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The Impact of The House Proposed IRA Expansion on the US Biopharma Ecosystem

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Executive Summary

- Vital Transformation (VT) modeled the impacts of the drug pricing provisions of the Inflation Reduction Act, with the expansions proposed by Representative Frank Pallone, Jr. (NJ-06) called the, "H.R. 4895: Lowering Drug Costs for American Families Act", which would impose government price setting for up to **50 selected Medicare Drugs** starting in 2029 and expand those negotiated prices to the commercial market.
- We modeled the impacts on industry revenues, future R&D investments for the Medicare aged population, and lost innovation including industry jobs.
- We estimate a loss of 136,000 – 216,000 direct biopharmaceutical industry jobs and 678,000 – 1,076,000 indirect jobs across the U.S. economy if the House Bill, H.R. 4895, were to be implemented.
- We estimate that the expanded government price setting could result in roughly 134 fewer FDA approvals of new medicines treating primarily the Medicare aged population over a ten-year period:
    - Impacts will be felt most heavily in many areas of unmet need, including in rare disease, oncology, neurology, and infectious disease targeting those over 65 years of age.
    - H.R. 4895 impacts the entire commercial market at the point of negotiated prices entering Medicare..
    - The most significant ecosystem impacts would be concentrated primarily in CA and MA.
- Had the drug pricing provisions of the House Bill H.R. 4895 been in place prior to the development of today's top-selling medicines, we estimate that 76 of the 198 therapies we identified as selected for Medicare price setting would likely have not been developed.

Changes & refinements to our first IRA models

- Given the introduction of CMS' first 10 drugs to be negotiated:
  - We now assume that the point of "applicability" for generic competition as stated in the IRA law is now moved back to the point of negotiation as per CMS guidance, not at market entry of the negotiated product as was implied by the actual legislation.
  - We include all insulin products, regardless if their baseline cost-sharing is now mandated to be capped at $35.
  - Given the lack of clarity regarding the impact of new mandates requiring vaccine coverage without cost sharing for all adults in Medicare Part D, we've opted to exclude vaccines in this analysis.
- CMS' 2021 Medicare Parts B & D dashboards have been projected forward to 2022, based upon corporate audited and reported sales of all CMS eligible products.
- Given the inclusion of therapies that were assumed in previous models to be excluded due to their going generic at 'the point of applicability', our cohort of negotiation eligible products has expanded from 216 in our previous Smart Pricing Study, to 346 in the House Bill.

Overview: Modeling the House Bill's IRA Expansion (1/2)

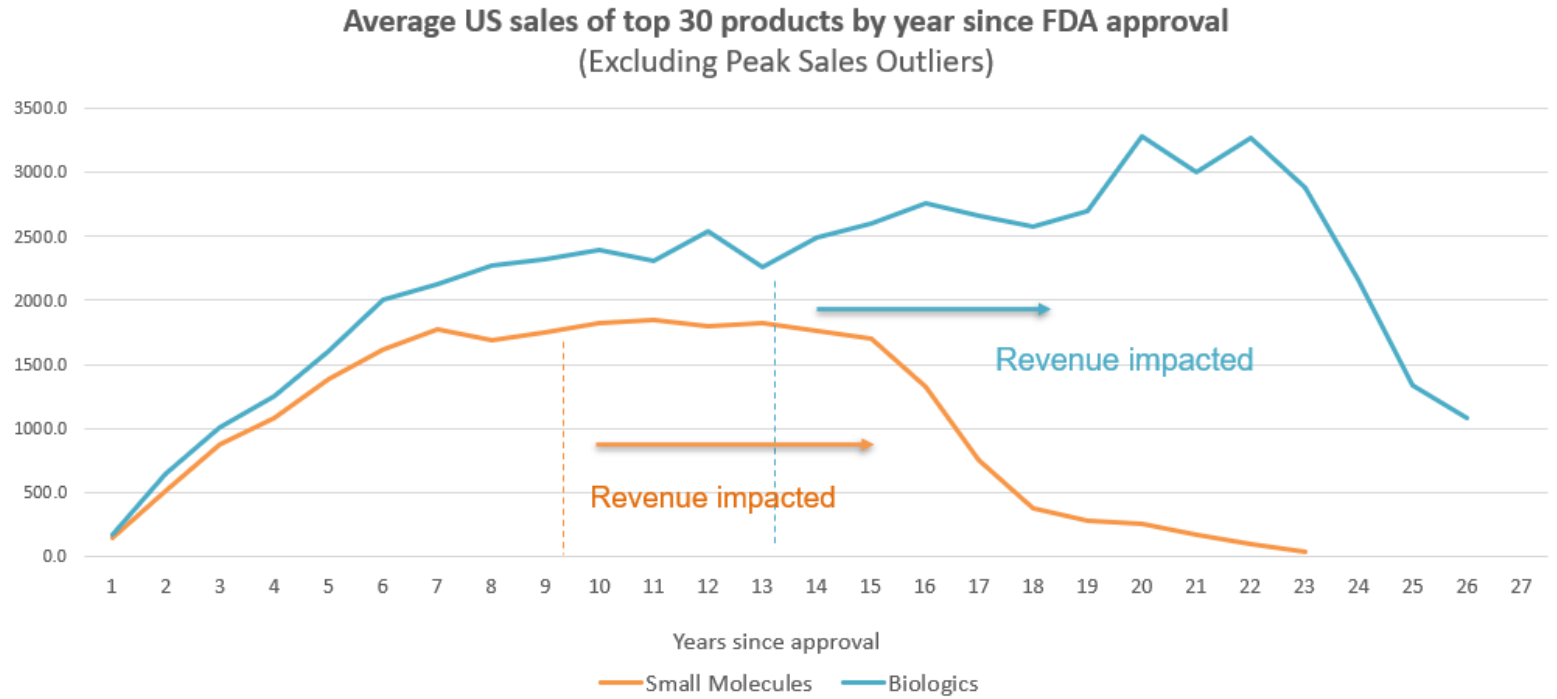
- Based on the 30 largest selling products over the last 10 years, we generated two baseline average US revenue curves over the product lifecycle (pre- and post- loss-of-exclusivity); one for small molecule medicines and one for biologics. This profile was used to forecast revenues 2023-2035 for each of the 346 drugs.
- Given the expansion of the cohort in 2029, we increased our cohort to 346 top-selling Part B and D drugs, All revenue values were adjusted to 2023 constant dollars. US revenues were allocated to the commercial or Medicare markets using SEC, FDA, and Biomedtracker data to determine the prevalence, by disease group, of those over or under the age of 65.
- Impacts from price setting begin in 2026 for the group selected in 2023, 2026 single source small molecules and 2028 for large molecules.
- 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" followed the same approach as small molecules, delayed until year 13.

Overview: Modeling the House Bill's IRA Expansion (2/2)

- Reduction of Net Present Value (NPV, at WACC 10%) resulting from revenue losses relative to baseline revenues (assuming no-IRA) was used to compute reduction in investment in R&D and, subsequently, drug losses.
- We identify products selected for price setting that would likely not have been developed had the House Bill been in place prior to investment decisions by estimating the change in revenue for therapies that our model predicts will be negotiated.
- Reduction of company-level EBIT (margin) are calculated by using SEC-based data (10-k Reports, the Biomedtracker Database, and Pitchbook) on current company EBITs and assuming cost structure remains unaltered resulting from IRA.
- Company-level R&D investments were extracted from SEC forms and allocated to each US state by company headquarter. Reduction of investment and number of jobs assumes an inelastic market coefficient of 1.

House Bill’s Impact on Drug Discovery

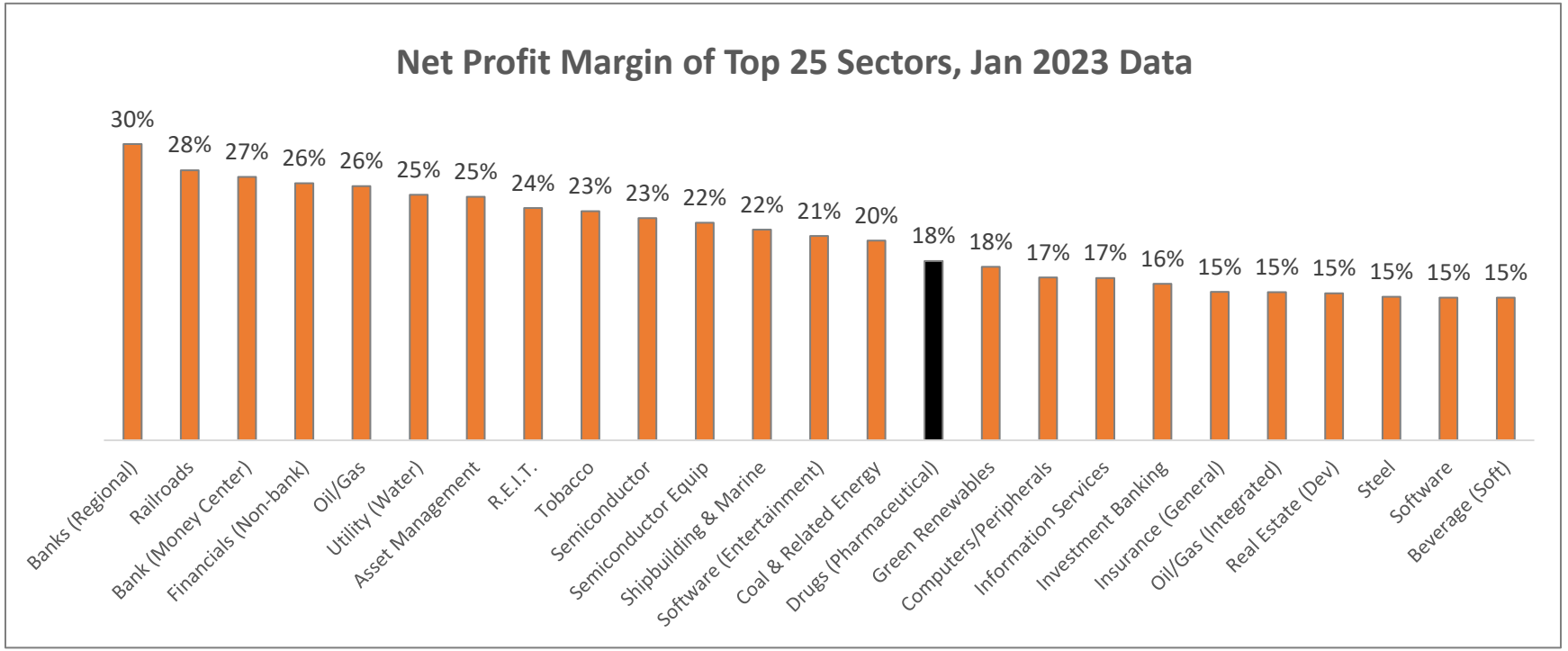
To estimate future revenues of drugs approved by CMS and FDA, we modeled the performance of the top selling 30 drugs over the last 10 years from market entry through to generic competition.



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

Despite the rhetoric, the biopharmaceutical sector is not overly profitable

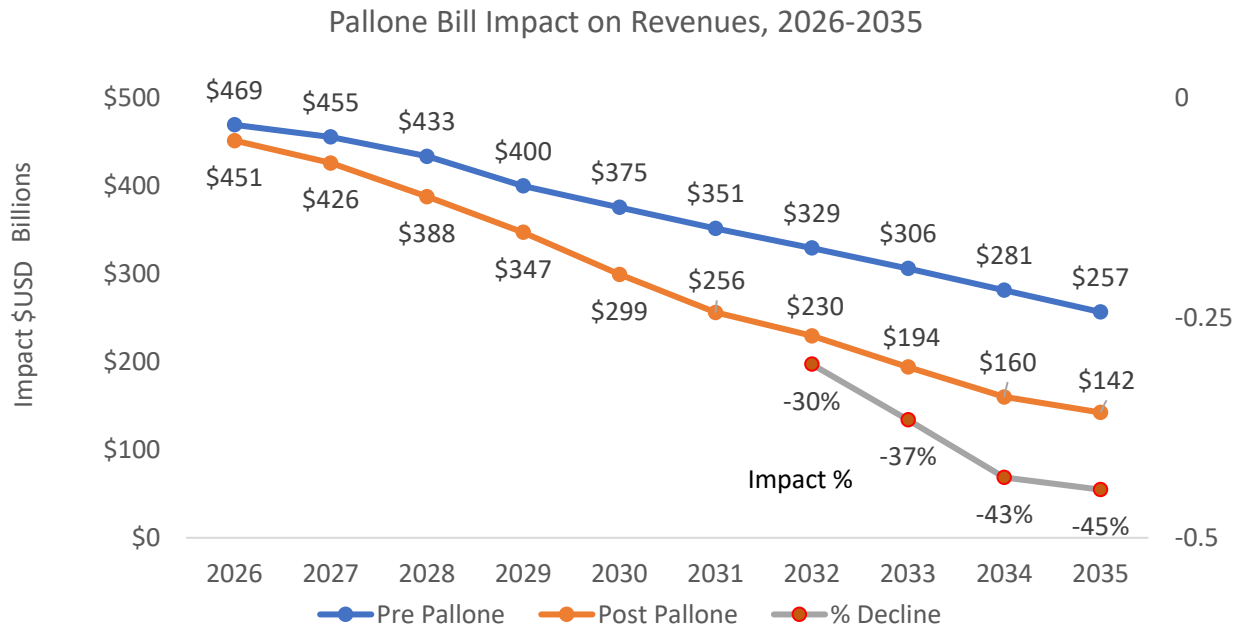
Biotechnology is excluded as it is ranked 92nd



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

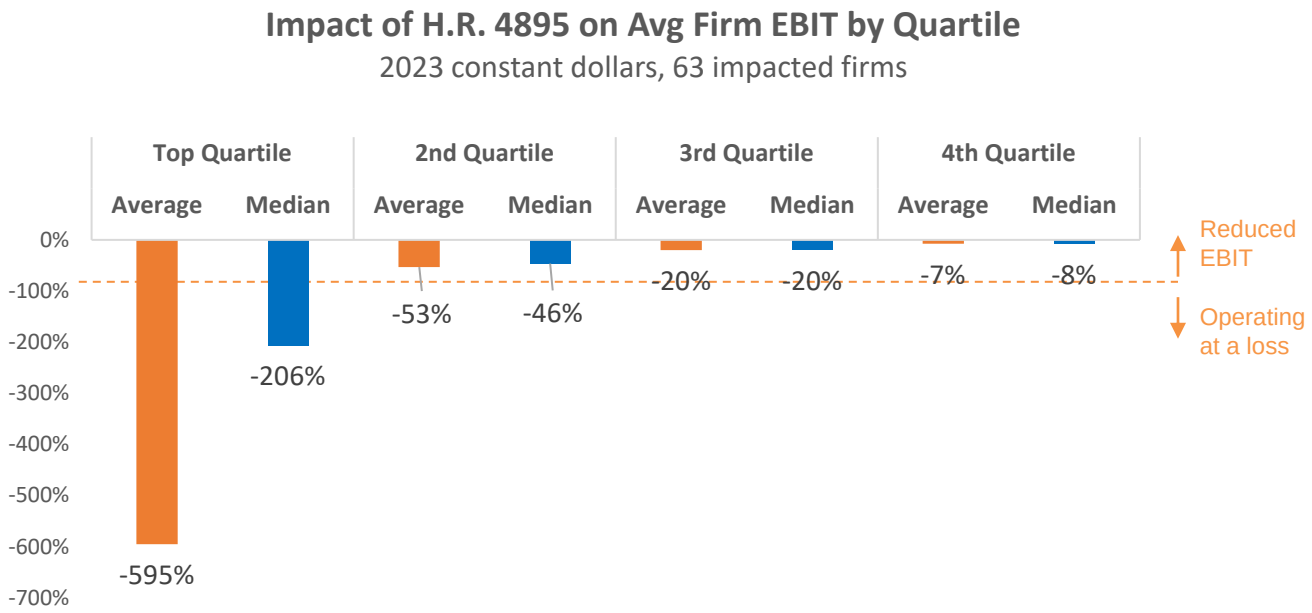
House Bill reduces company revenues in combined Medicare and commercial markets by 45%

64 firms, 348 therapies*, 2023 constant dollars



*Pallone Bill negotiates198 therapies in our model

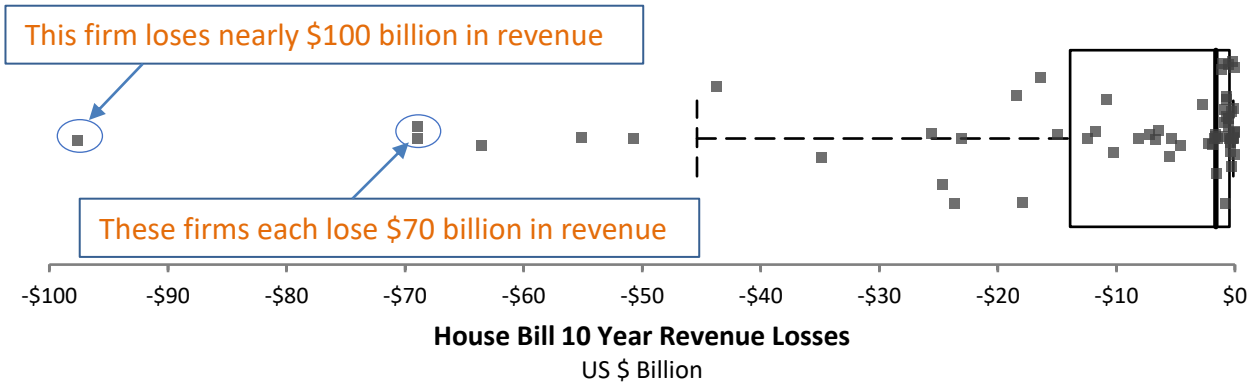
House Bill's impact on available cash for investments/pipelines 2026 - 2035



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

- H.R. 4895 reduces the ability of companies to reinvest their free cashflow into their pipelines as they lose on average 36% of their net earnings (EBIT).
- Had H.R. 4895 been in place from 2018-2022, the 25% most impacted firms would have incurred annual earnings losses nearing -600%.
- H.R. 4895's projected impact on the most impaired firms is larger than that modeled in the Smart Pricing Act.
- H.R. 4895 primarily impacts the companies with the most successful and innovative therapies targeting the Medicare aged population as well as their commercial sales.

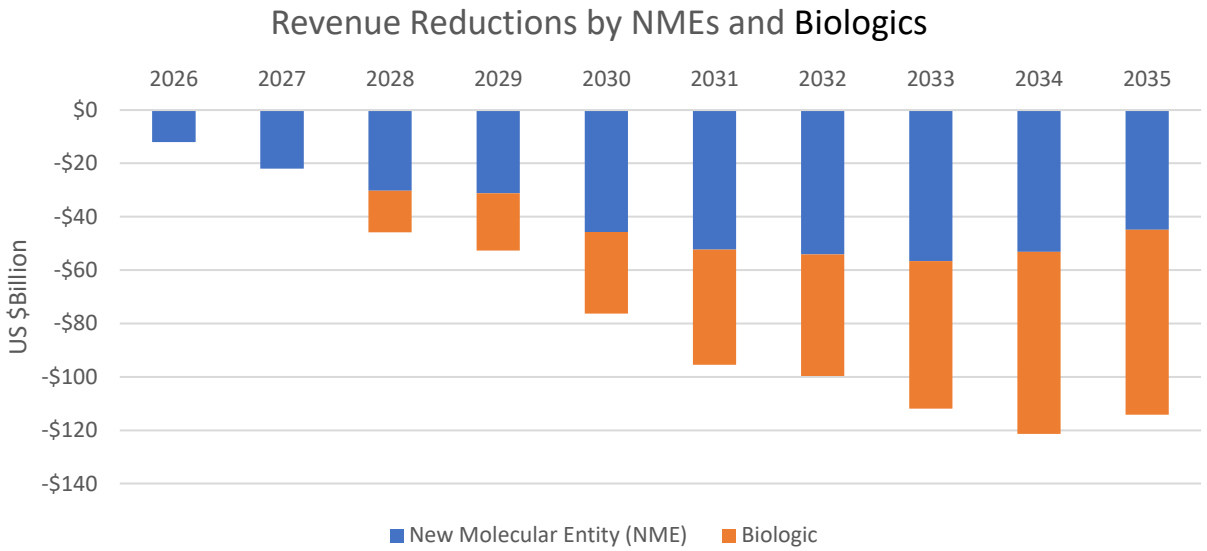
House Bill's impacts concentrate in companies which will see devastating revenue impacts 2026 - 2035



- Most companies with nominal Medicare sales are only minorly impacted by the expanded cohort to 50 therapies.
- However, the House Bill H.R. 4895 would have enormous impacts on 18 of the firms in our cohort.
- Our model projects that one major U.S. firm could lose nearly $10 billion dollars a year, $100 billion in total – these are unsustainable losses.
- H.R. 4895 specifically, and IRA generally, will create an enormous incentive for companies to avoid the Medicare aged population for new therapies.

Annual impact on revenue for small molecules and biologics

($US billion)



- At its peak in 2034, the projected losses for both large and small molecules addressing the Medicare aged population in our cohort is roughly equal, $60 billon dollars for each class of therapies.
- This is an enormous disincentive if investing in products to treat the Medicare aged population.

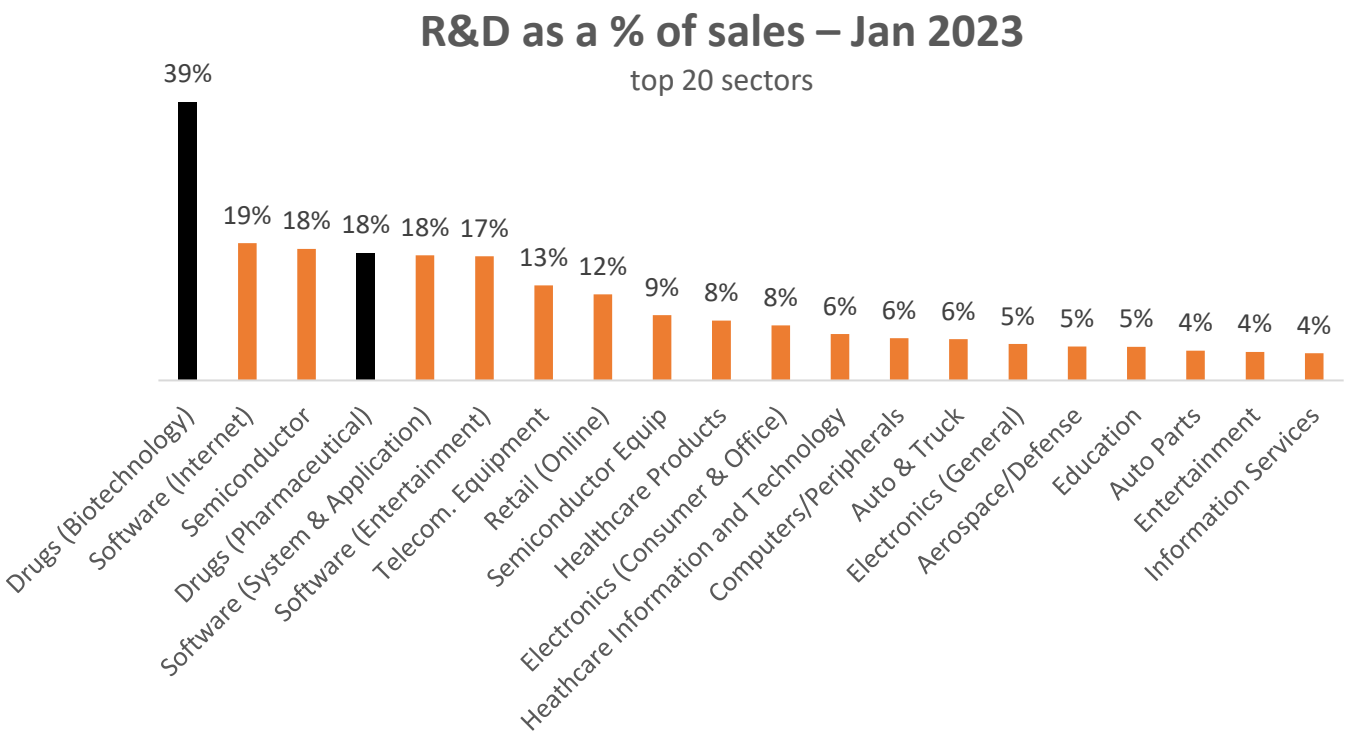
R&D programs will be cut if revenues are reduced under the bill

"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 the House Bill, we can model the subsequent impact on R&D spending if 20%, 30%, or 40% of revenue is allocated to R&D.
- The impacts on R&D spending allows one to determine the impact of the House Bill on the drug development ecosystem.

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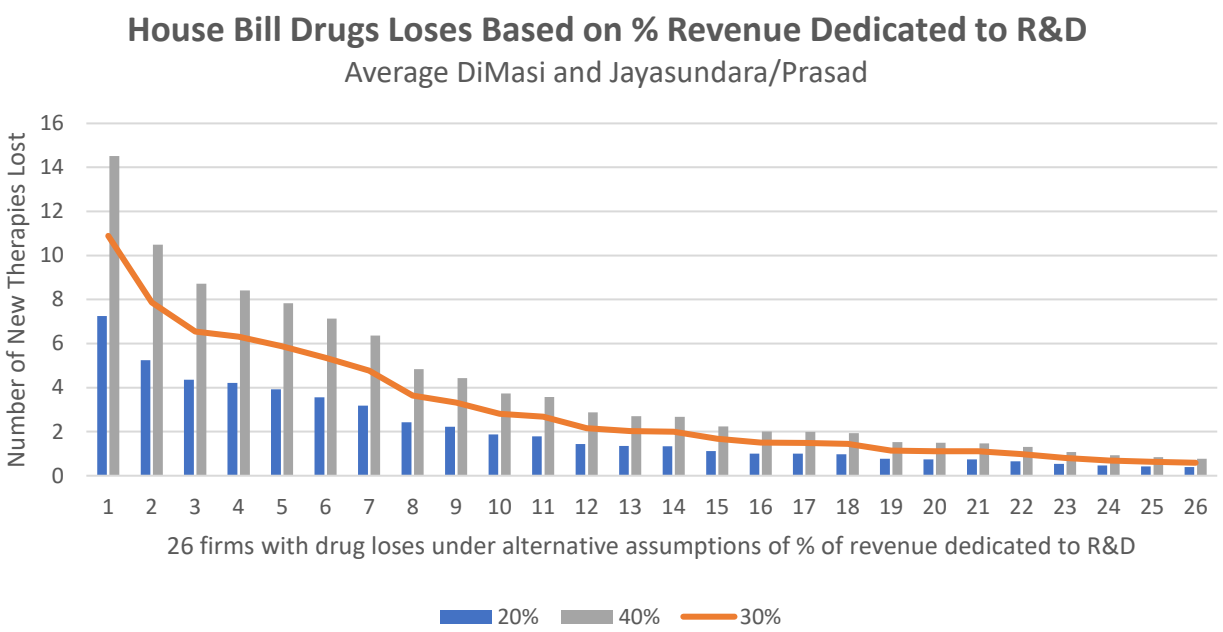
https://doi.org/10.1016/j.jhealeco.2016.01.012 Get rights and content

Number of price-controlled therapies retrospectively at risk, by firm

Had this bill been in place prior to initial investment decisions, 76 of the 198 price-controlled medicines in our cohort may not have been developed for Medicare



- The revenue reductions for 26 of 64 firms in our cohort imply a loss of 76 new FDA approved therapies in Medicare.
- 64 firms in our cohort have 198 FDA approved therapies that are price controlled by the House Bill; a loss of 76 of these developed therapies represents 38% of the total.
- Losses of one new approved medicine per firm or more on average are concentrated in 26 of the 64 companies in our cohort.

Impact of the House Bill's revenue reductions on Medicare therapies

Cost Impact (USD 2022)	Drugs Lost by R&D Revenue Allocation		
	20%	30%	40%
DIMasi ($2 billion)	34	51	68
Jayasundara/Prasad ($1 billion)	67	101	134
Average	**51**	**76**	**101**

- Using the risk weighted cash cost estimates of DiMasi and Jayasundara/Prasad for developing a new therapy, we can calculate the impact of the House Bill on future FDA approvals on our cohort.
- This retrospective analysis implies that companies with exposure to the Medicare aged population will move away from drugs that are likely to be negotiated, opting instead to develop therapies with mean ages far below 65 years of age.
- On average, between 51 and 101 new therapies would not come to market; our revenue analysis indicates these lost therapies will be concentrated in a few firms that are highly impacted by the House Bill.
- The above estimates of therapies lost implies that, on average, there will be 76 fewer new FDA approved therapies in Medicare over a 10-year period once the House Bill's impacts are felt at the firm level.

Price-controlled therapies retrospectively at risk, by type

Had H.R. 4895 been in place prior to investment decisions, companies may have forgone the development of 76 medicines in many areas of continued unmet need in Medicare, 38.3% of total.

Indication	Current		Post H.R. 4895		# Lost	
	Non-Orphan	Orphan	Non-Orphan	Orphan	Non-Orphan	Orphan
Oncology	35	28	22	17	13	11
Autoimmune/immunology	23	12	14	7	9	5
Neurology	16	5	10	3	6	2
Infectious Disease	12	4	7	2	5	2
Cardiovascular	9	3	6	2	3	1
Endocrine	8	1	5	1	3	0
Respiratory	7	1	4	1	3	0
Hematology	2	6	1	4	1	2
Psychiatry	6		4	0	2	0
Ophthalmology	4	2	2	1	2	1
Metabolic	3	3	2	2	1	1
Gastroenterology	4	1	2	1	2	0
Urology	2		1	0	1	0
Obstetrics/Gynecology	1		1	0	0	0
Grand Total	**132**	**66**	**81**	**41**	**51**	**25**
Total	**198**		**122**		**76**	

House Bill's potential impact on drug discovery:

Once the impacts of price controls are fully reflected in pipelines, the House Bill could see reductions of up to 134 new FDA approvals in Medicare after IRA's implementation

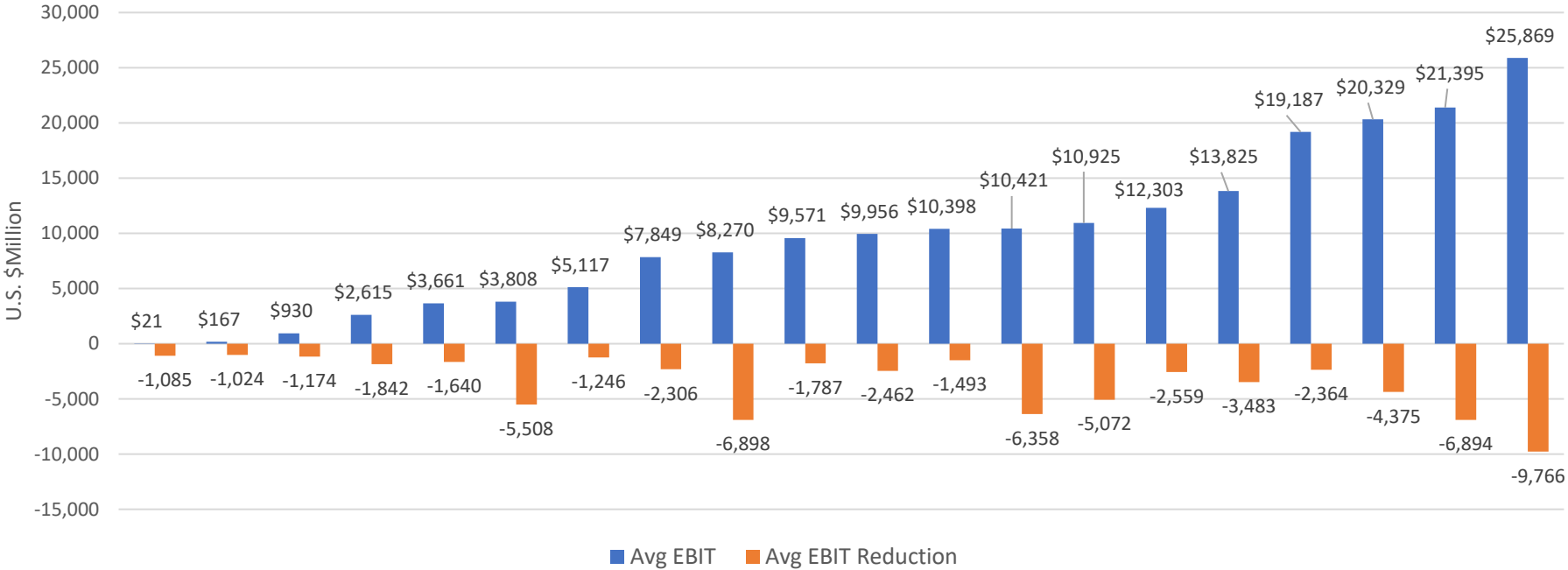
Number of Novel New FDA Approvals Per Year	Rate of H.R. 4895 Losses	10 Year Total of Therapies Lost From Medicare
35	**38.3%**	**134**

- 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 134 approvals over the next 10 years, for those drugs specifically targeting the Medicare aged population if the House Bill is approved.
- It is assumed that companies will adjust to these penalties and avoid therapeutic areas which are likely to be price controlled and/or shift to biologics where possible.

House Bill’s impact on the biopharma ecosystem

House Bill's impact on future pipeline investments

2023 constant dollars, 20 most impacted companies by drug losses, Avg EBIT reduction 2018 – 2022, US $Million



- The 20 firms which we project to be most likely to lose Medicare revenue due to the House Bill see an average weighted annual loss of free cash flow (EBIT) of 35%.

State investments by 20 impacted firms by drug development

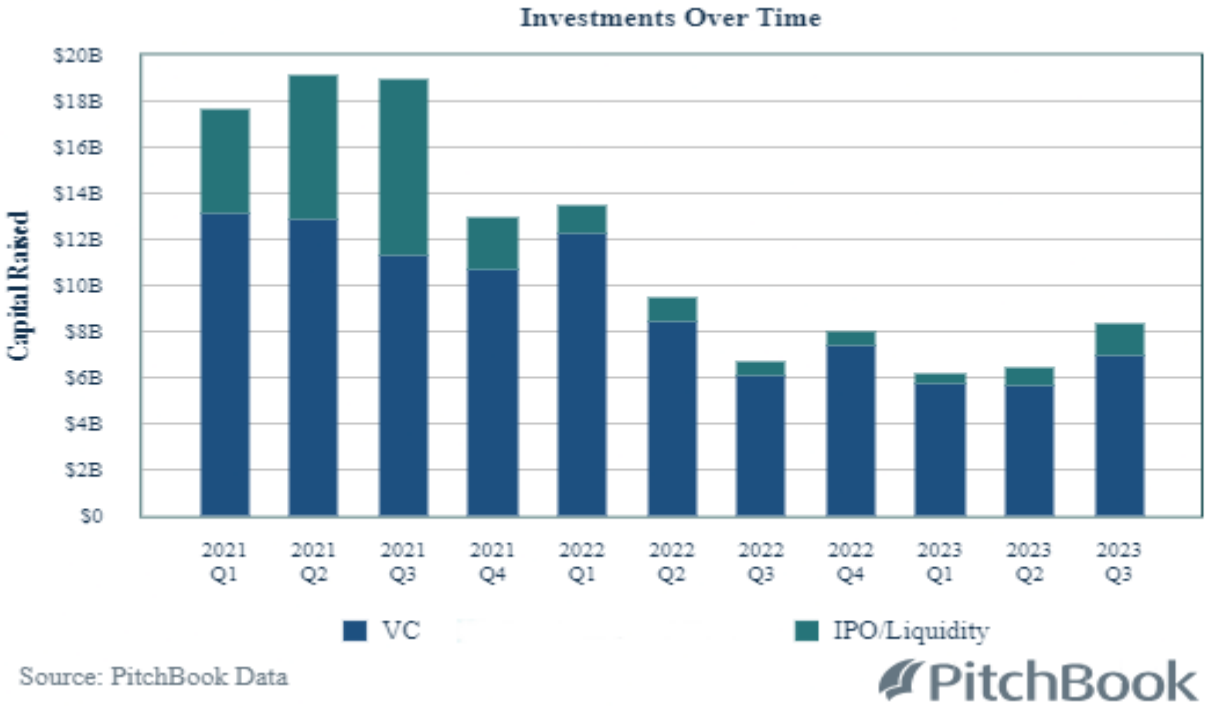
4/1/2014 - 3/31/2023

Investments by State 4/1/2013 - 3/31/2023	Value US $Million	H.R. 4895 Reduction 35%	Total Deals
California	$60,808	-$21,465	56
Massachusetts	$53,543	-$18,901	54
New York	$18,140	-$6,403	8
New Jersey	$4,256	-$1,503	9
Connecticut	$4,067	-$1,436	4
Washington	$3,249	-$1,147	6
Maryland	$2,450	-$865	5
North Carolina	$2,403	-$848	3
New Hampshire	$1,465	-$517	3
Wisconsin	$1,100	-$388	1
Illinois	$1,055	-$372	2
Texas	$600	-$212	1
Virginia	$500	-$177	1
Pennsylvania	$445	-$157	2
Florida	$275	-$97	1
Delaware	$245	-$86	1
Indiana	$225	-$79	1
Iowa	$20	-$7	1
Nevada	$20	-$7	1
	$154,866	**-$54,668**	**160**

- Our 20-firm cohort invested $155 billion into 160 deals identifiable by indication and location.
- House Bill reduces this available capital by 35%, which will impact a firm's deal selection.
- Our model projects a total loss of $55 billion of investments into new therapies for Medicare due to the House Bill.

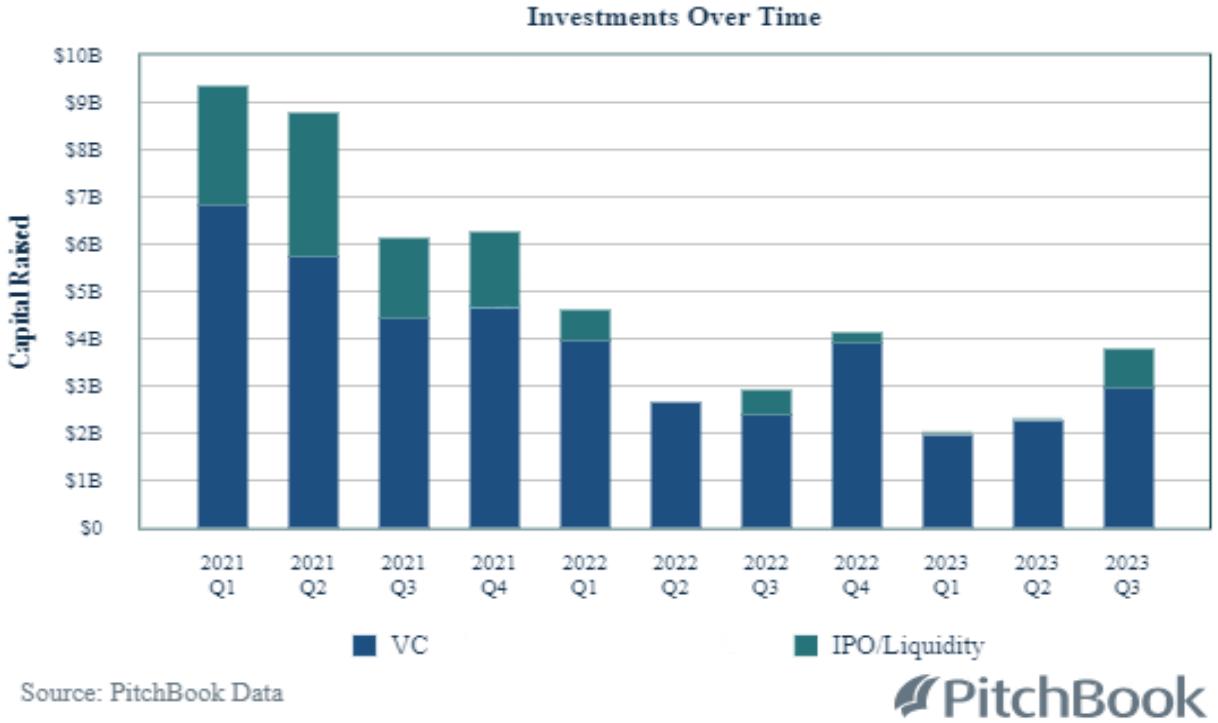
Evidence of the Ecosystem Impacts of IRA's Passage

Reductions in funding new therapies post IRA's approval



- IPOs for biopharma firms have dropped by more than 70% since the introduction of IRA.
- VC investments into biopharma firms have dropped by 50% since the introduction of IRA.

Reductions in cancer funding for new therapies post IRA's approval



- IPOs in biopharma companies targeting cancer therapies have dropped by more than 2/3rds since the introduction of IRA.
- VC investments into biopharma companies targeting cancer therapies have dropped by more than 50% since the introduction of IRA.

Steve Potts U.S. House Committee on Energy and Commerce Congressional testimony - Sept 20, 2023

Survey - 100 Venture funds in the pharma or biotech industry

Are you currently experiencing changes in funding/support for small molecules vs biologics as a result of the IRA?	OVERALL	VENTURE CAPITALISTS	BIOTECH EXECUTIVES	BIOTECH EMPLOYEES
I am seeing less funding of small molecule programs (excluding rare indications and targeted therapies)	76%	85%	71%	77%
Same funding of small molecule programs as before the IRA	24%	15%	29%	23%

- VC Steve Potts surveyed 100 funds regarding their desire to fund small molecules targeting Medicare.
- Overwhelming, his survey responders said they were moving way from small molecules.
- Solid tumors in cancer and Neurological disorders are key areas for small molecule research, these areas are now disincentivized for new therapies targeting the Medicare aged population

Demand for biopharma lab space is in radical decline

BIOTECH

STAT+

Biotech lab-space demand falls sharply as industry's 'sugar high' turns into a 'reset'

By Jonathan Wosen Sept. 19, 2023

Reprints

https://www.statnews.com/2023/09/19/biotech-lab-space-demand-falls-sharply/

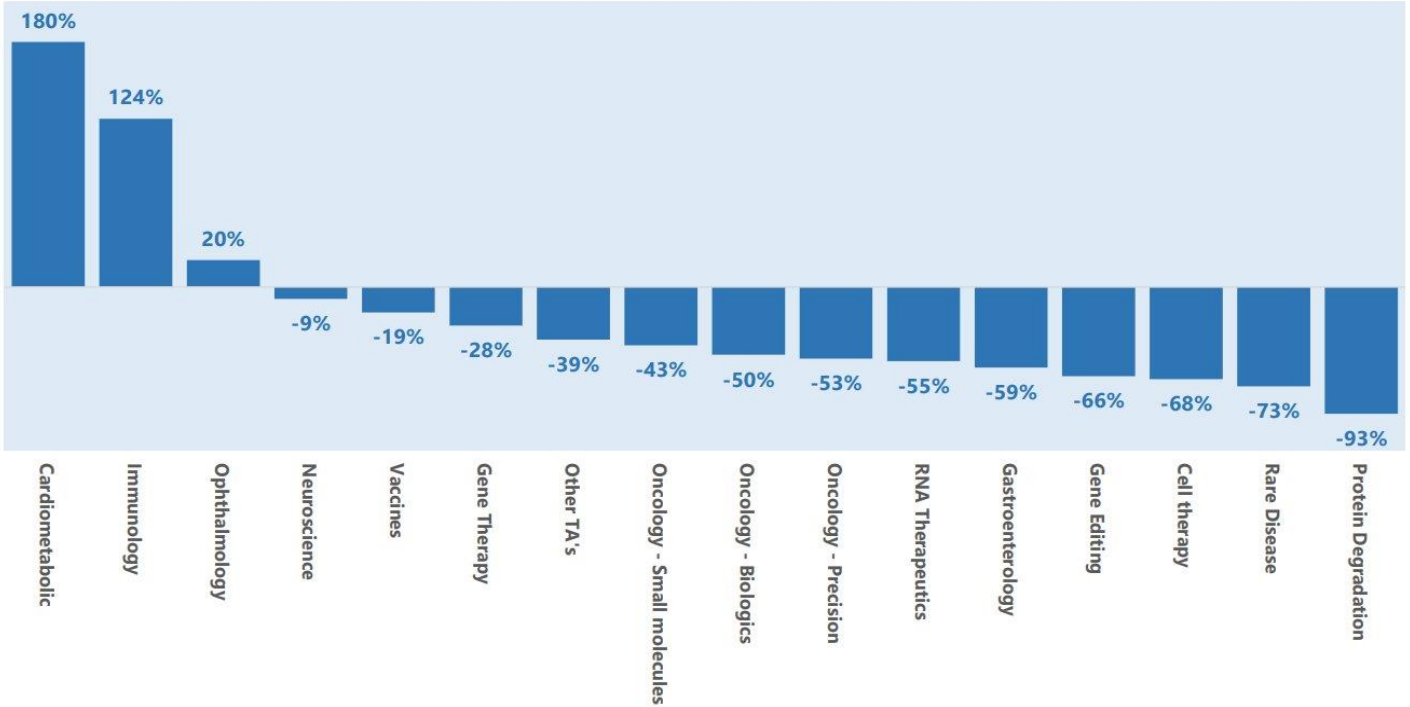
"Tenant demand, measured by the total amount of new space that companies are looking to lease, dropped from 25.3 million square feet at the end of 2021 to 10.1 million square feet by the second quarter of this year across eight top life science markets: Boston, the Bay Area, San Diego, Raleigh-Durham, Philadelphia, Seattle, Los Angeles, and the Washington, D.C., area."

VC valuations of biopharma firms have declined since the passage of IRA

VitalTransformation

Paras Sharma Toronto, Canada genesyscapital.com

% change in avg. enterprise value of biotech by lead asset (Dec 31, 2021 to June 30, 2023)



Source: CapitalIQ and Stifel research

H.R. 4895's impact on Jobs

House bill direct and total supported annual job losses by avg cohort impact

Total US and Puerto Rico by State/District/Region

Jobs Impact: 2026 - 2035 $76 Billion Avg Annual Revenue Reductions (Cohort)							
State	Direct Biopharma Jobs Impact	Total Biopharma Supported Jobs Impact	Biopharma Supported Output Impact ($Million)	State (Cont)	Direct Biopharma Jobs Impact (Cont)	Total Biopharma Supported Jobs Impact (Cont)	Biopharma Supported Output Impact ($Million)
Totals, U.S. & Puerto Rico	**-136,285**	**-678,604**	**($193,133)**				
California	-23,463	-127,652	($38,713)	South Carolina	-863	-4148	($1,146)
New Jersey	-10,201	-51,288	($14,019)	Maine	-763	-3887	($867)
Massachusetts	-10,205	-47,776	($11,912)	West Virginia	-787	-3816	($1,266)
Pennsylvania	-7,868	-42,655	($11,308)	Iowa	-940	-3665	($991)
North Carolina	-7,556	-42,180	($12,511)	Kentucky	-888	-3227	($738)
Illinois	-6,849	-41,457	($12,264)	Oregon	-703	-2907	($647)
New York	-9,268	-38,782	($11,274)	Delaware	-834	-2886	($642)
Texas	-6,391	-32,973	($9,039)	Nebraska	-524	-2459	($697)
Indiana	-4,143	-23,513	($9,345)	Alabama	-589	-2417	($679)
Florida	-4,328	-21,994	($4,877)	Rhode Island	-324	-2227	($614)
Maryland	-5,133	-21,806	($5,681)	New Mexico	-600	-2098	($439)
Ohio	-3,511	-15,258	($3,708)	New Hampshire	-404	-1887	($455)
Michigan	-2,685	-14,531	($3,828)	Oklahoma	-466	-1829	($430)
Puerto Rico	-3,007	-13,106	($9,685)	Nevada	-360	-1660	($402)
Utah	-2,071	-12,303	($2,909)	Louisiana	-462	-1566	($354)
Missouri	-2,061	-11,098	($2,712)	Mississippi	-303	-1345	($381)
Washington	-2,587	-9,580	($2,267)	Vermont	-194	-788	($189)
Georgia	-1,951	-9,574	($2,243)	Idaho	-157	-649	($153)
Wisconsin	-1,837	-8,656	($2,022)	Arkansas	-139	-643	($171)
Tennessee	-2,040	-7,802	($1,756)	Montana	-142	-473	($96)
Colorado	-1,449	-7,684	($1,885)	Hawaii	-152	-434	($81)
Arizona	-1,413	-6,978	($1,536)	DC	-107	-250	($74)
Virginia	-1,630	-6,824	($1,663)	Wyoming	-51	-184	($66)
Minnesota	-1,277	-6,739	($1,645)	South Dakota	-54	-166	($30)
Connecticut	-1,506	-5,953	($1,515)	North Dakota	-47	-137	($35)
Kansas	-975	-4,636	($1,162)	Alaska	-27	-60	($12)

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

House bill direct and total supported annual job losses by peak year impact

Total US and Puerto Rico by State/District/Region

Jobs Impact: 2026 - 2035 $121 Billion Avg Annual Revenue Reductions (Peak Sales Projection)							
State	**Direct Biopharma Jobs Impact**	**Total Biopharma Supported Jobs Impact**	**Biopharma Supported Output Impact ($Million)**	**State (Cont)**	**Direct Biopharma Jobs Impact (Cont)**	**Total Biopharma Supported Jobs Impact (Cont)**	**Biopharma Supported Output Impact ($Million)**
Totals, U.S. & Puerto Rico	**-216,190**	**-1,076,477**	**($306,369)**				
California	-37,220	-202,496	($61,410)	South Carolina	-1369	-6580	($1,818)
New Jersey	-16,182	-81,358	($22,238)	Maine	-1211	-6165	($1,375)
Massachusetts	-16,188	-75,788	($18,895)	West Virginia	-1248	-6053	($2,008)
Pennsylvania	-12,482	-67,664	($17,939)	Iowa	-1491	-5814	($1,571)
North Carolina	-11,985	-66,911	($19,846)	Kentucky	-1408	-5119	($1,171)
Illinois	-10,864	-65,764	($19,455)	Oregon	-1115	-4612	($1,027)
New York	-14,702	-61,520	($17,885)	Delaware	-1323	-4578	($1,018)
Texas	-10,138	-52,306	($14,339)	Nebraska	-831	-3900	($1,106)
Indiana	-6,572	-37,299	($14,824)	Alabama	-934	-3835	($1,076)
Florida	-6,865	-34,889	($7,737)	Rhode Island	-514	-3533	($973)
Maryland	-8,142	-34,591	($9,012)	New Mexico	-952	-3328	($697)
Ohio	-5,569	-24,204	($5,881)	New Hampshire	-641	-2993	($722)
Michigan	-4,259	-23,050	($6,073)	Oklahoma	-739	-2902	($682)
Puerto Rico	-4,771	-20,790	($15,363)	Nevada	-571	-2633	($638)
Utah	-3,286	-19,516	($4,615)	Louisiana	-733	-2485	($562)
Missouri	-3,270	-17,605	($4,303)	Mississippi	-480	-2133	($604)
Washington	-4,104	-15,197	($3,595)	Vermont	-308	-1250	($300)
Georgia	-3,095	-15,188	($3,558)	Idaho	-250	-1030	($242)
Wisconsin	-2,914	-13,732	($3,208)	Arkansas	-220	-1020	($271)
Tennessee	-3,237	-12,376	($2,785)	Montana	-226	-750	($152)
Colorado	-2,298	-12,189	($2,990)	Hawaii	-241	-689	($129)
Arizona	-2,241	-11,069	($2,437)	DC	-170	-396	($117)
Virginia	-2,586	-10,825	($2,639)	Wyoming	-81	-292	($105)
Minnesota	-2,026	-10,691	($2,609)	South Dakota	-85	-263	($48)
Connecticut	-2,389	-9,444	($2,402)	North Dakota	-75	-217	($55)
Kansas	-1,547	-7,354	($1,843)	Alaska	-43	-96	($19)

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

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Conclusions

Implications of House Bill

Conclusions and implications of House Bill

- The House Bill reduces net earnings for a 64-company cohort by 36%, but these impacts are highly concentrated in 18 companies, representing a substantial loss of their free cashflow for pipeline investments in Medicare.
- As measured by EBIT (annual net earnings):
  - The House Bill induced revenue reductions exceed nearly 600% of the annual earnings for 18 of the 64 companies in our cohort.
  - The House Bill penalizes the most innovative, successful therapies in Medicare.
  - The House Bill creates enormous disincentives for companies to continue to address the population over 65 years of age; these are most in need of novel cures and therapies for cancer and neurological disorders.
- At the firm level, the revenue reductions caused by the House Bill imply a 38% reduction in future FDA approvals for therapies targeting Medicare within our cohort.
- The inclusion of the commercial market has outsized impacts on several U.S. firms, one loses nearly $100 billion dollars over 10 years if the House Bill were to become law.
- The House Bill combined with the IRA will create enormous disincentives to develop new therapies for the Medicare aged population; we see evidence of a 2/3rds drop in IPOs and 50% drop in VC funding with IRA's passage.
- The House Bill will cause a 35% drop in partnership investments by the most impacted firms totaling $55 billion; these investments losses will be concentrated in CA and MA.
- We model losses of between 136,000 – 216,000 direct biopharmaceutical industry jobs and 678,000 – 1,076,000 indirect jobs across the U.S. economy.

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 the House Bill H.R. 4895 on the biopharmaceutical innovation ecosystem.
- We investigated the House Bill's impacts on investments in therapies targeting the Medicare aged population.
- Our focus was on new drug pipeline developments in small molecule and biological products, as well as the House Bill's impact on the U.S. biopharma ecosystem writ large.
- The analysis was performed by Vital Transformation's Research Manager Dr Daniel Gassull, Research Partner Gwen O'Loughlin and CEO Duane Schulthess.
- This study was funded by We Work for Health.
- The opinions included in this work are those of Vital Transformation LLC, and not necessarily those of the project's sponsors.
- The raw data behind this study is being held in preparation for peer review; questions are taken about the data on request.