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Who Develops Medicines?: An Analysis of NIH Grants

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PREPARED FOR

Bio Biotechnology Innovation Organization

PhRMA

Executive Summary

- There is a misguided perception that NIH funding, not private market investment, is largely responsible for the creation and approval of new therapies.
- This study tests that hypothesis by identifying patents linked to NIH grants from a single year, identifying those associated with clinical trials and approved medicines, and quantifying the public and private investments made for those investigational and approved medicines. Key findings include:
  - **23,230 NIH grants** in the year 2000 were linked – by NIH-supported patents – to **18 FDA-approved medicines** by 2020.
  - **None of these medicines** reached approval **without significant private investment.**
    - In fact, total private investment for the 18 approved medicines exceeded NIH funding by orders of magnitude: **$44.2 billion in private investment compared to $670 million in NIH funding.**
  - As industry's share of total investment increased, so did the likelihood of approval.
- These findings are consistent with the substantial literature describing the complementary roles of public and private R&D funding, and the significant long-term investments shouldered by industry with no guarantee of approval – in fact just 12% of medicines in clinical development are ultimately approved by the FDA.
- **Public policies that would seek to replace private sector investment with publicly-funded drug development or that would reduce industry's ability to build upon publicly-funded discoveries to bring medicines to market are therefore likely to slow drug development.**

Background and Context (1)

- A substantial literature exists describing the complementary roles of public and private funding in biopharmaceutical research and development.
  - The federal government is the primary funder of basic research in biomedical sciences through the National Institutes of Health (NIH). This research is essential for informing all medical progress including the development of medicines. It is not, however, drug development.
  - The biopharmaceutical industry's role in the U.S. research ecosystem is to take the necessary risks and undertake the drug development research required to advance basic science research into safe and effective treatments that can be made available to patients.
  - In 2018, the biopharmaceutical industry invested $102 billion in R&D, 100% of which was focused on drug development.[1] Meanwhile, the entire NIH budget in 2018 was $35.4 billion, only 8% of which was focused directly on research related to drug development.[2]

[1] Research!America, U.S. Investments in Medical and Health Research and Development 2013 – 2018, Fall 2019.
[2] PhRMA, ChartPack: Biopharmaceuticals in Perspective, Fall 2020, p29.

Background and Context (2)

- There is nevertheless a perception among some that NIH funding, not private market investment, is largely responsible for the creation and approval of new therapies.
- Sometimes NIH research supports the creation of patented discoveries, which may have an application for medicines.
- While the large majority of FDA-approved medicines are not associated with NIH-supported patents (about 90% according to the most recent estimate)[1], and while even medicines associated with NIH-supported patents typically rely on multiple other patents supported entirely by private investment[1], this study looks at cases where NIH-supported patents were associated with the development of medicines and what it takes to bring these medicines to market.
- This study adds to the evidence by following NIH discoveries – identified through patents related to NIH grants from a single year – and quantifying the public and private investments made in the research and development of medicines associated in some way with these discoveries.

[1]Genia Long, Federal government-interest patent disclosures for recent top-selling drugs, J Med Econ 2019 Dec; 22(12):1261-1267

Research Questions

- To better understand public and private roles in biopharmaceutical R&D, this study asks:
  - How many NIH research grants from a single year contribute to patented discoveries associated either directly or indirectly to an approved medicine?
  - In cases where patents linked to NIH-funded research are associated with medicines in development, what are the relative financial contributions of NIH and private investors to the development of new therapies?
- What are the implications for public policies intended to promote innovation?

Methodology

1. We identified all NIH extramural grants in FY 2000 across six major NIH Institutes and Centers* (see appendix for search criteria). This accounted for 70% of NIH's extramural grant funding in 2000. 23,230 NIH grants were identified.
2. Using data from the NIH Research Portfolio Online Reporting Tools, we identified all patents linked to discoveries funded by these FY 2000 NIH grants. 8,226 NIH-supported patents were identified.
3. Using data from BioMedTracker and ClinicalTrials.gov, we identified all investigational medicines reaching clinical trials that were associated with the NIH-funded patents identified in step 2. 41 pipeline products were identified.
4. To capture all potential government funding for therapies reaching clinical trials, the investigational medicines identified were audited to identify any other NIH grants (from any NIH Institute or Center) and associated patents that may have contributed to development of drugs in our cohort. This identified another 376 NIH-supported patents, for a total of 511.
5. Therapies were then categorized by whether they resulted in an FDA-approved therapy or, if not, the highest phase of clinical research development achieved. 18 of the 41 had reached FDA approval.
6. Data from SEC 10-K audits, corporate reports, and BioCentury IQ Tools were used to identify private investments, including funding before and after 2000 (see appendix for data sources). Types of transactions included equity, royalty, licensing, IPO, acquisition, debt, and finance.

*(1) National Cancer Institute, (2) National Heart Lung and Blood Institute, (3) National Institute for Allergy and Infectious Diseases, (4) National Institute of Arthritis and Musculoskeletal and Skin Diseases, (5) National Institute of Diabetes and Digestive and Kidney Diseases, and (6) National Institute of Neurological Disorders and Stroke.

Findings (1)

- The NIH funded **23,230 grants** across six major NIH Institutes and Centers through extramural grants in FY 2000. Patents supported by these grants were associated with **41 investigational medicines** that reached clinical trials.
  - The data sources used apply a liberal inclusion criteria for patents "associated with" investigational products in clinical trials, resulting in a conservatively large number of NIH-supported patents linked to products in development.
- **NIH funding totaled $2.4 billion** for these 41 investigational medicines
  - To ensure we captured all potentially relevant NIH funding, this includes any other NIH extramural grants for these 41 medicines from other years outside of 2000. Altogether, NIH grants from all years were associated with 511 patents.
- At the same time, **the private sector contributed a total investment of $50.2 billion** to the research and development of these 41 investigational medicines.
  - Investments were quantified through transactions including equity, royalties, licensing, IPO, acquisition, debt, and financing.

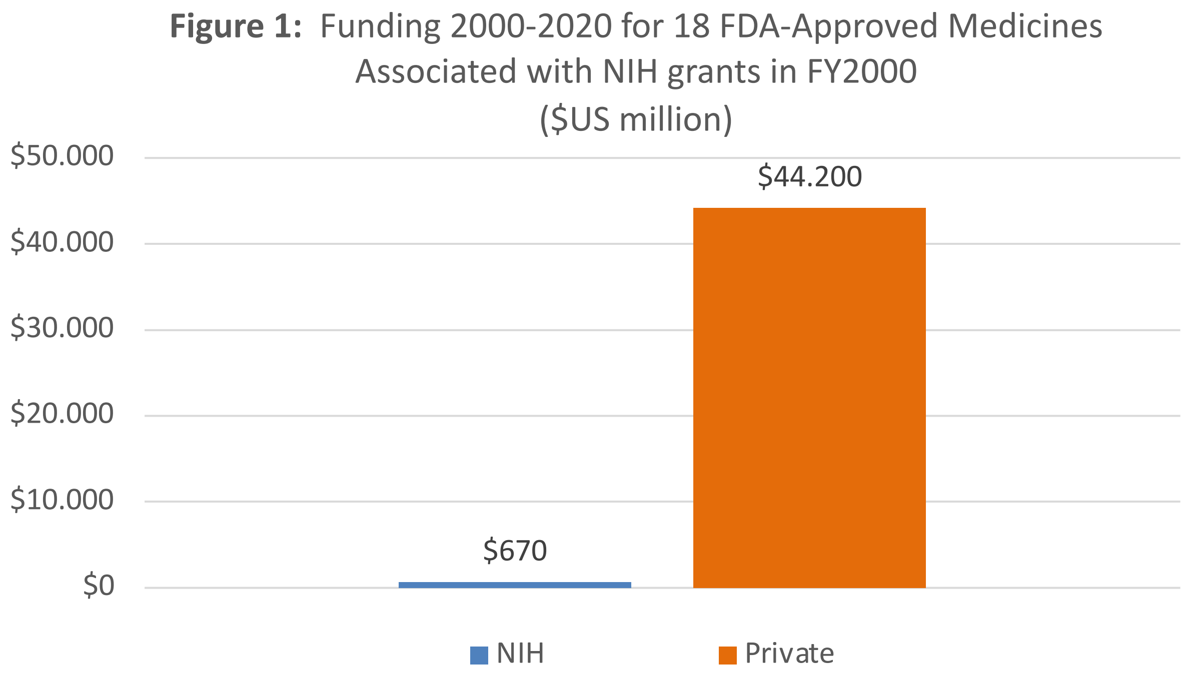
Findings (2)

- Of the 41 investigational medicines identified as associated with NIH-supported patents, **18 became FDA approved medicines**.
- **NIH funding totaled $670 million** for these 18 approved medicines *(Figure 1)*
- At the same time, **the private sector contributed a total investment of $44.2 billion** to bring these 18 approved medicines to market *(Figure 1)*.
- Industry investment exceeded NIH funding for 17 of the 18 approved medicines, typically by orders of magnitude *(Figure 2).*
- Industry investment far exceeded NIH funding across therapeutic classes *(Figure 3)*.
    - Cancer was the therapy area that accounted for the greatest number of approved therapies (5). The average private investment per cancer therapy was $5.5 billion, while average NIH funding was $5 million.
- Even for pipeline projects not resulting in an FDA-approved medicine, private investment was much larger than NIH funding, regardless of when projects were terminated *(Figure 4)*.

Findings (3)

- Companies investing in these medicines faced investment risks even after FDA approval.
- While 4 of the 18 approved medicines exceeded annual peak sales of $1 billion, 4 had sales that were not large enough to be reported as revenue in any SEC declaration *(Figure 5).*
- The larger the percentage of private investment, the higher the likelihood of a product being FDA-approved. *(Figure 6)*

Total private investment was markedly higher than NIH funding for the approved medicines associated with NIH-supported patents



Private investment and NIH funding varied markedly across the 18 approved medicines identified in the study. For all but one of these, private investment exceeded NIH funding, typically by orders of magnitude.

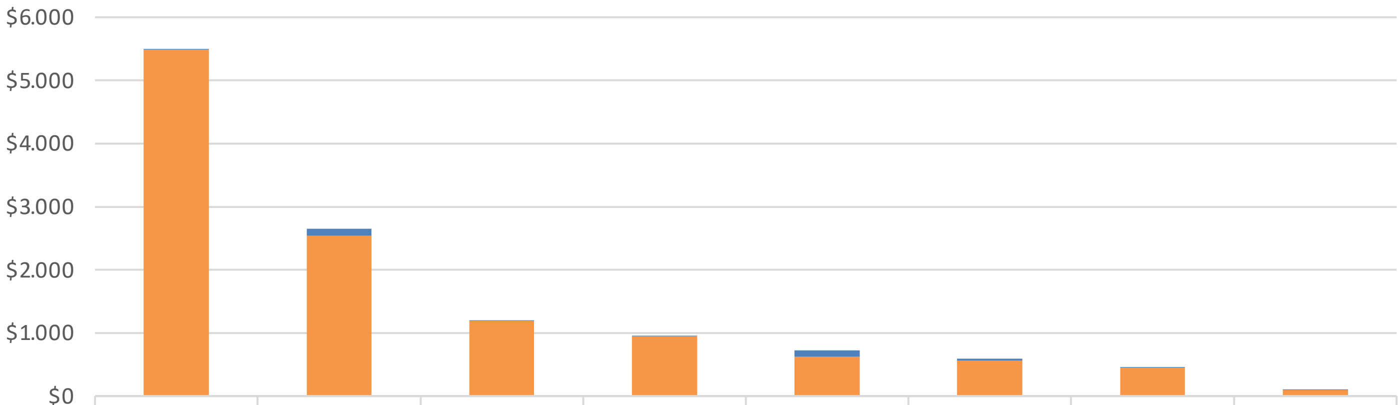
Figure 2: NIH funding and Private Investment by Product, for the 18 Approved Medicines Identified

Target	Total NIH Funding ($US Mil)	Total Private Funding to Approval ($US Mil)	Year Approved
Product #1	$1	$22,519	2020
Product #2	$8	$8,757	2004
Product #3	$8	$3,180	2014
Product #4	$5	$1,384	2005
Product #5	$5	$1,384	2012
Product #6	$7	$1,093	2003
Product #7	$7	$1,048	2011
Product #8	$2	$965	2016
Product #9	$6	$951	2003
Product #10	$104	$625	1995
Product #11	$38	$558	2012
Product #12	$4	$508	2015
Product #13	$7	$400	2014
Product #14	$1	$326	2005
Product #15	$453	$220	2011
Product #16	$4	$200	2006
Product #17	$5	$97	2018
Product #18	$4	$65	2002
Total	**$669**	**$44,280**	

Note: Products were identified as associated with NIH grant from the year 2000. In come cases these included multi-year grants that began prior to 2000. This explains the existence of one product with an approval date prior to 2000.

Private investment far exceeded NIH funding regardless of clinical area

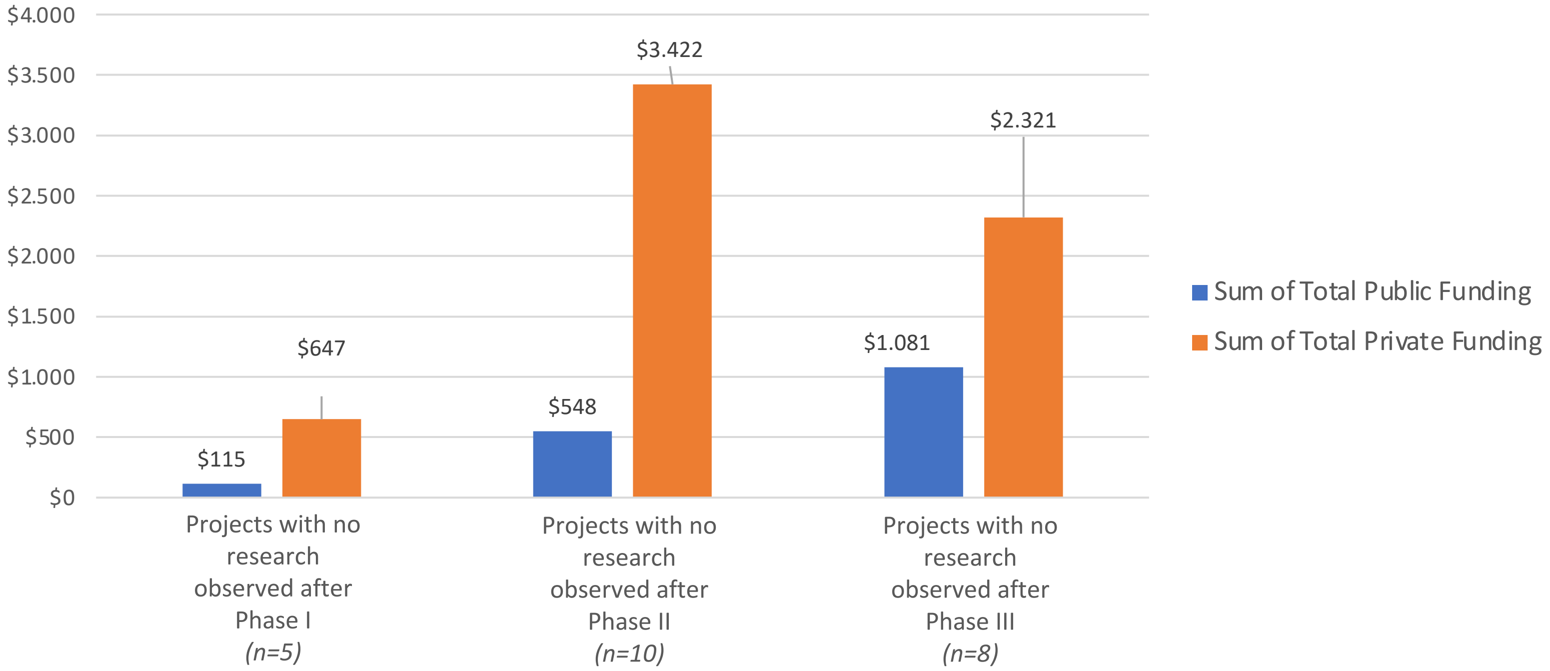
Figure 3: Average NIH and private investment per approved medicine, for the 18 medicines identified, by therapeutic area ($US million)



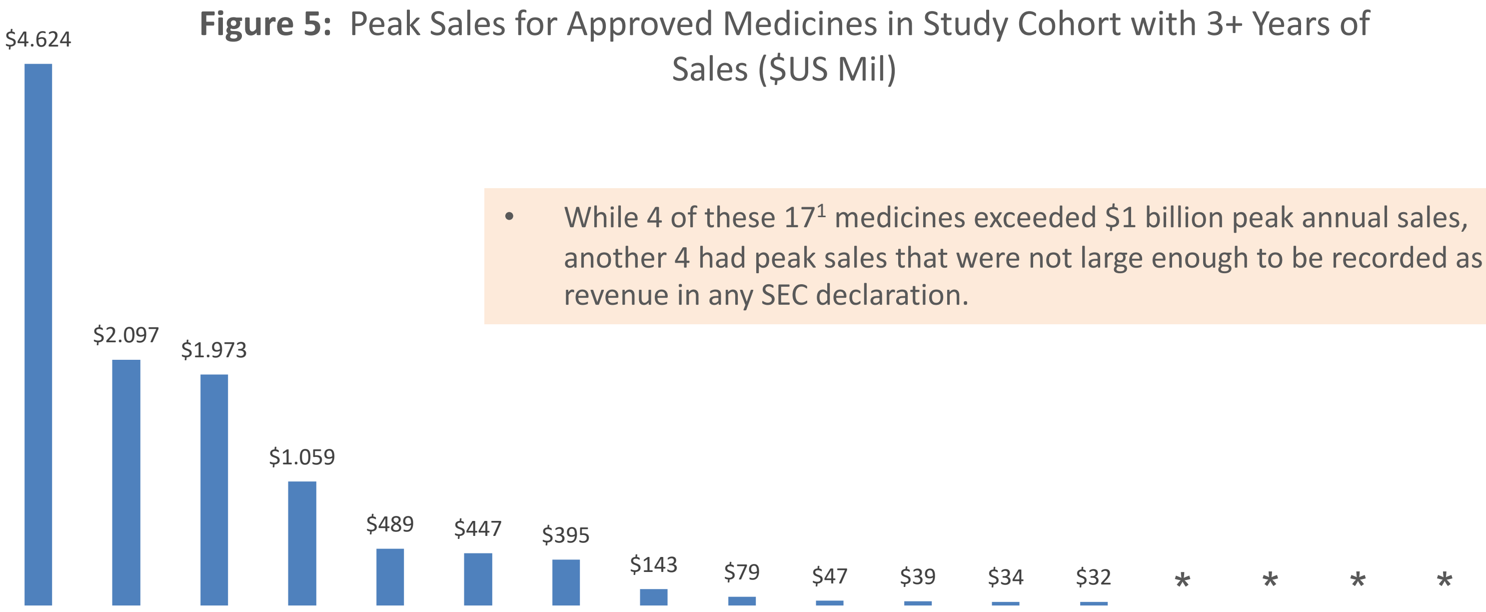
	Oncology	Neurology	Endocrinology	Immunology	Cardiology	Neonatology	Hematology	Dermatology
Average of Total Public Funding	$5	$117	$5	$6	$104	$38	$5	$5
Average of Total Private Funding to Approval	$5.486	$2.536	$1.190	$951	$625	$558	$454	$97
Number of products	5	4	3	1	1	1	2	1

Even for therapies not resulting in an FDA-approved medicine, private investment was much larger than NIH funding, regardless of when projects were terminated

Figure 4: Total aggregate project funding by highest phase of development reached, for projects *not* resulting in an FDA-approved medicine ($US million)



Even among the medicines in the study cohort that reached FDA approval, not all were commercially successful



- While 4 of these 17[1] medicines exceeded $1 billion peak annual sales, another 4 had peak sales that were not large enough to be recorded as revenue in any SEC declaration.

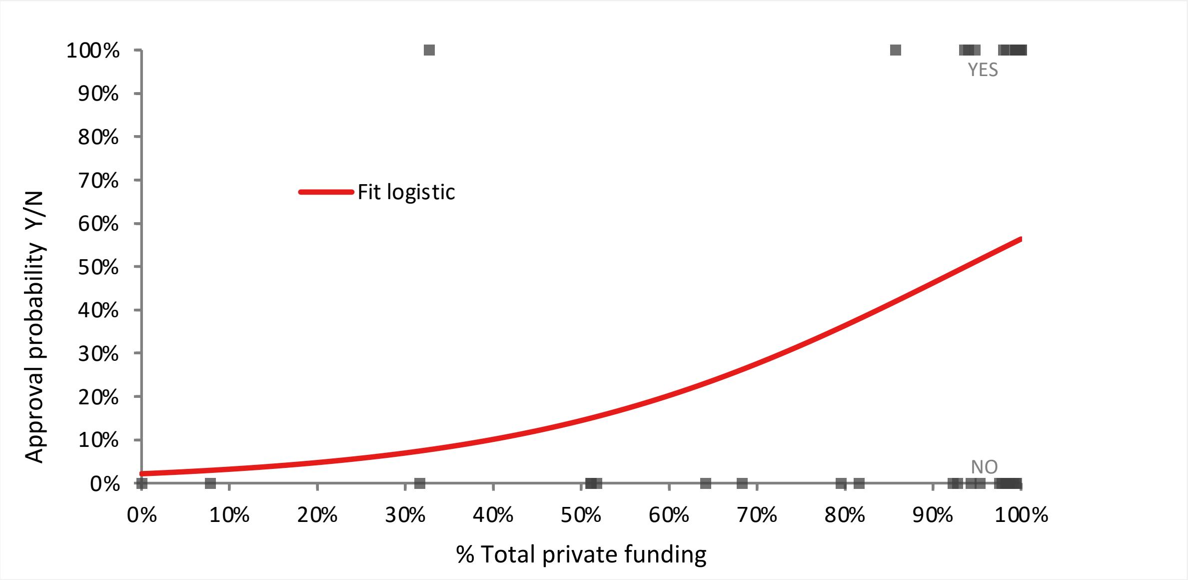
* Sales for these four products were not large enough to be reported as revenue in any SEC declaration.

[1] One of the 18 approved medicines identified in the study is excluded because it was approved in 2020, and would not yet have achieved annual sales approaching peak lifetime sales.

The larger the percentage of private investment, the higher the likelihood of a product being FDA-approved

Figure 6: Regression test -- % private funding to FDA approval

Source	-LogLikelihood	DF	G^2 statistic	p
Difference	2.9874	1	5.97	0.0145
Fitted model	25.126	39		
Null model	28.113	40		



Discussion

- NIH data show that the large majority of the NIH budget goes to basic research and activities complementary to drug development.[1] Consistent with these earlier findings, this study finds that the large majority of NIH grants from a single year did not directly contribute to drug development as measured through Bayh-Dole patent awards. When NIH-funded research is linked to patented discoveries, NIH requires partnership, investment, and the shouldering of financial risk by private sector companies for those ideas to contribute to an FDA-approved medicine.
  - No medicine identified in the analysis was approved without significant private investment.
  - In fact, the larger the percentage of private investment, the higher the likelihood of a product being FDA-approved.
  - The overwhelming majority of funding for the 18 approved medicines identified came from private sector investment; this was true across all stages of R&D and all therapeutical classes observed.
- Risk for private sector investment does not end at product approval. Many of the medicines in this study that came to market had limited revenues, including four with zero reported revenues in company financial documents.
- These findings suggest that public policies that would seek to replace private sector investment with publicly-funded drug development or that would reduce industry’s ability to build upon publicly-funded discoveries to bring medicines to market are therefore likely to slow drug development.

[1] PhRMA, Chart Pack: Biopharmaceuticals in Perspective, Fall 2020, p.29.

Discussion (2)

- It is important to put these findings in the larger context of *all* drug development.
- For the medicines and investigational medicines included in the analysis, we are looking solely at patents associated with NIH. However, medicines typically have multiple patents that are critical to their development, and most of these are supported entirely with private investment.[1]
  - For example, for the 12 approved products in our analysis that appear in the FDA Orange Book, the NIH-supported patents we identified account for only 5 of the 41 patents listed as protecting these products.
- Furthermore, most approved medicines do not rely on *any* NIH-supported patents. This analysis looks only at the minority of medicines that have some potential NIH involvement.
  - A 2019 analysis of 197 top-selling medicines found that only 10.2% had at least one patent listed in the Orange Book that had a government interest statement or U.S. government agency assignee.[1]

[1] Genia Long, Federal government-interest patent disclosures for recent top-selling drugs, J Med Econ 2019 Dec; 22(12):1261-1267.

Limitations

- Ascertaining the relevance and importance of every NIH-supported patent identified was outside the scope of this analysis. The analysis used public and commercially available business intelligence data sources to link NIH grants to products in the pipeline using patents listed in these sources as the link. This link is imperfect and appears to capture some NIH-supported patents that may be tangential or potentially even unrelated to the development of the pipeline products identified, thus overstating NIH investments and inventions related to these investigational medicines.
    - For example, for the 12 approved products in our analysis that appear in the FDA Orange Book, only 3 identify one of the NIH-supported patents we identified as protecting the product. In addition, one of the 18 approved medicines we identified was associated with multiple NIH-supported patents, but all were granted a decade or more *after* the product's approval.
- The analysis uses publicly reported financial transaction data (e.g., equity, royalties, licensing, IPOs, acquisitions) as a proxy for industry investment. This does not explicitly include the considerable internal R&D investments typically made by biopharmaceutical firms after these transactions.
- To the extent the NIH RePORTER database underreports patents, the number of patents and products associated with NIH grants may be understated. However, total NIH investment for identified products is not likely to be significantly affected.
- In order to have sufficient time to observe NIH-supported research being translated into approved medicines, we looked at grants from FY 2000. This single year of grants is not necessarily representative of all grant years.
- NIH intramural research grants (e.g., Z grants) were excluded as data for these are not available before FY 2007.

Appendix: Data Sources

NIH Search Criteria

https://projectreporter.nih.gov/reporter.cfm

Fiscal Year: 2000 – i.e. how many marketed therapies are linked to IP created from NIH grants awarded for fiscal year 2000?

NIH Centers Evaluated: NCI, NHLBI, NIAID, NIAMS, NIDDK, NINDS

Activity Code: P01 Program Projects, R01 Equivalents
DP2, R01, RF1, SBIR/STTR, R41, R42, R43, R44

Centers: P20, P30, P50, U54

R & D contracts

Non-SBIR/STTR Contracts

SBIR/STTR Contracts

Data, Financial, and IP Sources

- Biomedtracker - https://www.biomedtracker.com/
- Biocentury IQ Tools https://bciq.biocentury.com/home
- Securities and Exchange Commission corporate reports (10-k) https://www.sec.gov/edgar/searchedgar/companysearch.html
- Drug Patent Watch https://www.drugpatentwatch.com/
- Google Patents https://patents.google.com/
- US Patent and Trademark office https://www.uspto.gov/
- NIH Research Portfolio Online Reporting Tools (RePORTER) https://projectreporter.nih.gov/reporter.cfm
- NIH US National Library of Medicine https://druginfo.nlm.nih.gov/drugportal/name
- NIH US National Library of Medicine https://clinicaltrials.gov/
- FDA “Orange Book” https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm
- Center for Drug Evaluation and Research (CDER) “Purple Book” https://purplebooksearch.fda.gov/
- Association of University Technology Managers AUTM 2018 Survey https://autm.net/

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