VitalTransformation

The impact of health technology made simple

The US Ecosystem For Medicines

How new drug innovations get to patients

Government, Academia, Small firms, and Large firms

2011 – 2020

Updated as of 3/22/2023

PREPARED BY

Gwen O'Loughlin
Project Manager

Harry Bowen
Consulting Economist

Duane Schulthess
CEO

Intro – Background

1. In November of 2010, Robert Kneller published a landmark study outlining the importance of biotech to the US and global innovation ecosystem.
2. The data indicated that drugs initially discovered in biotechnology companies or universities accounted for approximately half of the scientifically innovative drugs approved.
3. The fundamental evidence presented by Kneller is now being called into question, as demonstrated by:
    a. the belief that the NIH, not industry, is primarily responsible for the development of new medicines, and the use of march-in rights is an appropriate method to control drug prices
    b. the current attacks questioning the validity of the Accelerated Approval pathway which is often used by small companies to bring new medicines targeting orphan indications to market
    c. the Biden Administration's decision to make mRNA IP available under WTO TRIPs waivers
    d. attacks from the US Congress regarding the role of 'Big Pharma' in the drug development ecosystem.
4. This research updates the Kneller 2010 study and contextualizes its findings with VT's recent research on the key roles played by the NIH and industry in the biopharma innovation ecosystem from 2011-2020.

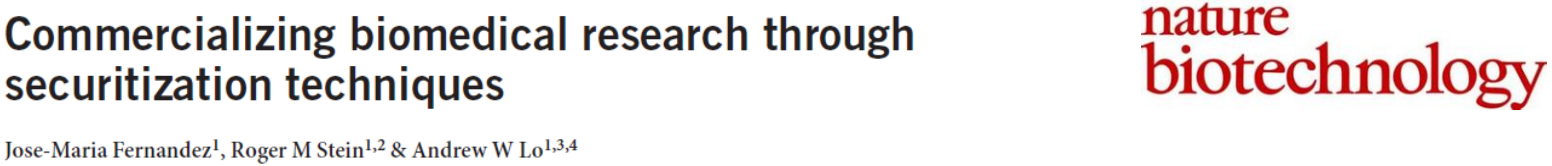
Objectives of this Research

1. Update Kneller's 2010 research using a cohort of therapies approved by the FDA between 2011 and 2020.
2. For each approved therapy, identify the geographic location and institution (university, researcher, company, and location) responsible for its 'origination' and compare them across relative geographic locations.
3. Compare the distribution of originator type (small company, large company, government, or academic) by the designations of priority review and standard review.
4. Make concrete determinations of the relative impact of originator type and location for sales.
5. Demonstrate the ecosystem evolution regarding internal/external IP innovation, and the role of NIH and government to novel IP creation since Kneller 2010.

Methodology

1. Used FDA orange and purple books to identify origin of the foundational IP of 363 FDA approved non-generic new medicines between 2011 and 2020.
2. Patent records for Biologics required a manual search (information absent in purple book):
   - Searched the U.S. Patent and Trademark Office (USPTO) for patent extension claims related to a specific BLA, as recorded in the federal register.
   - Federal USPTO rulings ("Determination of Regulatory Review Period for Purposes of Patent Extension") were then cross referenced and validated using a drug's application number, approved use, and FDA approval date from CDER data to the federal register.
3. An investigation was conducted to identify NIH funded CRADAs and Intermural grants for patents directly created under government contract.
4. The pathway of IP ownership was identified and tracked at three core points; origination, FDA filing, and post-FDA approval (i.e., current owner).
5. The originator of the IP was classified by their geographic location and sector (i.e., Small Biopharma <$500mil revenue, Large Pharma >$500mil Revenue, Government, Academia).

How Drug R&D Changed After the Great Financial Crisis of 2008


Commercializing biomedical research through securitization techniques

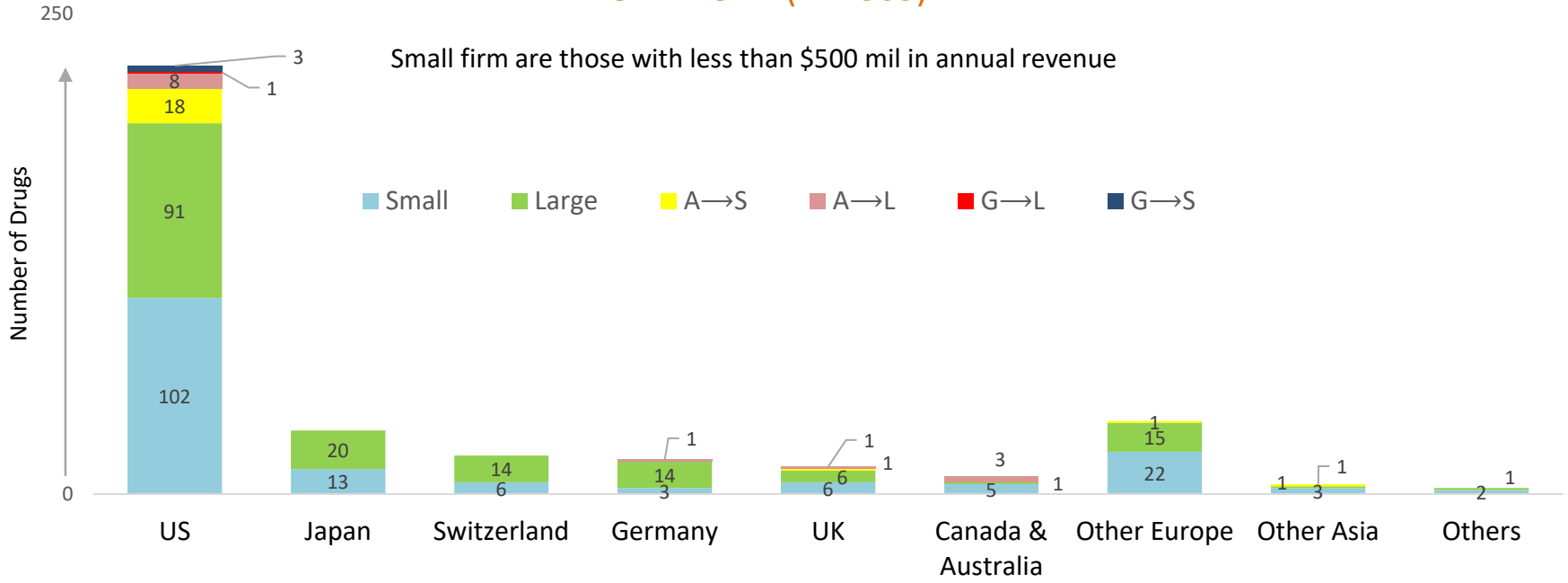
Jose-Maria Fernandez[1], Roger M Stein[1,2] & Andrew W Lo[1,3,4]

nature biotechnology

- Andrew Lo of MIT, in a highly influential Nature Biotechnology publication (2012), stated that rather than internally funded R&D, "biomedical programs at various stages of development [could be] funded by a single entity [with] megafunds of $5–15 billion."
- By 2012, the industry had already – for several years - begun to move from a mostly internal R&D model to a distributed R&D model of similar size and scope by allocating a substantial portion of their free cash flow toward R&D venture partnerships.
- Sanofi chief executive Chris Viehbacher was famously quoted in a keynote address at the 2012 CED Life Sciences Conference: "R&D is either a huge waste of money or too, too valuable…if you want to work with the best people, ***you're going to have to go outside your own company… venture capitalists… bring competencies we don't have***… in how to help a startup company."
- Considering the opinions of Lo and Viehbacher, exactly how has the IP innovation ecosystem changed since Kneller's highly influential 2012 publication?

State of the Art - Approvals by Geographic Location and Type of IP Originator

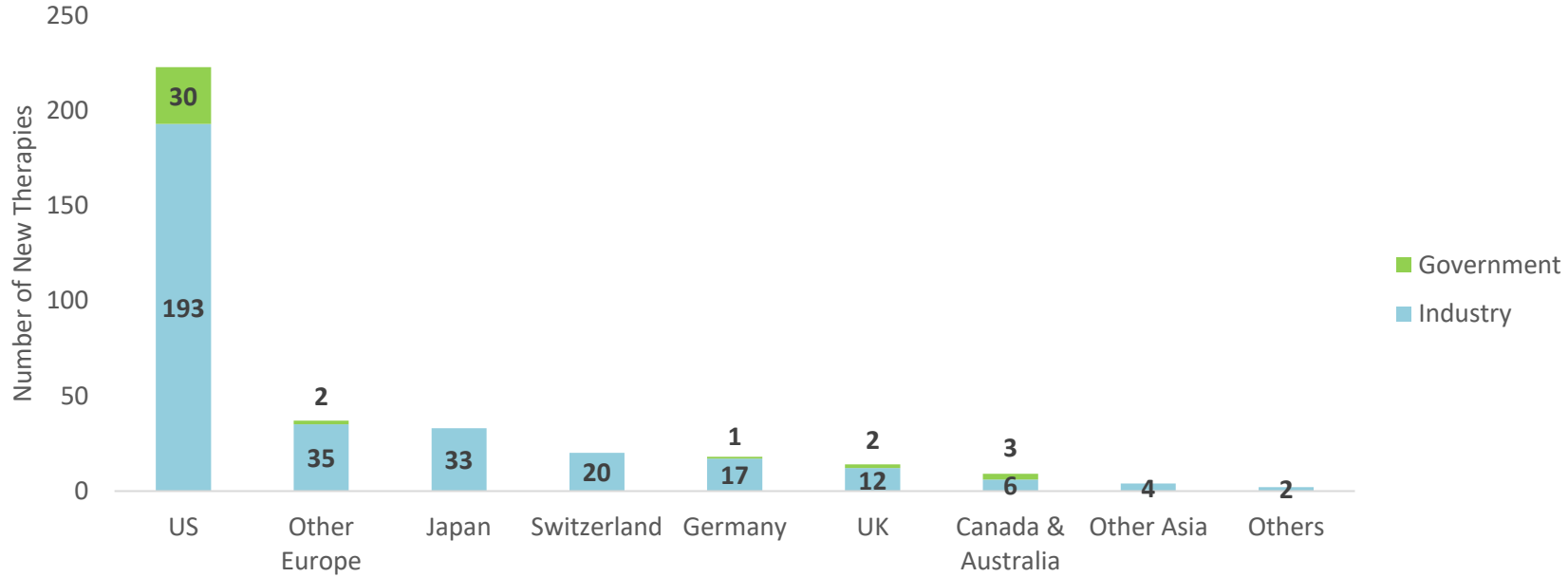
2011-2021 (N = 363)



- Academia ('A') is directly responsible for originating roughly 8% of U.S. derived new medicines, government ('G') for 1%.
- 55% of U.S. derived new medicines originated in small firms or small firms partnering w/academia and/or government.
- 45% of U.S. derived new medicines originated in large firms or large firms partnering w/academia and/or government

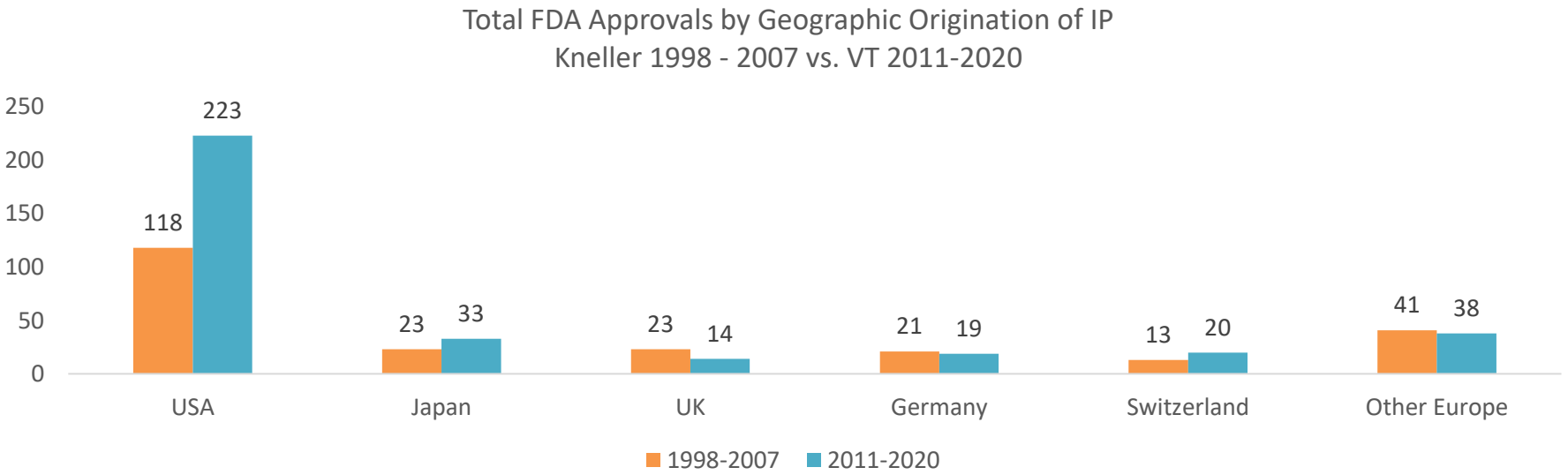
New Therapies Originated in Government or Industry Research by Geographic Location

2011-2021 (N = 360)



- Industry funded research originated the IP for roughly 90% of all new medicines globally.
- Government funded research originated the IP for roughly 10% of all new medicines globally.
- 62% of FDA approved medicines originated in the US.

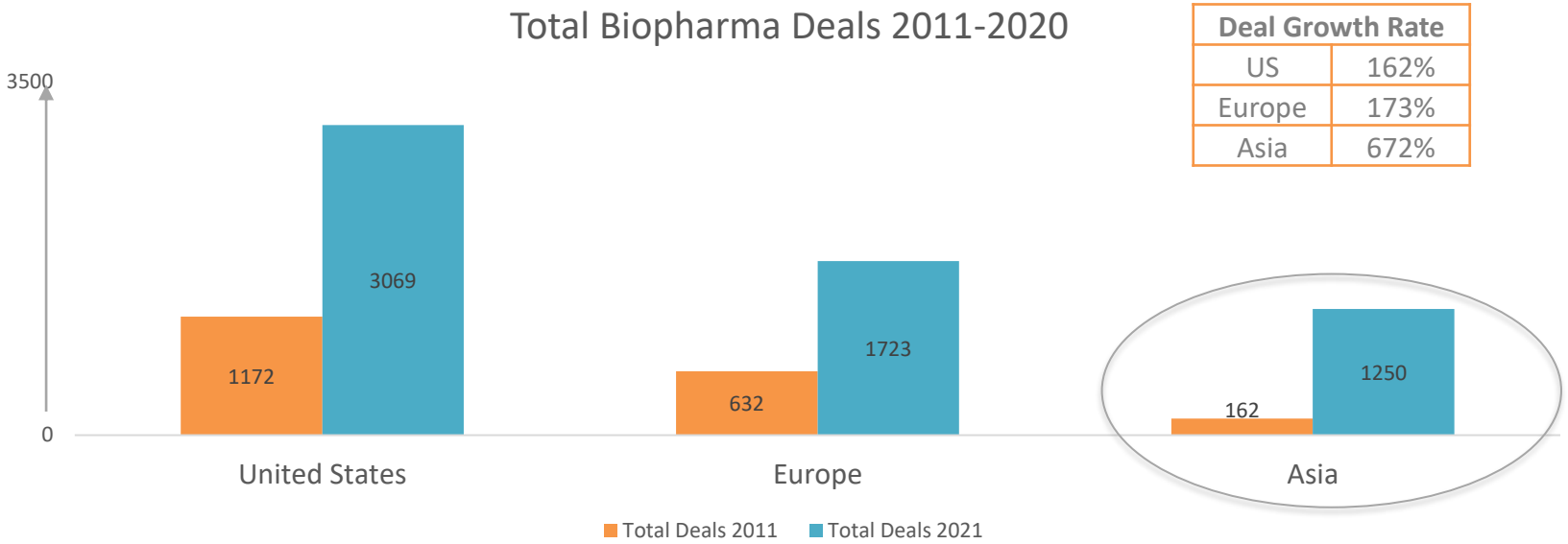
US vs Rest of World Biopharmaceutical Developments



The USA alone was responsible for 95% of the increase of 111 total FDA approvals in the 11 years between Kneller's 2007 publication and this research.

External deals have increased dramatically

Asia (China, Japan, S. Korea, Taiwan) will have more deals than Europe in 24 months at current trends



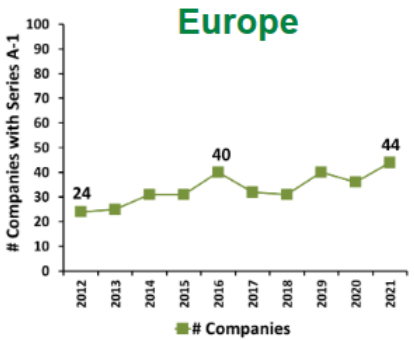
Deal Growth Rate	
US	162%
Europe	173%
Asia	672%

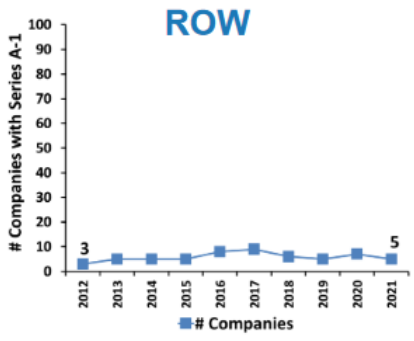
There has been a marked and profound transition to distributed partnership developments as endorsed by Lo and Viehbacher, this change suggests it was the core driver of the increase in drugs approved by FDA since the publication of Kneller (2010).

Global Early-Stage Venture Backed Biopharma Start-ups

2021 = barely a record

2021 = record #, by 2x vs 2020



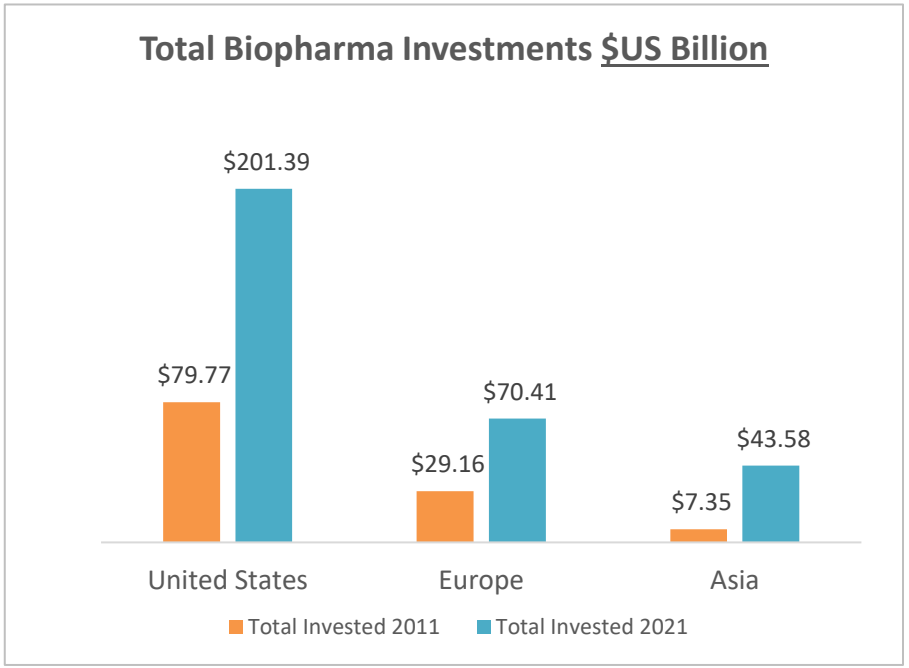


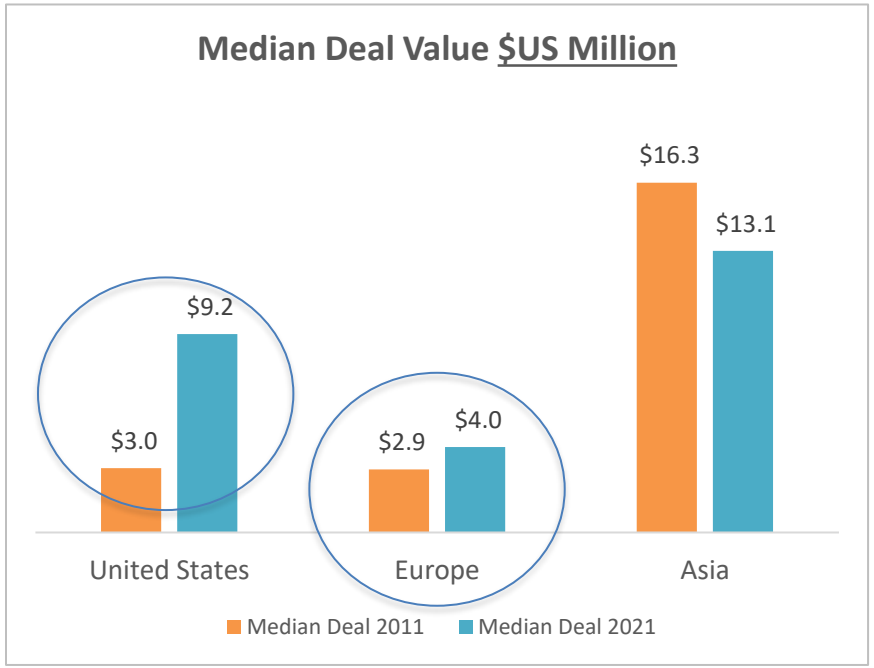
Primary Databases used: Primary: Cortellis/TR, EvaluatePharma, Informa, Biocentury BCIQ

www.bio.org/iareports, BIO Industry Analysis, 2022

- Transition appears to be occurring from infrastructure to innovative R&D in Asia.
- Asia (primarily China) has 93 venture backed start-ups; this is roughly equal to the annual US total.
- EU is flat with limited innovative early-stage growth.

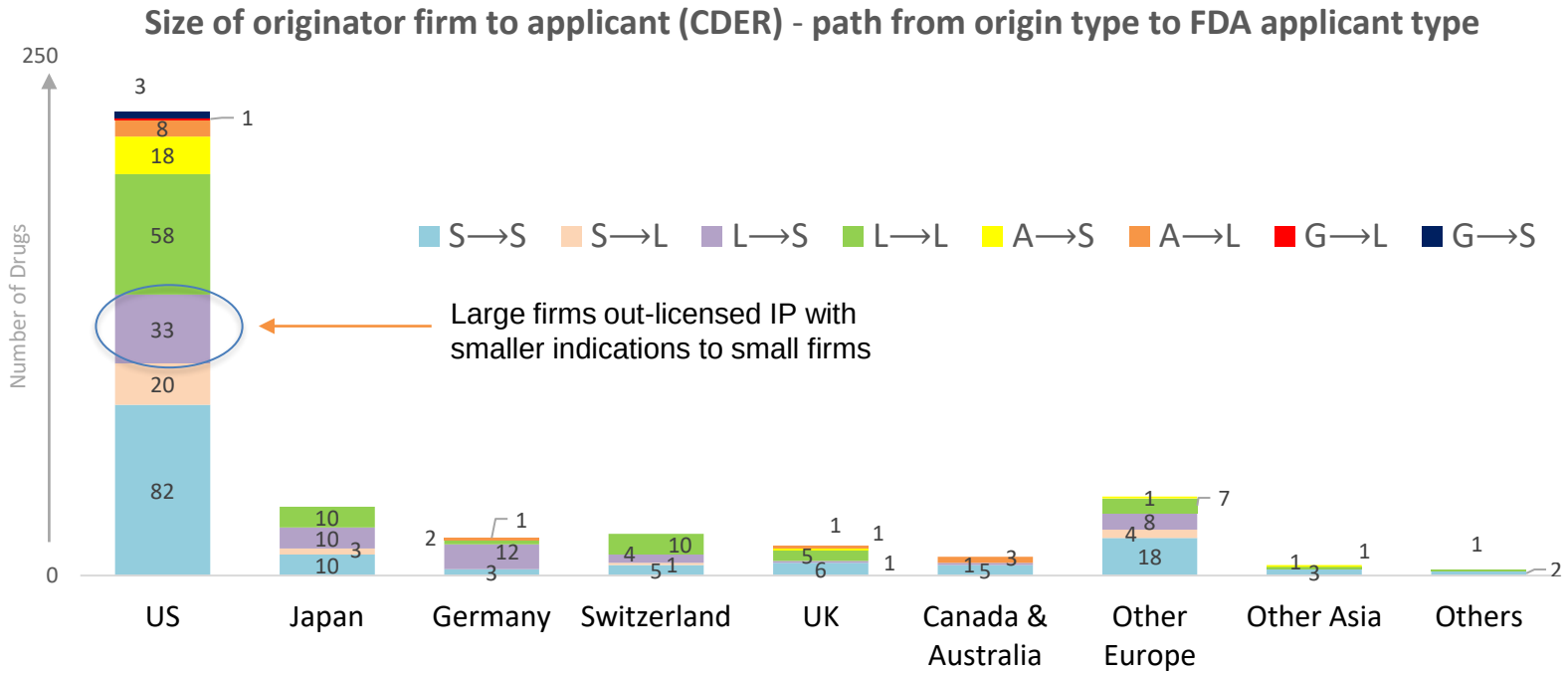
US External Partnerships and Investments Have Increased by 152% (CPI Base 2011)





US deals have more than tripled in size, there is limited growth in the size of individual EU deals

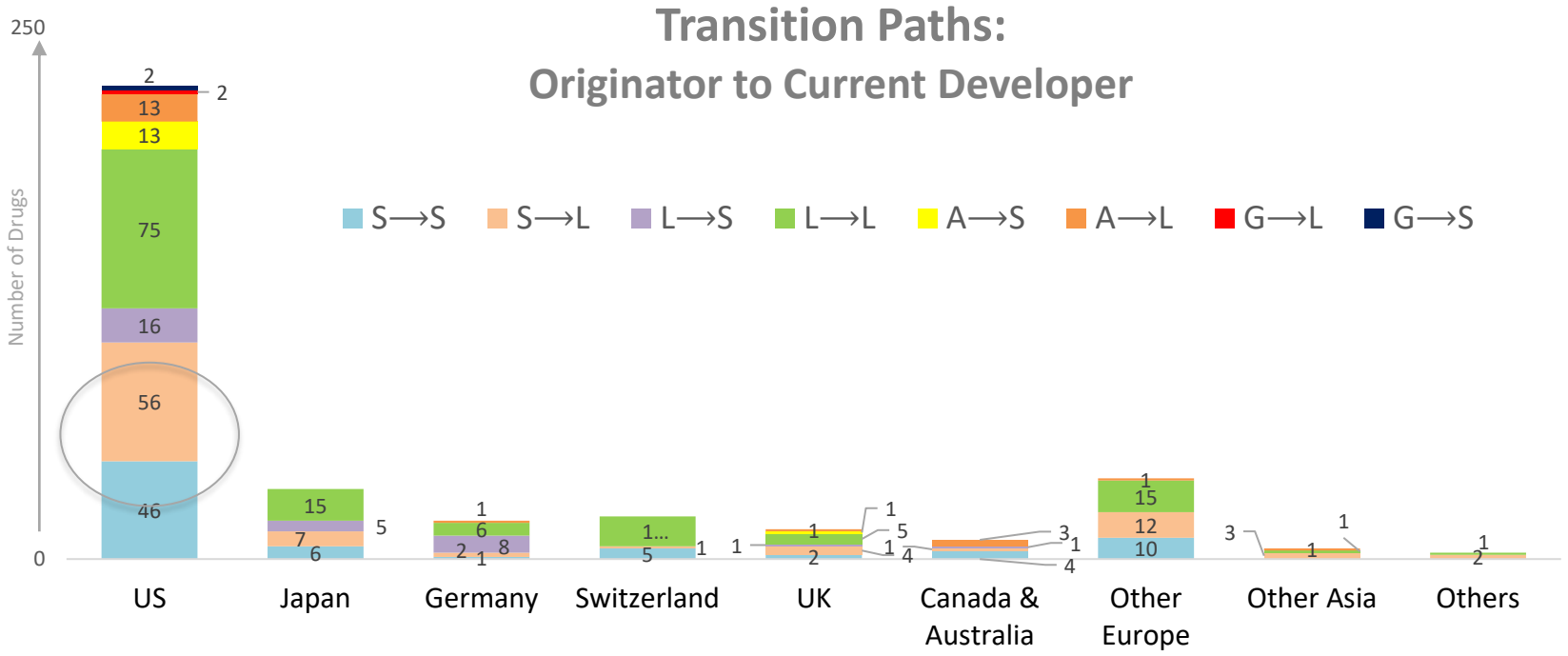
The US Ecosystem sees a tremendous movement of IP to optimize approvals



- Small firms have the ability to quickly scale their development while also managing FDA and global regulatory approval, indicating vital role of large pharma partnerships (e.g., Pfizer & BioNTech).
- Large firms out-license roughly 1/3rd of their discoveries to smaller firms based on the size of the indication (n=33).

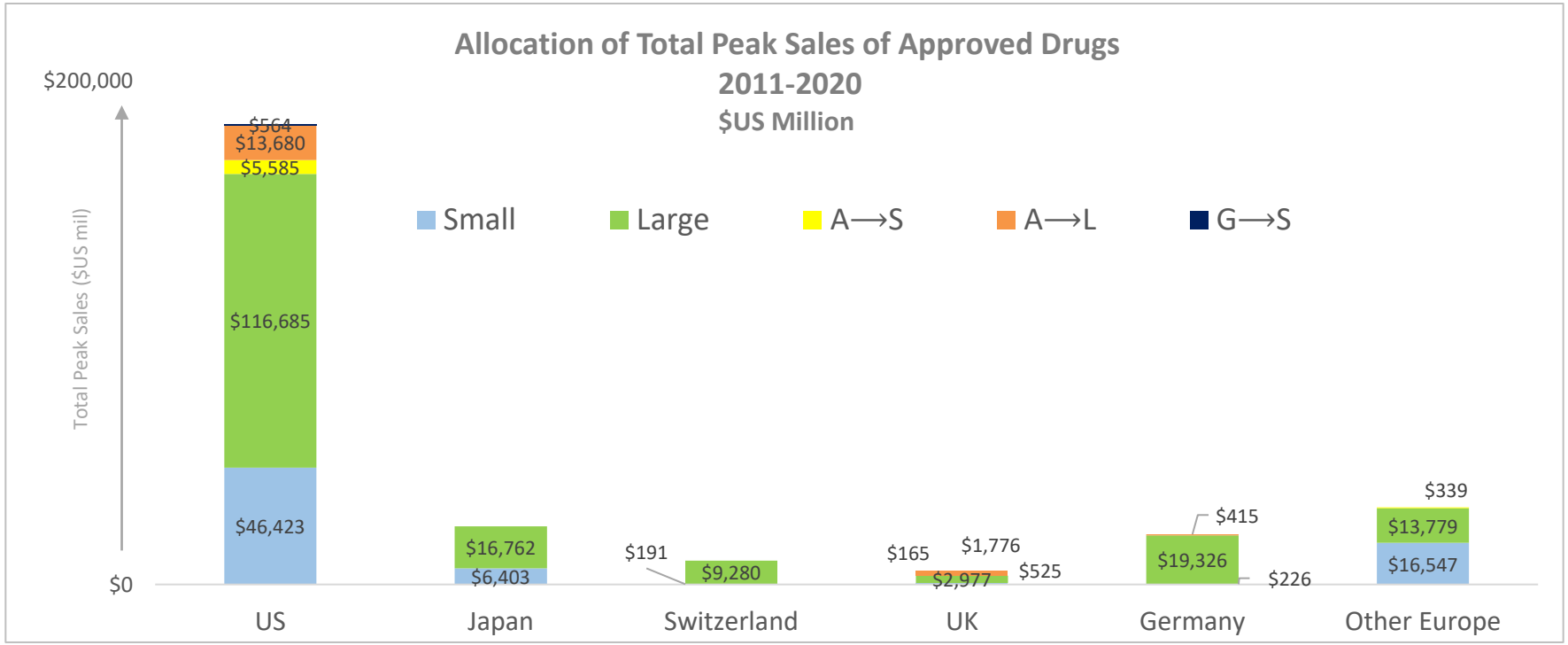
Who manages development after FDA approval?

Among our initial 102 therapies developed by small companies, 56 are fully managed and developed after FDA approval by large pharma in order to scaleup production, handle global regulatory policy, and provide access – enhancing development efficiencies.

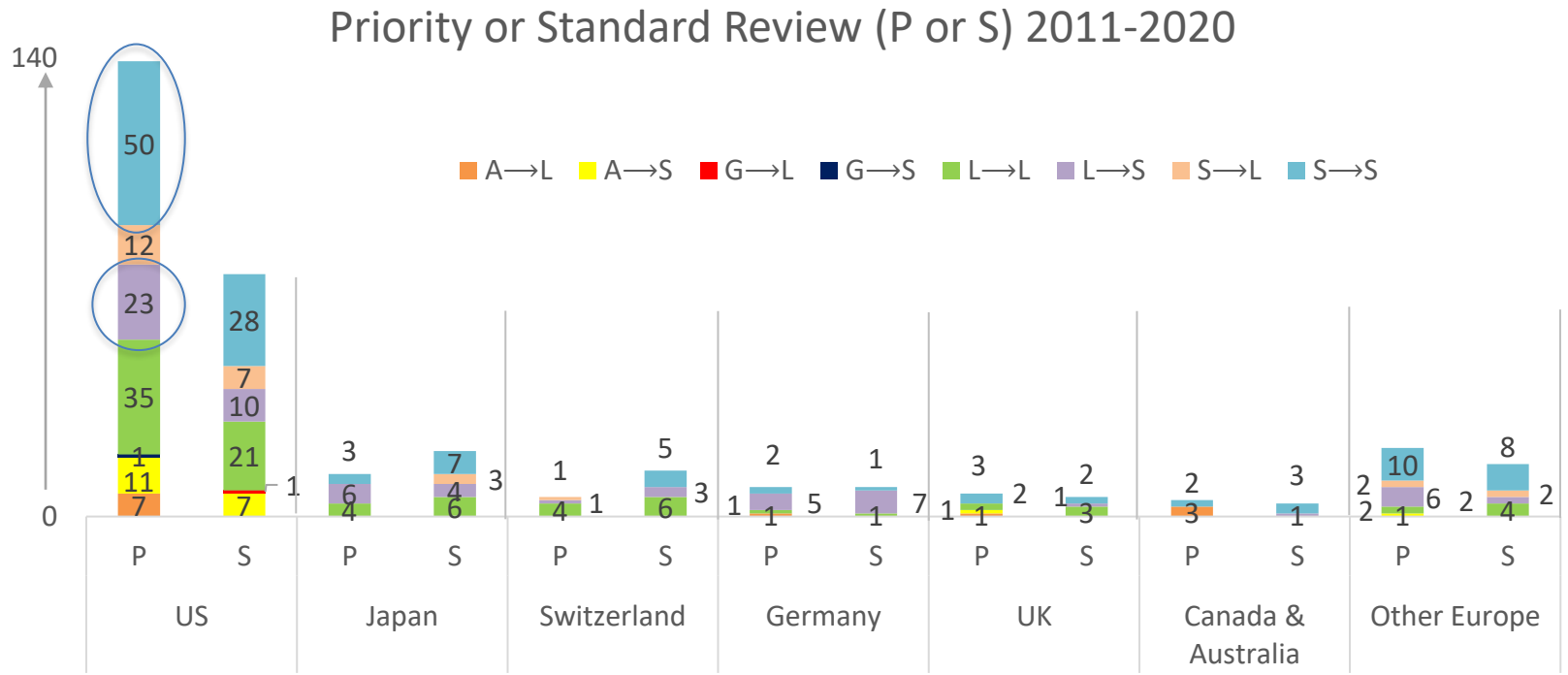


Who manages development after FDA approval?

Our hypothesis, that therapies targeting large indications require the scale of 'big pharma', is supported by the total sales by type of firm. Smaller firms appear to target indications with less revenue potential from 2011-2020



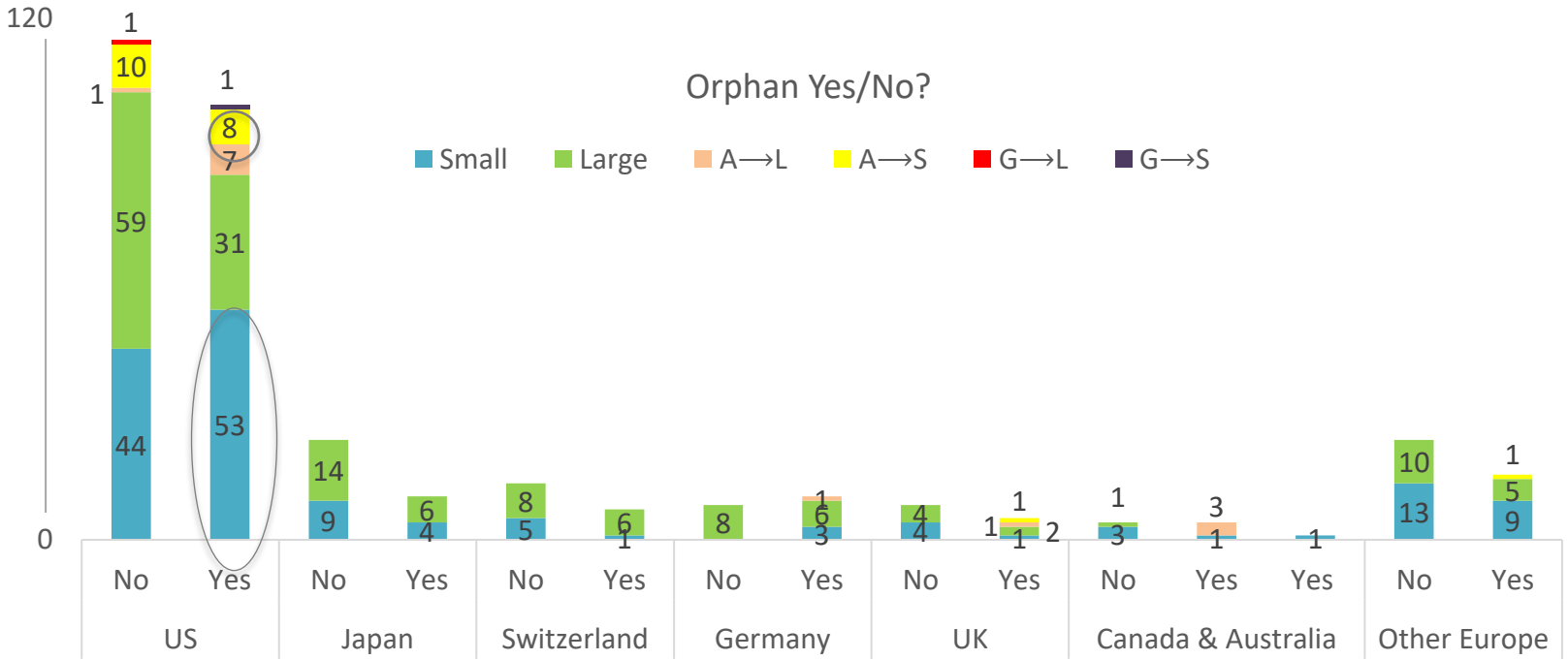
Development Paths at Time of FDA Approval by Country/Region of Originator



Small companies often focus on priority review therapies. These therapies are commonly orphan medicines which are generally more innovative, but less profitable due to their targeted populations than larger indications.

Development Paths at Time of FDA Approval by Country/Region of Originator

As previously stated, most ‘orphan’ therapies are managed and developed by small firms from 2011-2020.



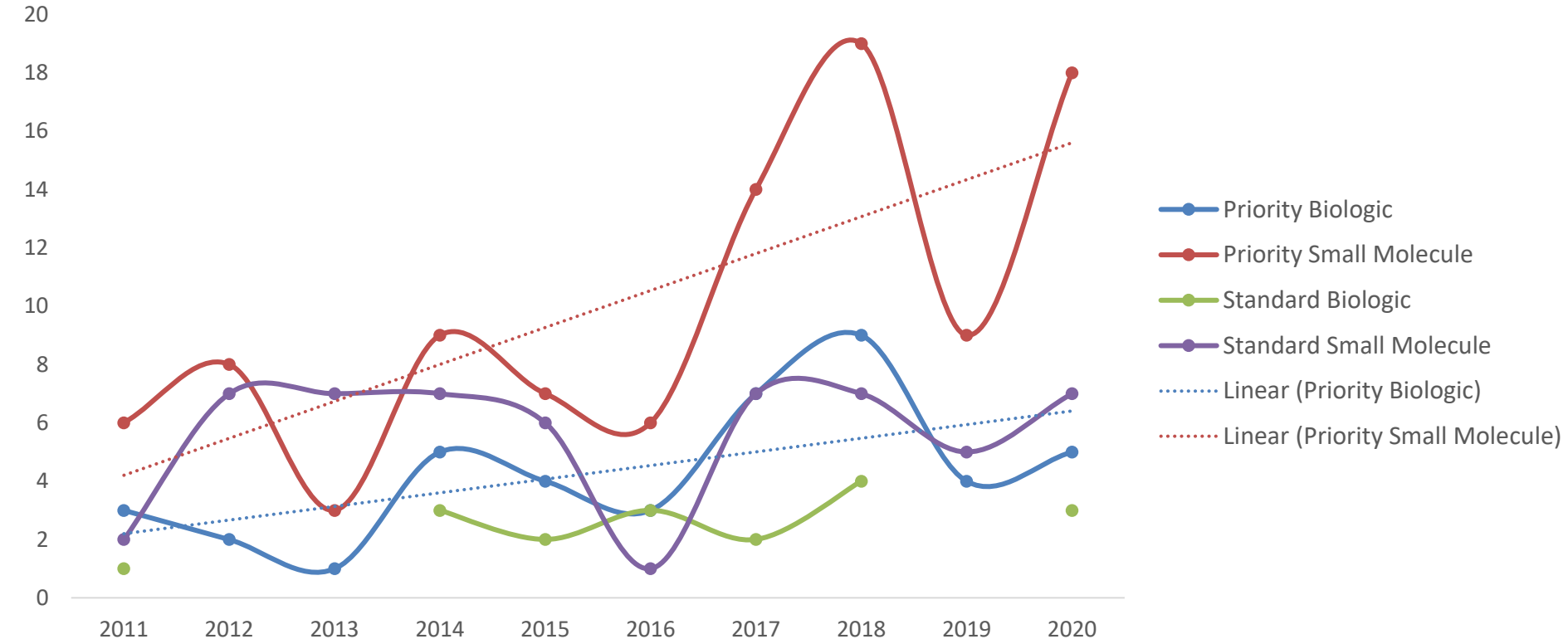
What is the probability that a ‘blockbuster’ therapy originated in…

Originator Sector	Probability a blockbuster originated in indicated sector
Small Company	64%
Large Company	28%
Academia	8%

Development Path: Originator –> Current Developer	Probability a blockbuster followed the indicated path
Small Co.–> Large Co.	39%
Small Co. –> Small Co.	25%
Large Co. –> Large Co.	25%
Academia	8%
Large Co. –> Small Co.	4%

Timeframe 2011-2020

Trends in IP Creation
Number of NDA or BLA FDA Approvals by Type of Review, 2011-2020



NIH Funds “every one of the 210 NMEs approved from 2010–2016”?

VitalTransformation

RESEARCH ARTICLE | SOCIAL SCIENCES |

Contribution of NIH funding to new drug approvals 2010–2016

Ekaterina Galkina Cleary, Jennifer M. Beierlein, Navleen Surjit Khanuja, +1, and Fred D. Ledley Authors Info & Affiliations

Edited by Solomon H. Snyder, Johns Hopkins University School of Medicine, Baltimore, MD, and approved December 27, 2017 (received for review September 1, 2017)

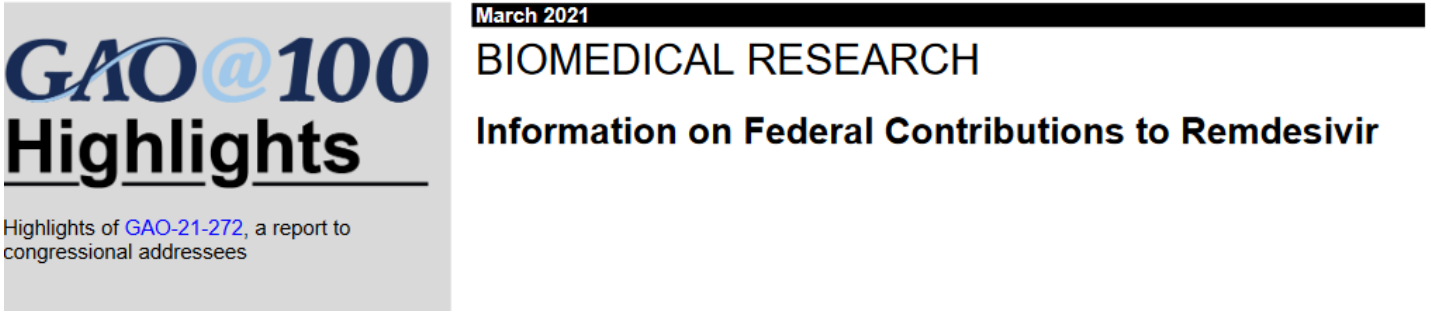
February 12, 2018 | 115 (10) 2329-2334 | https://doi.org/10.1073/pnas.1715368115

A highly quoted and publicized research study (Cleary, et al., 2018) claimed that every FDA approved NME in a six-year cohort had funding directly tied to the NIH.

IS THIS ACCURATE?

- Cleary, et al. claim that the discovery of NIH funded biological targets should be considered core IP for drug development; i.e., NIH identified platforms/targets that facilitate new approaches for drug development have a public IP claim for ownership.
- The entire motivation for the establishment of the NIH was to identify such new platforms and targets for future developments and medical breakthroughs in a pre-competitive environment.
- An analogy to consider would be any privately developed goods or services transported on the federally funded US Interstate freeway system are thusly owned by the US taxpayer; the concept is absurd and confiscatory.
- VT researched 23,230 NIH grants from the year 2000 and found no statistical evidence of NIH funded research having any statistical relationship to the probability on FDA approval.
- FDA approval is statistically predictable by the total amount of private funding and investments a drug receives.

Further Debunking the NIH Platform/Target Public Claim


GAO@100 Highlights

Highlights of GAO-21-272, a report to congressional addressees

March 2021

BIOMEDICAL RESEARCH

Information on Federal Contributions to Remdesivir

At the peak of the pandemic, Dr. Cleary again made a highly quoted and publicized claim that the COVID-19 treatment drug remdesivir had received, "$6.5 billion in NIH funding," and further stated that this, "underscores the scale and significance of the public-sector investments that enable new drug discovery and development."

A Government Accountability Office (GAO) report investigated this claim by Dr. Cleary et al and concluded, "Gilead's collaborations with government scientists with respect to remdesivir generated no intellectual property rights for federally funded researchers or government agencies."

The Relative Contributions of NIH and Private Sector Funding to the Approval of New Biopharmaceuticals

Duane Schulthess, Harry P. Bowen, Robert Popovian, Daniel Gassull, Augustine Zhang & Joe Hammang

Therapeutic Innovation & Regulatory Science (2022) | Cite this article

Published: 03 September 2022

- "NIH funding for the 18 FDA-approved therapies totaled $0.670 billion, whereas private sector funding (excluding post-approval funding) totaled $44.3 billion. . .The relationship between public funding and the likelihood of FDA approval is found to be negative and not statistically significant."

- "Our results indicate that, when NIH-funded research is linked to patented discoveries, additional public funding may have a significant ($p \leq 0.0965$) negative impact on the probability of FDA approval."

Summary and Conclusions

VitalTransformation

- The dominance of American biopharma in global innovation has increased since Kneller's publication; the USA is responsible for 95% of the increase of 111 total FDA approvals since 2010.
- The diversified external R&D ecosystem, emerged since 2008, has led to an increase of more than 160% in the value of external R&D partnership in Europe and the US.
- Industry funded research (small and large) originated the IP of roughly 90% of all new medicines globally.
- 1/3rd of Large Industry's originated U.S. IP is out-licensed to smaller firms, this is unique to the global ecosystem, and shows the ability of firms to adapt to the scale required to develop new medicines by indication.
- The NIH's CRADA and Intermural grants were directly responsible for the creation of 4 of the 363 new drugs in our cohort; US academic institutions and government created 10% of all indigenously originated U.S. IP.
- 55% of U.S. originated therapies are created by small biotech companies, large companies are responsible for 45%.
- The majority of biologics undergo priority review and target orphan indications at the time of FDA approval.
- The NIH's role in drug discovery, while vital, is not directly responsible for the development of new therapies.