VitalTransformation

The impact of health technology made simple

March-in rights under the Bayh-Dole Act & NIH contributions to pharmaceutical patents

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What is the Bayh-Dole Act?

Passed in December of 1980, Bayh-Dole Act permits universities, non-profit organizations, and companies that receive federal funding to elect ownership to resulting inventions, rather than obligating those organizations to assign invention rights to the federal government.

Since the Bayh-Dole Act's inception, several petitions have been filed under the march-in provision outlined in the act, however, the NIH has denied all the petitions as evidentiary findings have proven the patent holder and/or licensees to be in continued compliance with all statutory criteria.

Three Policies That Gave Us the Jobs Economy

THE WALL STREET JOURNAL. October 17, 2011

"Sponsored by Sens. Birch Bayh of Indiana and Bob Dole of Kansas, the measure clarified murky intellectual property rights so that universities and professors, especially, knew they owned their own ideas and could sell them. That knowledge gave professors and lab teams an enormous incentive to put to commercial use plans and ideas for inventions that they had long ago shelved in their minds and offices."

Intro and Background

Understanding march-in rights under the Bayh-Dole Act in the pharmaceutical sector

- On October 7, 2022, HHS Sec. Xavier Becerra was quoted by Axios as saying that the Federal Government's use of march-in rights to control drug prices were not “off the table.”
- On January 10, 2023, a group of 25 senators led by Sen. Elizabeth Warren (D-MA), sent a letter to HHS Sec. Xavier Becerra advocating for him to exercise march-in rights for a prostate cancer treatment specifically “to lower prescription drug prices.”
- On March 21, 2023, the NIH denied a petition received in November 2021 to exercise march-in rights under the Bayh-Dole Act to control the price of a prostate cancer treatment as the NIH’s analysis found the treatment was widely available to the public and satisfies the practical application requirement of the provision.
- Given the above, the questions that need to be addressed are the following:
  - What are march-in rights?
  - What is the government’s actual (not rhetorical) fiscal contribution to new therapies that come to market that could be subject to Bayh-Dole march-in provisions?
  - What would happen practically if march-in rights are exercised?

Under the Bayh-Dole Act, march-in rights are defined to ensure patents are exploited and developed

The Bayh-Dole Act specifies only four circumstances under which march-in rights may be exercised:

1. The patent holder has not taken effective steps to achieve ***practical application*** of the subject invention in such field of use. ***Practical application*** includes making a product available to the public based on the "reasonable terms" of the license, not the terms of a sale.

2. The patent owner or licensee has not ***reasonably satisfied*** health or safety needs as outlined by the contractor, assignee, or their licensees;

3. The patent owner or licensee's actions to meet requirements for public use ***specified by Federal regulations*** have not been met and therefore requirements are not reasonably satisfied by the contractor, assignee, or licensees; OR

4. The patent owner or licensee's exclusive right to use or sell any subject invention in the United States ***is in breach of its agreement*** should the licensee not agree to or is breach of an agreement to manufacture the patented product substantially in the United States (unless such requirement has been waived by the government).

https://www.govregs.com/uscode/35/203

Government Interest Statements & march-in provision triggers

- A Government Interest Statement (GIS) is required by law for any patent application filed by an individual or entity that "conceived or first actually reduced to practice" an invention under a federal grant or funding agreement, and must include the following language:
  - ***"This invention was made with government support under (identify the contract or grant) awarded by .... The government has certain rights in the invention."***

- Should a Bayh-Dole Act patent holder or licensee's non-compliance with any of the four march-in requirements trigger the government to 'march-in' on the patent, the law only requires competitors be licensed where the government had materially contributed to the product's discovery.

Patent types important to the development of FDA approved medicines

Types of patents

- Composition of matter patents (CoM):
  - Cover novel drug compounds or compositions not previously described in scientific literature such as new chemicals, biologics, polymers, alloys, and other materials.
- Mechanism of action patents (MoA):
  - Cover the therapeutic use of an agent, such as a method of treatment, a dosing regimen, or a combination therapy.

Types of FDA approved drugs

- Small molecules: approved through a New Drug Application (NDA)
  - typically synthesized chemically, have a low molecular weight, and often act on intracellular targets.

- Large molecules: approved through a Biologics License Application (BLA)
  - large complex molecules derived from living organisms that target extracellular proteins or receptors

Methodology

1. Vital Transformation (VT) has developed a methodology to determine the impact NIH funding involvement has on unexpired patents from a cohort of 361 novel, non-generic, small and large molecule medicines from 2011-2020 listed in the FDA's orange and purple books.

2. Mechanism of action and composition of matter patents were identified in the FDA's orange book for small molecules and patent records for biologics were manually extracted from USPTO patent filings and BioMedtracker.

3. All patents connected to our cohort which have a federal Government Interest Statement (GIS) have been identified using The Lens database.

4. All NIH program grant numbers and funding amounts associated with patents including a GIS have been identified.

5. Patents identified as co-developed or in partnerships with the federal government through CRADAs, Intermural, or Congressional/Department of Defense (DOD) funding programs are included, although these patents do not possess a GIS.

*federal government interest statement 310-Government License Rights to Contractor-Owned Inventions Made Under Federally Sponsored Research and Development (uspto.gov)

Innovation is overwhelmingly driven by the private sector, with a vast majority of novel therapies invented by industry

- **92%** of the therapies in our cohort have no GIS, federally funded co-development, or partnership program associated with any identified patents: 334 of 361 novel FDA approved therapies from 2011 - 2020.
- **8%** of the therapies in the cohort have at least one patent with a GIS or associated federally funded co-development program: (n=27).
  - **4%** of the therapies in our cohort have at least one patent that includes a GIS (n = 15)
  - **3%** of the therapies in our cohort have at least one patent that was developed in partnership with the federal government (n = 12)
- **2%** of all patents in the cohort include a GIS or a co-development partnership agreement: 49 of 2324 patents.

Large Molecules 2011-2020

Large molecule therapies in the cohort with a federal GIS connected to either a mechanism of action or a composition of matter patent.

Therapeutic Area	# of Government Patents
Oncology	1 of 2 patents
Oncology	1 of 6 patents
Oncology	1 of 1 patents
Oncology	1 of 3 patents

Small Molecules 2011-2020

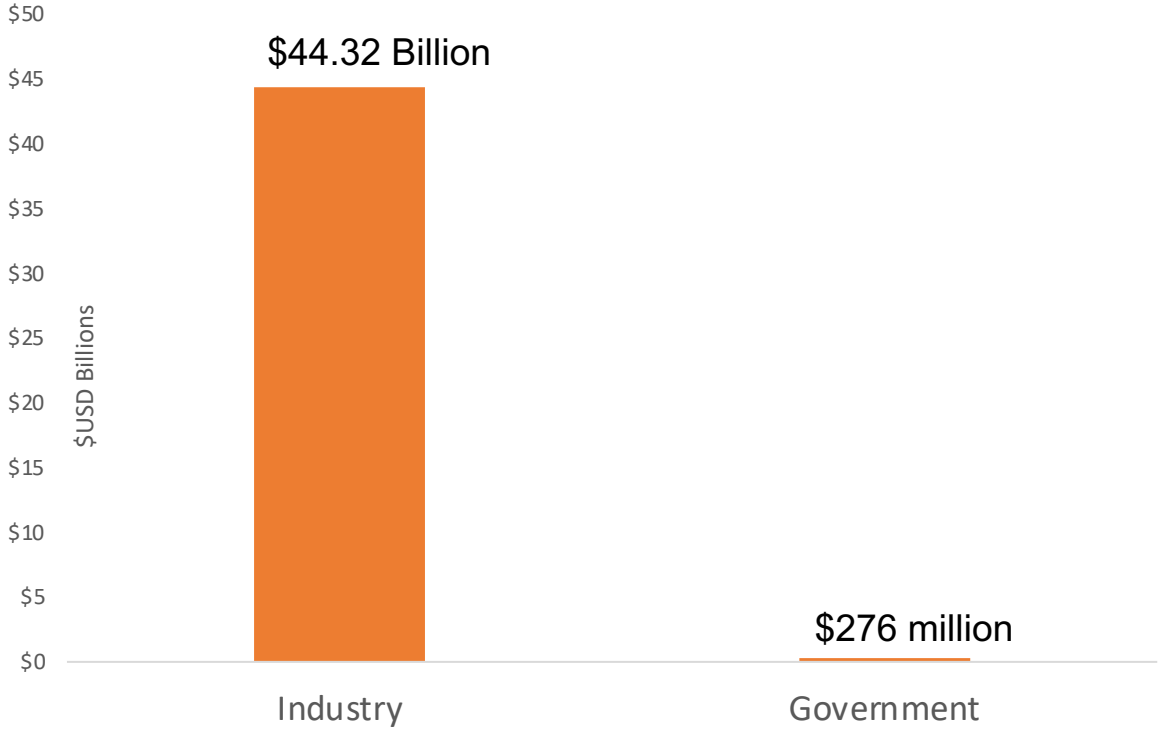
Small molecule therapies in the cohort with at least one patent that includes a federal GIS in connection to either mechanism of action or composition of matter patents

Therapeutic Area	# of Government Patents
Oncology	4 of 9 patents
Oncology	3 of 3 patents
Radiology	2 of 2 patents*
Radiology	1 of 1 patents*
Neurology	3 of 4 patents
Virology	6 of 6 patents
Neurology	3 of 9 patents
Rheumatology	3 of 5 patents
Anti-Microbial	1 of 3 patents
Neurology	1 of 9 patents
Neurology	5 of 8 patents

* Imaging agents using the same government patents.

Industry investment vs government contributions

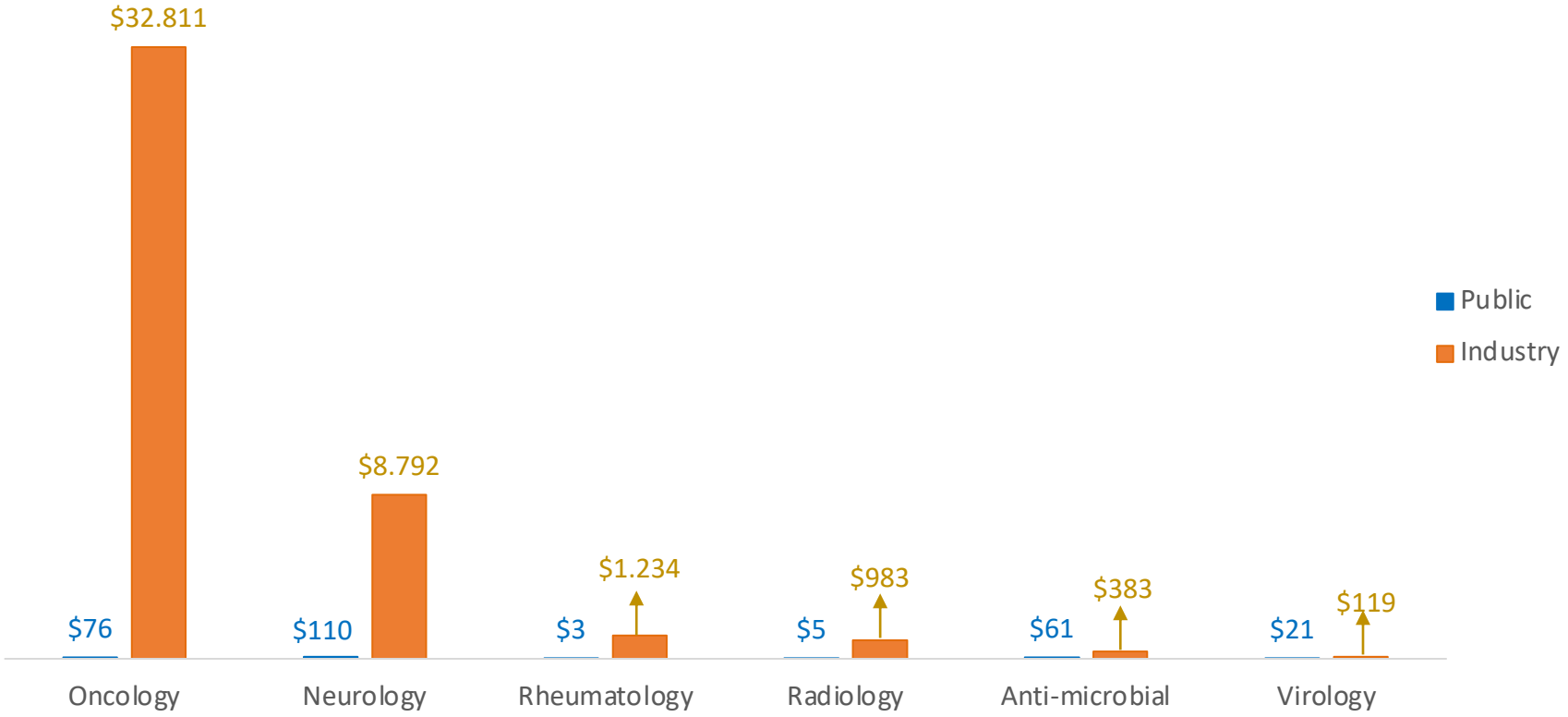
Total industry investments up to FDA approval vs Government contribution in connection to patents including a Government Interest Statement (GIS)



For the 36 unexpired patents with a GIS, which cover 15 approved novel therapies, this chart compares the specific government contribution to the total industry contribution from 2011-2020. Funding is calculated to the point of FDA approval.

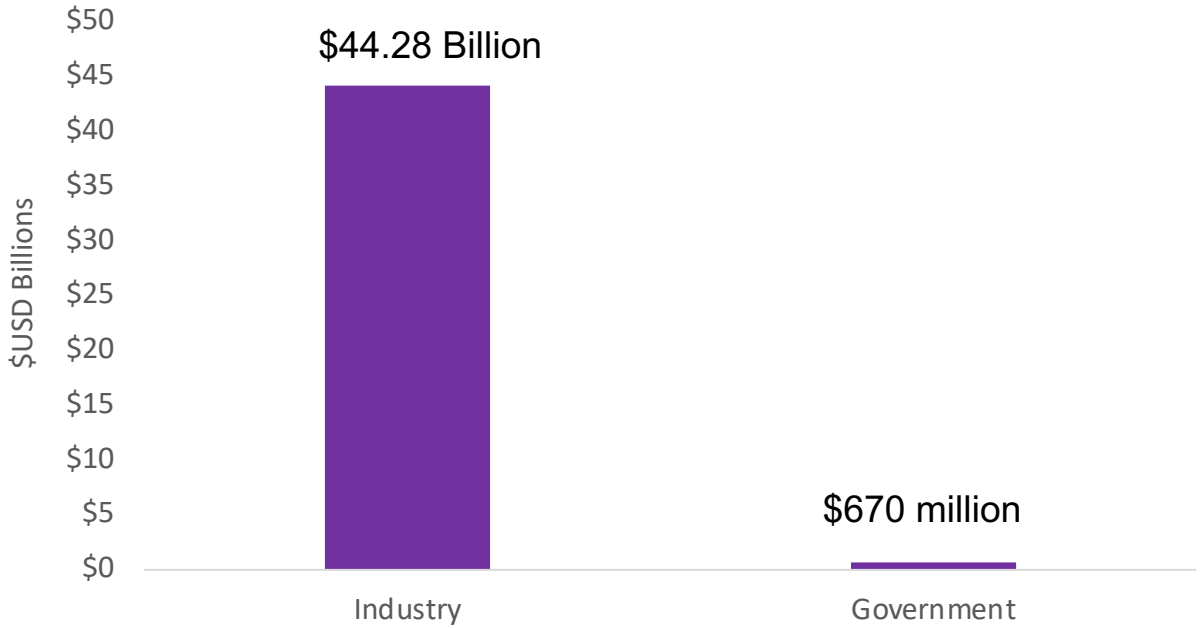
Total Financial Contributions by Therapeutic Area

Grant funding totals of unexpired patents with government interest statements vs total Industry contribution
$Mil USD



Relevant findings from VT's 2020 study

Total industry investments vs government contribution from 2000-2020 for the 18 FDA-approved medicines linked to FY2000 NIH program grants



To demonstrate the impact of research made possible by the Bayh-Dole Act, this chart compares the total government contribution to the **18 FDA approved medicines linked to a cohort of 23,230 NIH program grants** from FY 2000-2020 to the total industry contribution. Funding is calculated to the point of FDA approval.

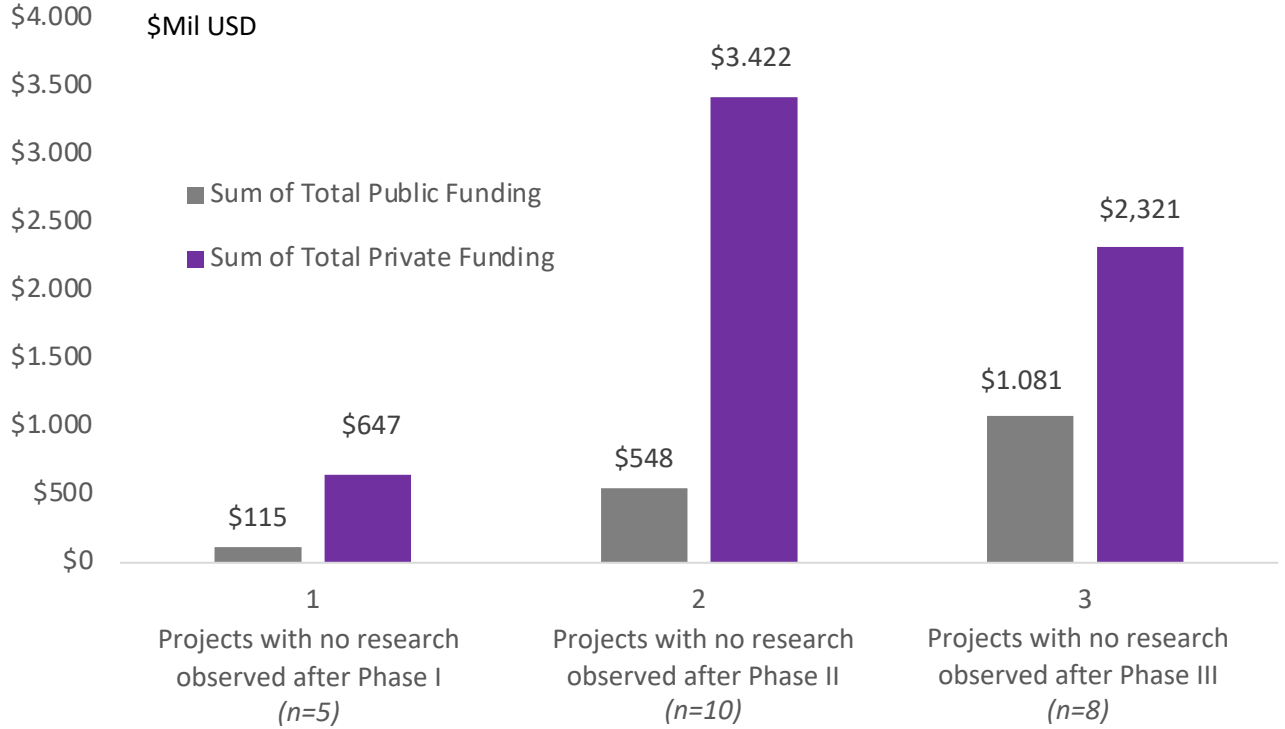
Schulthess, D., Bowen, H.P., Popovian, R. *et al.* The Relative Contributions of NIH and Private Sector Funding to the Approval of New Biopharmaceuticals. *Ther Innov Regul Sci* **57**, 160–169 (2023). https://doi.org/10.1007/s43441-022-00451-8

Clinical drug development fails >90% of the time

2020 Study: Even for therapies not resulting in FDA approval after early clinical development, private investment is much larger than NIH funding, regardless of when projects were terminated

Relevant findings from VT's 2020 study

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

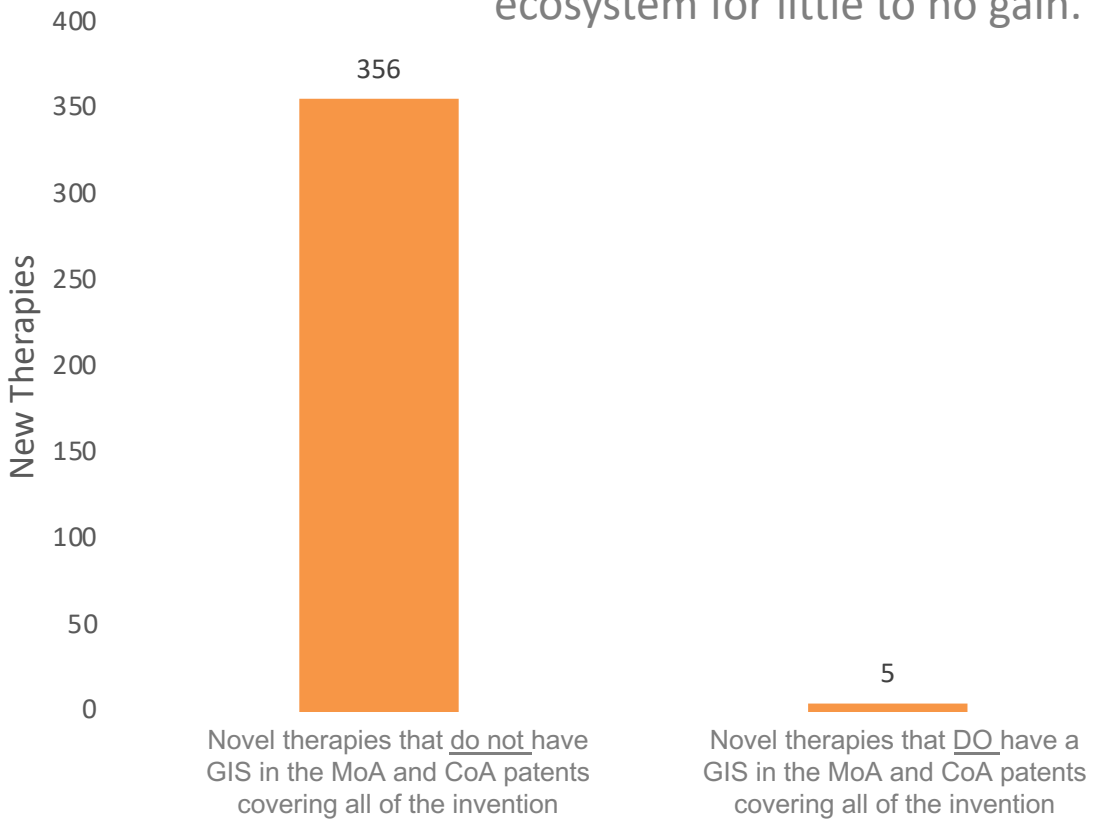


2020 Study:
Total aggregate project funding from 2000-2020 by highest phase of development reached, for projects not resulting in an FDA approval, linked to 23,230 multiyear NIH grants active in FY2000 **($Mil USD)**

Schulthess, D., Bowen, H.P., Popovian, R. et al. Correction: The Relative Contributions of NIH and Private Sector Funding to the Approval of New Biopharmaceuticals. Ther Innov Regul Sci 57, 170–171 (2023). https://doi.org/10.1007/s43441-022-00461-6

Using march-in to control prices would be ineffective

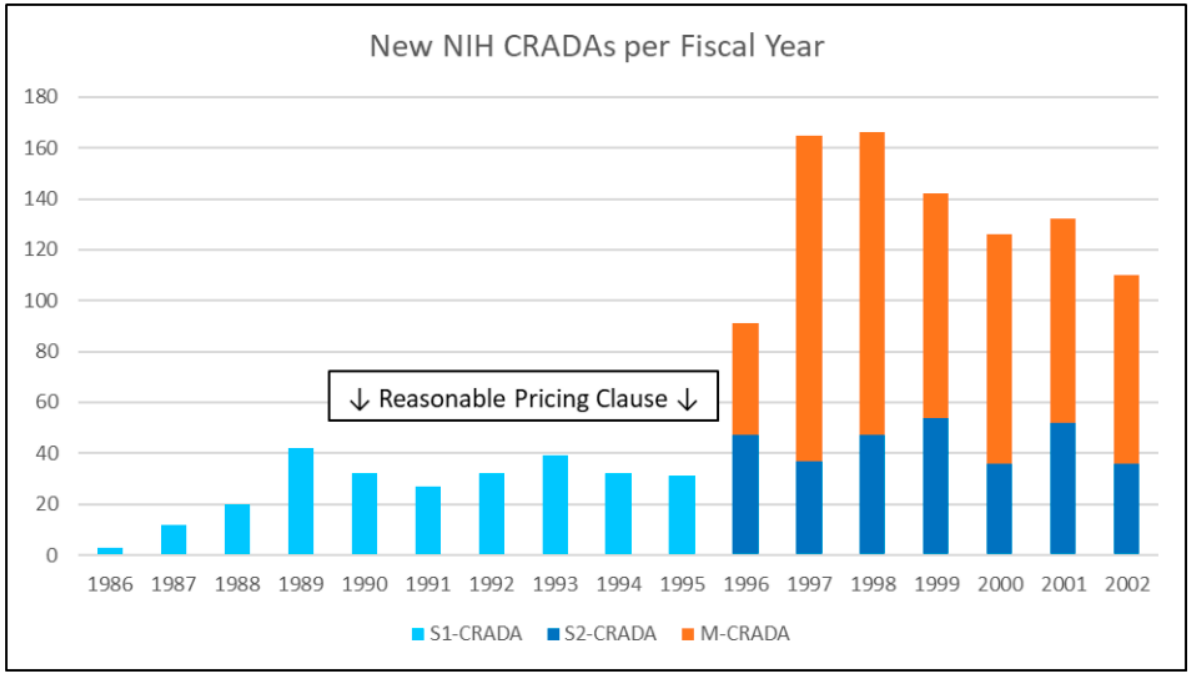
Exercising march-in rights as a cost control would risk chilling the entire innovation ecosystem for little to no gain.



The overwhelming majority of drugs in our cohort have no associated patents with a GIS. Only 5 of the 361 novel therapies in the cohort include a GIS in all MoA and CoA patents covering the inventions in the medicine. Because march-in rights apply to patents, not products, exercising march-in would serve no purpose unless every invention and every patent covering a drug is subject to Bayh Dole. Such drugs are exceedingly rare.

Impact of the U.S. Congress fair pricing clauses placed in NIH CRADA Grants

NIH research partnerships were negatively impacted



NIH press release from 1995:

"An extensive review of this matter over the past year indicated that the pricing clause has driven industry away from potentially beneficial scientific collaborations with PHS scientists without providing an offsetting benefit to the public," said Dr. Varmus.

"Eliminating the clause will promote research that can enhance health of the American people," he said.

Source: The NIH Experience with the Reasonable Pricing Clause in CRADAs FY1990-1995
Source: NIH News: April 11, 1995
https://www.techtransfer.nih.gov/

Final Conclusions

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1. Industry is the dominant source of innovation for novel FDA approved medicines; industry funding for novel patented therapies approved by the FDA from 2011 – 2020 was $44.3 billion, compared to the $276 million the US government contributed to patented drugs that are subject to Bayh Dole. Relevant to this, the previously published report by VT found that over the 20 years leading up to FDA approval of 18 innovative new therapies, the funding contribution from industry to the development of these therapies was 66 times higher than the public funding from all linked NIH grants.

2. Research and development investments are a significant risk to the pharmaceutical industry and their investors as not all assets result in a marketed product. The high rate of failure in drug development underscores the challenges and risks associated with bringing new treatments to patients.

3. 92% of the therapies in our cohort have no mechanism of action or composition of matter patents with a government interest statement or federally funded co-development program in connection to them

4. 99% of the therapies in our cohort cannot be marched-in upon, as the key patents studied do not cover the entire asset's intellectual property. There are only 5 out of 361 pharmaceutical products in which all available MoA and CoM patents include a government interest statement and could be subject to march-in rights.

5. Enacting march-in rights to control prices will create uncertainty and increase risk for inventors based upon previous experiences with fair pricing requirements for NIH CRADAs:
    - Industry, venture capital will avoid investing in commercializing academic inventions and partnerships with the NIH will plumet
    - US biopharma productivity will drop significantly, providing an opportunity for competing foreign biopharma markets to expand, with a high potential for industry to relocate their enterprises

Disclosure

- Vital Transformation, an international health economics and strategy consultancy, was asked to conduct an analysis of the impact of using march-in rights on FDA approved medicines.
- The opinions included in this work are those of Vital Transformation, LLC, and not necessarily those of the sponsors: the Biotechnology Innovation Organization (BIO), the National Pharmaceutical Council, Pfizer, Sanofi, Novartis, Merck, Astellas, and Gilead. The sponsors appreciate the critical insights from the Bayh-Dole Coalition.
- The analysis is being performed by Vital Transformation's Project Manager Gwen O'Loughlin and CEO Duane Schulthess.

Appendix

Other Research on IP and Govt interest statements

Federal government-interest patent disclosures for recent top-selling drugs, Journal of Medical Economics

- Results were generally comparable to a prior analysis that found that 9.0% of new drugs approved between 1988 and 2005 had either a Government Interest Statement disclosure or a government agency first-listed patent assignee.
- Utilized FDA Orange Book and results from the Freedom of Information Request (FOIA) response

Table 2. Orange Book-listed patents for top-selling 2013–2017 drugs, by patent claim type and government-interest patent disclosure.

	All Orange Book-listed patents	Patents with government-interest patent disclosure	Percent with government-interest patent disclosure
Method of use patents	666	21	3.2%
Drug product patents	677	11	1.6%
Drug substance patents	335	12	3.6%
Total Orange Book patents	1,151	30	2.6%

Genia Long (2019) Federal government-interest patent disclosures for recent top-selling drugs, Journal of Medical Economics, 22:12, 1261-1267, DOI: 10.1080/13696998.2019.1631832

Other Research on IP and Govt Funding

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What Are The Respective Roles of the Public and Private Sectors in Pharmaceutical Innovation?

- All NME approvals 1998-2005 (n=478). Focused on new drug applications (NDA).

- Patent citation data was used to assess the indirect role of pharmaceutical innovation however the march-in policy will only apply to drugs whose development included a direct role
  - Cohort analysis suggests direct role "was relatively small, and the aggregate economic impact of such policies would therefore be limited"
  - Generalizing by drug class: HIV/AIDS is an outlier in both direct and indirect involvement

New Drugs Approved By The Food And Drug Administration, 1988–2005, With Direct Or Indirect Public-Sector Support

	Standard-review drugs	Priority-review drugs	All drugs
Number of drugs	224	155	379
Had public-sector patent	3.1%	17.4%	9.0%
Patent cited at least one public-sector patent	15.6%	39.4%	25.3%
Patent cited at least one government publication	31.3%	56.1%	41.4%
Patent cited either a public-sector patent or a government publication	36.2%	64.5%	47.8%

Bhaven N. Sampat and Frank R. Lichtenberg What Are The Respective Roles Of The Public And Private Sectors In Pharmaceutical Innovation? Health Affairs 30, no.2 (2011):332-339 doi: 10.1377/hlthaff.2009.0917

Other Research on IP and Govt interest statements

The Role of Public-Sector Research in the Discovery of Drugs and Vaccines

Table 2. FDA-Approved Drugs Discovered through Public-Sector Research, According to Type of Review and Chemical Type, 1990–2007.*

Type of Review	New Molecular Entity	New Ester, Salt, or Derivative	New Formulation	New Combination	New Manufacturer	New Indication	Already Marketed	Total
Priority review								
Discovered by PSRI (no.)	44	1	17	3	0	1†	0	66
All FDA approvals (no.)	209	6	99	20	14	0	0	348
Rate of PSRI discovery (%)	21.1	16.7	17.2	15.0	0	NA	NA	19.0
Standard review								
Discovered by PSRI (no.)	20	0	36	6	7	8	0	77
All FDA approvals (no.)	274	33	631	96	137	10	12	1193
Rate of PSRI discovery (%)	7.3	0	5.7	6.3	5.1	80.0	0	6.5
All approvals								
Discovered by PSRI (no.)	64	1	53	9	7	9	0	143
All FDA approvals (no.)	483	39	730	116	151	10	12	1541
Rate of PSRI discovery (%)	13.3	2.6	7.3	7.8	4.6	90.0	0	9.3

* NA denotes not applicable, and PSRI public-sector research institution.
† The second new-drug application approved for Pfizer's Sutent, in 2006, was classified as type 6 (new indication) and given a priority review. However, the totals supplied by the FDA showed no priority reviews for new-indication applications in 2006 or any other year.