



VitalTransformation

The impact of health technology made simple



H.R.3 - International Reference Pricing

Calculating the Impact on the U.S. BioPharmaceutical Innovation Ecosystem

Nov 22, 2019

Support Provided By

PhRMA



Introduction

- Vital Transformation, an international health economics and healthcare real world evidence strategy consultancy, was asked to conduct an analysis of the impact of international pricing, as proposed in H.R. 3, on the U.S. BioPharmaceutical innovation ecosystem, and specifically the impact on investments into small company capital formation for new drug pipeline development.

Study Summary Overview

Medicare Part D International Reference Pricing

- 2017 Medicare total drug spend and per dose pricing taken directly from [Medicare Part D Spending Dashboard](#)
- Reference pricing for 79 assets (69 in this analysis after the removal of diagnostics and consolidation of insulin platforms) is taken directly from House Ways and Means study, “Using External Reference Pricing In Medicare Part D To Reduce Drug Price Differentials With Other Countries”, So-Yeon Kang et al, 2019
- Reduced international reference pricing in the House Ways and Means [study](#) is applied directly to corporate product revenue taken from 2017 audited annual reports, SEC 10-k filings, and cross referenced with Medtrack “Pharma Intelligence”
- Reference pricing 1.2x ‘margin’ taken from “H.R. 3 - Drug Price Negotiation Bill Summary” and applied directly to House Ways and Means reference pricing
- Our modeling predicts an annual reduction in revenue for the impacted firms of \$71.6 bil (five year impact of \$358 bil), compared to CBO analysis of ‘savings’ of \$334 over 5 years. Our financial impact is for the entire market, and is likely underestimated as we look at only the 79 assets in the Ways and Means study, not the 125 drugs included in the CBO analysis. However, given the results, we feel the impact will be clear to all readers.
- We do not agree with the CBO's assessment of market reduction of 8-15 drugs over 10 years as they do not fully analyze and depict anticipated investment behavior under H.R. 3. The data in our study shows a much greater impact: using a logistic regression of probability, the number of new medicines developed by innovative biotechnology companies supported by revenue generated by Medicare Part D products would fall from 64 to 8 over the next 10 years, all things being equal and with a 58% reduction in revenue.

Overview:

- [House Ways and Means](#) reference pricing methodology
- House reference pricing and H.R. 3 overall impact on commercial pricing and industry revenue
- Reference pricing revenue reductions and the impact on investor behavior
- Impact assessment of reference pricing on the U.S. Innovative BioPharma Market
- US BioPharma sector growth, EU Regulation's impact on innovation
- H.R. 3 impact on U.S. jobs, and stock market value

Methodology: Ways And Means Study

“Using External Reference Pricing In Medicare Part D To Reduce Drug Price Differentials With Other Countries”

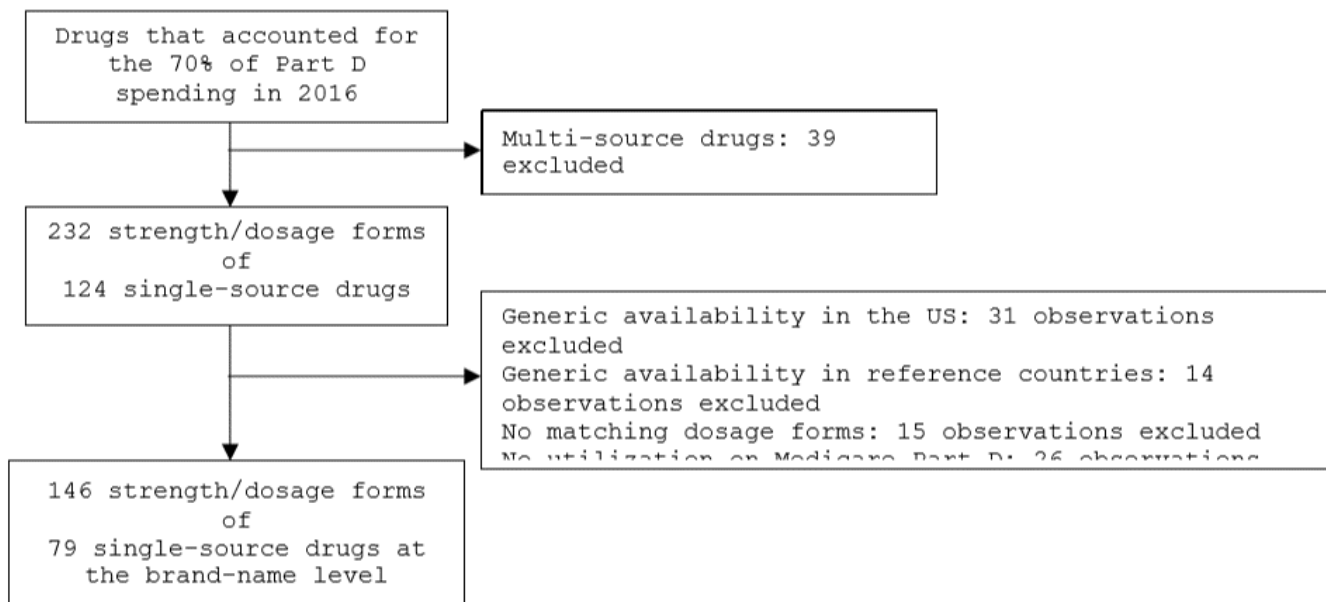
So-Yeon Kang et al, : 10.1377/hlthaff.2018.05207 HEALTH AFFAIRS 38, NO. 5 (2019): 804–811 ©2019 Project HOPE— The People-to-People Health Foundation, Inc

- Study compared the price differentials in the US and the UK, Japan, and Ontario (Canada) for [79 single-source brand-name drugs](#) that had been on the market for at least three years, and consumed 70% of Part D spending.
- Combined with U.S. House Ways and Means Committee paper “[A Painful Pill to Swallow: U.S. vs. International Prescription Drug Prices](#)” adding further reference pricing for Australia, Portugal, France, Netherlands, Germany, Denmark, Sweden, and Switzerland.
- US prices averaged 3.2–4.1 times higher after rebates were considered. The price differential for individual drugs varied from 1.3 to 70.1.
- The estimated cost reduction to Medicare Part D of adopting the average price of drugs in the reference countries was \$72.9 billion in 2018.

Ways and Means Selection Methodology – 79 Drugs

So-Yeon Kang et al, : [10.1377/hlthaff.2018.05207](https://doi.org/10.1377/hlthaff.2018.05207) HEALTH AFFAIRS 38, NO. 5 (2019)

Appendix Exhibit 1. Sample selection strategy



Medicare Part D – Reference Price Impact at the Firm Level



Company	Number of Drugs	US Medicare D Sales 2017 \$US Mil	New Medicare Revenue Based on Reference Price	Change in Medicare Revenue	Reduction in Part D Revenue %	Total R&D Spend 2017	Lost Revenue as a % of R&D	Lost Revenue as 20% of R&D
Company A	1	\$542	\$157	-\$385	-71%	\$361	-107%	-21%
Company B	4	\$3,677	\$577	-\$3,100	-84%	\$3,078	-101%	-20%
Company C	5	\$4,400	\$855	-\$3,545	-81%	\$3,925	-90%	-18%
Company D	2	\$3,952	\$1,193	-\$2,760	-70%	\$3,274	-84%	-17%
Company E	3	\$1,947	\$342	-\$1,604	-82%	\$2,254	-71%	-14%
Company F	6	\$4,643	\$2,080	-\$2,563	-55%	\$3,734	-69%	-14%
Company G	2	\$3,197	\$891	-\$2,306	-72%	\$3,562	-65%	-13%
Company H	4	\$3,758	\$855	-\$2,903	-77%	\$4,894	-59%	-12%
Company I	4	\$5,591	\$2,547	-\$3,044	-54%	\$5,472	-56%	-11%
Company J	2	\$2,818	\$584	-\$2,235	-79%	\$4,482	-50%	-10%
Company K	5	\$3,187	\$646	-\$2,541	-80%	\$5,357	-47%	-9%
Company L	1	\$724	\$210	-\$514	-71%	\$1,326	-39%	-8%
Company M	4	\$3,885	\$536	-\$3,350	-86%	\$9,818	-34%	-7%
Company N	1	\$855	\$302	-\$553	-65%	\$1,957	-28%	-6%
Company O	1	\$462	\$134	-\$328	-71%	\$1,161	-28%	-6%
Company P	3	\$4,935	\$1,901	-\$3,034	-61%	\$14,014	-22%	-4%
Company Q	6	\$3,002	\$1,077	-\$1,925	-64%	\$9,143	-21%	-4%
Company R	2	\$1,913	\$904	-\$1,009	-53%	\$5,007	-20%	-4%
Company S	3	\$1,928	\$504	-\$1,425	-74%	\$7,645	-19%	-4%
Company T	2	\$586	\$92	-\$494	-84%	\$2,930	-17%	-3%
Company U	3	\$1,150	\$278	-\$871	-76%	\$8,510	-10%	-2%
Company V	1	\$278	\$81	-\$198	-71%	\$1,991	-10%	-2%
Company W	1	\$271	\$79	-\$192	-71%	\$2,108	-9%	-2%
Company X	2	\$554	\$119	-\$435	-79%	\$5,455	-8%	-2%
Company Y	1	\$314	\$81	-\$233	-74%	\$10,529	-2%	0%
TOTAL	69	\$58,569	\$17,023	-\$41,546	-71%	\$121,986	-34%	-7%

Medicare Part D – Reference Price Impact with H.R. 3 1.2 Margin

Company	Number of Drugs	Medicare D Sales 2017 \$US Mil	Change in Medicare Revenue	Medicare D Reference Price	H.R. 3 1.2 x Margin	Change in Revenue	Revenue Reduction as %	Total R&D Spend 2017	Lost Revenue % of R&D	Lost Revenue as 20% of R&D
Company A	1	\$542	-\$385	\$157	\$189	-\$353	-65%	\$361	-98%	-20%
Company B	4	\$3,677	-\$3,100	\$577	\$693	-\$2,985	-81%	\$3,078	-97%	-19%
Company C	5	\$4,400	-\$3,545	\$855	\$1,026	-\$3,374	-77%	\$3,925	-86%	-17%
Company D	2	\$3,952	-\$2,760	\$1,193	\$1,431	-\$2,521	-64%	\$3,274	-77%	-15%
Company E	3	\$1,947	-\$1,604	\$342	\$411	-\$1,536	-79%	\$2,254	-68%	-14%
Company F	2	\$3,197	-\$2,306	\$891	\$1,069	-\$2,128	-67%	\$3,562	-60%	-12%
Company G	6	\$4,643	-\$2,563	\$2,080	\$2,496	-\$2,147	-46%	\$3,734	-57%	-11%
Company H	4	\$3,758	-\$2,903	\$855	\$1,026	-\$2,732	-73%	\$4,894	-56%	-11%
Company I	2	\$2,818	-\$2,235	\$584	\$700	-\$2,118	-75%	\$4,482	-47%	-9%
Company J	4	\$5,591	-\$3,044	\$2,547	\$3,056	-\$2,535	-45%	\$5,472	-46%	-9%
Company K	5	\$3,187	-\$2,541	\$646	\$775	-\$2,412	-76%	\$5,357	-45%	-9%
Company L	1	\$724	-\$514	\$210	\$252	-\$472	-65%	\$1,326	-36%	-7%
Company M	4	\$3,885	-\$3,350	\$536	\$643	-\$3,242	-83%	\$9,818	-33%	-7%
Company N	1	\$462	-\$328	\$134	\$161	-\$301	-65%	\$1,161	-26%	-5%
Company O	1	\$855	-\$553	\$302	\$362	-\$493	-58%	\$1,957	-25%	-5%
Company P	3	\$4,935	-\$3,034	\$1,901	\$2,281	-\$2,654	-54%	\$14,014	-19%	-4%
Company Q	6	\$3,002	-\$1,925	\$1,077	\$1,292	-\$1,709	-57%	\$9,143	-19%	-4%
Company R	3	\$1,928	-\$1,425	\$504	\$604	-\$1,324	-69%	\$7,645	-17%	-3%
Company S	2	\$1,913	-\$1,009	\$904	\$1,085	-\$828	-43%	\$5,007	-17%	-3%
Company T	2	\$586	-\$494	\$92	\$110	-\$475	-81%	\$2,930	-16%	-3%
Company U	3	\$1,150	-\$871	\$278	\$334	-\$816	-71%	\$8,510	-10%	-2%
Company V	1	\$278	-\$198	\$81	\$97	-\$182	-65%	\$1,991	-9%	-2%
Company W	1	\$271	-\$192	\$79	\$95	-\$176	-65%	\$2,108	-8%	-2%
Company X	2	\$554	-\$435	\$119	\$143	-\$411	-74%	\$5,455	-8%	-2%
Company Y	1	\$314	-\$233	\$81	\$97	-\$217	-69%	\$10,529	-2%	0%
TOTAL	69	\$58,569.15	-\$41,545.83	\$17,023.32	\$20,427.98	-\$38,141	-65%	\$121,986	-31%	-6%

Part D – Reference Price H.R. 3 Impact on the Entire Commercial Market

Company	Number of Drugs	Reference Discount	US Total Sales 2017	Revised Total Sales	Revised Total Sales H.R. 3 1.2 Margin	Change In Revenue	Total R&D Spend 2017	Reduction as a % of R&D	Reduction as 20% R&D ratio
Company S	2	73%	\$14,505	\$3,965	\$4,758	-\$9,747	\$5,007	-195%	-39%
Company C	5	77%	\$8,719	\$2,016	\$2,419	-\$6,300	\$3,925	-161%	-32%
Company E	3	83%	\$6,479	\$1,129	\$1,355	-\$5,124	\$2,254	-227%	-45%
Company F	2	73%	\$6,580	\$1,801	\$2,161	-\$4,419	\$3,562	-124%	-25%
Company G	6	57%	\$9,032	\$3,883	\$4,659	-\$4,373	\$3,734	-117%	-23%
Company Q	6	69%	\$6,563	\$2,025	\$2,429	-\$4,134	\$9,143	-45%	-9%
Company D	2	70%	\$6,434	\$1,942	\$2,331	-\$4,103	\$3,274	-125%	-25%
Company K	5	78%	\$5,518	\$1,200	\$1,440	-\$4,078	\$5,357	-76%	-15%
Company H	4	73%	\$6,023	\$1,654	\$1,985	-\$4,038	\$4,894	-83%	-17%
Company B	4	83%	\$4,711	\$779	\$935	-\$3,776	\$3,078	-123%	-25%
Company R	3	74%	\$4,879	\$1,254	\$1,505	-\$3,374	\$7,645	-44%	-9%
Company M	4	84%	\$3,790	\$590	\$708	-\$3,082	\$9,818	-31%	-6%
Company P	3	56%	\$5,655	\$2,506	\$3,008	-\$2,647	\$14,014	-19%	-4%
Company I	2	79%	\$3,400	\$708	\$850	-\$2,550	\$4,482	-57%	-11%
Company U	3	76%	\$3,448	\$844	\$1,012	-\$2,436	\$8,510	-29%	-6%
Company J	4	57%	\$4,834	\$2,057	\$2,468	-\$2,366	\$5,472	-43%	-9%
Company O	1	65%	\$1,331	\$470	\$564	-\$768	\$1,957	-39%	-8%
Company L	1	71%	\$1,133	\$329	\$394	-\$739	\$1,326	-56%	-11%
Company W	1	71%	\$1,120	\$327	\$392	-\$728	\$2,108	-35%	-7%
Company X	2	78%	\$829	\$186	\$223	-\$606	\$5,455	-11%	-2%
Company T	2	85%	\$733	\$109	\$130	-\$602	\$2,930	-21%	-4%
Company N	1	71%	\$826	\$239	\$287	-\$538	\$1,161	-46%	-9%
Company Y	1	74%	\$662	\$171	\$205	-\$457	\$10,529	-4%	-1%
Company A	1	71%	\$666	\$193	\$232	-\$434	\$361	-120%	-24%
Company V	1	71%	\$377	\$109	\$131	-\$246	\$1,991	-12%	-2%
TOTAL	69	72%	\$108,246	\$30,484	\$36,581	-\$71,665	\$120,920	-59%	-12%

Industry Impact % of Total Annual Earnings (EBIT), 2017 Base

Company	2017 Total Annual EBIT (\$Mil Base)
Company Q	\$17,673
Company G	\$13,529
Company R	\$12,304
Company Y	\$12,287
Company F	\$9,597
Company S	\$9,314
Company U	\$8,999
Company P	\$7,194
Company M	\$6,521
Company J	\$6,201
Company H	\$5,131
Company E	\$5,129
Company C	\$4,453
Company D	\$4,314
Company O	\$2,602
Company I	\$2,559
Company W	\$2,352
Company K	\$2,197
Company X	\$2,186
Company T	\$1,324
Company N	\$1,091
Company B	-\$246
Company L	-\$312
Company A	-\$1,741
Company V	-\$10,386
Total	\$124,272

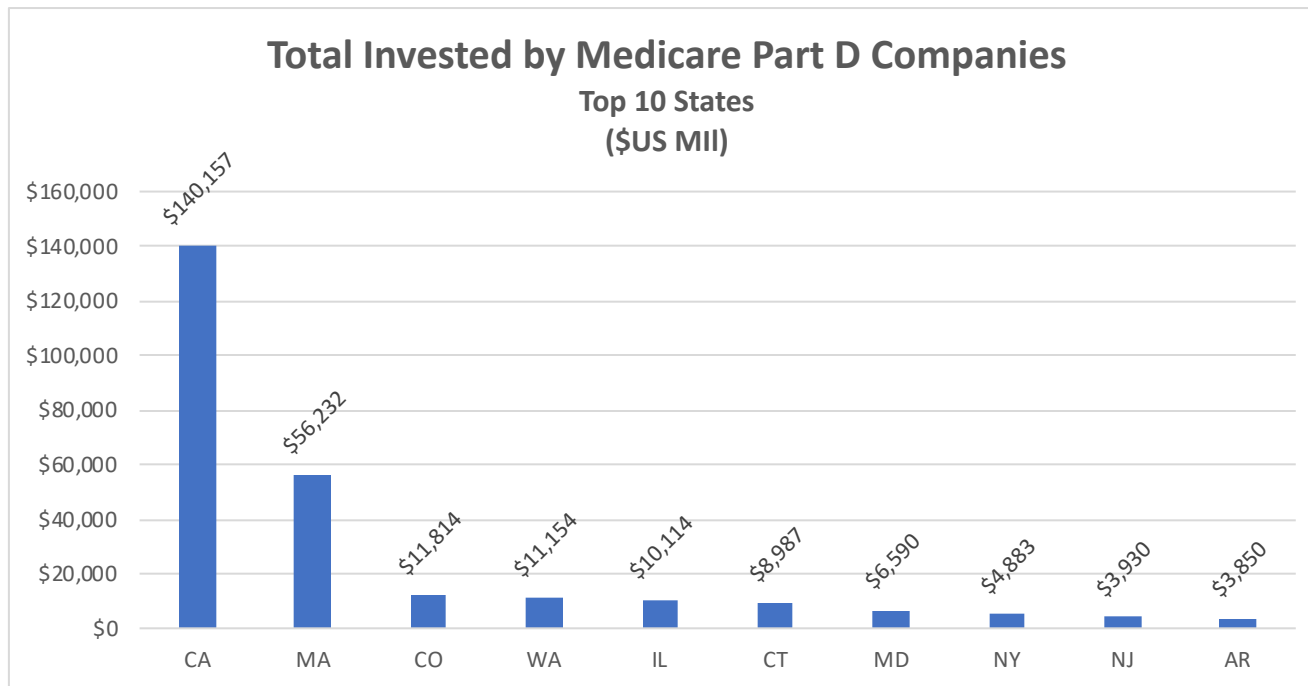
	Revenue Impact	% Reduction
Medicare D Reduction Ways and Means	-41,546	33%
Part D H.R. 3 1.2 Multiple	-38,141	31%
Part D H.R. 3 1.2 Full Market	-71,665	58%

Under H.R. 3, the model anticipates a -\$71.6 Bil annual revenue impact, or a 58% reduction in total annual earnings of \$124.3 Bil under the House Ways and Means International Reference Pricing methodology

H.R. 3 International Reference Pricing – Impact on U.S. BioPharma Investment

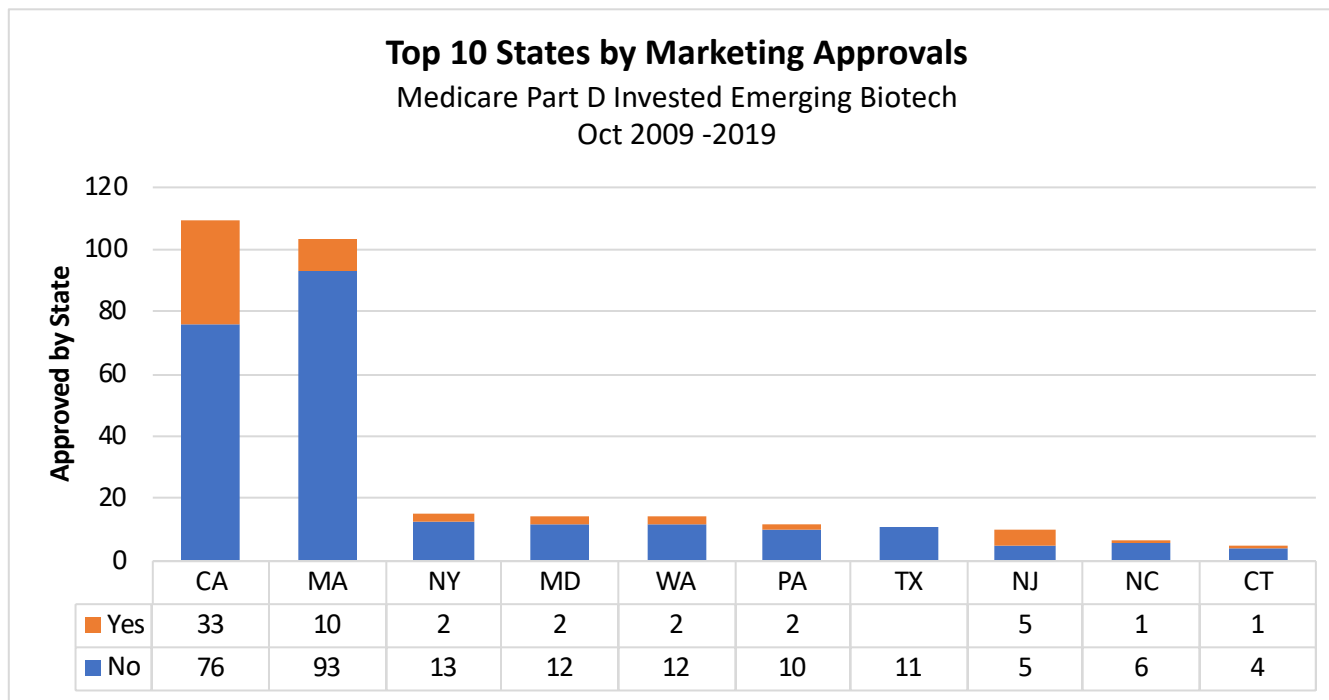
- Methodology: The Medtrack database was searched for all U.S. deals from October 2009 – 2019 involving BioPharma partnerships, venture capital financing, licensing agreements, and acquisitions made by firms potentially impacted by Medicare Part D pricing proposals.
- U.S. firms invested \$621 billion in these partnerships, this funding was taken primarily from free cash flow from operations.
- OTC companies, veterinary medicine, corporate level M&A/partnerships, manufacturing, diagnostics, non-us companies, and dermatological products were removed from our analysis to focus on U.S. based innovative emerging biotech.
- From October 2009 – 2019, a total of 331 biotech assets in the U.S. received nearly \$300 Bil in direct investments in partnerships, licensing, marketing, and venture agreements.
- Of the 331 assets receiving investments, 64 received marketing authorization for a new product (19%)
- Statistical tests modeling the impact of a 58% reduction in revenue due to the proposed international reference pricing were run to predict the revised market access for new medicines and investor behavior/willingness to invest

California Dominates in U.S. Biotech Investments



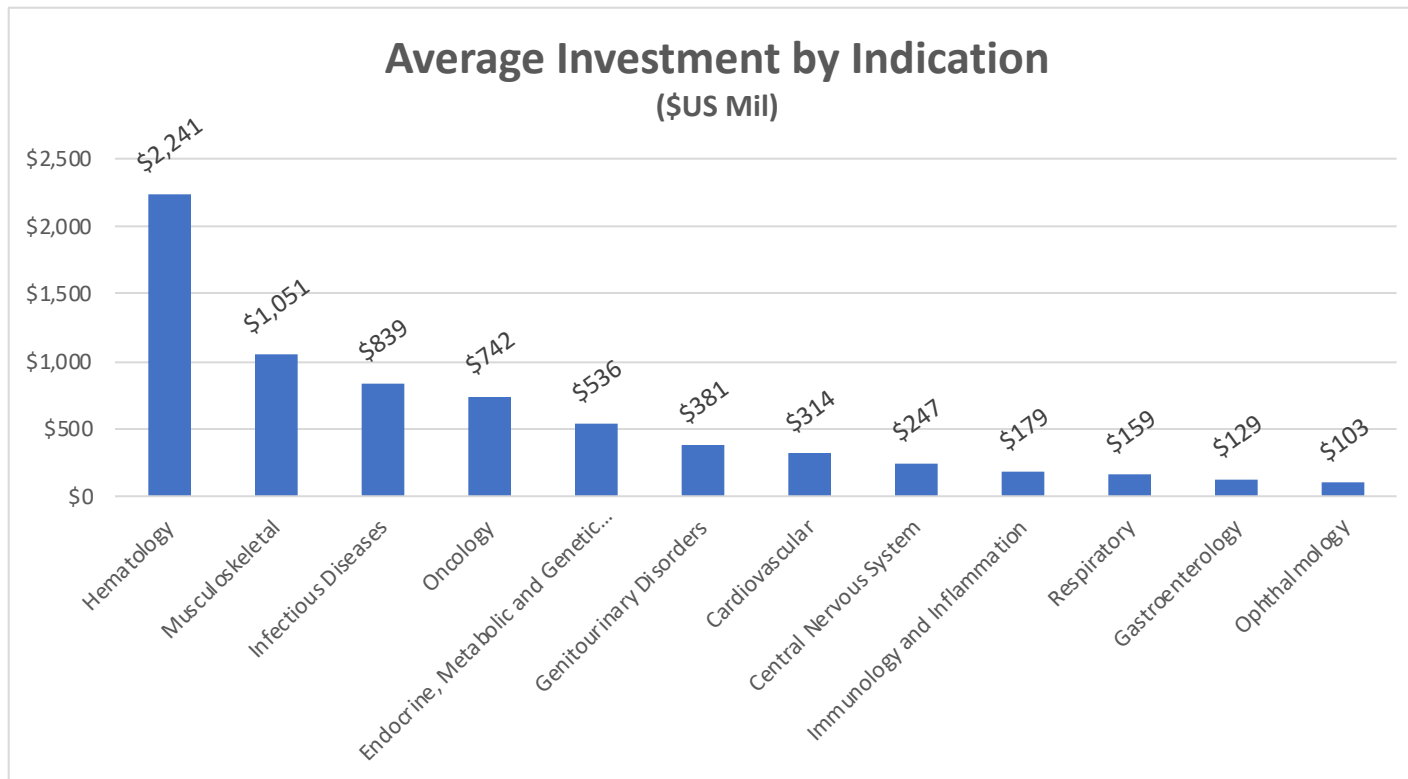
Medicare Part D firms' Investments into 331 Emerging U.S. Biotech firms, Oct 2009 -2019

CA and MA Provided 2/3rds of the 64 Approved Therapies



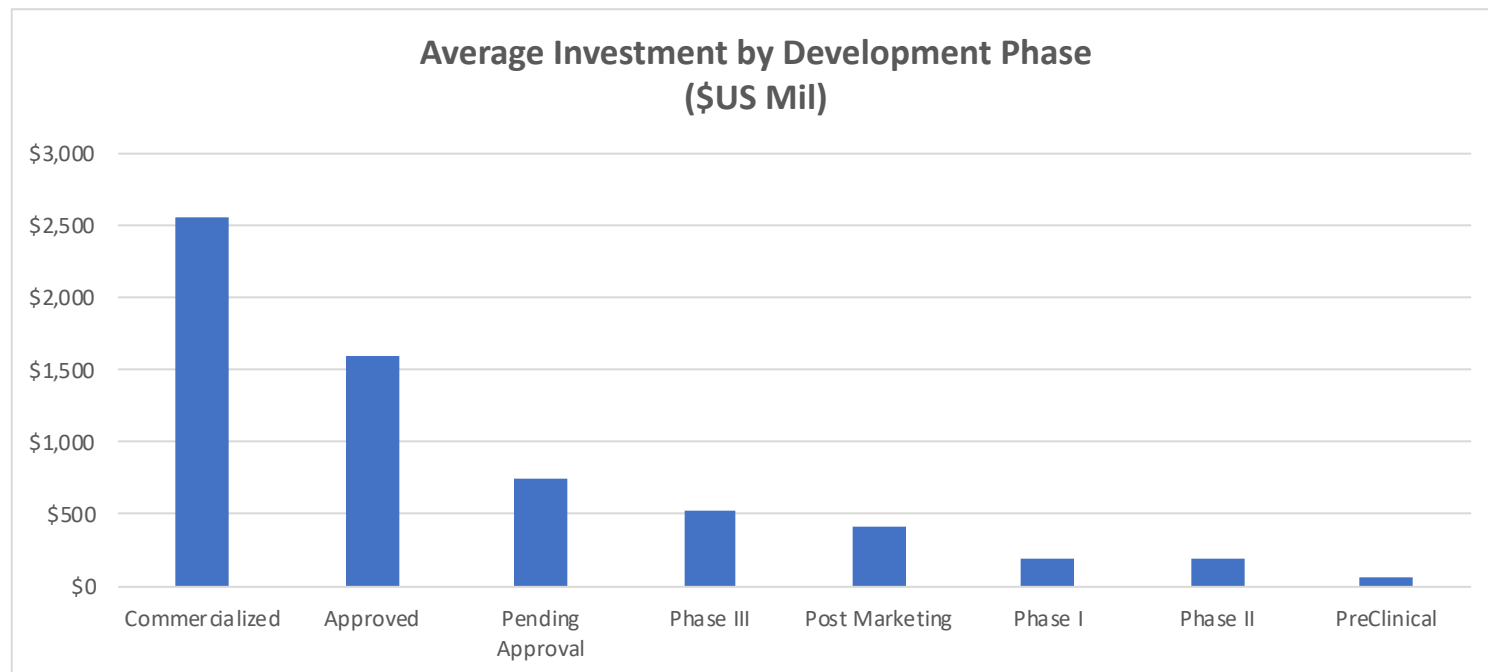
Medicare Part D firms' Investments into 331 Emerging U.S. Biotech firms, Oct 2009 -2019

Average Investment Size is Dependent Upon Therapeutic Area



Medicare Part D firms' Investments into 331 Emerging U.S. Biotech firms, Oct 2009 -2019

Average Investment Size is Dependent Upon Clinical Research Phase



Medicare Part D firms' Investments into 331 Emerging U.S. Biotech firms, Oct 2009 -2019

BioPharma Investors – Are Investments Rational?

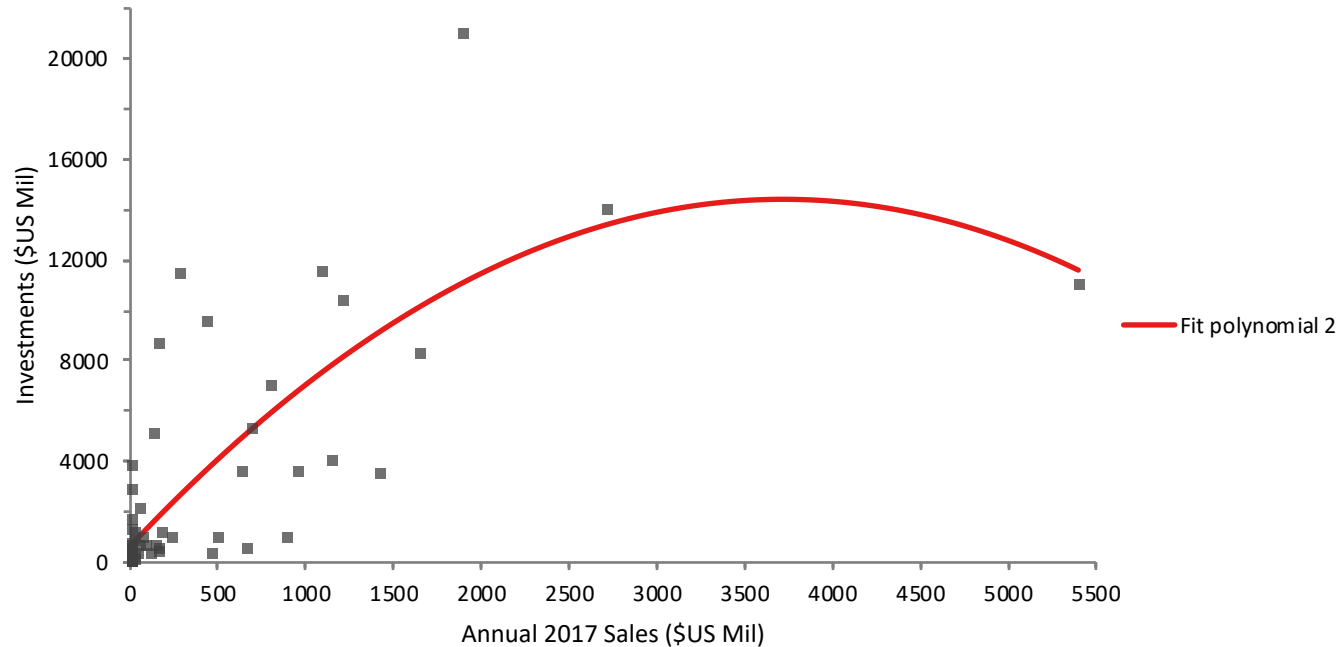
Acquired Company Location	Category	Status	Investments (\$US Mil)	Annual 2017 Sales (\$US Mil)
NJ	Endocrine, Metabolic and Genetic Disorders	Marketed	\$15	\$0.00
MA	Oncology	Marketed	\$32	\$1.72
CA	Endocrine, Metabolic and Genetic Disorders	Marketed	\$75	\$0.47
MA	Oncology	Marketed	\$91	\$13.84
CA	Infectious Diseases	Marketed	\$133	\$1.20
PA	Infectious Diseases	Marketed	\$208	\$0.00
PA	Central Nervous System	Marketed	\$270	\$0.00
CA	Endocrine, Metabolic and Genetic Disorders	Marketed	\$315	\$31.34
CA	Respiratory	Post Marketing	\$342	\$463.00
NJ	Endocrine, Metabolic and Genetic Disorders	Marketed	\$443	\$0.00
CA	Ophthalmology	Marketed	\$488	\$160.30
CA	Central Nervous System	Marketed	\$680	\$0.00
CT	Infectious Diseases	Marketed	\$750	\$0.00
WA	Musculoskeletal	Marketed	\$885	\$28.20
CA	Central Nervous System	Marketed	\$973	\$231.00
CA	Oncology	Marketed	\$1,000	\$63.00
CA	Oncology	Marketed	\$1,160	\$175.00
CA	Musculoskeletal	Marketed	\$1,260	\$3.00
TN	Cardiovascular	Marketed	\$3,600	\$944.76
AR	Infectious Diseases	Marketed	\$3,850	\$0.00
MA	Oncology	Marketed	\$5,340	\$688.50
CA	Endocrine, Metabolic and Genetic Disorders	Marketed	\$7,000	\$798.00
MA	Infectious Diseases	Marketed	\$9,500	\$433.02
CO	Oncology	Marketed	\$11,400	\$284.38
MA	Hematology	Marketed	\$11,600	\$1,089.00

- A random sample of 25 of the 64 therapies approved for market access from 2009 – 2019 was selected; a Welch ANOVA test was performed to validate the sample.
- A common criticism is that investors ‘over pay’ for assets; is this true?
- An exponential regression was run to test if the 2017 audited revenue generated by a therapy could predict the size of its investment of the entire marketed cohort (n=57).
- The relationship shows that investors accurately anticipate revenue, i.e. the smaller the investments, the lower the revenue potential of the asset.
- This relationship is highly statistically significant ($p = 0.0001$) in that the amount of 2017 revenue accurately predicts the amount of investment that is made.

BioPharma Investors – Relationship to Revenue

Statistical Significance of 2017 Therapy Revenue Predicting Investment Size

N=57 (Marketed and Post-Marketing)



Source	SS	DF	MS	F	p-value
Difference	626431698.9	2	313215849.5	36.92	<0.0001
Error	458160312.5	54	8484450.2		
Null model	1084592011.4	56	19367714.5		

BioPharma Investors – Impact of Modeling

Acquired Company Location	Category	Status	Investments (\$US Mil)	Annual 2017 Sales (\$US Mil)
NJ	Endocrine, Metabolic and Genetic Disorders	Marketed	\$15	\$0.00
MA	Oncology	Marketed	\$32	\$1.72
CA	Endocrine, Metabolic and Genetic Disorders	Marketed	\$75	\$0.47
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CA	Oncology	Marketed	\$1,160	\$175.00
CA	Musculoskeletal	Marketed	\$1,260	\$3.00
TN	Cardiovascular	Marketed	\$3,600	\$944.76
AR	Infectious Diseases	Marketed	\$3,850	\$0.00
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MA	Hematology	Marketed	\$11,600	\$1,089.00

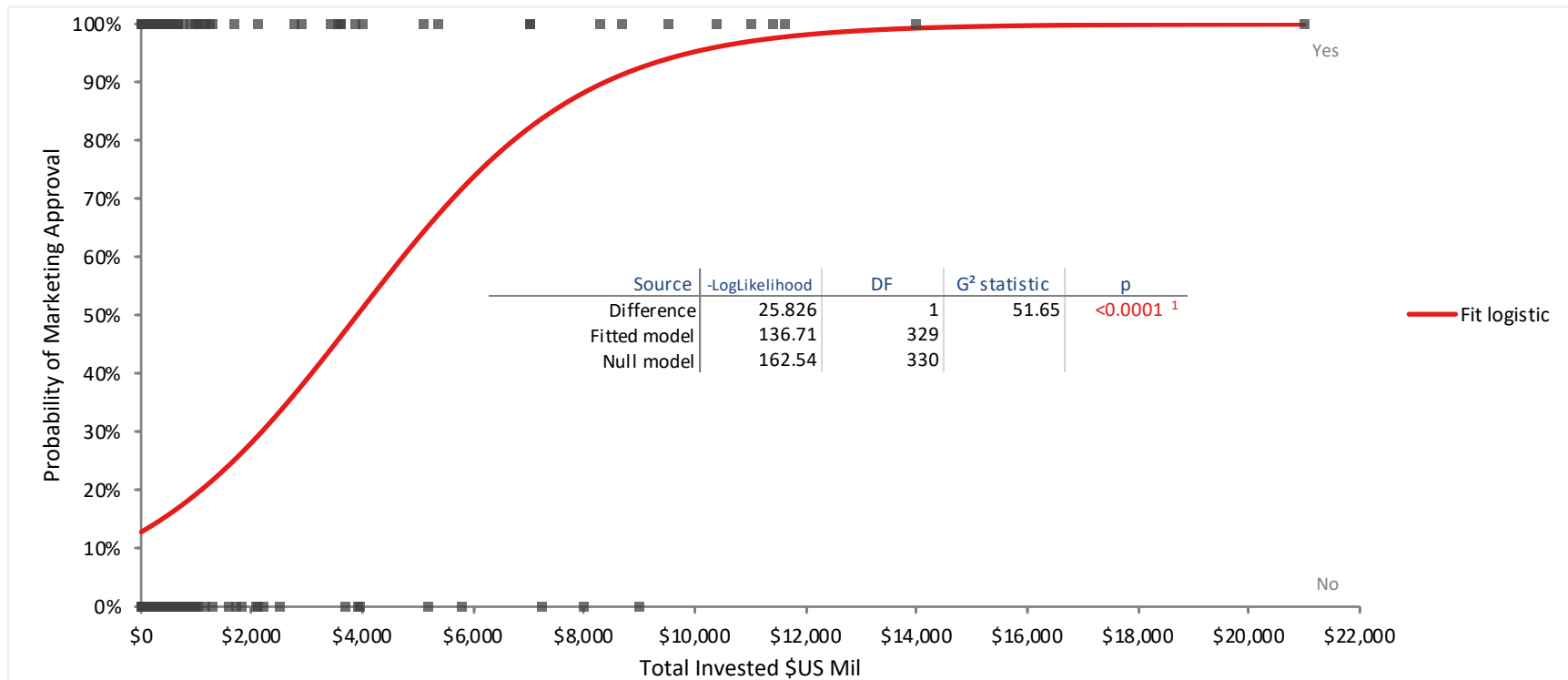
- Based on our model, an across the board revenue reduction of 58% will influence which assets classes are ‘investible’.
- Small market indications, early stage platforms with lower revenue potential, or products that risk not breaking even will not be brought to market (i.e. Alzheimer’s and neurological disorders may further be hindered, as will research requiring long-term outcomes [CVD] as well as targeted therapies in smaller indications).
- Investors will dedicate their reduced available capital to those assets with the largest market potential.
- However, investors need to invest large amounts of money to know which assets have market potential; our research finds the average cost across all indications is \$800 mil through Phase III, ergo the only option available to investors is fewer investments.
- Far fewer of the 64 assets from small, emerging biotech firms would have gained market access from 2009 - 2019.

Investments Predicting Market Entry

- Given the rate of success for BioPharma market entry is low, any reduction in revenue will mean that a firm will need to make fewer investments in proportion to their drop of free cashflow.
- Using a logistic regression, we have modeled the probability of our 331 products from small emerging U.S. biotech firms from 2009-2019 gaining market entry based on the total investment they received; the total amount received is a statistically significant predictor of successful market entry.
- We then model the impact of revised revenues on the probability of market entry and the decision to invest in the same cohort assuming two scenarios, the House Ways Means impact on Medicare Part D only, and the full impact on the commercial market adding in a 1.2 margin in H.R. 3.
- We find that H.R. 3 will reduce market entry from 64 products from emerging biotech companies to 8, all things being equal and with a 58% drop in free cashflow.

Investments Predicting Market Access

Amount of Cumulative Investments is a Statistically Significant Predictor of the Approval of New U.S. BioPharma Products from Emerging Biotech – A \$4 Bil investment has a 50% probability of Market Access



Current Probability of 64 U.S. Therapies Coming to Market 2009 - 2019

Indication	Investment	Probability
Oncology	\$21,000	100%
Oncology	\$14,000	99%
Hematology	\$11,600	98%
Oncology	\$11,400	98%
Infectious Diseases	\$11,000	97%
Oncology	\$10,400	96%
Infectious Diseases	\$9,500	94%
Musculoskeletal	\$8,700	91%
Musculoskeletal	\$8,300	90%
Hematology	\$7,000	82%
Endocrine, Metabolic and Genetic Disorders	\$7,000	82%
Oncology	\$5,340	67%
Oncology	\$5,100	64%
Oncology	\$4,000	51%
Infectious Diseases	\$3,850	49%
Cardiovascular	\$3,600	46%
Infectious Diseases	\$3,600	46%
Oncology	\$3,550	46%
Oncology	\$3,430	44%
Surgery	\$2,900	38%
Endocrine, Metabolic and Genetic Disorders	\$2,755	36%

Indication	Investment	Probability
Endocrine, Metabolic and Genetic Disorders	\$2,100	29%
Endocrine, Metabolic and Genetic Disorders	\$1,695	25%
Musculoskeletal	\$1,260	21%
Cardiovascular	\$1,240	21%
Oncology	\$1,160	21%
Respiratory	\$1,150	21%
Oncology	\$1,000	19%
Oncology	\$1,000	19%
Endocrine, Metabolic and Genetic Disorders	\$1,000	19%
Central Nervous System	\$997	19%
Central Nervous System	\$973	19%
Musculoskeletal	\$885	19%
Infectious Diseases	\$750	18%
Central Nervous System	\$680	17%
Infectious Diseases	\$675	17%
Oncology	\$640	17%
Oncology	\$640	17%
Hematology	\$560	16%
Respiratory	\$550	16%
Oncology	\$510	16%
Ophthalmology	\$488	16%
Oncology	\$465	16%

Indication	Investment	Probability
Endocrine, Metabolic and Genetic Disorders	\$443	15%
Oncology	\$415	15%
Cardiovascular	\$350	15%
Respiratory	\$342	15%
Endocrine, Metabolic and Genetic Disorders	\$315	15%
Central Nervous System	\$270	14%
Musculoskeletal	\$220	14%
Infectious Diseases	\$208	14%
Gastroenterology	\$200	14%
Musculoskeletal	\$140	14%
Infectious Diseases	\$133	14%
Oncology	\$91	13%
Endocrine, Metabolic and Genetic Disorders	\$75	13%
Infectious Diseases	\$46	13%
Oncology	\$43	13%
Immunology and Inflammation	\$41	13%
Oncology	\$32	13%
Respiratory	\$30	13%
Endocrine, Metabolic and Genetic Disorders	\$29	13%
Ophthalmology	\$26	13%
Endocrine, Metabolic and Genetic Disorders	\$15	13%

Many of our therapies came to market with a low probability, based on investments predicting limited revenue potential. What will be the impact on probability given a 33% and 58% reduction in investment capital, based on the current congressional proposals?

Revised Probability of 64 U.S. Therapies Coming to Market

House Ways and Means and H.R. 3 Proposals

Asset Class	Total Invested Capital \$181 Bil	Current Probability	Ways & Means Revenue Reduced 33% Capital \$121 Bil	H.R. 3 Revenue Reduced 58% Capital \$76 Bil
Oncology	\$21,000	100%	99%	92%
Oncology	\$14,000	99%	94%	73%
Hematology	\$11,600	98%	87%	62%
Oncology	\$11,400	98%	86%	61%
Infectious Diseases	\$11,000	97%	85%	59%
Oncology	\$10,400	96%	82%	56%
Infectious Diseases	\$9,500	94%	77%	51%
Musculoskeletal	\$8,700	91%	72%	47%
Musculoskeletal	\$8,300	90%	69%	45%
Hematology	\$7,000	82%	60%	38%
Endocrine, Metabolic and Genetic	\$7,000	82%	60%	38%
Oncology	\$5,340	67%	46%	31%
Oncology	\$5,100	64%	44%	30%
Oncology	\$4,000	51%	35%	25%
Infectious Diseases	\$3,850	49%	34%	25%
Cardiovascular	\$3,600	46%	33%	24%
Infectious Diseases	\$3,600	46%	33%	24%
Oncology	\$3,550	46%	32%	23%
Oncology	\$3,430	44%	31%	23%
Surgery	\$2,900	38%	28%	21%
Endocrine, Metabolic and Genetic	\$2,755	36%	27%	21%
Endocrine, Metabolic and Genetic	\$2,100	29%	23%	18%
Endocrine, Metabolic and Genetic	\$1,695	25%	20%	17%

64 Assets
of
Declining
Probability



GIVEN AVAILABLE CASH AND REVISED PROBABILITY	
BRING TO MARKET	DO NOT BRING TO MARKET

Where is the Pharmacy to the World?

International Regulatory Variation and Pharmaceutical Industry Location.

Table 4. New Chemical Entities by Headquarter Country of Inventing Firm¹³

	1961 – 1970		1971 – 1980		1981 – 1990		1991 – 2000	
	NCEs	% Total	NCEs	%Total	NCEs	%Total	NCEs	%Total
USA	209	30	157	31	145	32	75	42
France	172	25	98	19	37	8	10	6
Germany	115	17	96	20	67	15	24	13
Japan	80	12	75	15	130	29	16	9
Switzerland	68	10	53	10	48	11	26	14
U.K.	48	7	29	6	29	6	29	16
Total NCEs	692		508		456		180	

“Between 1961 and 1980, firms based on the European continent invented and brought to market over sixty percent of new therapeutic molecules. . .By the decade beginning in 1991, however, firms in the United States were inventing over forty percent of new drugs . . .Germany’s relative ranking slipped further after 2001”

Arthur Daemmrich, Copyright © 2009
Harvard Business School

Pharmaceutical regulation in Europe and its impact on corporate R&D

[Stephan Eger](#) & [Jörg C Mahlich](#), *Health Economics Review* volume 4, Article number: 23

Published online 2014 Oct 3. doi: [10.1186/s13561-014-0023-5](https://doi.org/10.1186/s13561-014-0023-5)

“The higher the share of sales made in the EMA region, the higher is the negative impact. . .in other words the more sales a company makes in the EMA region beyond a certain threshold the higher is the decline in R&D investment.”

Abstract

Objectives

Many European countries regulate the markets for prescription drugs in order to cope with rising health expenditures. On the other hand, regulation distorts incentives to invest in pharmaceutical R&D. This study aims at empirically assessing the impact of regulation on pharmaceutical R&D expenditures.

Results

Beyond a threshold of 33% of sales generated in Europe, a higher presence in Europe is associated with lower R&D investments.

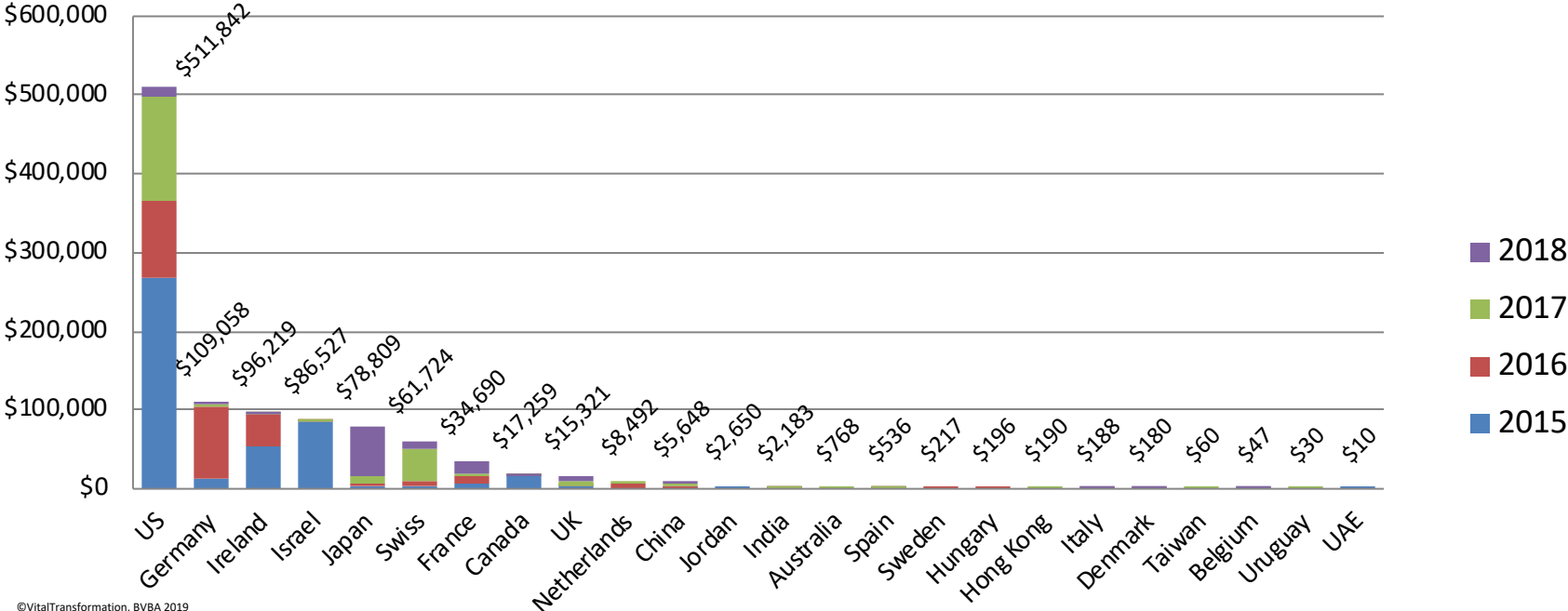
Conclusion

The results can be interpreted as further evidence of the deteriorating effect of regulation on firm's incentives to invest in R&D.

BIOTECH M&A BY BUYING COUNTRY, 2015 - 2018

\$US Millions

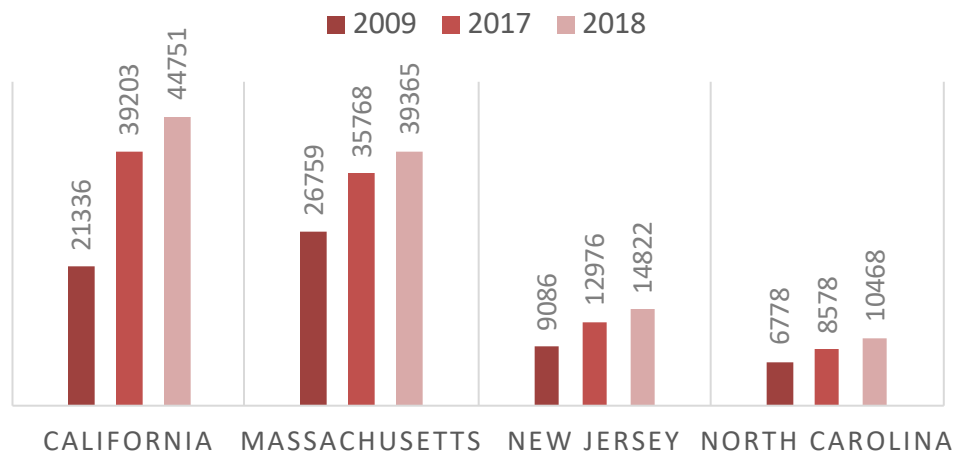
In order to commercialize, international biotech is locating to the U.S. due to a lack of market opportunity in Europe. This chart shows that, over the last 4 years, 70% of all global biotech IP in mergers and acquisitions are being acquired by US interests.



©VitalTransformation, BVBA 2019
<https://www.thepharmaletter.com/article/an-all-time-record-year-for-pharma-biotech-m-a>
<https://www.thepharmaletter.com/article/volume-and-value-of-pharma-biotech-m-a-slowed-down-in-2016>
<https://www.thepharmaletter.com/article/pharmaceutical-m-a-deals-in-2017>
<https://www.thepharmaletter.com/article/pharmaceutical-m-a-deals-in-2018>

BioPharma – A U.S. Innovation Growth Engine

10 YEAR JOB GROWTH BIOTECH R&D



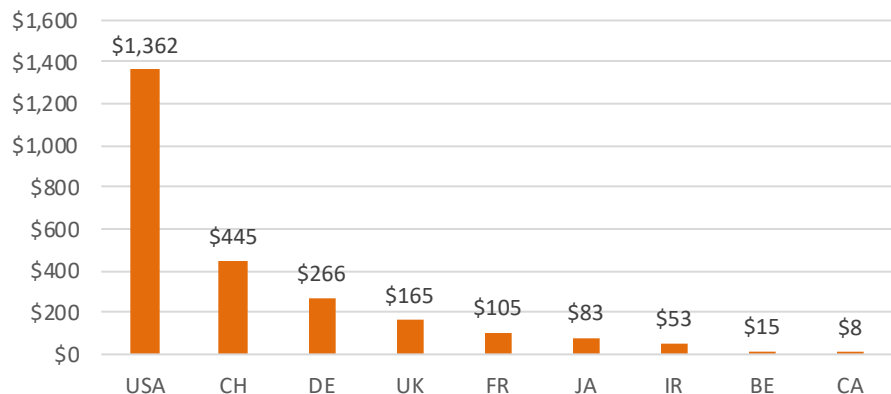
The BioPharma sector is growing organically as well as through capturing emerging international companies to move to the U.S. to commercialize. This growth will be curtailed by a revenue reduction of 58%.

Source: MassBIO, U.S. Bureau of Labor Statistics, Quarterly Census of Employment and Wages (QCEW)

International Reference Pricing Overwhelmingly Impacts US Shareholder Value

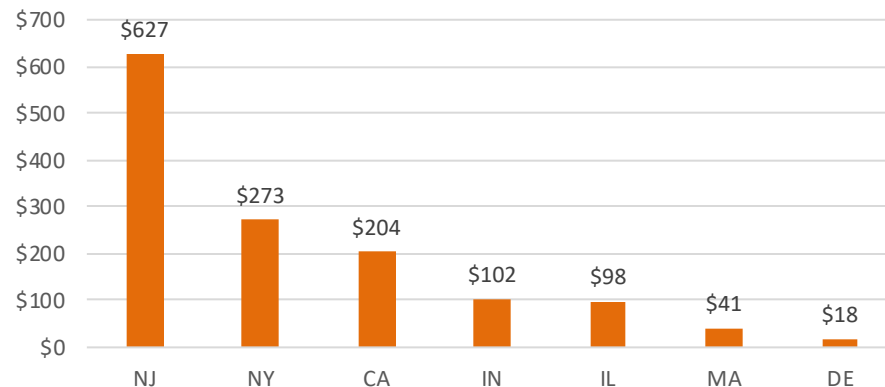
Medicare Part D

International Reference Pricing Companies
Market Capitalization By Country \$US Bil



US Market Capitalization

State Corporate Headquarters
Medicare Part D Impacted Firms \$US Bil



A cut of 58% of BioPharma revenue will likely result in a reduction in excess of \$500 billion in the Market Capitalization of US firms

Key Messages

- International Reference Pricing reductions in Part D will not be contained to the Medicare market and will impact all U.S. commercial pricing, regardless if this is the stated goal.
- H.R. 3 will cause, at minimum, a reduction of \$72 bil a year in industry revenue (House Ways and Means, CBO, and Vital Transformation's estimate); this represents a reduction of 58% of the annual net industry revenue of Medicare Part D impacted companies of \$124.3 bil.
- A 58% reduction in revenue will radically impact vital marketing, commercialization, licensing, and venture funding provided to emerging innovative biotech.
- 19% of our cohort has gained market access (64 of 331); determining if a therapy has market potential requires roughly \$800 Mil on average through Phase III.
- Of our 331 emerging biotech firms that received investments from 2009-2019, \$4 Bil of funding committed to an asset had only a 50/50 probability of gaining market access.
- Our model predicts that a 58% reduction in revenue will see a drop in the number of innovative biotech assets brought to market from 64 to 8 over a 10 year period (all things being equal).
- 70% of global BioPharma intellectual property is now owned and developed in the U.S. which has seen 100% job growth in CA and MA in biotech R&D employment over the last 10 years; this will be arrested and likely reversed by H.R. 3 and international reference pricing.



VitalTransformation

The impact of health technology made simple

DATA APPENDIX



H.R.3 - International Reference Pricing

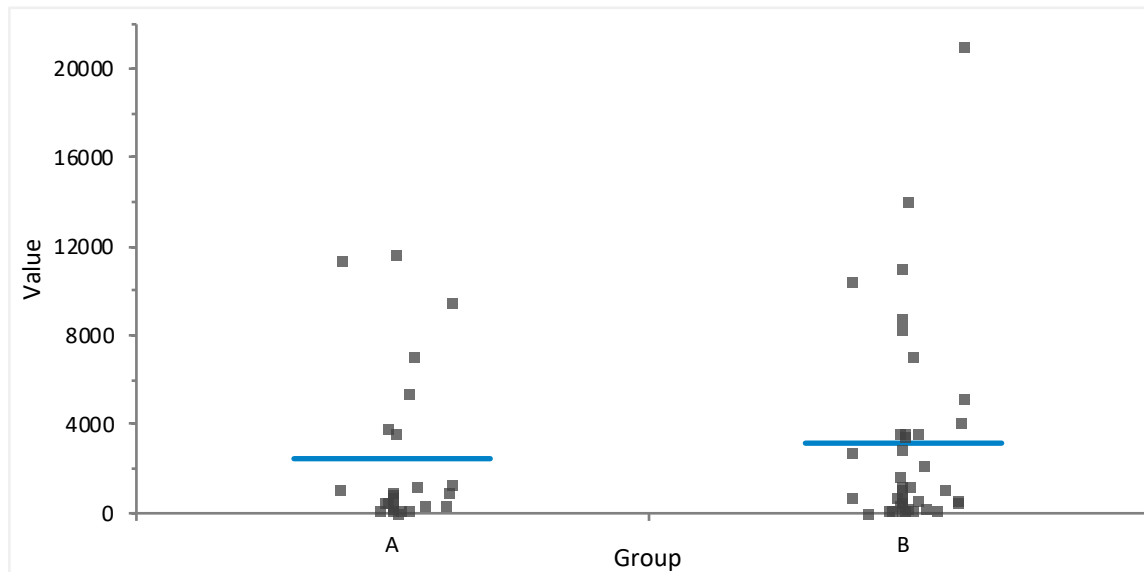
Calculating the Impact on the U.S. BioPharmaceutical Innovation Ecosystem

Nov 22, 2019

Support Provided By

PhRMA





Welch ANOVA

F statistic	0.46
Numerator DF	1
Denominator DF	59.0
p-value	0.5013 ¹

N | 64

H0: $\mu_1 = \mu_2 = \mu...$

The mean of the populations are all equal.

H1: $\mu_i \neq \mu_j$ for at least one i, j

The mean of the populations are not all equal.

¹ Do not reject the null hypothesis at the 5% significance level.

Value by Group	N	Mean	Mean SE	SD
A	25	2456.40	726.532	3632.66
B	39	3154.38	732.287	4573.13

Fit

N | 57
 Mean of Y | 2910.2

Equation | Investments (\$US Mil) = 663.3 + 7.399 Annual 2017 Sales (\$US Mil) - 0.0009949 Annual 2017 Sales (\$US Mil)²

R² | 0.578
 R² adjusted | 0.562
 RMSE | 2912.81

Parameter	Estimate	95% CI	SE	t	p-value
Constant	663.3	-281.4 to 1608	471.21	1.41	0.1649
Annual 2017 Sales	7.399	5.301 to 9.498	1.0468	7.07	<0.0001
Annual 2017 Sales ²	-9.949E-04	-0.001456 to -5.334E-04	2.3018E-04	-4.32	<0.0001

H0: $\beta = 0$

The parameter is equal to 0.

H1: $\beta \neq 0$

The parameter is not equal to 0.

Effect of Model

Source	SS	DF	MS	F	p-value
Difference	626431698.9	2	313215849.5	36.92	<0.0001
Error	458160312.5	54	8484450.2		
Null model	1084592011.4	56	19367714.5		

Fit

N	331		
Parameter	Estimate	99% CI	SE
Constant	-1.917	-2.363 to -1.472	0.17293
Total	4.920E-04	2.485E-04 to 7.355E-04	9.4527E-05

$$\beta = \log \Phi_{\text{Yes}}$$

Effect of Model

Source	- LogLikelihood	DF	G ² statistic	p
Difference	25.826	1	51.65	<0.0001 ¹
Fitted model	136.71	329		
Null model	162.54	330		

$$H_0: g(x) = \beta_0$$

The model is no better than a null model $Y=\pi$.

$$H_1: g(x) = \beta_0 + \beta x$$

The model is better than the null model.

¹ Reject the null hypothesis in favour of the alternative hypothesis at the 1% significance level.