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The Historical Impact of Price Controls on the Biopharma Industry

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PREPARED BY

Duane Schulthess
CEO

Harry Bowen
Consulting Economist

Executive Summary

- With US congressional proposals now advocating in favor of government price setting for prescription medicines, the impacts of historical price setting in Europe provides a robust data source to test and predict the impact of price controls in the US on the biopharma ecosystem.
- Previous research has shown a decline in the biopharma ecosystem in Europe relative to the United States, corresponding to increasing price controls in European countries.
- This study uses statistical and economic modeling to calculate the net impact of EU price controls upon the domestic biopharma ecosystem in Europe; US and EU prices were compared for the top 10 selling drugs in the US for each year from 2003 – 2020, and impacts upon biopharma R&D ecosystem key performance indicators (KPIs) were measured.
- Our research shows that every 10% drop in the price of medicines in price-controlled EU markets was associated with a 14% decrease in total VC funding (10% early stage and 17% late state), a 7% decrease in biotech patents, a 9% decrease in biotech start up funding relative to the US, and an 8% increase in the delay of access to medicines.
- Our model also proved robust at predicting the trend impacts of drug pricing on Japanese biopharma KPIs, which acts as a validation of our methodology; we posit that similar drops measured by biopharma KPIs in the US would be seen over time with similar price controls.
- Drug pricing controls implemented in the US would likely have an even greater impact on biopharma KPIs given its global leadership in investment and innovation.

“Reducing revenues from highly profitable drugs will deter VCs from making high-risk investments in biotechs… [they are] going to be very sensitive to the upper tail of profits being lopped off.”

Harvard Professor Amitabh Chandra, BioCentury, September 2021.

Project Background

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- Previous research has shown measurable declines in the EU biopharma ecosystem relative to the United States, as government price controls on medicines expanded in Europe.
    - In 2009, Arthur Daemmrich of the Harvard Business School noted, “Between 1961 and 1980, firms based on the European continent invented and brought to market over sixty percent of new therapeutic molecules. . .By. . .1991, . . .firms in the United States were inventing over forty percent of new drugs . . . Germany’s relative ranking slipped further after 2001.”
    - Stephan Eger and Jörg Mahlich, in the Health Economics Review in 2014, found that, “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 the decline in R&D investment.”
- The objective of this study is to determine if the EU biopharma ecosystem continues to be negatively impacted by price controls on medicines, and to quantify any statistically measurable impacts that could be extrapolated to the US biopharma ecosystem as U.S. policymakers consider drug pricing reform.

*European Medicines Agency

Research Methodology

1. A basket of the top 10 selling drugs in the US were selected for each year from 2003 – 2020 to determine their average cost and average access delay relative to the US in Belgium, France, Germany, Ireland, Italy, Spain, Sweden, and the United Kingdom.

2. Using data from both public and private sources, a multivariate analysis was conducted to estimate the impact of Europe-US price differences with respect to the following:
   - Evidence of causality between the use of biopharma price controls on core key performance indicators (KPIs) regarding the European R&D biotech ecosystem.
   - The impact of EU-US price differences, driven by price controls in European countries, on delays in access to needed new medicines.

3. We then tested our model's ability to accurately predict the impact of Japanese pharmaceutical pricing on our different biopharma KPIs.

4. In all cases, an elasticity value measuring the impact of price-controls for medicines in European markets upon our various biopharma KPIs were calculated.

44 drugs included in our test baskets

The top 10 selling US medicines in each year from 2003 – 2020s

Therapy Area	Count
NEUROLOGY	10
ONCOLOGY	5
IMMUNOSUPPRESSANTS	5
CVD	4
DIABETES	4
RESPIRATORY	3
BLOOD AND BLOOD FORMING ORGANS	3
OPHTHALMOLOGY	2
GASTROENTEROLOGY	2
HEPATITIS C	2
RHEUMATOLOGY	1
DERMATOLOGY	1
HIV	1
HEMATOLOGY	1

- Basket is compared to all countries for price and date of access to the medicine*, weighted by population and GDP.
- The top 10 drugs are by US sales.
- Drugs in the baskets include best in class novel treatments addressing high unmet needs in stroke, heart attack, hepatitis, depression, anxiety, pain, eyesight, COPD, cancer, eczema, and HIV/AIDS, among others.

*For European countries, refers to the date at which the national HTA or government body includes the drug for national reimbursement schemes.

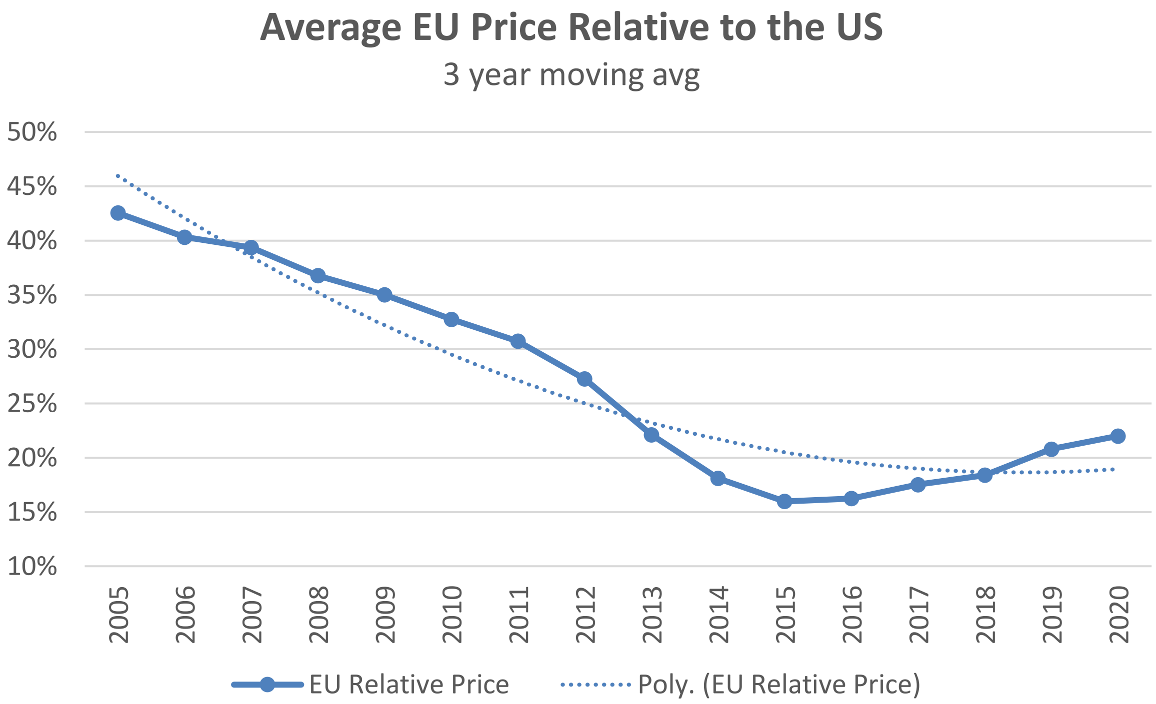
Data Sources Used

Datasets used in this research include:

1. OECD
2. US Department of Commerce
3. BioCentury
4. Medtrack/Informa
5. Pricentric
6. IQVIA MIDAS - data combine country-level data, healthcare expertise and therapeutic knowledge in 90+ countries to deliver data in globally standardized forms to facilitate multi-country analyses, a leading source of insight into international market dynamics relating to the distribution and use of medicines. IQVIA MIDAS data is designed to support multi-country analyses of trends, patterns, and similar types of analyses. All of the calculations, algorithms and methodologies used to produce these estimates of real-world activity makes the data highly reliable for these intended uses.
7. Social Survey Research Information Company, Ltd (Japan only)

The Impact of EU Price Controls on Biopharma Ecosystem KPIs

Basket of medicines sees significant price decreases in price-controlled EU markets relative to the US



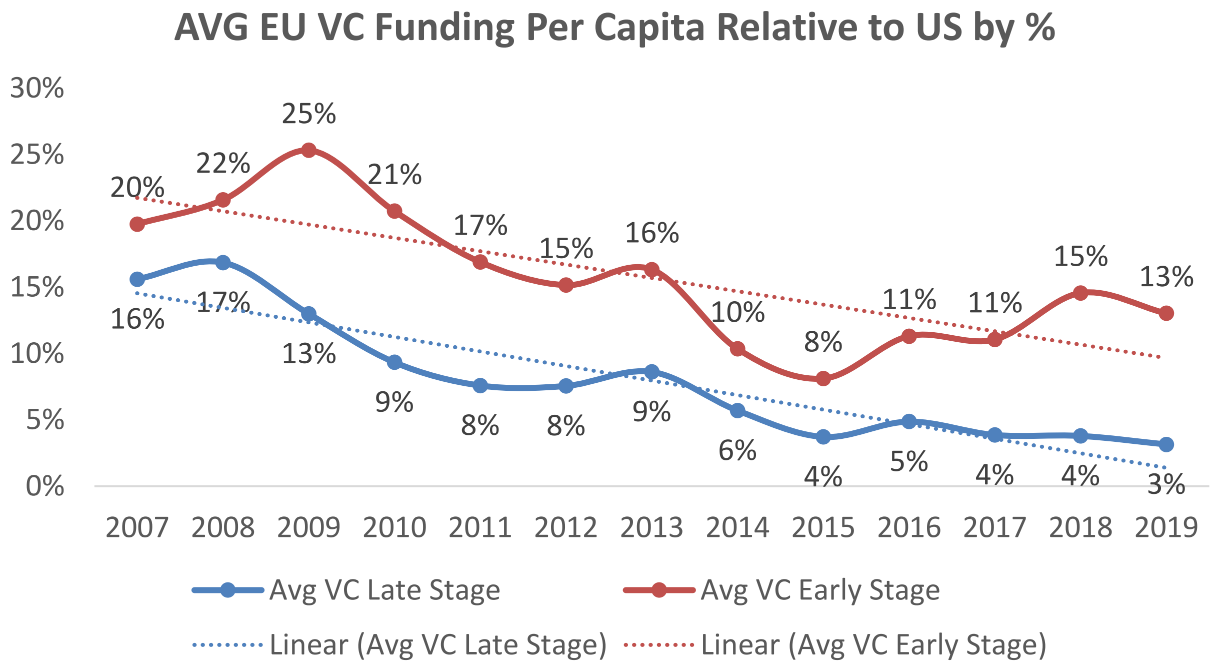
Sample countries are Belgium, France, Germany, Ireland, Italy , Spain, Sweden, United Kingdom, and United States

Why is VC important in biotech?

"Initial public offerings (IPOs) . . .started strongly in 2020, with biopharma firms comprising 80% of all US IPOs in the first quarter . . . the US NASDAQ Biotechnology Index . . . neared a five-year high"

Nature Biotechnology, May 2020

Early & late stage VC have declined significantly in the EU relative to the US

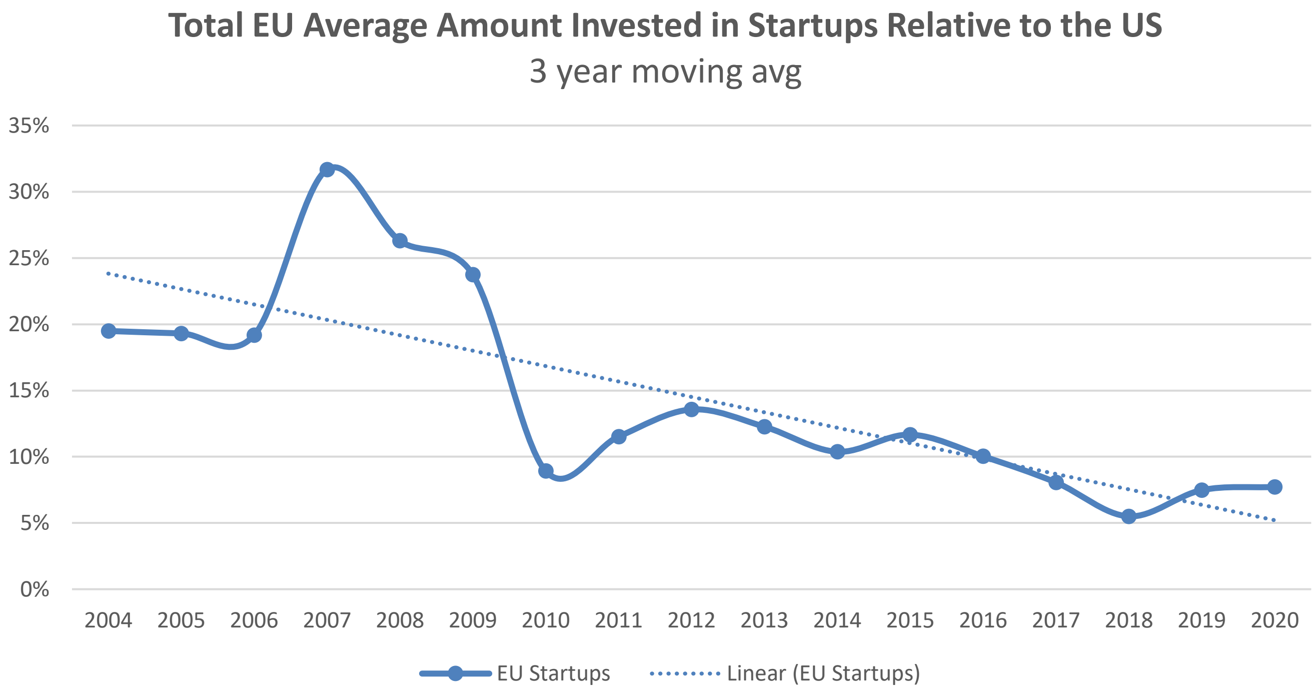


By 2019, EU late-stage VC was just 3% of US late-stage VC.

Sample countries are Belgium, France, Germany, Ireland, Italy , Spain, Sweden, United Kingdom, and United States

Biopharma startup investments have declined significantly in the EU

relative to the US



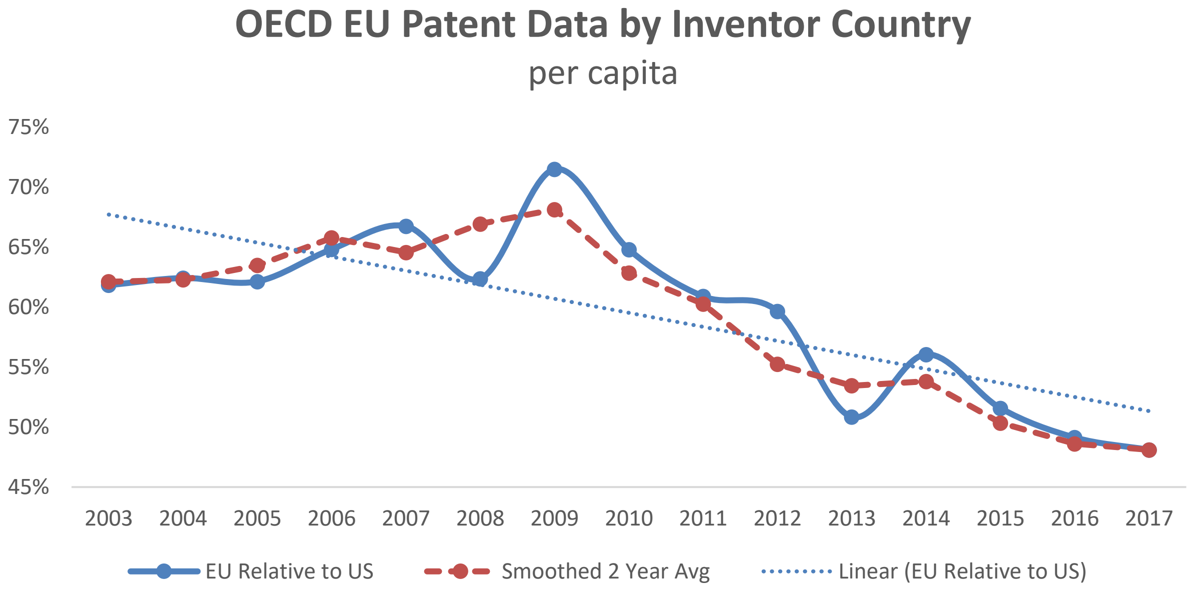
Sample countries are Belgium, France, Germany, Ireland, Italy , Spain, Sweden, United Kingdom, and United States

Biopharma startup investments in the EU were less than 10% of the level in the US by 2020.

Startup investments include foreign direct investments as well as investments made within the country.

Biotech patents* per capita have declined significantly in the EU

relative to US

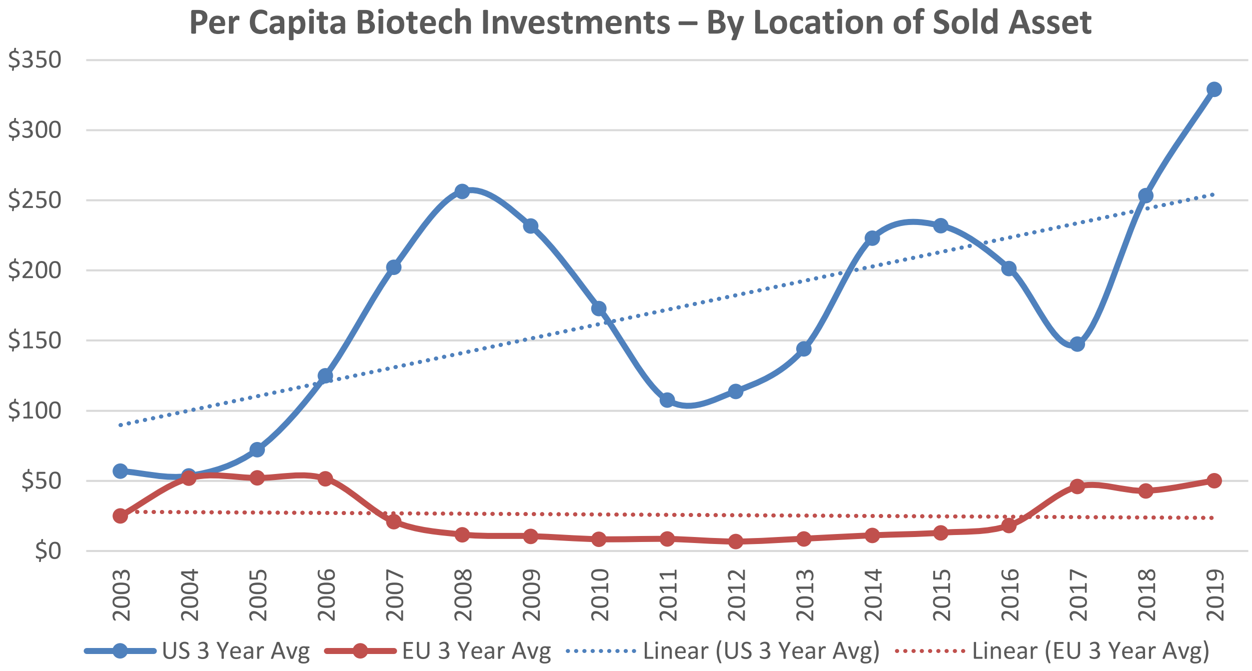


By 2017, EU biotech patents per capita were roughly 48% of the US total.

*IP5 patents-BioTech-Priority date, Inventor country of residence – OECD.

Sample countries are France, Germany, Italy, Spain, Sweden, United Kingdom, and United States

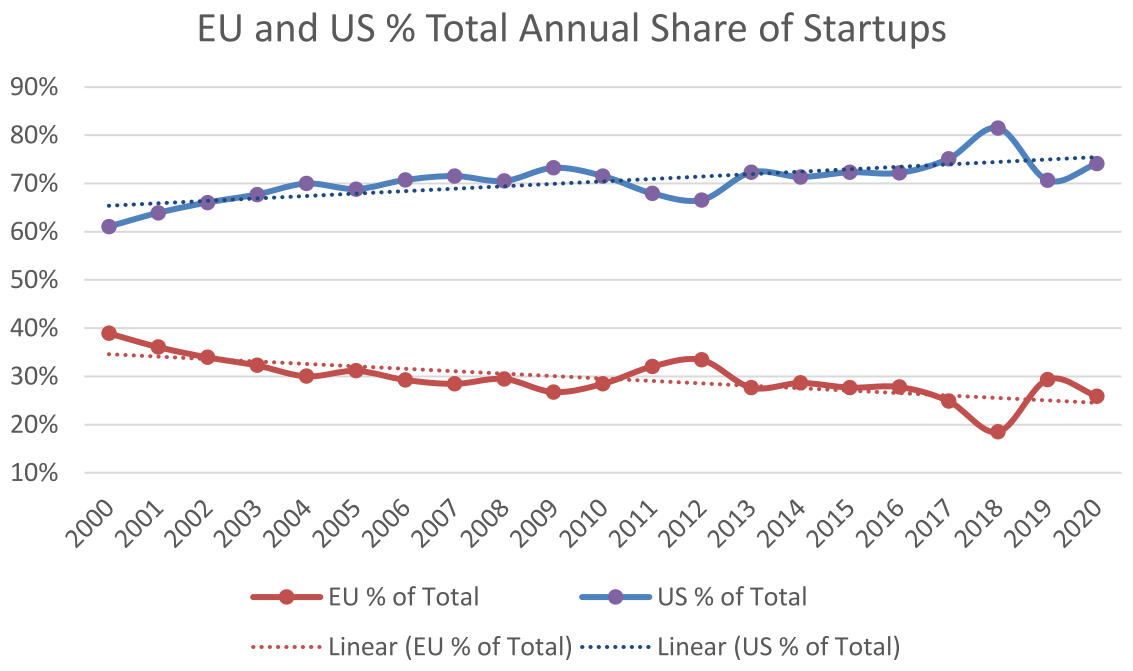
US biotech investments per capita have grown, EU investments have been flat



From 2003 to 2019, biotech investments in the US increased sixfold, while they remained static in the EU.

Sample countries are Belgium, France, Germany, Ireland, Italy , Spain, Sweden, United Kingdom, and United States.

The US share of total biotech startups has grown, the EU share has declined



In 2020, the US share of total annual biotech startups was roughly three times greater than the EU share.

Sample countries are Belgium, France, Germany, Ireland, Italy , Spain, Sweden, United Kingdom, and United States.

The lower the EU price relative to the US, the longer is the delay in patient access

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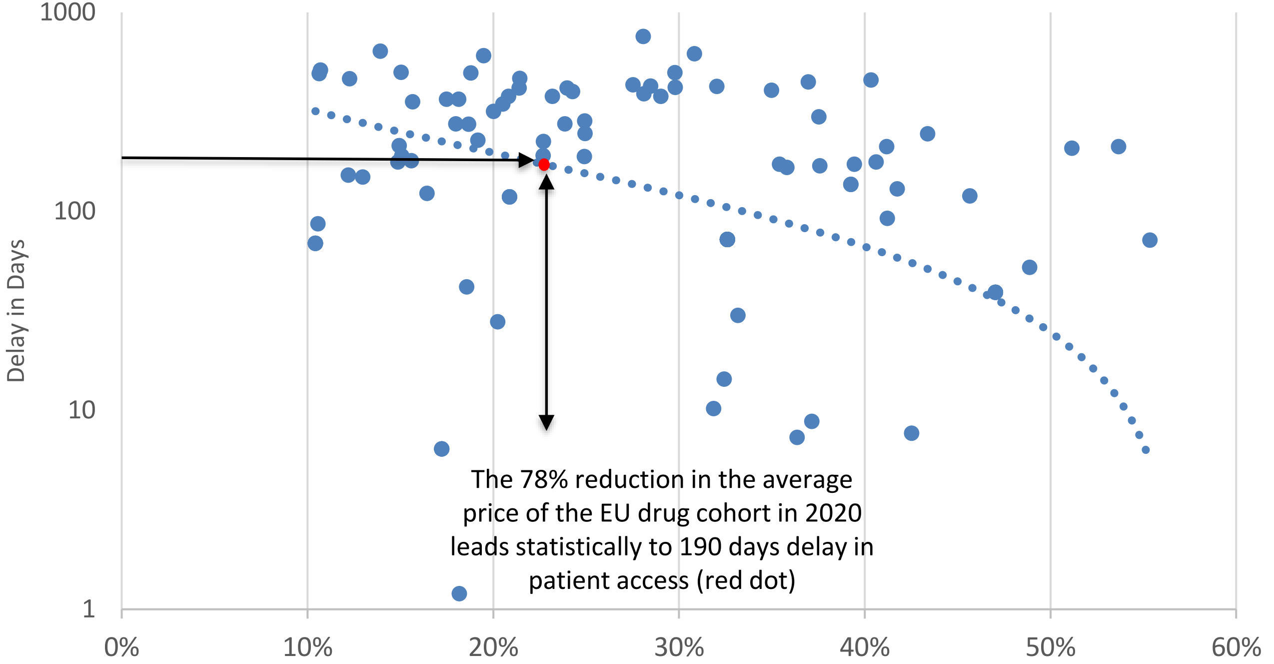
Delay in EU Access Per Drug Relative to US Approval Date and Price



Lower % of US Price → Higher % of US Price

Lower drug prices caused by price controls in the EU, statistically predict the delay in patient access compared to the FDA approval date.

The current EU average lower price of 78% in our drug cohort leads to 190 days of delays for patient access.

For every 10% reduction in the price of medicines, we see a one month (30.6) day delay in patient access measured from the date of FDA approval ($p < 0.05$). Most of these are best in class treatments for high unmet medical needs.

Sample countries are France, Germany, Italy, Spain, Sweden, United Kingdom, and United States.

Biopharma industry KPIs declined significantly with EU price controls on drugs

For every 10% reduction in the price of medicines in a given market:

- Early-stage VC funding across all industries* declined by 14% ($p < 0.001$)
  - Early stage declined by 10% ($p < 0.001$)
  - Late-stage declined by 17% ($p < 0.001$)
- Biotech patents created per capita declined by 7% ($p < 0.05$)
- Biotech investments by location of asset sold per capita declined by 2% ($p<0.001$)

- Funds raised by biopharma startups relative to the US declined by 9% ($p<0.05$)
- The number of biopharma startups in the EU relative to the US declined by 2% ($p < 0.01$)

- The delay in EU access (relative to FDA approval) increased by 8% ($p < 0.05$).

*Data were not available for VC funding by industry. However, biotech represents roughly a quarter of all VC investments and a high percentage of all IPO listings and VC ROI.

Testing our model's predictive ability - Japan

- To validate our model, predictions for different biopharma KPIs were computed using Japanese pricing data.
- The resulting trend predictions generated by our model were then compared to the actual Japanese outcomes using a regression analysis (see appendix for regression tables).
- Our model proved robust at predicting with 95% statistical probability the level of Japanese enterprise R&D funding per capita and Japanese biotech patents per capita.
- Our model proved robust at predicting with 90% statistical probability the level Japanese VC funding per capita and the level Japanese startup funding relative to the US.
- These findings indicate high confidence in the model's ability to predict the effects of drug price changes and price controls on biopharma KPIs.

Summary of Findings

- Continued EU controls on the price of medicines has had a statistically measurable impact on their biopharma ecosystem KPIs.
- Our estimates demonstrate that each 10% drop in drug prices in a given market led to a/an:
  - 14% decrease in total VC funding; 10% early-stage VC funding, 17% late-stage VC funding.
  - 9% decrease in biotech start up funding relative to the US.
  - 8% increase in the delay of access to medicines.
  - 7% decrease in biotech patents per capita.
- Our model statistically predicts the impacts of price controls on Japanese pharma R&D, patent creation, VC funding, and start-up funding, providing evidence that the impact of drug price controls are generalizable to other countries.

Conclusions/Implications

- Many studies have shown lost biotech productivity, a declining share of global biopharma R&D, and a general movement of novel biotech assets from the EU to the US, but they have not tied these trends to price control policies in the EU.
- This study finds evidence suggesting that EU drug price control policies since 2003 have negatively affected the EU biopharma ecosystem.
- We would also expect similar negative impacts in other countries that adopt government mandated drug price controls.
- Drug pricing controls implemented in the US would likely have an even greater impact on biopharma KPIs given its global leadership in investment and innovation.
- This study's conclusions are consistent with VT's prior research which found negative and substantial impacts of H.R.3 price controls on both US VC funding and its biopharma innovation ecosystem.

Appendix A: Model Results

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Elasticity Estimates (% change in indicator for each 1% change in price variable)

Indicator (all measured per capita)	Drug Price	Std. Error	Drug Price Relative to US Price	Std. Error
Total VC Funding per capita	1.427***	0.115		
Early Stage Funding per capita	1.012***	0.095		
Later Stage Funding per capita	1.705***	0.146		
Biotech Patents (resident applicant), per capita	0.691*	0.279		
Biotech investments by location of asset sold per capita	0.18***	0.042		
R&D per capita (Pharma Business Enterprises)	0.056*	0.027		
Biotech start-ups, total funds raised relative to U.S.			0.874*	0.366
Biotech start-ups, number of, relative to U.S.			0.243**	0.086
Drug Launch Delay (days after FDA approval)			-0.788*	0.319

* p < .05, ** p < .01 *** p < .001; Elasticity estimates computed at data means. Country sample included on slides 24 and 25. Monetary variables measured in constant 2017 US dollars.

Elasticity Estimates – Confidence Intervals

Indicator	Elasticity	Std. Err.	z-stat	p-value	95% confidence limits	
					Lower	Upper
Total VC Funding per capita	1.427	0.115	12.420	0.000	1.202	1.652
Early Stage Funding per capita	1.012	0.095	10.630	0.000	0.826	1.199
Later Stage Funding per capita	1.705	0.146	11.670	0.000	1.418	1.991
Biotech Patents (resident applicant), per capita	0.691	0.027	2.050	0.041	0.002	0.109
Biotech investments by location sold per capita	0.18	0.278	2.480	0.013	0.145	1.237
Biotech start-ups, total funds raised relative to U.S.	0.874	0.366	2.390	0.017	0.157	1.590
Biotech start-ups, number of, relative to U.S.	0.243	0.086	2.810	0.005	0.073	0.412
Drug Launch Delay (days after FDA approval)	-0.788	0.319	-2.470	0.013	-1.412	-0.163

Elasticity estimates computed at data means. Country sample included on slides 24 and 25. Monetary variables measured in constant 2017 US dollars.

Pooled Data Regression Results using Level of Drug Price Index

Variable	Total VC Funding per capita	Early Stage Funding per capita	Later Stage Funding per capita	Biotech Patents (resident applicant), per capita	Biotech investments by where sold, per capita
Drug Price	21.0113***	6.2246***	13.4469***	0.1577++	11.4903**
GDP per capita	505.6393	266.4984+	93.8312	-244.2963***	-900.2002
Year2003					
Year2004				0.0493	
Year2005				0.4833	
Year2006				0.5948	
Year2007	-12.4084	-10.9127	-1.0926	1.0142++	
Year2008	-14.2953	-10.7328	-3.2583	0.5599	
Year2009	-27.6715	-15.4253++	-11.9505	0.2556	
Year2010	-51.0503++	-22.6361**	-26.5451++	-0.3039	
Year2011	-44.1146++	-21.4271++	-21.0912+	-0.4002	
Year2012	-39.9032++	-19.8897++	-19.1134	-0.3288	
Year2013	-38.7844++	-18.5654++	-19.3372	-0.359	
Year2014	-36.4794+	-19.7059++	-15.5995	-0.0509	
Year2015	-39.8049++	-20.4477++	-17.9328	0.2517	
Year2016	-33.3870+	-16.3350++	-16.9561	0.2246	
Year2017	-53.8315++	-22.2588++	-31.6244++	-4.0766***	
Year2018	-28.5333	-11.1102	-16.6818		
Year2019	-42.0551++	-14.8453++	-25.5996++		
Intercept	-7.3642	3.911	-3.1889	18.0054***	58.9927
R-square	0.910	0.878	0.908	0.069	0.275
F-statistic	20.120	15.942	18.167	11.547	3.661
p-value	0.000	0.000	0.000	0.000	0.029
Observations	118[a]	118[a]	118[a]	105[b]	115[a]

+ p<0.15, ++ p<0.10, ** p<0.01, *** p<0.001. All estimations made using country fixed effects and year time dummies (where indicated). Monetary variables measured in constant 2017 US dollars.

[a] Country sample: Belgium, France, Germany, Ireland, Italy, Spain, Sweden, United Kingdom, United States

[b] Country sample: France, Germany, Italy, Spain, Sweden, United Kingdom, United States

Pooled Data Regression Results using Country Drug Price Index Relative to U.S Price Index

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Variable	Biotech start-ups, total funds raised, relative to U.S.	Biotech start-ups, number of, relative to U.S.	Drug Launch Delay (days since FDA approval date)
Price/US Price	0.057++	0.036**	-383.6066++
GDP per capita	-0.457	0.120	-7372.645
Year2003			
Year2004			31.8864
Year2005			-96.4564++
Year2006			-163.8602**
Year2007			48.3724
Year2008			260.9861***
Year2009			244.3579***
Year2010			198.4423***
Year2011			206.2832***
Year2012			135.611++
Year2013			123.5568++
Year2014			230.3389***
Year2015			208.0999**
Year2016			4.434
Year2017			-29.5213
Year2018			37.9657
Year2019			103.0503+
Year2020			236.993***
Intercept	0.0566++	0.0364**	481.0672+
R-square	0.011	0.002	0.467
F-stat	5.193	4.302	14.765
p-val	0.0066	0.0155	0.000
Observations	142 [a]	142 [a]	108 [b]

+ p<0.15, ++ p<0.10, ** p<0.01, *** p<0.001; Estimation made using country fixed effects and year time dummies (where indicated). Monetary variables measured in constant 2017 US dollars.

[a] Country sample: Belgium, France, Germany, Ireland, Italy, Spain, Sweden, United Kingdom, United States.

[b] Country sample: France, Germany, Italy, Spain, Sweden, United Kingdom, United States.

Appendix B: Model Predictions in Japan

Regression - Japanese biotech patents per capita

Fit

N	15
Mean of Y	0.000009851

Equation	pc_patents_biotec = 4.454e-07 + 1.053 pc_patents_biotec_hat

R^2	0.599
R^2 adjusted	0.569
RMSE	0.000001207

Parameter	Estimate	95% CI	SE	t	p-value
Constant	4.454E-07	-4.211E-06 to 5.101E-06	2.1552E-06	0.21	0.8395 [2]
pc_patents_biotec_hat	1.053	0.5373 to 1.569	0.23881	4.41	0.0007 [1]

H0: β = 0

The parameter is equal to 0.

H1: β ≠ 0

The parameter is not equal to 0.

[1] Reject the null hypothesis in favour of the alternative hypothesis at the 5% significance level.

[2] Do not reject the null hypothesis at the 5% significance level.

Effect of Model

Source	SS	DF	MS	F	p-value
Difference	0.000000000	1	0.000000000	19.45	0.0007 [1]
Error	0.000000000	13	0.000000000		
Null model	0.000000000	14	0.000000000		

Regression - Japanese enterprise R&D funding per capita

Fit

N	17
Mean of Y	97.285134

Equation	pc_berd_by_pharma = 42.87 + 0.9029 pc_berd_by_pharma_hat

R^2	0.630
R^2 adjusted	0.606
RMSE	9.8670652

Parameter	Estimate	95% CI	SE	t	p-value
Constant	42.87	19.38 to 66.37	11.021	3.89	0.0015
pc_berd_by_pharma_hat	0.9029	0.5224 to 1.283	0.17852	5.06	0.0001

H0: β = 0
The parameter is equal to 0.
H1: β ≠ 0
The parameter is not equal to 0.

Effect of Model

Source	SS	DF	MS	F	p-value
Difference	2490.368626	1	2490.368626	25.58	0.0001 [1]
Error	1460.384629	15	97.358975		
Null model	3950.753255	16	246.922078		

Regression - Japanese VC funding per capita

Fit

N	18
Mean of Y	11.2503524

Equation	ppp_pc_vc_total_funding = 7.543 + 0.08171 ppp_pc_vc_total_funding_hat

R^2	0.178
R^2 adjusted	0.127
RMSE	3.49753345

Parameter	Estimate	95% CI	SE	t	p-value
Constant	7.543	2.974 to 12.11	2.1555	3.50	0.0030 [1]
ppp_pc_vc_total_funding_hat	0.08171	-0.01135 to 0.1748	0.043900	1.86	0.0812 [1]

H0: β = 0

The parameter is equal to 0.

H1: β ≠ 0

The parameter is not equal to 0.

[1] Reject the null hypothesis in favour of the alternative hypothesis at the 10% significance level.

Effect of Model

Source	SS	DF	MS	F	p-value
Difference	42.3785389	1	42.3785389	3.46	0.0812 [1]
Error	195.7238436	16	12.2327402		
Null model	238.1023825	17	14.0060225		

Regression - Japanese startup funding relative to the US

Fit

N	18
Mean of Y	-5.492086929

Equation: Acutal Funding 3 Year Avg = 0.001711 * 5.139e+12 $^{\text{Projected Funding 3 Year Avg}}$

R^2	0.169
R^2 adjusted	0.117
RMSE	0.873809357

Parameter	Estimate	95% CI	SE	t	p-value
Constant	-6.371	-7.493 to -5.249	0.52940	-12.03	<0.0001
Projected Funding 3 Year Avg	29.27	-5.165 to 63.70	16.242	1.80	0.0904

H0: β = 0
The parameter is equal to 0.
H1: β ≠ 0
The parameter is not equal to 0.

Effect of Model

Source	SS	DF	MS	F	p-value
Difference	2.479206745	1	2.479206745	3.25	0.0904
Error	12.216684666	16	0.763542792		
Null model	14.695891411	17	0.864464201		

Disclosure

- Vital Transformation, a real-world evidence international health economics and healthcare strategy consultancy, was asked to conduct an analysis of the predictability of outcomes of a proposed implementation of pricing controls placed upon novel medicines emerging from the U.S. biopharma ecosystem.
- The present study is a follow-up to our study on H.R. 3, which sees sharp reductions in revenue specifically impacting VC and early-stage investments and small company capital formation within the pipeline of new drug development.
- The opinions included in this work are those of Vital Transformation LLC, and are not necessarily those of the project sponsors.
- The analysis was performed by Vital Transformation's Consulting Economist Dr. Harry Bowen and Vital Transformation's Managing Director Duane Schulthess.
- This project was made possible with the financial support of the Pharmaceutical Research and Manufacturers of America (PhRMA), the Biotechnology Innovation Organization (BIO), Amgen, Pfizer, Alexion, AbbVie, Genentech, and Bristol Myers Squibb.