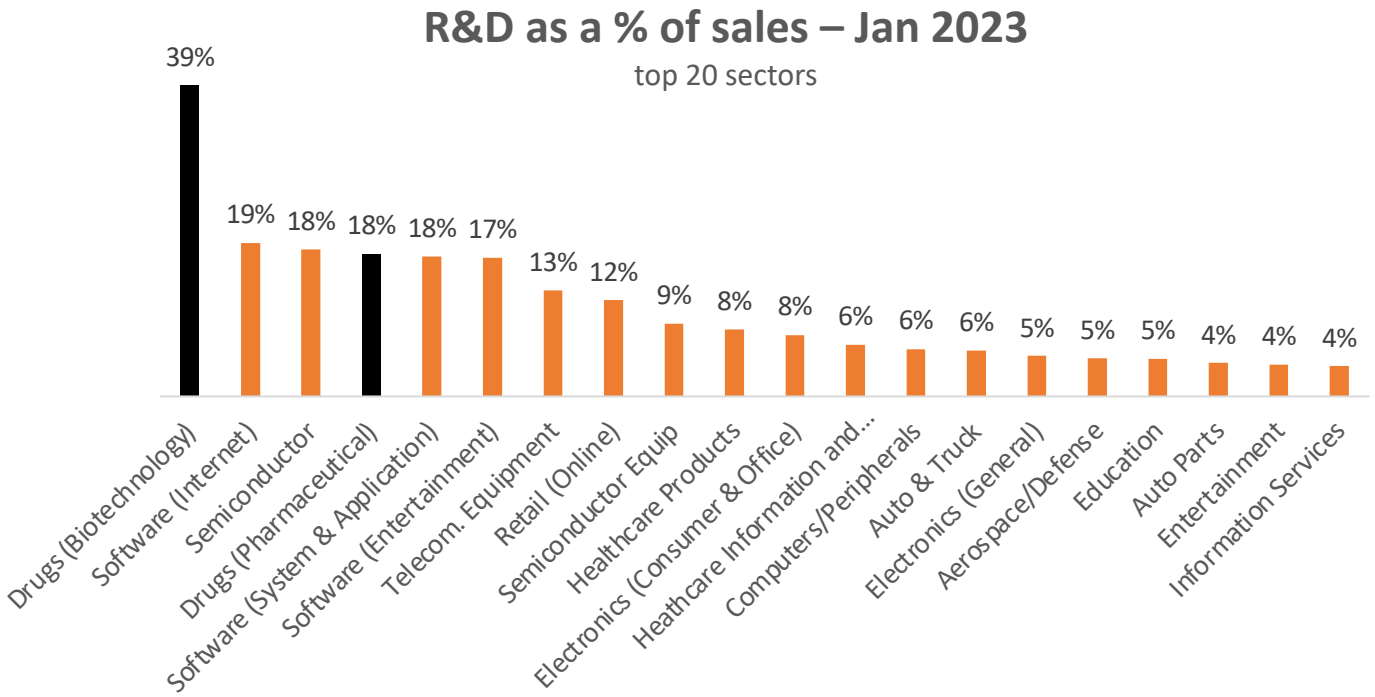
R&D programs will be cut when revenues are reduced under IRA

"The pharmaceutical industry invests 25% of total sales into R&D. . . what is a company going to do with less revenues? When Lipitor went off patent . . we closed research sites around the globe. Fewer researchers, and fewer research programs. Is this really what we want to do?"

John LaMattina, former President of Pfizer Global Research and Development, Forbes contributor.

Biopharma allocated, on average, 28% of revenues toward R&D in 2022

Biotech allocated 39%, Pharma allocated 18%



- The biopharma sector, on average, allocates 50% more of it's revenues to R&D than the next closest sector (Software and Internet companies).
- Given projected revenue reductions from IRA, we can model the subsequent impact on R&D spending assuming that 20%, 30%, or 40% of revenue is allocated to R&D.
- The impacts on R&D spending then allows one to determine the impact on drug development.

Source: https://pages.stern.nyu.edu/~adamodar/New_Home_Page/datafile/margin.html

Sources of the cost basis of our analysis

Research | Open Access | Published: 10 January 2019

Estimating the clinical cost of drug development for orphan versus non-orphan drugs

Kavisha Jayasundara, Aidan Hollis, Murray Krahn, Muhammad Mamdani, Jeffrey S. Hoch & Paul Grootendorst

Orphanet Journal of Rare Diseases **14**, Article number: 12 (2019) | Cite this article

28k Accesses | **48** Citations | **51** Altmetric | Metrics

Journal of Health Economics

Volume 47, May 2016, Pages 20-33

Innovation in the pharmaceutical industry: New estimates of R&D costs ☆

Joseph A. DiMasi [a], Henry G. Grabowski [b], Ronald W. Hansen [c]

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https://doi.org/10.1016/j.jhealeco.2016.01.012 Get rights and content

Impact of IRA Revenue Reductions on FDA Approvals

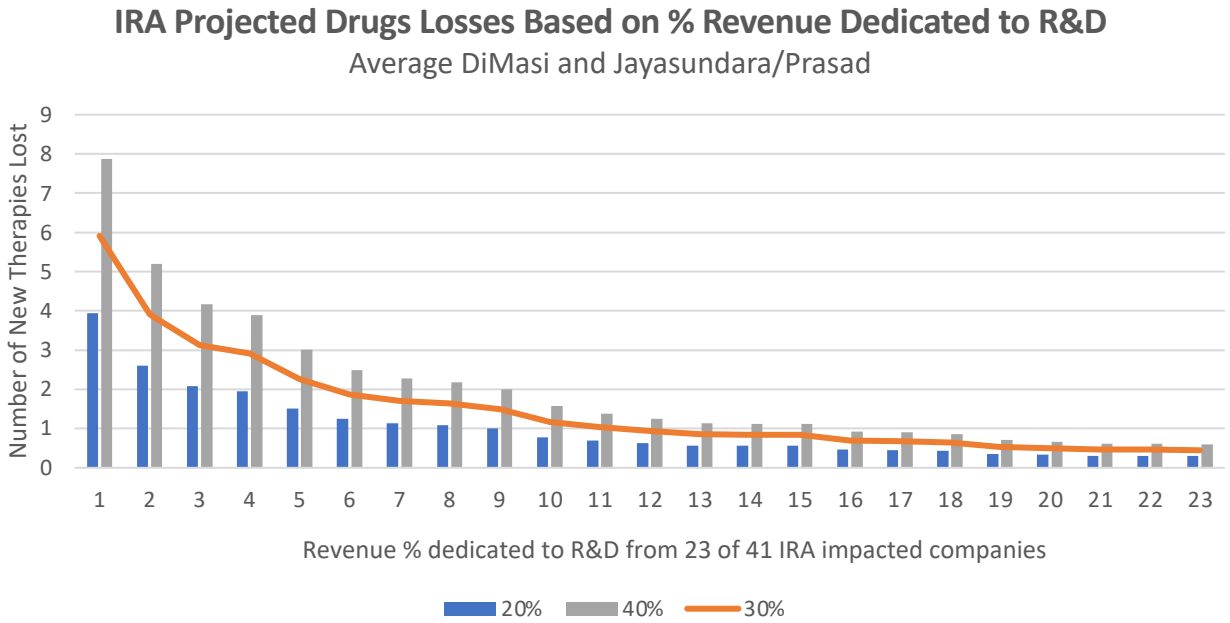
Cost Impact (USD 2022)	Drugs Lost by R&D Revenue Allocation 20%	30%	40%
DiMasi ($2 bil)	-16	-25	-33
Jayasundara/Prasad ($1 bil)	-32	-49	-65
Average	**-24**	**-37**	**-49**

- Using the risk weighted cash cost estimates of DiMasi and Jayasundara/Prasad for developing a new therapy, we can calculate the impact of IRA on our cohort of firms.

- Had the IRA been in place beginning in 2014, we estimate the reductions in revenue on the impacted drugs to be so large to the impacted firms that between 24 and 49 therapies currently available today would most likely not have come to market and therefore, not available for patients and their providers.

Projected losses of new FDA therapies per firm

On average, 23 firms would no longer develop 37 new medicines



- The revenue reductions for 23 of 41 firms in our cohort imply a loss of 37 new FDA approved therapies.
- The 41 firms in our cohort have 92 approved therapies impacted by IRA; a loss of 37 of their developed therapies represents 40% of their drug approvals in this cohort.
- IRA's potential impact on new drug development varies depending on sales volume and how close a therapy is to becoming generic.

IRA's Impact on Drug Discovery:
Our IRA model predicts a 40% reduction in FDA approvals

23 impacted firms, 2026 – 2035

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Indication	Current		Post IRA		# Lost	
	Non-Orphan	Orphan	Non-Orphan	Orphan	Non-Orphan	Orphan
Oncology	16	19	10	11	6	8
Autoimmune	5	4	3	2	2	2
Infectious Disease	6	3	4	2	2	1
Neurology	6	1	4	1	2	0
Endocrine	7		4		3	
Respiratory	5	1	3	1	2	0
Cardiovascular	3	2	2	1	1	1
Psychiatry	4		2		2	
Hematology	2	2	1	1	1	1
Ophthalmology	2	1	1	1	1	0
Gastroenterology	2		1		1	
Metabolic		1		1		0
Grand Total	**58**	**34**	**35**	**20**	**23**	**14**
Total	**92**		**55**		**37**	

IRA's Impact on Drug Discovery:
Over 10 years, IRA could lead to reductions of up to 139 new FDA approvals

41 impacted firms, 2026 – 2035

Number of Novel New FDA Approvals Per Year	Rate of IRA Losses	10 Year Losses of New Therapies
35	**40%**	**139**

- The challenge with any analysis of IRA is that we can only calculate its impacts upon a fixed CMS dataset at one point in time (2022).
- However, the FDA approves, on average, 35 new therapies per year.
- As new therapies will enter the CMS cohort each year, if we assume the current impact rates remain constant, all things being equal, we could see declines of up to 139 approvals over the next 10 years.

IRA Impact on Small Molecules and Biologics

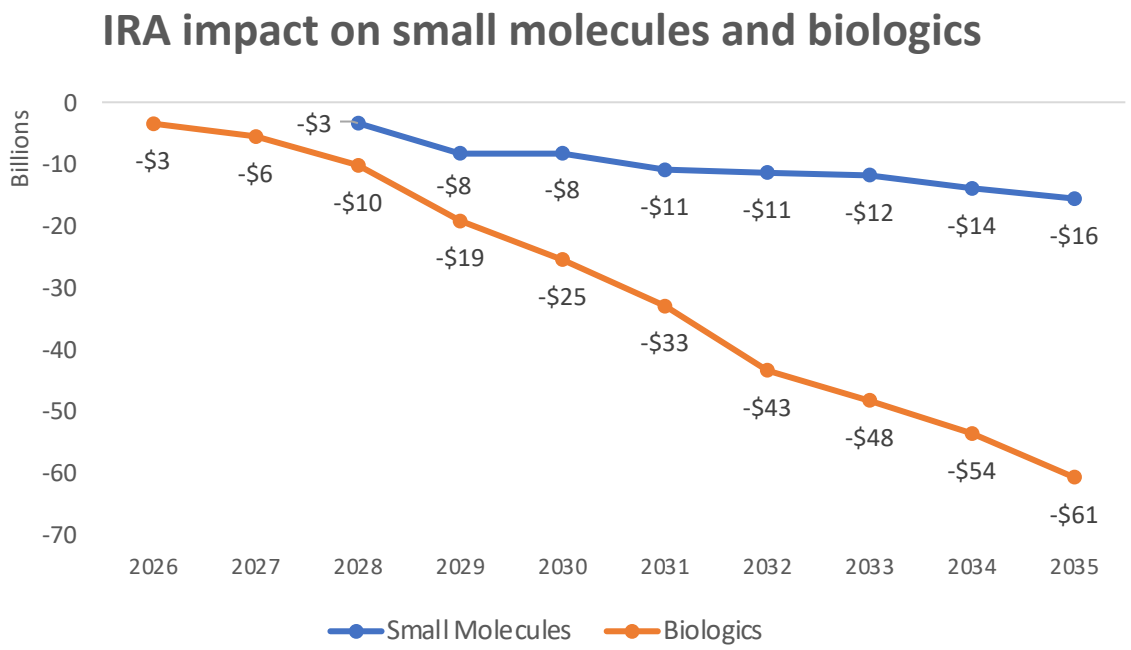
Average revenue declines by type of therapy under IRA

Type of Therapy	Number in Cohort	Average Reduction in revenue per therapy ($US billion)
Biologic	17	-$4.9 billion
Small Molecule	75	-$4 billion

- On average, the cost per use of an individual biologic therapy is slightly higher than the cost per use of a small molecule therapy.
- Although the number of individual biologics impacted by IRA is lesser than the number of individual small molecules, the average impact on each biologic therapy is larger when IRA is implemented.

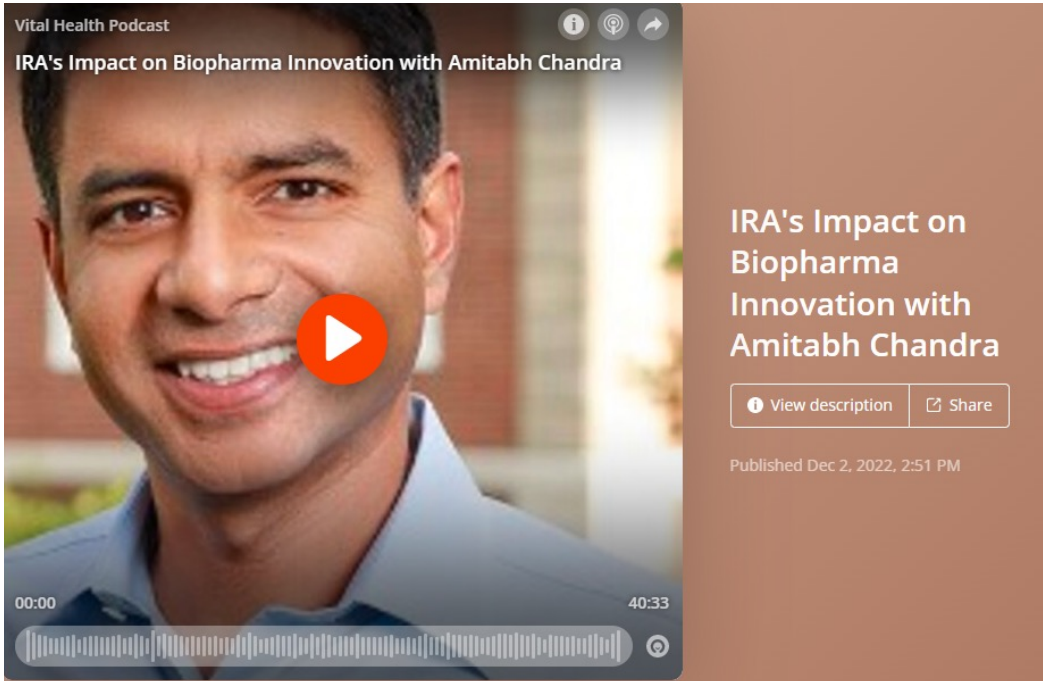
Average annual impact on revenue for the entire class of small molecules and biologics

($US bil)



While the impacts to both small molecule and biologics are significant, on average, the annual revenue loss on the entire class of small molecules is greater largely because there are more small molecules on the market and because Medicare negotiation begins 2 years earlier for small molecules.

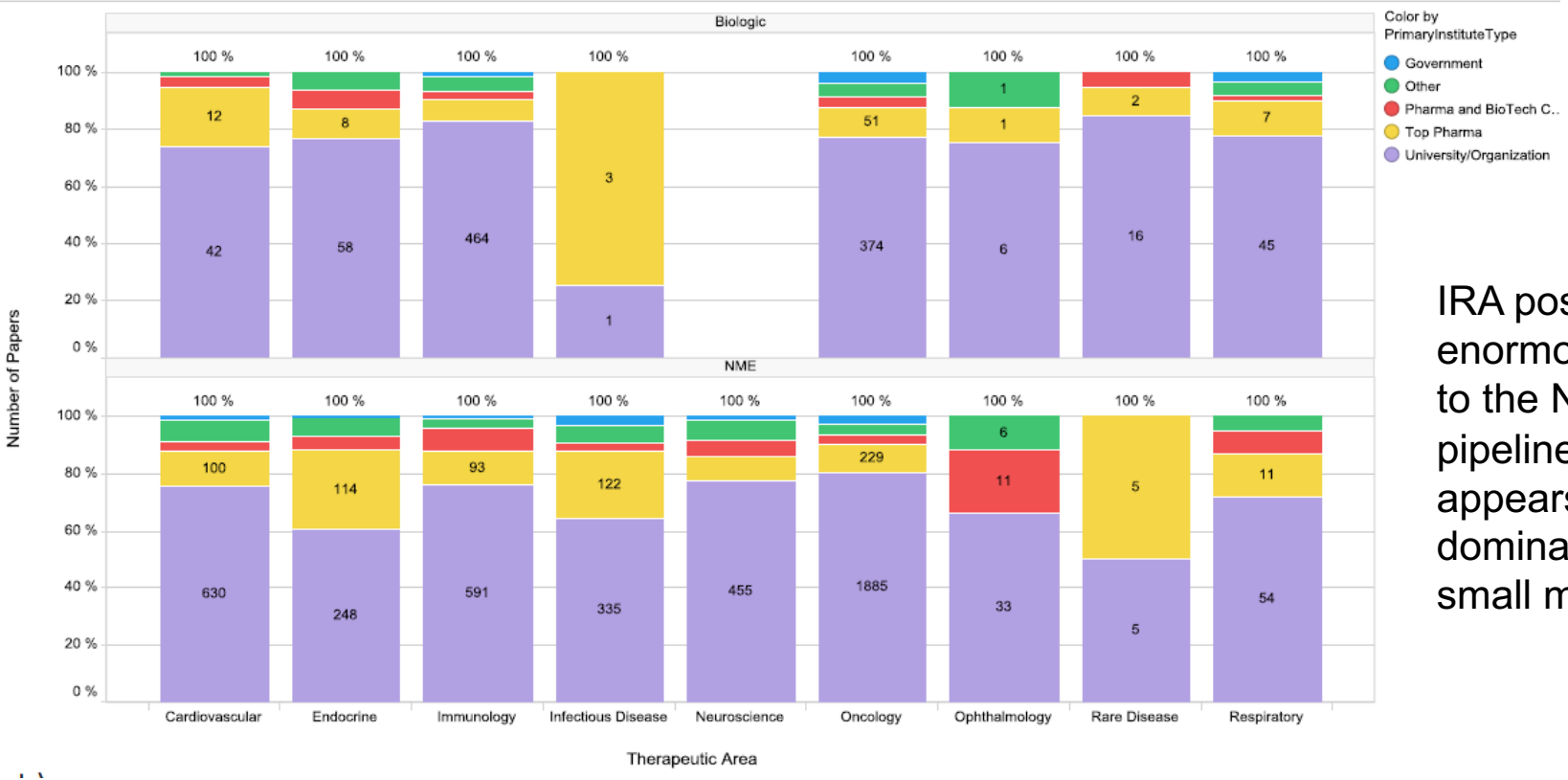
Small molecules eventually go generic and can be taken at home



"You want to encourage the small molecule drugs, they go generic…as a society, we want more small molecule drugs. So it's weird we're squeezing the small molecule manufacturers"

Amitabh Chandra, Director of Health Policy Research, Harvard Kennedy School of Government.

Groupings by first author/primary institute for papers published on approved drugs separated by therapeutic area (2006 – 2016)



IRA poses enormous risks to the Neurology pipeline which appears to be dominated by small molecules.

Source: "The impact of external innovation on new drug approvals: A retrospective Analysis," Xiong Liua et al, International Journal of Pharmaceutics, 564 (2019) 273-281

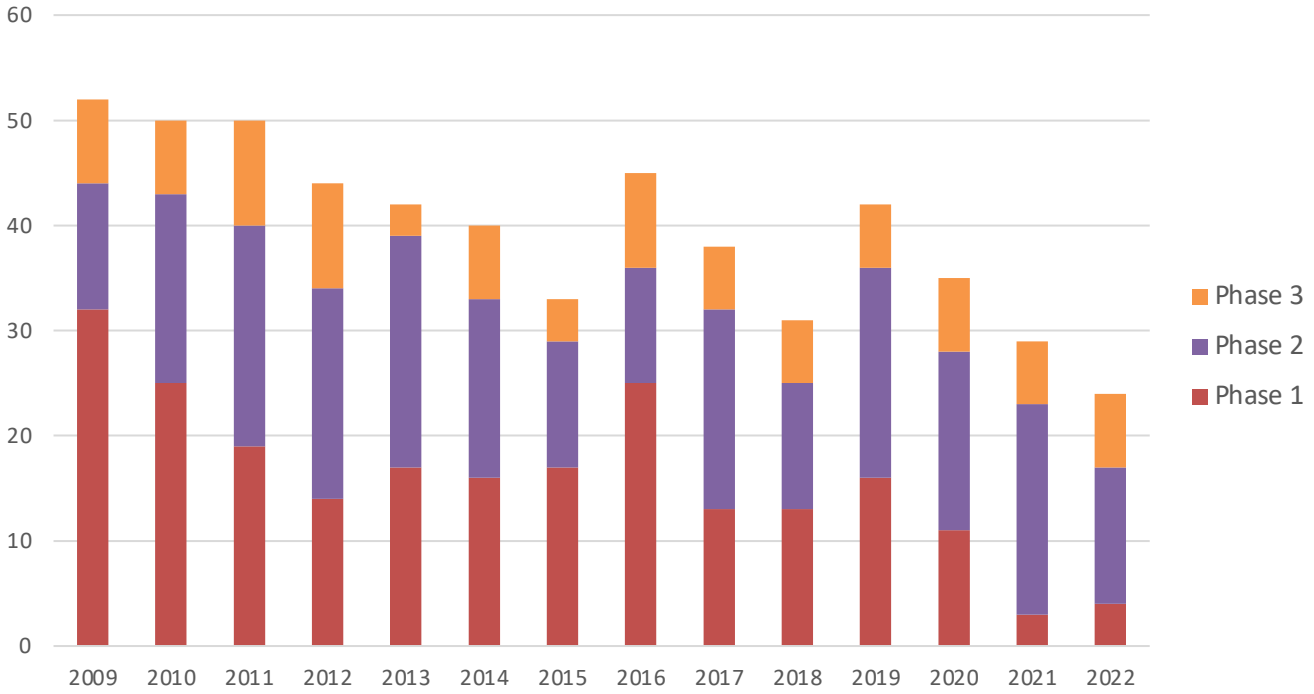
The IRA poses risks to Neuroscience (CNS) Research

CNS Program Portfolios in Large Pharma		
Company	**2009**	**2014**
Abbott/AbbVie	17	10
AstraZeneca	21	7
Bristol-Myers Squibb	12	2
GlaxoSmithKline	40	14
Johnson & Johnson	18	17
Lilly	16	9
Merck/Schering-Plough	32	7
Novartis	14	15
Pfizer/Wyeth	46	15
Roche/Genentech	22	21
Sanofi/Genzyme	29	12
Total Programs	**267**	**129**

- Biopharma companies have downsized their neuroscience research.
- IRA will likely accelerate the decline in neurological research particularly in small molecule therapies.

Neuron, Volume 84, Issue 3, Medicines for the Mind: Policy-Based "Pull" Incentives for Creating Breakthrough CNS Drugs; Dennis W. Choi, Robert Armitage, et al.; 2014, Pages 554-563; ISSN 0896-6273, https://doi.org/10.1016/j.neuron.2014.10.027. (https://www.sciencedirect.com/science/article/pii/S0896627314009477)

The number of Alzheimer's RCTs declined by 50% between 2009 and 2022



Source clinicaltrials.gov

Unintended Consequences - IRA's impact on orphan indications

IRA disincentivizes investments in additional orphan indications

Year	Initial Indication No IRA Impat	2nd indication 40 % Increase	2nd Indication w/ IRA Impact	IRA Impacts
Pre Clincial	-$450	-$450	-$450	100%
1	$60	$60	$60	100%
2	$120	$120	$120	100%
3	$180	$180	$180	100%
4	$200	$150	$150	100%
5	$300	$250	$250	100%
6	$400	**$510**	**$510**	100%
7	$550	$770	$770	100%
8	$700	$980	$980	100%
9	$840	$1,176	$882	**75%**
10	$941	$1,317	$988	**75%**
11	$1,054	$1,475	$1,106	**75%**
12	$1,180	$1,652	$1,074	**65%**
13	$1,180	$1,652	$1,074	**65%**
14	$1,121	$1,570	$1,020	**65%**
15	$1,065	$1,491	$969	**65%**
16	$1,012	$1,417	$567	**40%**
17	$961	$1,346	$538	**40%**
NPV	**$3,421**	**$4,646**	**$3,421**	

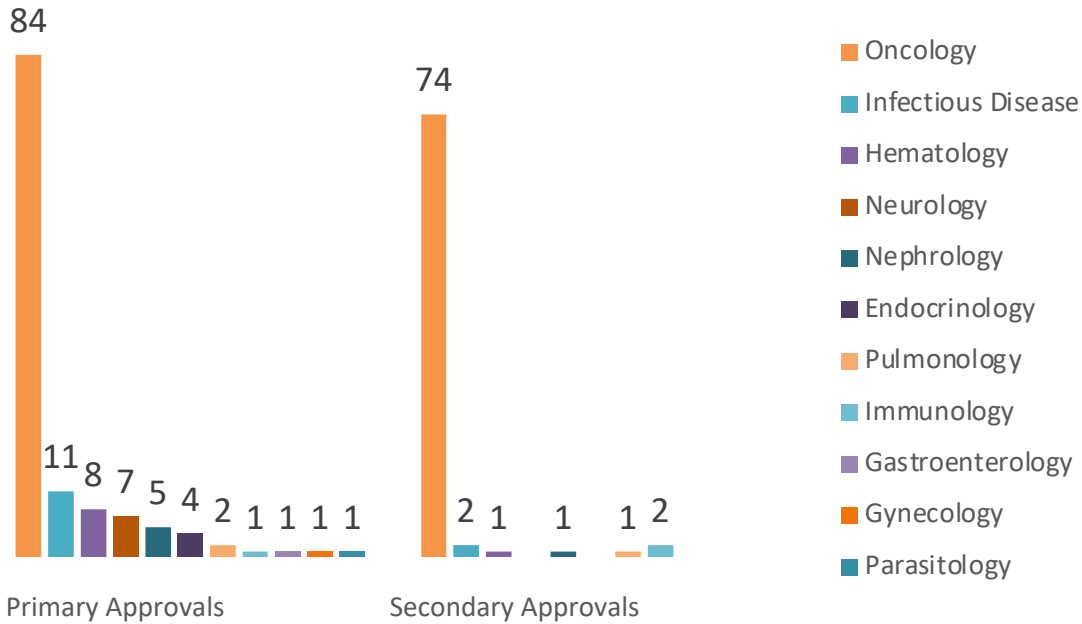
$US Mil, 10% cost of capital, 2023 constant dollars

- IRA allows an exemption from negotiation for drugs only commercialized for a single indication and orphan therapies.
- Genetic based orphan therapies are limited in their ability to target additional indications, IRA may cause companies to question if the revenue penalties are worth the risk of investing in a 2nd indication.
- Our model (left), demonstrates that adding an indication does increase revenues by 40% starting in year 6, however, it will be impacted by IRA, therefore it generates the same NPV as not adding an indication at all.
- Our model assumes that the extra label required an investment of $50 mil a year for three years ($150 mil total) to fulfil in years 4 – 6.

IRA's Impact on Orphan Dugs Including Oncology

N=206 (oncology = 158, non-oncology = 48)

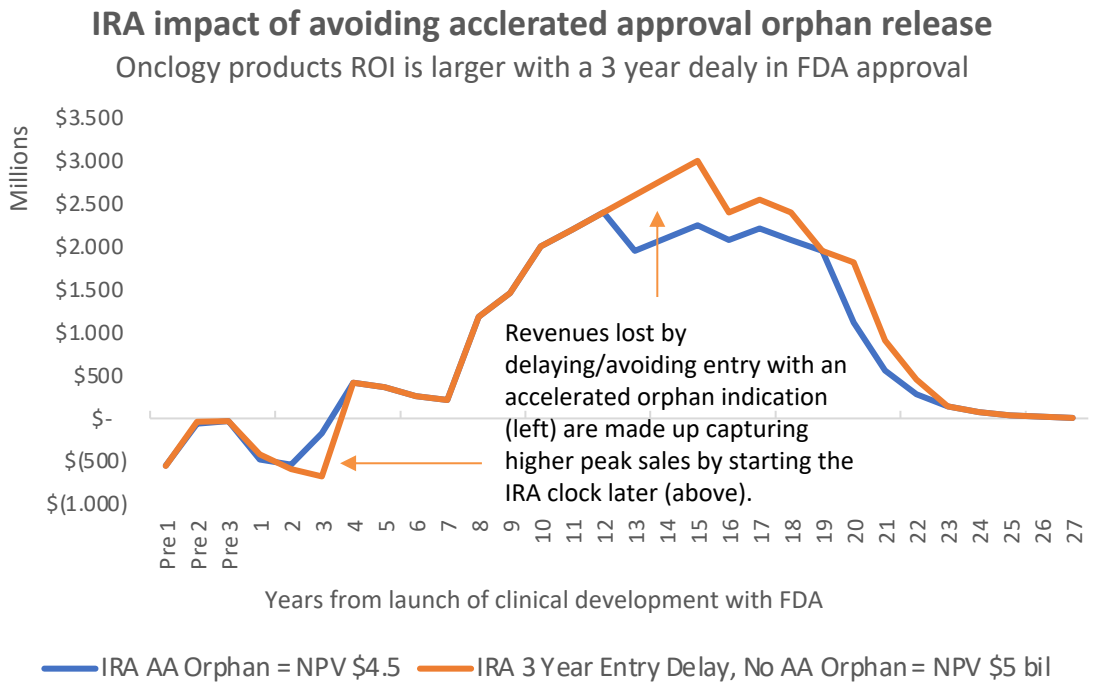
Accelerated Approvals by Primary and Secondary Indications, 2001 – 2021



- From 2001 -2021, 160 of 206 accelerated approvals were for orphan oncology therapies, 78% of the cohort.
- The accelerated approval of orphan oncology products is considered an enormous success of the US innovation and regulatory ecosystems.
- IRA puts the current approach at risk.

IRA penalizes accelerated orphan oncology indications

The preferred approach to oncology approvals is disincentivized to the detriment of patients



$US Mil, 10% cost of capital, 2023 constant dollars

- Entering the market with an orphan approval creates a ‘penalty’ due to IRA’s impact upon peak sales; the IRA clock starts ticking when you have your first approval.
- The model on the left shows that delaying market entry by three years, and focusing on a non-orphan indication at launch, improves the NPV by $500 mil $USD.
- Leading with an accelerated oncology indication to de-risk R&D appears to be a far less favorable strategy under IRA; this may require a radical shift in biopharma’s current go-to market paradigm.

IRA’s impact on Jobs

IRA Direct and Total Supported Annual Job Losses by Avg Cohort Impact

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Total US and Puerto Rico by State/District/Region

Jobs Impact: 2026 - 2035 $38.7 Billion Avg Annual Revenue Reductions (Cohort)							
State	Direct Biopharma Jobs Impact	Total Biopharma Supported Jobs Impact	Biopharma Supported Output Impact ($M)	State (Cont)	Direct Biopharma Jobs Impact (Cont)	Total Biopharma Supported Jobs Impact (Cont)	Biopharma Supported Output Impact ($M)
Totals, U.S. & Puerto Rico	**-68,874**	**-342,944**	**($97,603)**				
California	-11,857	-64,511	($19,564)	South Carolina	-436	-2096	($579)
New Jersey	-5,155	-25,919	($7,085)	Maine	-386	-1964	($438)
Massachusetts	-5,157	-24,144	($6,020)	West Virginia	-398	-1928	($640)
Pennsylvania	-3,976	-21,556	($5,715)	Iowa	-475	-1852	($501)
North Carolina	-3,818	-21,316	($6,323)	Kentucky	-449	-1631	($373)
Illinois	-3,461	-20,951	($6,198)	Oregon	-355	-1469	($327)
New York	-4,684	-19,599	($5,698)	Delaware	-422	-1458	($324)
Texas	-3,230	-16,664	($4,568)	Nebraska	-265	-1243	($352)
Indiana	-2,094	-11,883	($4,723)	Alabama	-298	-1222	($343)
Florida	-2,187	-11,115	($2,465)	Rhode Island	-164	-1125	($310)
Maryland	-2,594	-11,020	($2,871)	New Mexico	-303	-1060	($222)
Ohio	-1,774	-7,711	($1,874)	New Hampshire	-204	-954	($230)
Michigan	-1,357	-7,343	($1,935)	Oklahoma	-235	-924	($217)
Puerto Rico	-1,520	-6,623	($4,894)	Nevada	-182	-839	($203)
Utah	-1,047	-6,217	($1,470)	Louisiana	-233	-792	($179)
Missouri	-1,042	-5,609	($1,371)	Mississippi	-153	-680	($192)
Washington	-1,307	-4,841	($1,145)	Vermont	-98	-398	($96)
Georgia	-986	-4,839	($1,134)	Idaho	-80	-328	($77)
Wisconsin	-928	-4,375	($1,022)	Arkansas	-70	-325	($86)
Tennessee	-1,031	-3,943	($887)	Montana	-72	-239	($49)
Colorado	-732	-3,883	($953)	Hawaii	-77	-220	($41)
Arizona	-714	-3,526	($776)	DC	-54	-126	($37)
Virginia	-824	-3,449	($841)	Wyoming	-26	-93	($33)
Minnesota	-645	-3,406	($831)	South Dakota	-27	-84	($15)
Connecticut	-761	-3,009	($765)	North Dakota	-24	-69	($18)
Kansas	-493	-2,343	($587)	Alaska	-14	-30	($6)

Source: TEConomy analysis; IMPLAN U.S. 2017 Model, VT adjusted for average annual reduction of IRA cohort revenue, 2023 constant dollars.

IRA Direct and Total Supported Annual Job Losses by Peak Year Sales Impact

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Total US and Puerto Rico by State/District/Region

Jobs Impact: 2026 - 2035 $76.3 Billion Avg Annual Revenue Reductions (Peak Sales Projection)							
State	Direct Biopharma Jobs Impact	Total Biopharma Supported Jobs Impact	Biopharma Supported Output Impact ($M)	State (Cont)	Direct Biopharma Jobs Impact (Cont)	Total Biopharma Supported Jobs Impact (Cont)	Biopharma Supported Output Impact ($M)
Totals, U.S. & Puerto Rico	**-135,948**	**-676,928**	**($192,656)**				
California	-23,405	-127,337	($38,617)	South Carolina	-861	-4137	($1,143)
New Jersey	-10,176	-51,161	($13,984)	Maine	-761	-3877	($865)
Massachusetts	-10,180	-47,658	($11,882)	West Virginia	-785	-3807	($1,263)
Pennsylvania	-7,849	-42,550	($11,280)	Iowa	-937	-3656	($988)
North Carolina	-7,537	-42,076	($12,480)	Kentucky	-886	-3219	($736)
Illinois	-6,832	-41,355	($12,234)	Oregon	-701	-2900	($646)
New York	-9,245	-38,686	($11,247)	Delaware	-832	-2879	($640)
Texas	-6,375	-32,892	($9,017)	Nebraska	-523	-2453	($696)
Indiana	-4,133	-23,455	($9,322)	Alabama	-588	-2411	($677)
Florida	-4,317	-21,939	($4,865)	Rhode Island	-323	-2221	($612)
Maryland	-5,120	-21,752	($5,667)	New Mexico	-599	-2093	($438)
Ohio	-3,502	-15,220	($3,698)	New Hampshire	-403	-1882	($454)
Michigan	-2,678	-14,495	($3,819)	Oklahoma	-464	-1825	($429)
Puerto Rico	-3,000	-13,073	($9,661)	Nevada	-359	-1656	($401)
Utah	-2,066	-12,272	($2,902)	Louisiana	-461	-1562	($353)
Missouri	-2,056	-11,071	($2,706)	Mississippi	-302	-1342	($380)
Washington	-2,581	-9,556	($2,261)	Vermont	-194	-786	($189)
Georgia	-1,946	-9,551	($2,237)	Idaho	-157	-648	($152)
Wisconsin	-1,832	-8,635	($2,017)	Arkansas	-138	-641	($170)
Tennessee	-2,035	-7,782	($1,751)	Montana	-142	-472	($96)
Colorado	-1,445	-7,665	($1,880)	Hawaii	-151	-433	($81)
Arizona	-1,409	-6,961	($1,532)	DC	-107	-249	($73)
Virginia	-1,626	-6,807	($1,659)	Wyoming	-51	-183	($66)
Minnesota	-1,274	-6,723	($1,640)	South Dakota	-54	-165	($30)
Connecticut	-1,502	-5,939	($1,511)	North Dakota	-47	-136	($35)
Kansas	-973	-4,624	($1,159)	Alaska	-27	-60	($12)

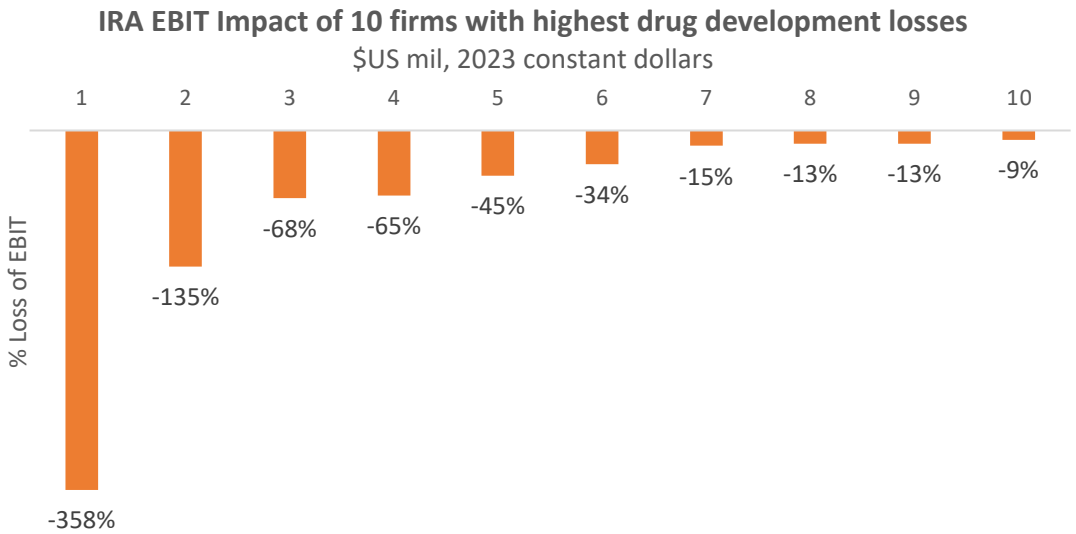
Source: TEConomy analysis; IMPLAN U.S. 2017 Model, VT adjusted for projected reductions in peak sales, 2023 constant dollars.

IRA’s impact on Investments in US start-ups by state

IRA's impact on Investments in US start-ups by state

Calculating the impact of cash flow - 10 IRA firms

Avg Annual EBIT	Ave Annual EBIT Loss from IRA by Firm	% Loss EBIT
$10,242	($3,103)	-30%



- The 10 firms which we project to be most likely to lose new approved therapies due to IRA see an average annual loss of free cash flow by 30%.
- We now investigate the firm's investing behavior over the previous 10 years to see how their partnering activities would have been reduced if the IRA been in place.

State investments by 10 IRA impacted firms with the most projected lost therapies

4/1/2014 - 3/31/2023

State	Total Deal Value Per State	Number of Deals
California	$27,927,600,000	44
Massachusetts	$21,178,500,000	44
New York	$14,894,999,990	7
Washington	$2,385,000,000	4
North Carolina	$1,888,000,000	2
Maryland	$1,380,000,000	4
New Jersey	$625,000,000	3
Virginia	$500,000,000	1
Wisconsin	$456,500,000	1
Illinois	$420,000,000	2
Connecticut	$342,500,000	1
Delaware	$245,000,000	1
Pennsylvania	$170,000,000	1
Iowa	$20,000,000	1
Nevada	$19,500,000	1
Totals	**$72,452,599,990**	**117**

- Our 10 firm cohort invested $72.4 billion in partnerships in roughly 117 deals, an average of $619 million per deal.
- IRA reduces the available capital in these firms by 30%, which will impact deal selection.

Projected lost investments by 10 IRA impacted firms with a 30% reduction in EBIT in CA

4/1/2014 - 3/31/2023

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California Lost Investments 4/1/2014 - 3/31/2023			
Indication	**Investments by Indication**	**Indication**	**Loses by Indication**
Hemophilia	$3,560,000,000	DLBCL	$1,205,000,000
Solid Tumors	$3,544,766,667	Chronic Myelogenous Leukemia (CML)	$1,205,000,000
Amyloidosis	$3,385,000,000	Rheumatoid Arthritis (RA)	$1,170,000,000
Cancer	$3,355,000,000	Non-Alcoholic Steatohepatitis (NASH)	$1,035,000,000
Inflammatory Disorders	$2,625,000,000	Alzheimer's Disease (AD)	$1,007,500,000
Crohn's Disease	$1,390,000,000	Alpha-1 Deficiency (A1AD or AATD)	$740,000,000
Ulcerative Colitis (UC)	$1,390,000,000	NSCLC	$603,666,667
		Anemia Due to Chronic Kidney Disease	$492,000,000
		Pancreatic Cancer	$480,000,000
		Multiple Myeloma (MM)	$280,000,000
		Thyroid Cancer	$228,000,000
		Colorectal Cancer (CRC)	$166,666,667
		Hypercholesterolemia	$55,000,000
		Dry AMD	$10,000,000
		IRA EBIT Impact - 30% loss of investments	**-$8,378,280,000**

We base our selection of indications by cumulative investment size as a proxy for demand

Projected lost investments by 10 IRA impacted firms with a 30% reduction in EBIT in MA

4/1/2014 - 3/31/2023

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Massachusetts Lost Investments 4/1/2014 - 3/31/2023			
Indication	**Investments by Indication**	**Indication**	**Loses by Indication**
Muscular Dystrophy	$5,190,000,000	Sickle Cell Anemia	$1,977,500,000
Solid Tumors	$2,492,500,000	Hypercholesterolemia	$980,000,000
Cystic Fibrosis (CF)	$2,357,500,000	Epstein Barr Virus (EBV)	$872,500,000
Asthma	$2,100,000,000	Hematologic Cancer	$608,000,000
Cancer	$2,000,000,000	Inflammatory Disorders	$270,000,000
Psoriasis	$2,000,000,000	Hereditary Angioedema (HAE)	$195,500,000
		Crohn's Disease	$100,000,000
		Pulmonary Fibrosis	$25,000,000
		Chronic Pain	$10,000,000
		IRA EBIT Impact - 30% loss of investments	**-$6,353,550,000**

We base our selection of indications by cumulative investment size as a proxy for demand

Projected lost investments by 10 IRA impacted firms with a 30% reduction in EBIT in NY, WA

4/1/2014 - 3/31/2023

NY, WA Lost Investments 4/1/2014 - 3/31/2023					
State	**Indication**	**Investments by Indication**	**State**	**Indication**	**Loses by Indication**
NY	Psoriasis	$13,400,000,000	WA	Breast Cancer	$1,125,000,000
			WA	Systemic Lupus Erythematosus (SLE)	$730,000,000
			NY	Seizure Disorders (Epilepsy)	$660,000,000
			NY	Melanoma	$625,000,000
			WA	Cancer	$530,000,000
			NY	Undisclosed	$170,000,000
			NY	DLBCL	$39,999,990
			IRA EBIT Impact - 30% loss of investments		**-$5,183,999,997**

We base our selection of indications by cumulative investment size as a proxy for demand

Projected lost investments by 10 IRA impacted firms with a 30% reduction in EBIT in MD, NC, VA, NJ, WI, IL, CT, DE, PA, IA, NV

4/1/2014 - 3/31/2023

MD, NC, VA, NJ, WI, IL, CT, DE, PA, IA, NV - Lost Investments 4/1/2014 - 3/31/2023					
State	**Indication**	**Investments by Indication**	**State**	**Indication**	**Loses by Indication**
MD	Wet AMD	$1,380,000,000	WI	Cancer	$456,500,000
NC	Cystic Fibrosis (CF)	$1,090,000,000	IL	Celiac Disease	$420,000,000
NC	Antibacterial	$798,000,000	CT	Solid Tumors	$342,500,000
VA	Inflammatory Disorders	$500,000,000	DE	Desmoid Tumors	$245,000,000
NJ	Solid Tumors	$475,000,000	PA	Retinal Dystrophy	$170,000,000
			NJ	Celiac Disease	$150,000,000
			IA	Ebola	$20,000,000
			NV	Melanoma	$19,500,000
			IRA EBIT Impact - 30% loss of investments		**-$1,819,950,000**

We base our selection of indications by cumulative investment size as a proxy for demand

US disease prevalence of therapies in our cohort we project will no longer receive investments

Analysis of investing activity before IRA implementation, if 21% of free cash flow was lost by firms: 4/1/2014 - 3/31/2023

Indication	Disease Prevelance	Indication (cont)	Disease Prevelance (cont)
Epstein Barr Virus (EBV)	297,000,000	Colorectal Cancer (CRC)	1,369,005
Chronic Pain	50,200,000	Melanoma	1,361,282
Non-Alcoholic Steatohepatitis (NASH)	39,600,000	Thyroid Cancer	915,664
Chronic Kidney Disease	37,000,000	NSCLC	576,924
Rheumatoid Arthritis (RA)	32,500,000	Systemic Lupus Erythematosus (SLE)	345,000
Hypercholesterolemia	28,000,000	Retinal Dystrophy	184,048
Dry AMD	18,340,000	Multiple Myeloma (MM)	144,922
Solid Tumors	18,200,000	DLBCL	143,000
Alzheimer's Disease (AD)	6,700,000	Alpha-1 Antitrypsin Deficiency (A1AD or AATD)	100,000
Breast Cancer	3,771,794	Pulmonary Fibrosis	100,000
Epilepsy	3,400,000	Sickle Cell Anemia	100,000
Crohn's Disease	3,000,000	Pancreatic Cancer	89,248
Desmoid Tumors	3,000,000	Chronic Myelogenous Leukemia (CML)	62,895
Celiac Disease	2,481,203	Hereditary Angioedema (HAE)	6,000
Hematologic Cancer	1,650,000	Ebola	11

Conclusions

Implications of IRA

Conclusions and Implications of IRA

- IRA reduces net earnings for a 41 company cohort, but these impacts are highly concentrated in only 10 firms.
- As measured by EBIT (annual net earning):
  - The IRA induced revenue reductions exceed 350% of the annual earnings for 25% of the 41 companies in our cohort.
  - The IRA penalizes the most innovative, successful therapies which fund an outsized amount of research.
  - The IRA penalizes successful biopharma companies.
- The IRA's orphan drug carve-outs appear to have large unintended consequences for assets with limited ability to seek secondary indications – according to our modeling, any extra indication must produce at minimum 40% more revenue to offset the losses created by IRA.
- IRA may act as a disincentive to the current strategy in oncology of launching with an orphan indication to de-risk R&D – this will require a major paradigm shift for the industry, negatively impacting patients requiring new effective late-stage oncology treatments.
- We model a loss of U.S. jobs between loss of between 66,800 - 135,900 direct and 342,000 - 676,000 in the U.S. biopharma ecosystem. 252,000 and 365,000 based upon two impact scenarios.

Disclosure

- Vital Transformation, an international health economics and strategy consultancy, was asked to conduct an analysis of the impact of price controls as proposed in IRA, on the biopharmaceutical innovation ecosystem.
- We investigated IRA's impacts on investments and small company capital formation.
- Our focus was new drug pipeline developments in orphan, small molecule, and biological products.
- The opinions included in this work are those of Vital Transformation LLC, and not necessarily those of the project's sponsors.
- The analysis was performed by Vital Transformation's Consulting Economist Dr Harry Bowen, Research Manager Dr Daniel Gassull, and CEO Duane Schulthess.
- This study was funded by the Biotechnology Innovation Organization, BIO.
- The raw data behind this study is available by request.