The Effect of Financialization on Innovation in Biopharma:

Evolution Over Time and an Empirical Analysis of the Industry

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DECLARATION

I, Travis Whitfill, confirm that the work presented in my thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

ABSTRACT

The biopharmaceutical industry is inherently capital intensive due to the complexity of drug development. The sector has also increasingly experienced shareholder-driven corporate governance, or financialization. However, to date, the term “financialization” in biopharma has been poorly defined and generally restricted to describing share buybacks and dividends. Few studies have empirically examined the relationship between financialization and innovation in biopharma.

Through a neo-Schumpeterian framework, I first offer a definition of financialization in biopharma, which I interpret as the strategy of prioritizing financial accumulation over technical innovation, mediated by the influence of finance and shareholder-driven corporate governance, to benefit shareholders. I give operational definitions of financialization across institutional control, stock engineering practices, and corporate governance. I hypothesize that the industry is heavily financialized, more so over time, and that financialization leads to lower innovation.

I then investigate the degree of financialization in biopharma from 2011 to 2021, showing that the industry has become significantly more financialized.

Finally, I look at the empirical relationship between financialization and innovation in the top 50 biopharma companies. I use several metrics to define innovation, including new drug approvals, the medical benefit of drugs, and patent citations. Structural equation modeling reveals a significant inverse relationship between financialization and R&D spend, and a significant inverse association between M&A and internal R&D spend. Higher M&A spend is not associated with higher innovation.

Taken together, these findings show that higher financialization is associated with a decrease in internal R&D and an increase in M&A, which then is associated with a decrease in innovation. Profits from acquired companies flow back to investors, who perpetuate the cycle of increasing private valuations and earlier IPOs, leading to riskier investments. Despite the industry’s belief

that M&A is critical to innovation, my analyses do not support this claim. Instead, biopharma should focus on internal R&D for innovation.

IMPACT STATEMENT

The biopharmaceutical industry is a particularly financialized industry with significant share repurchases, rises in drug pricing, and a focus on delivering returns to shareholders and venture capital, all of which is driven by short-term returns. These forces create an inevitable tension between innovation and return for shareholders, and a financialized biopharma model may have several negative consequences for society. Prioritizing shareholders may hinder the innovation process for delivering medicines to patients; manager-driven capitalism does not necessarily coincide with patients' interests; rising drug costs benefit shareholders and may limit access for patients; and the short-termism of capital that dominates biopharma is often at odds with the long-term horizon of drug development.

My studies have shown that over the last decade the biopharma industry has become increasingly financialized, as characterized by skyrocketing venture capital funds and early-stage IPOs; increased stock engineering practices and egregious executive compensation; increased stock repurchases and dividends; and higher stock repurchases and dividends compared to R&D investments.

In this thesis, using empirical analyses, I show the impact of financialization and M&A on innovation and R&D in the 50 largest biopharma companies between 2011 and 2021. I demonstrate that there is a significant relationship between higher financialization and lower internal R&D, indicating that increased investments in R&D instead of share buybacks, executive compensation, dividends, or M&A could lead to increased innovation in biopharma. Additionally, higher M&A spend leads to lower R&D spend. I also show how higher R&D efficiency is associated with increased R&D intensity (R&D spend divided by revenues), smaller firm sizes, and specialized firms with a narrower, more focused pipeline. Taken together, my research suggests that larger, financialized companies have lower R&D spend, which, in turn, is associated with lower innovation and, specifically, fewer drug approvals.

I propose several policy changes as a result of these findings. First, the US Government could take mission-oriented initiatives and follow a venture capital model to invest in innovation, and provide a source of capital for innovation, while capturing returns for taxpayers. Second, I suggest restrictions on executive compensation, especially when those executives benefit heavily from taxpayer-funded R&D. Third, I propose more scrutiny of M&A in biopharma (e.g. via the Federal Trade Commission), given that more M&A may ultimately be detrimental to innovation. Finally, I suggest that the US enact policies that promote diffuse innovation (e.g. less consolidation), lower spend on financialization, and higher internal R&D spend, because these would lead to higher innovation in the biopharma industry, and ultimate benefit patients over shareholders.

DEDICATION

I dedicate this thesis to my mom, who is battling Stage IV ovarian cancer, and deserves equitable and fair access to affordable, innovative medicines and healthcare. To my dear friends, loved ones, and support system, who have supported me while working, studying, and helping me take care of my mom.

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ABBREVIATIONS AND ACRONYMS

AARCC	Advanced Agricultural Research and Commercialization Corporation
AEMPS	Agencia Española de Medicamentos y Productos Sanitarios
AIFA	Agenzia Italiana del Farmaco
APAC	Asia-Pacific
ARPA-H	Advanced Research Projects Agency for Health
ASMR	l'amélioration du service médical rendu
BARDA	Biomedical Advanced Research and Development Authority
CEO	Chief executive officer
CFI	Comparative fit index
CFO	Chief financial officer
CI	Confidence interval
CIA	Central Intelligence Agency
CMO	Chief medical officer
COVID	Coronavirus disease
CRSP	Center for Research in Security Prices
DARPA	Defense Advanced Research Projects Agency
DNA	Deoxyribonucleic acid
DoD	Department of Defense
EU	European Union
FDA	Food and Drug Administration
FTC	Federal Trade Commission
GDP	Gross domestic product
GVKEY	Global company key
HAS	Haut Autorité de Santé
HTA	Healthcare technology assessment
IP	Intellectual property
IPO	Initial public offering
JnJ	Johnson & Johnson
M&A	Mergers and acquisitions
mRNA	Messenger ribonucleic acid
MSV	Maximizing shareholder value
NASA	National Aeronautics and Space Administration
NBE	New biological entity
NBER	National Bureau of Economic Research
NDA	New drug approval

NFC	Nonfinancial corporation
NICE	National Institute for Health and Care Excellence
NIH	National Institutes of Health
NME	New molecular entity
NYSE	New York Stock Exchange
PhRMA	Pharmaceutical Research and Manufacturers of America
QALY	Quality-adjusted life-year
R&D	Research and development
rDNA	Recombinant DNA
RNA	Ribonucleic acid
RMSEA	Root mean standard error of approximation
SBIR	Small Business Innovative Research
S&P 500	Standard and Poor's 500
SD	Standard deviation
SEC	Securities and Exchange Commission
SEM	Structural equation modeling or Standard error of means
SG&A	Selling, general, and administrative
SME	Small and medium enterprise
SMR	Service Médical Rendu
SPC	Simple patent count
TC	Transparency Commission
TCJA	Tax Cuts and Jobs Act
USPTO	United States Patent and Trademark Office
USD	United States Dollar
VC	Venture Capital
WPC	Weighted patent counts
WRDS	Wharton Research Data Services
XML	Extensible Markup Language

Chapter 1: Introduction

1.1. Introduction and context

The modern biotechnology industry began in the 1970s with the first uses of recombinant DNA for developing medicines. It grew slowly for its first few decades, but after the completion of the Human Genome Project in 2003, and exponentially decreasing costs in genome sequencing, biotechnology has become integral to the pharmaceutical industry (together, the 'biopharma' industry), producing a wave of revolutionary new biological drugs.

While new technologies were invented to change the drug discovery and commercialization process, *the way in which biopharma companies innovate has also changed*. The rise of biotechnology in the 1980s shifted the division of innovative labor in the pharmaceutical sector—it was initially concentrated in and integrated into large pharma companies, but then diffused across a network of innovators in smaller biotech companies (Arora and Gambardella 1990, Gambardella 1995). Innovation policies and regulations in the 1980s also shaped this process, especially the 1980 Bayh-Dole Act, which played a major role in this innovative shift, allowing for the license and commercialization of intellectual property (IP) from universities (Pisano 2006).

Concurrently, the way the biopharma industry was financed changed drastically in response to the changing biopharma innovation landscape. Throughout the late 20th century, a number of policies were key to how finance shaped biopharma: deliberate monetary policy, deregulation of the finance industry, tax policies, and deregulation of corporate practices allowed for both finance and corporate governance to grow in their influence over the economy (van der Pijl 1984, Ferguson 1986, Duménil 2001, Wray 2009). At the same time, policies in the 1980s allowed venture capital to rise as a vehicle for financing innovation, and it has since grown to be one of the primary finance vehicles for biotech companies.

The two processes (innovation shifts and the growing influence of finance) are intertwined: innovation shifted from being concentrated in large

pharma to a decentralized network of small, innovative biotech companies that required a lot of capital. The pattern of change in innovation in biopharma increasingly necessitated a different model of finance; at the same time, finance itself changed and became increasingly dominant in biopharma companies, directing how they were governed and operated.

"Financialization" is a relatively new term that emerged in the 1990s to describe the growing influence of finance throughout the economy. Financialization resulted in a split between the real and financial economies (Lazonick and and O'Sullivan 2000, Stockhammer 2004, Epstein 2005, Krippner 2005, Orhangazi 2008, Davis 2016). Empirical studies of financialization have revealed similar macro trends in biopharma to those in other industries: (1) increases in debt; (2) the rise of intangible assets; and (3) the growth of payouts to shareholders. From a review of the literature (discussed in detail in the next section), there are two predominant streams of financialization at the meso/micro level that have been characterized in biopharma, one driven by a corporate governance ideology of maximizing shareholder value (MSV), the other by the financial institutions that capitalize the biopharma companies.

MSV ideology is characterized by the prioritization of share value over the general efficiency of the productive system. An MSV-driven firm aims to return capital back to shareholders instead of re-investing returns in R&D and tangible capital. Until the 1970s, US stockholders allowed management to retain control over most of a corporation's cash flow with little influence from shareholders (Chandler 1977). However, later in the 20th century this Chandlerian type of managerial practice eroded and shifted towards an emphasis on shareholder interests (Stockhammer 2004, Taylor 2015). This was accelerated by regulatory shifts that occurred in the late 20th century—e.g. growth in institutional investors, more stock-based executive pay, and encouraging stock buybacks (Davis 2017).

Financial institutions have also played a major role in a finance-dominated biopharma industry. These financial institutions (venture capital and

other institutional capital) are focused on short-term financial returns and thus exert their influence on biopharma firms accordingly. There is often inherent tension in the goals of venture capital and the goals of true biopharma innovation: for biopharma companies innovation is a long-term process (Lazonick and O'Sullivan 1996), and this often clashes with the goals of venture capital, which seeks short-term returns. Importantly, venture capital is also itself financialized: venture capital is controlled by shareholders who have expectations and determine the investing strategy of the VC firm. Thus, there is the compounding effect of shareholder ideology on the venture capital group, as well as the direct demands of the VC on the biopharma company.

While many have documented an increasingly financialized biopharmaceutical sector (e.g. (Serfati 2008, Lazonick 2009, Andersson, Gleadle et al. 2010, Lazonick and Tulum 2011, Montalban and Sakinç 2013, Lazonick 2016), the *empirical* relationship between financialization and innovation in the biopharmaceutical industry is under-researched. Few studies have looked at the empirical effect of financialization on innovation. How financialization actually drives innovation (whether positively or negatively) has not been well studied; empirical studies to more definitively answer this question are the focus of this thesis.

1.2. The significance of studying financialization in biopharma

The biopharmaceutical industry is a particularly financialized industry with significant share repurchases, rises in drug pricing, and a focus on delivering returns to shareholders and venture capital, all of which is driven by short-term returns. **These forces create an inevitable tension between innovation and return for shareholders, and a financialized biopharma model may have a number of negative consequences for society:**

(1) prioritizing shareholders may hinder the innovation process for delivering medicines to patients;
(2) manager-driven capitalism is often at odds with patients' interests;

(3) rising drug costs benefit shareholders and may limit access to patients; and

(4) the short-termism of capital that dominates biopharma is often at odds with the long-term horizon of drug development.

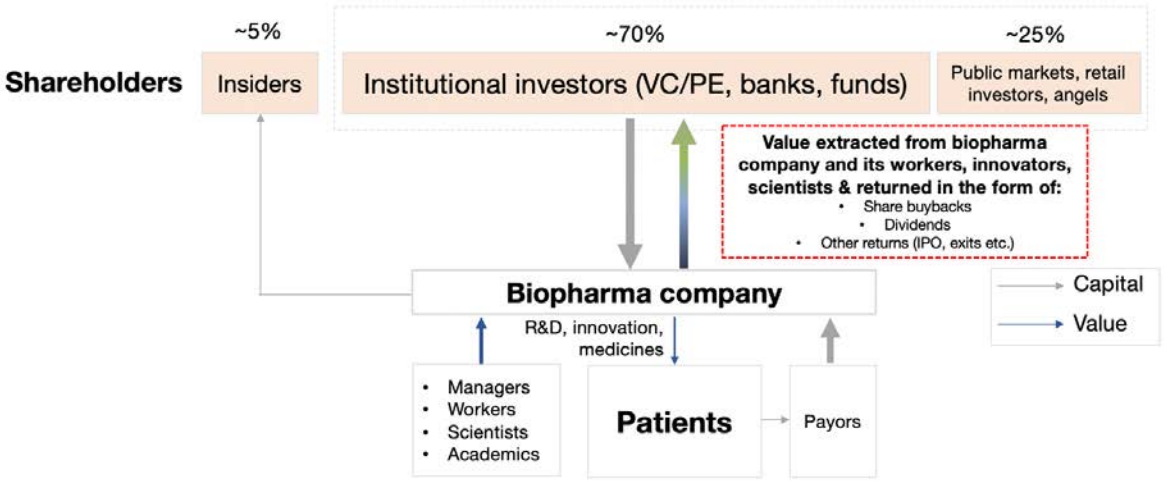
First, prioritizing shareholders may hinder the innovation process for delivering medicines to patients. An integrated approach to innovation in biopharma would prioritize delivering value to patients in the form of medicines, while a financialized approach in biopharma prioritizes delivering value to shareholders (Gleadle, Parris et al. 2014). Instead of reinvesting income into research and development (despite the claim that high drug prices are justified to fuel R&D), many larger biopharma companies instead invest accumulated capital into buying back their own shares or distributing dividends to shareholders (Lazonick 2016, Roy, Hawksbee et al. 2016).

Moreover, taking the number of new NMEs (new molecular entities) approved by the FDA as a function of spend on R&D, there has been a steady decline in productivity. This is in part due to the reorienting of investments toward high-risk/high-premium targets (Pammolli, Magazzini et al. 2011). This is indicative of MSV ideology, which prioritizes earnings over value to patients (Dosi, Marengo et al. 2023).

Second, a systemic problem across biopharma is that *incentives for management and shareholders are too closely aligned;* by selling shares in their companies and leveraging their own compensation packages, many pharma executives are able to buy shares from themselves *and* increase the value of their own and other shareholders' shares. Put another way, pharma executives' incentives are not aligned with those of patients. While MSV-focused strategies benefit shareholders, they extract value (i.e. therapeutic advances) out of the biopharma innovation process (Mazzucato 2018), and benefit venture capitalists and institutional investors over the intended beneficiary of value: patients. These relationships are depicted in **Figure 1** in

which value is extracted from a biopharma company (and thus, indirectly, patients) and returned in capital to institutional investors and insiders.

Figure 1. Maximizing shareholder value in biopharma



Third, drug prices continue to rise to the detriment of purchasers and patients. Many pharmaceutical companies insist that the dramatic rise in drug prices funds innovation, is necessary for research and development, and is justified by the high risks and high rate of drug failures (Mossinghoff 1999, Lazonick 2016). However, no empirical research supports this (Lazonick 2016). In 2013-2015, drug prices increased *annually* by 10% in the US, which was over six times the rate of general inflation (Schondelmeyer 2016, Hernandez, Good et al. 2019). Prices for new types of medicines coming to the market are approaching or exceeding $1 million USD per therapy (e.g. gene therapies). The result of these unregulated increases in drug prices is a large accumulation of capital among biopharma companies. Instead of reinvesting income into research and development (despite the claim that high drug prices are justified to fuel R&D), many larger biopharma companies instead invest accumulated capital into buying back their own shares or distributing dividends to shareholders (Lazonick 2016, Roy, Hawksbee et al. 2016). The cost of medicines places a clear burden on health systems, and even high-income countries struggle to afford high-cost medicines, e.g. particularly for cancer and orphan diseases (Ramsey, Whitley et al. 2009, Michel and Toumi 2012,

Simoens, Picavet et al. 2013, 2014, Brennan and Shrank 2014, Kmietowicz 2014). As an illustration, in 2014 the UK's National Institute for Health and Care Excellence (NICE) deemed an effective breast cancer drug, trastuzumab (Kadcyla, Roche), which had a £90,000 annual price tag, unaffordable (Kmietowicz 2014). However, the possibility that some orphan drugs do not qualify for full reimbursement is not generally accepted (Sheldon 2012, Simoens, Picavet et al. 2013), even though this creates political and ethical dilemmas around affordability and patients' access to life-saving medicines. These issues are exacerbated by conflicts of interest and lobbying from the pharmaceutical industry, particularly in the US (Neuman, Korenstein et al. 2011, Piller 2018).

Finally, there is inherent tension in the goals of true biopharma innovation and its sources of finance and capital. Smaller biopharma companies are primarily financed through venture capital funds, and larger biopharma companies are often financed by public markets and money managers at institutional funds. A key problem with both these sources of capital is their short-termism. Given the long-term time horizon of drug development (often ten to 15 years for the entire process), this is typically at odds with the focus of corporate managers and shareholders on short-term results—usually short-term financial gains for a fund (Rappaport 2005, Dallas 2012). This is especially true in venture capital, which is driven by goals of returning ≥10x on the portfolio in ~five years. This leads to VCs and funds encouraging companies to go through an IPO or M&A deal (Lazonick and Mazzucato 2013). Pisano sees the US biotech industry as in need of "patient capital" over the short-termism of venture capital (Pisano 2006). Venture capitalists—as a generalization—are more concerned about making a return than sustaining innovation.

1.3. Gaps and expected contributions to the literature

The tension between innovation and financialization in biopharma seems clear. However, in a review of the literature, there seem to be some key gaps that I

hope to address in my work: (1) there have been few and limited definitions of financialization in biopharma; (2) there have been few empirical analyses studying the effects that financialization has on innovation in biopharma; and (3) most analyses of financialization in biopharma to date have been limited to public companies. The goal of this thesis is to address these three primary gaps.

First, previous definitions of financialization seem narrow and primarily focus on MSV ideology. Lazonick is a key economist who has characterized corporate strategies and financialization in biopharma. He has shown that from 2012 to 2021, the 14 pharmaceutical companies in the S&P 500 Index spent $377 billion repurchasing their own shares and $370 billion in dividends to shareholders, which represents 110% of their net income (Lazonick and Tulum 2024).

However, looking at dividends and share repurchases is a quite narrow empirical approach to studying financialization. A key contribution of my thesis to the literature will be to expand and characterize the definition of financialization in biopharma.

Second, there have been few empirical analyses of the actual effect financialization has on *innovation.* Missing from the work of Lazonick and others is an examination of the *consequences* of some of these financialized business practices. Indeed, as Christophers described it in 2015, “There are limits to our quantitative research into actually existing financialization” (Christophers 2015). In 2013, Mazzucato pointed out that innovation has both a rate and direction, and, “the way in which finance affects this direction is not well understood; **how the financial structure of an industry affects this directional bias** is a key area for future research” (Mazzucato 2013). Similar conclusions can be drawn between the relationship between financialization and innovation. The empirical, directional relationship between financialization and innovation (whether positive or negative) in biopharma has been understudied, and empirical studies to examine this relationship are the focus of this thesis.

Finally, most of the analyses in the literature draw from companies that are listed on stock exchanges and often do not include private companies—mostly due to the lack of publicly available data. Including private companies (and their relationship to venture capital, public funding, M&A from pharma, and patents), provides a much richer dataset through which to explore relationships between innovation and financialization.

1.4. Aims and hypotheses

The goal of my thesis is to provide a definition of financialization and empirical evidence that financialization directionally affects innovation in biopharma. The aims of my thesis are:

Aim 1: Define financialization in biopharma
Aim 2: Characterize financialization in biopharma
Aim 3: Study relationships between financialization and innovation

I hypothesize that more financialized systems are detrimental for innovation; that higher financialization (i.e. more stock repurchases, dividends, valuations) leads to lower internal R&D efforts and, overall, to lower innovative outputs (i.e. patents, new molecular entities, and health outcomes).

Specifically, for Aim 2, I hypothesize that the biopharma industry is financialized by: a high degree of venture capital financing; an increasing number of low-quality IPOs; stock engineering practices both in private and public companies; a high degree of financing being derived from M&A activity; the offer of stock repurchases and dividends (absolute value); and stock repurchases being significantly close to 1.0 or higher as a ratio of stock repurchases and dividends to R&D expenditures. I hypothesize that these trends have increased over the last decade.

For Aim 3, I hypothesize that higher financialization (i.e. more stock repurchases, dividends, valuations) leads to lower innovative outputs (i.e. patents, innovative drugs, and R&D productivity). Higher M&A activity also

leads to lower innovative outputs. Additionally, higher internal R&D spend leads to higher innovative outputs. I also hypothesize that R&D efficiency remains low in the industry and is likely to be associated with firm size and R&D intensity, and that M&A number and intensity are associated with higher innovation by more drug approvals.

The overarching goal of this work is to explore and map out innovation and finance systems in biopharma to determine if these systems can be optimized to maximize biopharmaceutical innovation.

1.5. Overview of findings

In Chapter 2, I summarize the literature on financialization and financialized practices in biopharma. I give background on the origins of financialization, starting with globalization in the 1960s, but particularly how it became dominant, beginning in the 1980s after a series of policies and laws allowed for monetization of IP from universities, deregulation of the financial sector, lower capital gains taxes and looser policies for VCs, and allowances for share repurchases. I study financialization through several lenses to achieve a macro view (at the macroeconomic level), a meso view (at an industry level), and an individual-level view (at the firm level). Through each of these levels, I summarize evidence of financialization, then home in on financialization specific to the biopharma sector. I summarize financialized practices across corporate governance (e.g. MSV ideology, drug pricing, and intellectual property rights), institutional control (the short-termism of VCs and how that affects innovation), and stock engineering (e.g. share buybacks and dividends). Finally, I lay out the theoretical framework for my studies on financialization by using a neo-Schumpeterian lens, which allows for the entanglement of finance and innovation—an approach that is key for studying biopharma, which is an R&D-centric industry.

In Chapter 3, I provide the methodology for my studies, which includes an industry-level analysis of financialization in biopharma. I describe my empirical approach to studying the relationship between financialization and innovation

in biopharma, using original data collection to construct a database of key variables for financialization and innovation for the top 50 biopharma firms. I use structural equation modeling, which allows for (1) the construction of latent variables with multiple measures (e.g. innovation is measured by multiple variables, including drug approvals, drug therapeutic value, and patent citations); and (2) insights into causal relationships between variables. Using this approach, I look at the causal relationships between innovation and internal R&D, M&A, and financialization.

In Chapter 4, I define financialization in biopharma as the strategic prioritization of financial accumulation over technical innovation, mediated by the influence of finance and shareholder-driven corporate governance, to benefit shareholders. I contextualize this definition and give concrete examples by studying financialization, including corporate governance, institutional control, and stock engineering, at the meso and micro level. I then characterize financialization in biopharma at the industry level in the last decade by looking at venture capital (which increased 40-fold from 2011 to 2021), more and earlier stage IPOs (which have increased 10-fold from 2011 to 2021), increasing private company valuations (which have increased 5.5-fold from 2011 to 2021), more M&A, higher share repurchases ($513 billion from 2011 to 2021 among the top 20 biopharma firms), more dividends ($784 billion during the same period among the top 20 biopharma firms), and an increasing ratio of share repurchases and dividends to R&D (from 0.7 in 2009 to 1.3 in 2019, p=0.007). I also provide case studies to support these analyses—for example, Biogen and Moderna—on share repurchases and executive compensation, respectively. Together, these findings show that increases in VC dollars lead to increases in private valuations, more IPOs at higher prices and earlier stages, more M&A, more large pharma buybacks and dividends—all of which benefit shareholders—and lower internal biopharma R&D.

Finally, in Chapter 5, I take a sample of the world's top 50 public biopharma companies (defined by 2021 revenue) to look at trends in the firms over time (from 2011 to 2021), as well as the empirical relationship between innovation

and internal R&D, M&A, and financialization. Among the bivariate findings, there is a linear and significant relationship between simple patent count and R&D spend; as well as new drug approvals and new molecular entities (NMEs) and R&D spend; an overall increase in R&D efficiency (number of drug approvals per $1 billion of R&D spending); a weak but significant relationship between R&D efficiency and R&D intensity (R&D spending as a percent of revenue); an inverse relationship between R&D efficiency and firm size; egregious executive compensation ($17.5 billion to executives from 2011 to 2021); steady but high share repurchases ($639 billion from 2011 to 2021); increasing dividends ($903 billion total from 2011 to 2021); a peak in M&A spend in 2019 (a total of $1.09 trillion from 2011 to 2021); and an inverse relationship between M&A spend and NMEs. Structural equation modeling reveals that higher financialization leads to lower internal R&D spend (p=0.038), and that more financialized companies also spend more on M&A (p=0.011) and less on R&D (p=0.076). Additionally, there is a negative relationship between financialization and innovation, although this relationship is not statistically significant.

1.6. Summary

This thesis has five key conclusions about the financialization of the biopharma industry. **First, the biopharma industry is heavily financialized and has become more financialized over time.** There are increasing examples of egregious financialization, such as exorbitant executive compensation from government-funded innovation during COVID, or FDA lobbying, high drug pricing, and share buybacks that negatively impacted Alzheimer's patients. The industry is more financialized, as evidenced by spending on share buybacks and dividends relative to internal R&D. While my empirical findings do not directly link financialization to lower innovation, it is indirectly related: higher financialization leads to lower internal R&D spend, which is nonsignificantly associated with innovation, and leads to higher M&A activity. Profits from

acquired companies then flow back to investors, who perpetuate the cycle of increasing private valuations and early IPOs, leading to riskier investments.

Second, R&D efficiency is associated with smaller, concentrated firms with higher R&D intensity. Contrary to some of the literature suggesting that economies of scale may contribute to higher innovation, my studies show that several factors are associated with higher R&D efficiency: increased R&D intensity (R&D spend divided by revenues), smaller firm sizes, and specialized firms with a narrow, focused pipeline.

Third, mergers and acquisitions are not associated with higher innovation. It has been a long-held belief in the industry that M&A is critical for innovation. This has been especially important as pharma companies face looming patent cliffs that threaten to erode massive revenues from blockbuster drugs. However, my findings challenge the belief that M&A leads to higher innovation. I find that higher M&A spend relative to internal R&D spend is associated with *fewer new drug approvals*. I also show that M&A intensity (measure of M&A spend to revenues) is associated with lower M&A efficiency (number of new drugs per M&A spend). I also show in SEM models that M&A is not associated with higher innovation.

Fourth, the VC and IPO model in biopharma is flawed. Venture capital is a major source of financing for early-stage biotech companies early in the drug development life cycle. Although venture capital can be necessary for these companies, it is characterized by short-termism and driven by returns. There was an explosion of IPOs in the late 2010s. These IPOs have tended to take place at an earlier stage, which can be problematic due to volatility, pipelines, and clinical trial development.

Fifth, there are clear policy actions that can fix some of these problems in the industry. These include US Congress acting to allow federal agencies to use novel investment mechanisms into companies (e.g. equity investments, as in VC), using the FTC to scrutinize M&A activity, imposing limits on executive compensation—particularly recipients of federal funds, and using

the SEC to more closely regulate early IPOs to prevent VCs from commencing IPOs companies for liquidity.

Taken together, the results of these studies and examples triangulate several key takeaways on the relationship between innovation and financialization, M&A, VCs, and internal R&D. The rise of venture capital (which is short term-focused) has led to higher private company valuations and IPOs. Subsequently, in part due to patent cliffs and pressure to replenish pipelines, M&A from large biopharma firms has increased significantly, but—contrary to the industry's claim that M&A is critical to innovation—more M&A spend leads to *less* innovation. This is supported by the finding that the higher the ratio of M&A to R&D, the *fewer* NMEs are approved. More financialized biopharma firms spend more on M&A and less on internal R&D, which leads to less innovation. More internal R&D spend is consistently correlated with higher patent citations, more drug approvals, and more NME approvals.

In summary, financialization, mediated by higher venture capital, dividends and share repurchases, and executive compensation, leads to more benefit to investors than to innovation. Biopharma firms should spend less on dividends, share buybacks, executive compensation, and M&A, and should focus on the R&D spend and increased R&D intensity that could lead to higher innovation.

Chapter 2: Literature review

2.1. Introduction

The global economy and the biopharmaceutical industry have changed dramatically since the 1970s. It is clear that finance has taken an increasingly broad role in the global economy and in the biopharmaceutical industry; concurrently, globalization and deregulation of markets have allowed finance to gain political and economic power. This practice has even spilled over to nonfinancial corporations (NFCs), which, driven by shareholders, have adopted finance-dominated, stock market-driven corporate strategies. The biopharmaceutical ("biopharma") industry is a particularly financialized industry with significant share repurchases, rises in drug pricing, and a focus on delivering returns to shareholders and venture capital, driven by short-term returns.

At the same time, innovation in science and especially the biopharma sector has drastically changed since the 1970s. Not only have new technologies been invented to change the drug discovery and commercialization process, but *the way in which biopharma companies innovate has also changed*. The process can be characterized by the rise of biotechnology in the 1980s, which shifted the division of innovative labor, once concentrated and integrated in large pharma companies, into a network of innovators in smaller biotech companies (Arora and Gambardella 1990, Gambardella 1995). In the 1970s and early 1980s, almost all drug discoveries took place inside traditional pharma companies (Shepherd 2018). Universities played a role in the innovation process, but were only key in the diffusion of knowledge—and this knowledge was a public repository from which industry freely drew (Nelson 1986, Gambardella 1995). Instead of contributing any direct drug discoveries or innovation, universities contributed to the knowledge upon which pharma companies innovated. In addition, large pharmaceutical firms in the industry were primarily the innovators and patent holders (Shepherd 2018).

However, beginning in the 1980s, the innovation system in pharma shifted: universities were less instrumental in the diffusion of knowledge and more crucial in the actual innovation and drug development process (Berman 2011). The passage of the Bayh-Dole Act in 1980 was also a catalyst in this innovation shift, allowing for the license and commercialization of intellectual property (IP) from universities (Pisano 2006). This accelerated the formation of biotech companies that could license a commercializable asset from a university. The shift in the division of innovative labor from concentrated large pharma companies to a network of biotech companies can be essentially characterized by a shift from a Schumpeter Mark II industry, in which large, established firms dominate innovation (Schumpeter 1942), to more of a Schumpeter Mark I industry, in which entrepreneurs and new firms play a larger role in innovation (Schumpeter 1934, Nelson and Winter 1982, Malerba and Orsenigo 1996). Concurrently, changes in scientific policies beginning in the 1970s led to an increasing concentration of scientific innovation at universities, such as increased NIH investments, the creation of the New Technology Opportunities Program, and other federal initiatives investing in universities (Berman 2011).

At the same time, policies in the 1980s allowed venture capital to rise as a vehicle for financing innovation. The two processes are intertwined: innovation shifted from being concentrated in large pharma to a decentralized network of small, innovative biotech companies that required a lot of capital. Policies in the 1970s and 1980s allowed capital to drive this innovation in biotech companies. Thus, the pattern of change in the innovation in biopharma increasingly necessitated a different model of finance; at the same time, finance itself changed and increasingly dominated how biopharma companies were governed and operated.

“Financialization” is a relatively new term that emerged in the 1990s to describe the growing influence of finance throughout the economy. Financialization resulted in a split between the real and financial economies (Phillips 1994, Mazzucato 2013, Mazzucato 2015). This built off Minsky’s work

in the 1980s and 1990s on post-New Deal money manager capitalism in which money managers asserted financial control over industrial capital (Minsky 1992, Wray 2009). In Minsky's view, money manager capitalism emerged in the 1980s and was characterized by the fact that the largest share of US corporate stocks and bonds were held by financial institutions rather than individual investors (Minsky 1996). Furthermore, in the context of the risk-reward nexus in the relationship between innovation and inequality, the system rewards individuals who position themselves between firms and the product or financial market, and disproportionately share the rewards of the innovation process (Lazonick and Mazzucato 2013).

Although many have invoked the term financialization "without explaining what exactly is meant by the term" (Christophers 2015), and many have documented an increasingly financialized biopharmaceutical sector (Lazonick 2009, Andersson, Gleadle et al. 2010, Lazonick and Tulum 2011, Montalban and Sakinç 2013, Lazonick 2016), the *empirical* relationship between financialization and innovation in the biopharmaceutical industry is under-studied.

With the aim of laying the foundations for defining financialization in the biopharma industry in Chapter 4, as well as the empirical analyses in Chapter 5, this chapter conducts a broad literature review on financialization and contextualizes the findings within the biopharma industry.

I start this chapter by describing the origins of financialization, which can be traced back to the 1960s, and focus on the theoretical framework of neoliberalism and globalization as being heavily associated with the beginning of a financialized economy. Next, I offer a conceptual framework for studying financialization in biopharma, going beyond the definitions offered by Lazonick, Tulum, and others (e.g. Lazonick 2010, 2011, and 2016), which focus solely on share repurchases or dividends as measures of financialization, to look at broader financial, corporate, and innovative practices in the financialized biopharma industry. I then dive into corporate governance and financial institutions as two separate drivers of financialization in biopharma. Finally, I

look at financialization and R&D and examine empirical studies in financialization. This chapter aims to lay the foundations for defining financialization in the biopharma industry in Chapter 4, as well as the empirical analyses in Chapter 5.

2.2 R&D and innovation

Changes in innovation over time

Over the past decades the R&D process has evolved in the biopharma industry, with a change in the "division of innovative labor" that has shifted from large firms pre-1980s to mostly small biopharma companies post-1980s (Demirel 2010). In the 1970s and early 1980s, almost all drug discoveries took place inside traditional pharma companies (Shepherd 2018). The source of innovation significantly changed, beginning in the 1980s during the rise of biotechnology, as the pharma industry entered into an entirely new trajectory with biotechnology and genomics (Henderson, Orsenigo et al. 1999, Montalban and Sakinç 2013). The new era of biotechnology disrupted the long-established pharma companies, as new innovation shifted to emerging biotech companies (Chandler 2009).

Leading into the 1980s, universities played a role in the innovation process, but were only key in the diffusion of knowledge—and this knowledge was a public repository from which industry freely drew (Nelson 1986, Gambardella 1995). This knowledge base included substantial advances in genetics, physiology, biochemistry, and cell biology, from the 1950s to the 1980s, which led to a much better understanding of diseases and drug targets (Gambardella 1995). This pattern follows Pavitt's pattern of technical change in science-based firms in which successive waves of innovation depend on prior development of the relevant basic science (Pavitt 1984). These advances led to a first major shift in the pharmaceutical industry that enabled rational drug design and functional screens of chemical compounds (Malerba and Orsenigo 2002). Universities played a vital role in this shift as they contributed to the knowledge upon which pharma companies innovated. The distribution of this

knowledge was dependent on firm size and the ability to take advantage of publicly generated knowledge (Gambardella 1995, Cockburn and Henderson 1996).

In the middle of this transition to rational drug discovery and design, biotechnology was born in the 1980s, when molecular genetics and recombinant DNA technology opened a new frontier for pharmaceutical innovation (Malerba and Orsenigo 2002). Genentech, founded in 1976 by venture capitalist Robert Swanson and scientist Herb Boyer, was the first biotechnology firm. The first biotechnology product, Genentech's human insulin, was approved in 1982 (Grabowski and Vernon 1994). Genentech constituted the model for new biotech firms: they were primarily university spinoffs formed by a collaboration between scientists and business managers, and were backed by venture capital (Malerba and Orsenigo 2002). Collaboration allowed new biotech firms to survive (Arora A. and Gambardella 1995).

The passage of the 1980 Bayh-Dole Act in the US transformed the monetization of IP and the innovation model in biopharma. The Act encouraged universities to patent their IP and take steps to commercialize it (Pisano 2006). This set the stage for technology transfer from universities to enable federally funded research to be commercialized. This accelerated the formation of biotech companies that could license a commercializable asset from a university. The shift in the division of innovative labor from concentrated large pharma companies to a network of biotech companies can be essentially characterized by a shift from a Schumpeter Mark II industry—in which large, established firms dominate innovation (Schumpeter 1942)– to more of a Schumpeter Mark I industry in which entrepreneurs and new firms play a larger role in innovation (Schumpeter 1934, Nelson and Winter 1982, Malerba and Orsenigo 1996).

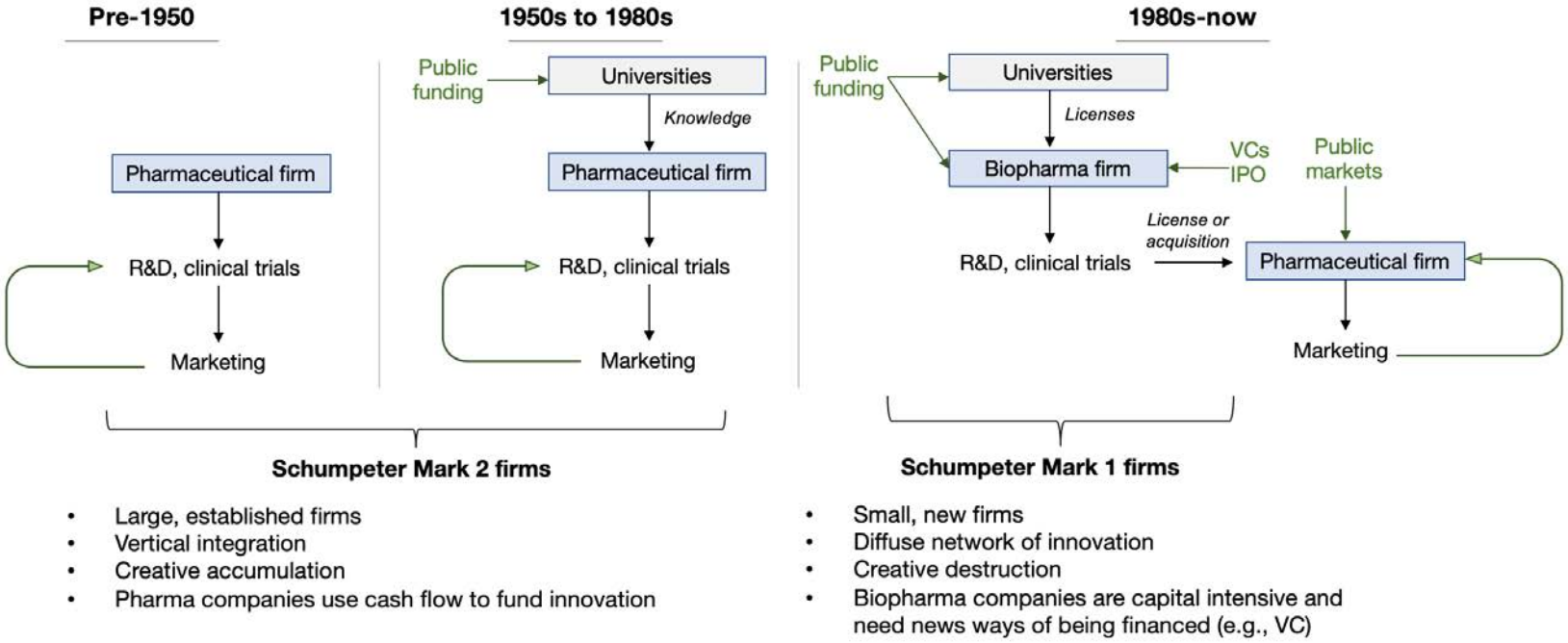
A Schumpeter Mark I pattern of innovation originated in Schumpeter's early work, *The Theory of Economic Development* (Schumpeter 1912). Such firms are characterized by "creative destruction" in which entrepreneurs and

new firms play a key role in innovative activities (Malerba and Orsenigo 1996). In contrast to Mark I, a Schumpeter Mark II model, which arose in Schumpeter's later work, *Capitalism, Socialism, and Democracy,* describes an innovation pattern in which large, established firms dominate, characterized by "creative accumulation" with barriers to entry for new innovators (Schumpeter 1942, Malerba and Orsenigo 1996). Before the 1980s (i.e. before the rise of biotechnology), pharmaceutical firms can be largely described as Schumpeter Mark II firms (Malerba and Orsenigo 1996): large, pharma companies using cash flow to invest in internal R&D for innovation. After the 1980s, however, more biotechnology firms were established, and these were largely the source of innovation in biopharma (i.e. largely Schumpeter Mark II firms). The innovation ecosystem became more diffuse, with most new drugs originating in biotech companies that are then acquired or licensed to larger pharma. While large biopharma firms still exist, the division of innovative labor more heavily relies on Mark I firms. I will show this in Chapter 4 by looking at the origination of innovation that is largely dominated by smaller, biotech firms.

Changes in biopharma innovation are intertwined with how they are financed

These two types of firms (Mark I, newer biotech firms or Mark II, established pharma firms) often require different kind of finance. Mark I firms depend more on venture capital and equity markets to fund R&D (BROWN, FAZZARI et al. 2009, Mazzucato 2013). In contrast, larger firms rely on retained earnings, debt, and large institutional investors (such as hedge funds) (Mazzucato 2013). **Figure 2** shows the changes in innovation and finance over three eras: pre-1950, 1950s to 1980s, and post-1980s.

Figure 2. Maximizing shareholder value in biopharma: changes over time



- Large, established firms
- Vertical integration
- Creative accumulation
- Pharma companies use cash flow to fund innovation

- Small, new firms
- Diffuse network of innovation
- Creative destruction
- Biopharma companies are capital intensive and need news ways of being financed (e.g., VC)

Source: original figure

2.3 Globalization of the economy and the origins of financialization

Most studies agree that the origins of financialization can be traced back to the end of the 1960s, when the Fordist accumulation of wealth came to an end (Stockhammer 2008), which then gave rise to a finance-dominated accumulation of wealth (Boyer 2000). Finance capitalism, a form of capitalism in which "finance" has become the dominant driver of the economy, has predominated in major economies, and has extended into other areas of life (van der Zwan 2014). The term *finance* itself refers to the management of money and other assets by a complex network of individuals, corporations, etc. (Duménil 2001). Finance refers to both institutions (the financial system of banks, pension funds, hedge funds, venture capital, insurance…) and individuals (capitalists, etc.) (Duménil 2001).

Several synchronous drivers contributed to the rise of financialization and the dramatic shift in the 1960s. First, globalization created a new international finance that developed in the 1960s. Concurrently, the rise of multinational firms and the internationalization of production created a demand for the circulation of assets internationally, which then created a rise in demand for financial institutions (Duménil 2001).

The pharmaceutical industry in particular experienced strong globalization, beginning in the 1960s, as a "new" way of drug development emerged that was characterized by extensive international partnerships and a higher degree of collaborations (Cantwell, Dunning et al. 2004, Jungmittag, Reger et al. 2013). This drug development model also included the industrialization of the drug discovery process and the expansion into foreign markets. In contrast to the historical way of drug development based on chemistry and limited collaborations with universities, drug development began to take advantage of new biological discoveries and molecular genetics, and partnerships with universities and international scientists. In other words, the shift in the 1960s and 70s can be described as a globalization of technical innovation (Dunning 1994, Pearce 1994,

Cantwell and Janne 1999, Pearce 1999), which enabled rapid innovation in the pharmaceutical industry. Around the same time, advances in biology were driving drug discovery, and the biopharma[1] industry arguably began in 1976 with the formation of Genentech, the first biotechnology firm—or, more explicitly, the first firm to exploit recombinant DNA (rDNA) technology (Grabowski and Vernon 1994). Genentech was founded by a venture capitalist (Robert Swanson) and scientist Herb Boyer.

Concurrently with globalization, monetary policy shifted dramatically in the 1970s—especially deliberate monetary policy related to price stability (van der Pijl 1984, Ferguson 1986, Duménil 2001). Some policies deregulated the finance industry in the late 1900s and early 2000s, for example, the Financial Modernization Act of 1999 (which eliminated segregation of distinct institutional parts of the financial system) or the Commodities Futures Modernization Act of 2000 (which excluded new instruments from regulation) (Wray 2009). Throughout the late 20th century, deregulation took place and allowed stronger corporate governance to grow in its influence over the economy. These trends allowed for larger mergers and favored the interest of shareholders (Duménil 2001). Indeed, the late 20th century was characterized by heavy consolidation in pharma; the industry saw significant mergers between pharmaceutical giants (Pfizer and Warner-Lambert, Glaxo and Wellcome, and Astra AB and Zeneca). Heavy consolidation and larger mergers remain characteristic of biopharma. Additionally, deregulation of the markets has also allowed tax inversions where global companies relocate their headquarters or operations overseas to find lower tax rates.

Collectively, from 1979 to 1981, several policies had a profound effect on the way in which biopharma is financed. In 1979, the Department of Labor allowed

[1] "Biopharmaceutical" or "biopharma" is loosely defined as the traditional pharmaceutical sector plus biotechnology companies that use recombinant DNA to make medicines.

pension funds to invest in venture capital (VC) funds, which enabled a lot more money to flow into venture financing (Lee and Dibner 2005, Shepherd 2018). In 1981, the Economic Recovery Tax Act then lowered the individual capital gains tax rate from 42% to 20%, which incentivized individual investment into VC funds (Lee and Dibner 2005). As a results of these policies, VC funds more than doubled between 1979 and 1982 (Lee and Dibner 2005).

Policy in the late 20th century also had an impact on intellectual property, as the US Patent Office was largely defunded, making it dependent on the fees it charged. This lowered examiners' wages relative to patent attorneys, and meant the volume of applications was prioritized due to the focus on fees (Perelman 2014). The result was a higher volume of patents and, in some cases, overlapping claims, which benefits larger multinational pharmaceutical corporations that are able to afford the legal costs of patent filings.

The convergence of these factors (globalization, internationalization of finance, monetary policy changes, and deregulation) allowed capitalism to enter a new phase: neoliberalism. As characterized by Stockhammer and Crotty, neoliberalism is primarily a shift in power from labor to capital, made possible by deregulation and privatization, and driven by a redefinition of monetary policy (Stockhammer 2008). Neoliberalism, while not synonymous with financialization, allowed financialization to eventually dominate the major global economies, including—and perhaps especially—the biopharmaceutical industry.

Despite the claim that neoliberalism leads to economic growth, through a broad, macroeconomic lens the evidence does not seem to support this. As Crotty and others have pointed out, neoliberalism led to a number of economic problems across the world between the 1980s and the financial crises in the 2000s: global income growth slowed; national gross domestic products (GDP) growth slowed; the rate of capital accumulation growth slowed; productivity growth slowed;

excessive debt accumulated; real wage growth declined; inequality rose sharply; real interest rates rose; and financial crises erupted (Crotty 2000).

The key characteristic of a firm-level analysis of financial firms and nonfinancial corporations (NFC) is summarized by Crotty as the "neoliberal paradox": that financial markets demanded perpetually increasing earnings, but market competition made it impossible for NFCs to achieve high earnings (Crotty 2003, Crotty 2005). As financial firms absorbed substantial economic rents from the rest of the economy (Tomaskovic-Devey and Lin 2011), NFCs increasingly pursued financial investment strategies (Krippner 2011). According to Crotty (2005: 104) (for similar conclusions, see Epstein 2005: 7; Epstein and Jayadev 2005: 64), "(m)any NFCs [non-financial corporations] responded . . . to the high returns they observed being made on financial assets and financial enterprises, in two innovative ways. First, an increasing per cent of NFC investment funds were used to acquire financial assets. Second, firms created or bought financial subsidiaries, and expanded those financial subsidiaries already in existence. These widely noted developments are sometimes referred to as the 'financialization' of the NFC in the neoliberal era." In short, two concurrent practices have occurred at the firm level: an increase permeance and influence of financial firms as well as an increase in financial practices of NFCs themselves.

However, some recent evidence has shown that financialized practices of NFCs do not necessarily reflect a rise in increased financial assets but an increase in intangible assets (e.g., patents, copyrights, licenses) as a function of R&D investments as well as globalization (Fiebiger 2016, Rabinovich 2019). Rabinovich and Orhangazi have noted a rise in intangible assets in NCFs in recent years, particularly in the pharmaceutical industry (Orhangazi 2018, Rabinovich 2019). Those authors and others have also pointed out that the decrease in financial assets may be obscured by a rise in overseas investments as NFCs are increasingly globalized (Fiebiger 2016).

To summarize the origins of financialization and the characterization of the economy since the 1960s, financial interests have significantly become more economically and politically influential—and this influence has extracted value from non-financial parts of the economy.

2.4. Defining financialization

Background

Definitions of financialization in the literature are somewhat inconsistent. As Dore says: "'financialization' is a bit like 'globalization'—a convenient word for a bundle of more or less discrete structural changes in the economies of the industrialized world" (Dore 2008). Krippner argues that, given that the concept is rooted firmly in empirical evidence, financialization is a distinct phenomenon from globalization and neoliberalism (Krippner 2005). However, some studies on financialization have been imprecise in their distinction between the components of the financial system, when financialization encompasses "all the sectors of capital that carry out productive activities" (Guillen).

The origins of the term "financialization" are somewhat obscure, but the literature (Sawyer , Foster 2007) typically points to the work of Philips, who employed the term in his book, *Boiling Point,* in 1993 (Philips 1993) and wrote a chapter on financialization in 1994 in *Arrogant Capital*, defining it as a "prolonged split between the divergent real and financial economies" (Phillips 1994). This built off Minsky's work in the 1980s and 1990s on the money manager capitalism that arose after the New Deal and in which money managers asserted financial control over industrial capital (Minsky 1992, Wray 2009). In Minsky's view, money manager capitalism emerged in the 1980s and was characterized by the fact that the largest share of US corporate stocks and bonds were held by financial institutions rather than individual investors (Minsky 1996).

Concurrently, some of the first to associate the growth of financial markets with the stagnation of industrial production were Marxist economists Magdoff and Sweezy, writing for the *Monthly Review* in 1987 (Magdoff 1987), as well as Arrighi (Arrighi 1994). In 1997, Sweezy wrote:

> "The three most important underlying trends in the recent history of capitalism, the period beginning with the recession of 1974-75 [are]: (1) the slowing down of the overall rate of growth; (2) the worldwide proliferation of monopolistic (or oligopolistic) multinational corporations; and (3) what may be called the financialization of the capital accumulation process." (Sweezy 1997).

Sweezy mentioned globalization as a fourth trend, but argued was more complex and reflective of the growth of imperialism.

2.5. Empirical studies on financialization

Conceptual framework of studying financialization

Studies on financialization have different foci and methods. My conceptual framework incorporates threads from various approaches and is based on van der Zwan, who noted several threads in the financialization literature: (1) financialization as a regime of accumulation; (2) financialization of the modern corporation; and (3) financialization of the everyday (van der Zwan 2014). I propose four lenses for studying financialization: a **macro view** (at the macroeconomic level), a **meso view** (at an industry level), and an **individual-level view** (at the firm level).

Empirical studies

Empirical analyses reveal a number of trends as evidence of financialization: at the macro level there have been increases in financial transactions with a rise of real interest rates and higher shares of national income accruing to holders of financial assets; at the meso level there have been increases in the profitability of financial firms yet decreases in the profitability of nonfinancial firms; and at the firm level there has been an increase in stock repurchases and other actions to benefit individual shareholders (Crotty 2000, Duménil 2001, 2005, Davis 2017).

Most studies on financialization have taken a firm-level analysis and analyze changes in corporate governance and labor over time. This level of view reflects the "varieties of capitalism" approach from Hall and Soskice (Hall 2001). This is "a firm-centered political economy that regards companies as the crucial actors in a capitalist economy" (Hall 2001) and argues that the major differences in developed economies can be accounted for by the organization of the firm. Tradeoffs between investment and profits at the firm level also aggregate at the macro-economic level (Amable, Palombarini et al. 2005, van Treeck 2009).

For the purposes of this thesis, I will take a micro- and meso-level lens, focusing on firm- and systems-level analyses, given that the nature of the innovation process depends on individual firms.

Characterizing financialization at the macro level

The financialization of the economy began in the 1970s and 1980s. Krippner took a macro lens to financialization, defining it as "a pattern of accumulation in which profits occur through financial channels rather than trade and commodity production" (Krippner 2005). Epstein, in *Financialization and the World Economy*, defines financialization as the "increasing role of financial motives, financial markets, financial actors, and financial institutions in the operation of the domestic and international economies" (Epstein 2005).

The growth of nonfinancial corporation profits has declined dramatically since the 1960s, as has been shown by Crotty, Krippner, Brenner and others (Glyn 1997, Dumenil and Levy 2002, Crotty 2003, Crotty 2005, Krippner 2005). Payments to financial markets have increased (Stockhammer 2008). During the last half of the 20th century, financial institutions grew rapidly relative to the nonfinancial sector, rising from about 10% added to GDP and a 10% share of corporate profits to 20% added to GDP and 40% share of corporate profits in the US (Mazzucato 2015).

Financialization at the meso level

At the same time, the profit rates of financial corporations have risen dramatically, while physical investment dynamics have tended to slow down (Philippon and Reshef 2013, Montecino, Levina et al. 2014). One of the most important financialization trends is that NFCs have increased payments to the financial sector through interest payments, dividends payments, and share buybacks (Crotty 2005).

Additionally, NFCs have experienced an increase in tangible assets in their balance sheets, as Orhangazi has noted a rise in intangible assets as a ratio to capital stock in the pharmaceutical industry in recent years (Orhangazi 2018). Such industries with high ratios of intangible assets to stock have higher markups and profits. Orhangazi also found a negative relationship between financialization and real investment from an analysis the last three decades in the 20th century (Orhangazi 2008).

Financialization at the firm level

In 1982, it became legal for corporations to repurchase their own stock after the SEC adopted Rule 10b-1, which provided a safe harbor for repurchasing firms against the anti-manipulative provisions in the 1934 Securities Exchange Act

(SEA)[2] (Grullon and Michaely 2002). An analysis by Gullon and Michaely revealed that the adoption of Rule 10b-1 led to ~1,000% increase in the average annual share repurchases (Grullon and Michaely 2002). Additionally, in 1993, the corporate tax deductibility of executive compensation was capped at $1 million (unless the additional compensation was "performance-based") (Tomaskovic-Devey and Lin). The result of this was the popularization of using stock-based compensation for executives to avoid tax liability (Rose and Wolfram 2002, DiPrete, Eirich et al. 2010). These two regulatory changes, directly and indirectly focused on stock prices, encouraged corporate executives to manipulate stock prices (Cicero 2009, Bebchuk, Grinstein et al. 2010, Zheng and Zhou 2012).

In short, managerial practices are heavily related to the importance of stock market performance.

Corporate policies can be distilled down to two competing policies—both of which relate to share price: a "retain-and-invest" policy in non-financialized economies (Hall 1994, Corbett and Jenkinson 1996, Lazonick and O'Sullivan 2000, Crotty 2003) or a "downsize-and-distribute" policy as a reflection of financialization, and as a result of increased shareholder value orientation and higher profitability pressures (Zorn and Dobbin , Hall 1994, Corbett and Jenkinson 1996, Lazonick and O'Sullivan 1996, Lazonick and O'Sullivan 2000, Lazonick 2016). A "retain-and-invest" philosophy retains profits and people and reinvests in productive activities (Tulum and Lazonick 2018).

The "downsize and distribute" policy is driven by the maximizing shareholder value (MSV) philosophy, which aims to return capital back to shareholders instead of re-investing returns in R&D and productivity. "Shareholder value" is a term that first originated in the 1980s and it refers to the concept that the primary purpose of the corporation is to make profit for its shareholders (van der Zwan 2014, Taylor 2015). Until the 1970s, US stockholders allowed

[2] 47 Fed. Reg. 53333 (November 26, 1982).

corporations' management to retain control over most of the company's cash flow with little influence from shareholders (Chandler 1977). However, this Chandlerian type of managerial practice eroded and shifted towards an emphasis on shareholder interests (Stockhammer 2004, Taylor 2015). These were driven and accelerated by regulatory shifts that occurred in the late 20th century—e.g. growth in institutional investors, more stock-based executive pay, and encouraging stock buybacks (Davis 2017).

2.6 Introduction on financialization in biopharma

Drug development in pharma (and especially in biotech) is a very capital- and risk-intensive process. Some studies have attempted to quantify the cost of bringing a new small molecule drug to the market—the latest figure estimates the cost to be over $2.8 billion USD per drug in 2016 (DiMasi, Hansen et al. 2003, DiMasi, Grabowski et al. 2016), and a 2020 *JAMA* study estimated new mean and median capitalized R&D development costs to be $1.3 billion and $985 million, respectively (Wouters, McKee et al. 2020).

However, these studies likely overestimate the cost of drug development—and the costs themselves are likely financialized—due to multiple factors: (1) most of these studies used survey-based methods with pharma companies self-reporting their own costs; (2) the estimates include capitalized costs that are poorly defined and likely inflated; and (3) the estimates also include the cost of R&D and failed drugs. Indeed, Light and Warburton point out that pharma companies have a strong interest in maximizing R&D figures and supporting researchers who help them do so (Light and Warburton 2011). Pharma companies often justify increases in drug prices by citing the high cost of drug development (Gagnon 2024). If pharma companies control the narrative and limit verifiable figures on the cost of drug development, they can support this narrative (Light and Warburton 2011).

A more accurate estimate of the cost of development is likely in the $200-400 million range per drug in direct costs, depending on disease and medicine type (Morgan, Grootendorst et al. 2011, Jayasundara, Hollis et al. 2019). Regardless, the financial requirements for bringing a drug to market at high technical risk are enormous. This makes the biopharma industry particularly sensitive to financialization, as drug development requires significant resources.

Two major streams of financialization in biopharma emerge from a review of the literature: one from a corporate governance ideology of maximizing shareholder value and one from the financial institutions that control biopharma companies. A third of stock engineering also exists, whereby private companies increase their share price (i.e. the valuation of the company) or companies listed on a stock exchange deliberately release news flow to raise capital at a higher price. **Table 1** summarizes these characteristics.

Table 1. Characteristics of financialization in biopharma

	Description	**Potential gaps in the literature**
Corporate governance	Driven by a "maximizing shareholder value" ideology, management aims to govern the company to maximize	Empirical evidence of the relationship between innovation and MSV ideology
Institutional control	Venture capital, hedge funds are the key agents	Some studies do not fully address the extent that venture capital and hedge funds exert on a biopharma company and what effect this has on innovation
Stock engineering	Manipulating share prices or speculating on the stock market	This strategy is not thoroughly addressed in the literature

Source: Original table

These forces create an inevitable tension between "innovation" (or at least therapeutic value) and return for shareholders. An integrated approach would

prioritize delivering value to patients in the form of medicines, while a financialized approach prioritizes delivering value to shareholders (Gleadle, Parris et al. 2014). Gagnon summarized some of these problems in the pharma industry as “ghost management” (Gagnon 2021) in which the pharmaceutical industry produces medical knowledge but exploits their narrative to their financial interests (for example, an overrepresentation of positive scientific studies and underrepresentation of failed studies, systematic suppression of opposing narratives, and devotion of more resources to shape medical knowledge than therapeutic development (Gagnon 2011).

2.7. Financialization in biopharma at the meso level

Financial institutions at the meso level

Investors and fund managers play a central role in the development of the healthcare industry (Hunter and Murray 2019). Given the long-term cycle inherent to innovation—especially in the biopharmaceutical industry—it needs to be financed by sources with a long-term commitment to return on investment; in other words “patient capital” is needed to sustain long-term innovation (Crotty 2005). Short-termism is defined as the excessive focus of corporate managers and shareholders on short-term results—usually short-term financial gains for a fund (Rappaport 2005, Dallas 2012). This is especially true in venture capital, which is driven by goals of returning ≥10x on the portfolio. The short-termism of venture capitalists (the major financier of biotech companies) contrasts with the long-term nature of drug development (Andersson, Gleadle et al. 2010). Venture capital tends to exert pressure on biotech companies, with strict oversight by investment managers, pressure to meet timelines, and tranched funding to meet predefined milestones (Shepherd 2018). All of these contribute to biased decision-making in biotech to appease investors and make short-term gains.

Venture capital in biopharma grew significantly in the late 1990s. Several factors and policies in the 1980s allowed VC to explode: (1) in 1979, the Department of Labor allowed pension funds to invest in VC funds; and (2) the Economic Recovery Tax Act of 1981 lowered the individual capital gains tax rate from 42% to 20%, which incentivized individual investment into VC funds (Lee and Dibner 2005, Shepherd 2018). Since then, rises in VC funding have only increased: VC funding increased by 842% between 1991 and 2001, and between 2004 and 2008 VC firms invested $21.5 billion in biotech drug R&D (Shepherd 2018). VC financing is even more dominant in biotech than other industries and has exploded in the last decade, as I outline in Chapter 4.

What role does venture capital play in biopharma? It plays a key role in financing the early stages of the innovation process, and—to a lesser extent—helps shape the strategy of the early biopharma company. VC firms in biopharma are sophisticated investors and typically have extensive technical knowledge of drug development. Broadly, the literature indicates that venture capital supports innovation within firms (Kortum and Lerner 2000, Penas 2007, Parris 2010). Kortum and Lenner (2000), for example, use an industry analysis of R&D and patent activity to show that VC investment was more productive than corporate R&D in producing patents. Others have drawn similar conclusions (Parris 2010, Hirukawa and Ueda 2011).

However, there exists inherent tension in the goals of venture capital and true biopharma innovation. A key problem with venture capital is its short-termism. Lazonick and O'Sullivan argue that the most important function of an organization's structure is to foster innovation over the long term (Lazonick and O'Sullivan 1996), and this often clashes with the goals of venture capital, which seek short-term returns. Pisano sees the US biotech industry as in need of "patient capital" over the short-termism of venture capital (Pisano 2006). It's an important distinction to note that venture capitalists can demand a return (i.e. an "exit") well before a drug

is commercialized; given that the innovation primarily occurs in early-stage biotech companies, and that there are many potential opportunities to monetize a company along the drug development process.

For example, an exit for VCs often comes in the form of an IPO (Ahn and Shaygan 2019, Cunningham, Ederer et al. 2021), at which point a VC's investment can become liquid (following a "lockup" period where shares are prohibited from being sold), depending on public market conditions (Gompers and Lerner 1999). Indeed, as VC investment in biopharma has increased over time, the number of biopharma IPOs has skyrocketed; in 2020—a year generally characterized by favorable public conditions for biopharma—there were over 100 biopharma IPOs with over $20 billion in proceeds raised (Cameron and Morrison 2021).

Early-stage IPOs are widely problematic for a variety of reasons. Early IPOs have been found to have negative impacts on innovation for small biopharma firms (Lo and Thakor 2022). Several studies have documented high volatility (beta often significantly higher than 1.0) in publicly traded biopharma firms (Harrington 2012, Lo and Thakor 2018) due to the high level of market risk inherent in R&D and the sector (Jørring, Lo et al. 2022). Drugs in preclinical and Phase 1 clinical development have a very small chance of getting approved—studies have shown that on average 10% of drugs (or less) will make it to approval (Wouters, McKee et al. 2020), and that percentage is even lower for preclinical drugs. The consequence of market volatility and market risk is a high cost of capital for biopharma firms (Cockburn and Lerner 2009, Harrington 2012), which adds constraints to biopharma, impacts their strategic decisions on their pipeline, and can lead biopharma firms to abandon early-stage drugs (Mace 2020).

There are also other impacts on innovation caused by early IPOs. Some studies have shown, for example, that innovation (as measured by patents) typically decreases when firms go public (Bernstein 2015). Additionally, biopharma

firms conduct fewer clinical trials and focus on less risky indications when they go public vs. staying private (Lerner, Shane et al. 2003, Aghamolla and Thakor 2022).

Instead of the traditional approach of VC funding early-stage drug R&D, VCs are getting ever more impatient and looking to exit (via IPOs) and transfer the risk to public market investors and publicly traded biopharma firms. Although IPOs can be a means for VCs to create liquidity and returns to their funds, public market investors—many of whom lack the expertise to understand complex science—as well as public biopharma firms themselves are exposed to higher risk, and this risk leads to negative impacts on biopharma innovation as measured by fewer patents, fewer clinical trials, fewer drugs, and less risky disease targets. For context, on average, the companies that had IPOs in 2021 fell 37% by the end of the year (Senior 2022).

Lazonick and O'Sullivan argue that if "the earnings of the enterprise come under control of people who demand liquidity rather than financial commitment, then the existing financial conditions for initiating and sustaining innovative investment strategies will disappear" (Lazonick and O'Sullivan 1996). Venture capitalists—as a generalization—are solely concerned about making a return over sustaining innovation. It is important to note that venture capital itself is financialized: venture capital is controlled by shareholders (limited partners, or "LPs") who have expectations and determine the investing strategy of the VC firm. Thus, there is a compounding effect of shareholder ideology on the venture capital group on top of the direct demands of the VC on the biopharma company. These are problematic and create a complex system of financialization that, to my knowledge, is not well documented in the literature.

While I would hypothesize that venture capital may indeed be beneficial for innovation in the short term, I would imagine it may have long-term consequences. For example, (1) creating long-term gaps in neglected diseases (e.g. antibiotics, tropical diseases) because they are not profitable; (2) decreasing R&D productivity

due to the lack of development infrastructure in small biotech companies; (3) increasing valuations and earlier stage IPOs; (4) creating strains on biopharma firms' balance sheets since venture capitalists demand a >10x return on investment; and (5) having potential downstream impact on patients. These are questions I hope to explore in Chapters 4 and 5 in my empirical analyses in looking at systems of finance and innovation in biopharma.

2.8 Financialization in biopharma at the micro level

Corporate governance in the financialized biopharma industry

At the micro level (i.e. firm level), companies exhibit financialized practices through profit-driven corporate policies. Lazonick and Tulum develop a description of a corporate "downsize and distribute" policy in their paper specific to the biopharma industry:

> "Since the 1980s the US business community, the [biopharmaceutical] industry included, has embraced the ideology that the performance of their companies and the economy are best served by the 'maximization of shareholder value. . .'
>
> It is an ideology that, among other things, says that any attempt by the government to interfere in the allocation of resources can only undermine economic performance. In practice, what shareholder ideology has meant for corporate resource allocation is that when companies reap more profits, they spend a substantial proportion of them on stock repurchases in an effort to boost their stock prices, thus enriching first and foremost the corporate executives who make these allocative decisions."
>
> (Lazonick and Tulum 2011).

MSV ideology is driven by “shareholder value” and is characterized by the prioritization of share value over the general efficiency of the productive system. Many authors in the literature have emphasized the dominant role of finance as the basis for corporate restructuring (Lazonick and O'Sullivan 2000, Crotty 2003).

What sets the financialized corporation apart from its industrial-age predecessor is that the financial gains from these operations are not reinvested in the firm’s productive facilities, but rather distributed to shareholders through dividend payouts and share buybacks (Lazonick and O’Sullivan 2000). A systemic problem across biopharma is that *incentives are too closely aligned between management and shareholders;* by selling shares of the companies and leveraging their own compensation packages, many pharma executives are able to buy shares from themselves *and* increase the value of their and shareholders’ shares. Put another way, pharma executives’ incentives are not aligned with those of patients. While MSV-focused strategies benefit shareholders, they extract value from the biopharma innovation process (Mazzucato 2018), and benefit venture capitalists and institutional investors over the intended beneficiary of value: patients.

Drug pricing as an MSV-driven practice

Many pharmaceutical companies have insisted that the dramatic rise in drug prices funds innovation and is necessary for research and development, particularly given the high risks and high rate of drug failures (Mossinghoff 1999, Lazonick 2016). Empirical research does not support this (Lazonick 2016), yet drug prices continue to rise drastically: from 2013 to 2015, drug prices increased *annually* by 10%, which was over six times the rate of general inflation (Schondelmeyer 2016, Hernandez, Good et al. 2019). A majority of the increases in specialty drug costs come from price increases (50-70%) (Hernandez, Good et al. 2019). Prices for new types of medicines coming to the market are approaching or exceeding $1

million USD per therapy. The first gene therapy approved in the US, Spark Therapeutics' Luxturna, was priced at $850,000 USD (Kaltenboeck and Bach 2018), and a new gene therapy that entered the market in 2019—Novartis' Zolgensma for spinal muscular atrophy—has a whopping $2.1 million price tag (Bach 2019).

The result of these unregulated increases in drug prices is a large accumulation of capital among biopharma companies. Instead of reinvesting income into research and development (despite the claim that high drug prices are justified to fuel R&D), many larger biopharma companies instead invest accumulated capital into buying back their own shares or distributing dividends to shareholders (Lazonick 2016, Roy, Hawksbee et al. 2016). From 2012 to 2021, for example, the 14 pharmaceutical companies in the S&P 500 Index spent $377 billion repurchasing their own shares and $370 billion in dividends to shareholders, which represents 110% of their net income (Lazonick and Tulum 2024).

Intellectual property and financialization

Patents and the intellectual property rights (IPR) system have become a key incentive for revenue in biopharma in order to prevent competition from the market, and offer incentives beyond market exclusivity alone (Levin, Klevorick et al. 1987, Grabowski 2002, Canoy and Versteegh 2022). Some in the literature argue that patents and patent citations could be an indicator of a firm's ability to innovate (Jaffe and Trajtenberg 2002, von Wartburg, Teichert et al. 2005), but most agree that patent citation data rather than simple patent counts represent a truer measure of innovation

The biopharma industry asserts that the IPR system is key to innovation in that it protects marketed drugs for longer by preventing competitors or generics from entering the market, thereby providing more revenue to fund innovation (Cockburn and Long 2015). However, the IPR system in biopharma is also

intertwined with financialization: increasingly, biopharma firms have employed legal barriers, IP monopolies, and patent evergreening to maximize profits as opposed to incentivize innovation (Dosi, Marengo et al. 2023). Dosi found that patenting activities in pharma does not correspond to innovative activities and summarized that IPR leads to intellectual monopolies rather than an incentive to reward innovation (Dosi, Marengo et al. 2023).

This is evidenced by biopharma firms' tactics of patent extension by filing new patents offering incremental and negligible benefits, such as a new dose level, a modified version of the original molecule (essentially a "me-too" drug), a new patient population or disease indication, a new formulation, or a new route of administration (Dubey and Dubey 2009, Grootendorst 2009, 2012, Daidoji, Yasukawa et al. 2013, Gupta 2023). The resulting effect is biopharma companies charging higher prices on medicines based on monopolistic IPR protection (Mazzucato and Li 2021).

Indeed, some in the literature go a step further on IPR in pharma and claim that patents are a form of monopolistic economic rent seeking (i.e. returns based on ownership over a scarce asset—in this case, patents on medicines and manufacturing processes) (Christophers 2020, Kang 2020, Mazzucato, Ryan-Collins et al. 2023). Although rent seeking could be "good" in that innovation and economic growth inherently generate rents as part of the creative destruction process, as described by Schumpeter (1942), rent seeking could also be used to establish more permanent rents that lead to inequality and monopolies (Mazzucato, Ryan-Collins et al. 2023). Indeed, patents in biopharma often fall into the latter form of rent seeking, as biopharma firms often use patents not only to enable monopolistic control of markets, but also as assets to be exploited—to be bought and sold and speculated upon (Kang 2020, Roy 2020, Bourgeron and Geiger 2022).

2.9 Empirical review of financialization studies in biopharma

Evidence of financialization

Similar evidence of financialization from other industries, as illustrated in Section 2.2, also hold true in biopharma. A recent analysis from Stichting Onderzoek Multinationale Ondernemingen (SOMO) revealed several key trends in biopharma: (1) increases in debt; (2) the rise of intangible assets; and (3) the growth of payouts to shareholders. Baranes analyzed the intangible assets of pharmaceutical companies from 2002 to 2015, showing that intangible assets have significantly risen over time (Izhar Baranes 2017).

Lazonick and colleagues have focused their analyses of biopharma financialization on share repurchases (Lazonick 2011, Lazonick 2012, Lazonick 2012, Lazonick, Hopkins et al. 2017, Lazonick 2018, Tulum and Lazonick 2018, Lazonick and Tulum 2024). Others in the literature have described the problems of financialization in biopharma, such as the prioritization of profits and its effect on drug price increases (Collington 2020, LaMattina 2022), inequitable access to vaccines or medicines (Stein 2021, Whitacre 2024), rising executive compensation (Lazonick and Tulum , Busfield 2020), stock price manipulation (Lazonick and Tulum), inequitable profit distribution (Fernandez and Klinge 2020), profiting from taxpayer-funded innovation (Lewis, Reichman et al. 2007, Mazzucato, Chow et al. 2018, Roy 2023), corporate greed during the pandemic (Lazonick and Tulum 2023), patents and rent-seeking (Mazzucato, Chow et al. 2018), and even innovation models (Gleadle, Parris et al. 2014),

However, beyond corporate greed and prioritizing profits over patients, these studies lack a deeper examination of the *consequences* of some of these financialized business practices on innovation. In Chapter 5, I empirically examine the relationship between financialization and innovation.

Decline in R&D productivity is a byproduct of MSV ideology

Gleadle et al. note a “decline in productivity” by looking at the number of new NMEs (new molecular entities) approved by the FDA as a function of spend on R&D. This is also highlighted by other studies (Paul, Mytelka et al. 2010, Bunnage 2011, Lendrem, Senn et al. 2015, Dosi, Marengo et al. 2023), including Scannell et al., who observe that the number of drugs approved by the FDA per $1 billion USD has halved roughly every nine years (Scannell, Blanckley et al. 2012). Pammolli et al. note that the reorienting of investments toward high-risk/high-premium targets accounted for most of the decline in productivity in pharma R&D, measured in terms of attrition rate, development times, and NMEs launched (Pammolli, Magazzini et al. 2011). This is indicative of MSV ideology, which prioritizes earnings over value to patients (Dosi, Marengo et al. 2023)

Defining innovation in biopharma

Innovation in biopharma is difficult to define. Are R&D expenditures sufficient to capture innovation? Patents? Number of NMEs? Each of these metrics has its limitations. Trajtenberg argues that patents are the primary manifestation of inventive activity (Trajtenberg 2002)—and patent citations offer a proxy for the technological impact of the value of innovation in biopharma. Historically, simple patent counts were used as measures for innovative output. However, Trajtenberg and Jaffe, beginning in the late 1990s, make a compelling case for the use of weighted citations from patent data as a measure of innovation and economic output. They outline in various works that weighted patent counts are more strongly associated with innovation. Patent counts weighted by citations (WPC) are good indicators of the value of innovations, while simple patent counts (SPCs) are not (Trajtenberg 2002). Nevertheless, SPCs could be good indicators of the *inputs* to the innovative process as measured by R&D expenditures, which is consistent with the literature showing strong relationships between R&D spend and total patents.

In the context of biopharma, a number of studies have used patent citations as a measure of innovation. For example, Mazzucato and Tancioni (Mazzucato and Tancioni 2012) looked at stock return performance and innovation measured by patent citations. Some studies have—perhaps misguidedly—used R&D *expenditures* as an *output* or proxy for measuring innovation, instead of R&D expenditures as an *input* (Danzon, Epstein et al. 2004). R&D expenditures are often not a reasonable measure of innovation (Ringel and Choy 2017). R&D productivity, which is the ratio of NMEs or other output to R&D expenditures, is a better metric than simple R&D expenditures. It is also well known that R&D productivity has been declining (Scannell, Blanckley et al. 2012).

A tangible innovative output in biopharma is an approved drug, which delivers value to consumers (i.e. patients). The number of approved drugs has commonly been used as a simple measure of innovative outputs (Kaitin and DiMasi 2011). Alternatively, an evaluation of the health impact a drug brings to patients can be used to measure innovative output. In many countries, health technology assessment (HTA) and therapeutic value are used to inform policy makers on reimbursement and pricing for medicines and health technologies (Kergall, Autin et al. 2021). In the European Union, even though drug approvals are issued by the European Medicines Agency (EMA), HTA evaluation remains at the country level, leading to a decentralized approach and lack of a unified HTA approach.

Example HTA systems include the UK's National Institute for Health and Care Excellence (NICE), Italy's Medicines Agency (AIFA—Agenzia Italiana del Farmaco), Spain's Agency of Medicines and Medicinal Products (AEMPS—Agencia Española de Medicamentos y Productos Sanitarios), and others (Raftery and Powell 2013, Akehurst, Abadie et al. 2017).

In France, the Transparency Commission (TC) of the French National Authority for Health (Haute Autorité de Santé*)* evaluates the added benefit of new

drugs in relation to the relevant comparator (Le Pen 2018). France sets its reimbursement level for new medicines based on a five-point system that reflects the medicine's added value. Each medicine receives two ratings: (1) one reflecting the medicine's actual benefit (**SMR**—service médical rendu); and (2) one reflecting the improvement in medical benefit (**ASMR**—mélioration du service médical rendu), which determines whether a medicine can have a price premium or if a discount is required. ASMR answers the question: "What is the progress made by this drug compared to existing therapies?" The SMR makes it possible to decide on the reimbursement of the drug and its reimbursement rate and the ASMR contributes to setting its price.[3]

The French ASMR scale ranks each drug compared to existing treatment options. There are five ranks:

- ASMR I: major improvement
- ASMR II: important improvement
- ASMR III: moderate improvement
- ASMR IV: minor improvement
- ASMR V: no improvement

The flow diagram in **Figure 3** shows this process and is based on Maison et al. (Maison, Zanetti et al. 2013).

[3] Haute Autorité de Santé website: https://www.has-sante.fr/jcms/c_2877573/fr/la-commission-de-la-transparence-precise-et-adapte-ses-principes-d-evaluation-des-medicaments

Figure 3. Healthcare technology assessment process in France

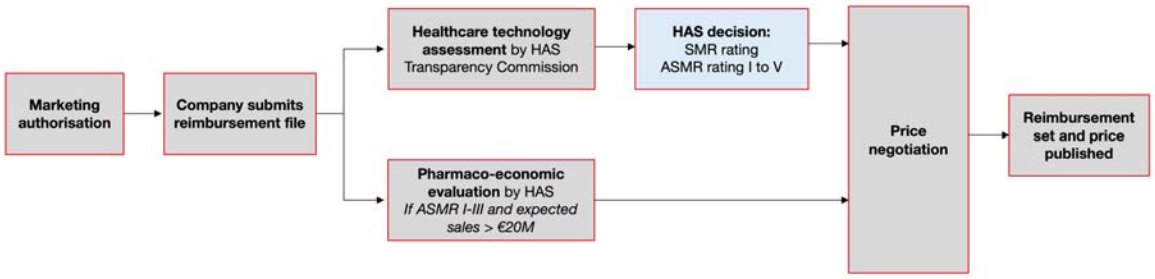


Table 2 summarizes various measures of innovative output in biopharma and weighs the advantages and disadvantages of each.

Table 1. Examples of measures of innovation in biopharma

	Patents		Drugs			R&D	
	Simple patent citations	Weighted patent counts	Total drug approvals	NMEs	ASMR	Expenditures	R&D productivity
Description	Number of patents assigned over a certain period of time to firms, industries, etc.	Counts the number of times that each patent has been cited in subsequent patents and uses that number to compute weighted patent counts	Number of drugs approved by regulatory authority (e.g.	New molecular entities	l'amélioration du service médical rendu, centralized evaluation of benefit/risk ratio to measure quality of a drug	Simple measure of R&D spend	Ratio of NMEs to R&D
Sources	(Trajtenberg 2002)	(Trajtenberg 2002) (Mazzucato and Tancioni 2012) (Kesselheim and Avorn 2009)	e.g. DiMasi (Kaitin and DiMasi 2011)	e.g. DiMasi (Kaitin and DiMasi 2011)	Abrams 2018	(Ringel and Choy 2017).	(Scannell, Blanckley et al. 2012)
Advantages	- Easily measurable - Highly correlated with R&D input	- High correlation with economic and innovative output - Well recognized across econometric analyses	- Easily measurable - Global metric of innovative output	- Easily measurable	- Evidence-based and validated approach to measure medical benefit	- Easily measurable	- Easily measurable - Better metric of R&D output
Disadvantages	- Not suitable for measure of innovative output	- Very difficult to construct - No available database	- Captures "me-too" drugs and other non-innovative drug approvals, such as generics or ANDAs	- Doesn't capture value of drug	- Is not evaluated for all drugs	- Not indicative of innovation	

2.10 Theoretical framework: a neo-Schumpeterian lens to study biopharma financialization and its effect on innovation

The passage of the 1980 Bayh-Dole Act in the US transformed the monetization of intellectual property (IP) and the innovation model in biopharma. The Act encouraged universities to patent their IP and take steps to commercialize it (Pisano 2006). This allowed technology transfer from universities to commercial entities, enabling federally funded research to be commercialized. The first major license agreement in biopharma occurred when Genentech licensed the use of insulin to a major pharmaceutical company, Eli Lilly. This agreement served as a template that would shape the evolution of the biopharma industry, even to this day (Pisano 2006).

Innovation in the biopharma industry is a complex system, with many stakeholders—universities, public laboratories, and corporations—shaping the innovation process (Cantwell, Dunning et al. 2004). Additionally, innovation in biopharma is a collective process, and instead of "big pharma" companies dominating the innovation process, it relies on smaller biotechnology companies and universities. Given the inherent nature of the biopharmaceutical industry, which is primarily focused on innovative outputs, analysis is needed at the micro- or meso-level, so I propose using a neo-Schumpeterian lens for studying financialization. This is based on Schumpeter's theory of creative destruction (Schumpeter 2003), meaning that new technologies come along and "destroy" the productivity of old technologies. Innovation competition is the core principle underlying the neo-Schumpeterian approach, and Hanusch and Pyka (2007) describe three pillars under neo-Schumpeterian economics: industry, finance, and the public sector.

Additionally, under the neo-Schumpeterian lens, technological transformations cannot be analyzed or understood at the macro level (Carlsson and Eliasson 2003), and are best found in the industry dynamics at the meso level, driven by technological innovation and decisions at the meso (Dopfer, Foster et al. 2004) or micro level (Hanusch and Pyka 2007). Moreover,

biopharma is a complex system and is technologically intensive—therefore, as Hanusch and Pyka point out, “Competition no longer takes place between single companies only, but often occurs between networks of actors, where new knowledge is created and diffused collectively. More importantly, firms often no longer compete in a price dimension only, as competition innovation has taken the dominant role” (Hanusch and Pyka 2007).

The biopharma industry is characterized more by Schumpeter Mark I firms in which entrepreneurs and new firms play a larger role in innovation (Schumpeter 1912, Schumpeter 1934, Nelson and Winter 1982, Malerba and Orsenigo 1996). These types of firms are characterized by creative destruction in which entrepreneurs and new firms play a key role in innovative activities (Malerba and Orsenigo 1996). After the 1980s, however, more biotechnology firms arose and became the source of innovation in biopharma (i.e. largely Schumpeter Mark II firms). The innovation ecosystem became more diffuse, with most new drugs originating in biotech companies that were then acquired or licensed to larger pharma. While large biopharma firms still exist, the division of innovative labor more heavily relies on Mark I firms.

Most Schumpeterian and neo-Schumpeterian studies have focused on innovation and have not thoroughly incorporated the broad influence of finance on innovation (Jan, David et al. , Mazzucato 2015, Mazzucato and Semieniuk 2017)—especially from an empirical perspective. Mary O’Sullivan points out that “contemporary economists of innovation have largely neglected the relationship between finance and innovation” (Jan, David et al.). Unique to biopharma, the financial sector has a technical orientation, and financial and technological knowledge are blended, and not always distinct from each other. Therefore, I take a neo-Schumpeterian approach to defining financialization in biopharma and empirically analyzing the complex relationships between financialization and innovation in biopharma.

2.11 Summary and conclusions

The global economy and innovation in biopharma have changed dramatically since the 1970s. With the explosion of biotechnology and the post-genomic era, new technologies have emerged to change the drug development process. In parallel, biopharma's innovation model has also changed: universities have increasingly become less instrumental in the diffusion of knowledge and more crucial in the actual innovation and drug development process.

At the same time, at a macro level, finance has taken an increasingly broad role in the global economy with globalization and deregulation of markets that have allowed finance to gain political and economic power. The biopharmaceutical industry has been particularly sensitive to these shifts, with finance and financialization taking a more dominant role in the corporate strategies of biopharma companies. Policies in the 1980s-2000s in the US (e.g. the Bayh-Dole Act of 1980, the Economic Recovery Tax Act of 1981, Rule 10b-1 at the SEC in 1982, the Financial Modernization Act of 1999, the Commodities Futures Modernization Act of 2000) allowed venture capital to rise as a vehicle for financing innovation—which has become increasingly dominant in biopharma. Neoliberalism has also allowed finance to dominate major global industries, especially the biopharma sector, leading to firms dominated by "financialization" (i.e. the increasing role of financial markets, motives, and institutions in the operation of firms and economies).

The shifts in both innovation and finance are intertwined: innovation shifted from being concentrated in large pharma (Schumpeter Mark II firms) to a decentralized network of small, innovative biotech companies (Schumpeter Mark I firms) that required a lot of capital. The pattern of change in biopharma innovation increasingly necessitated a different model of finance; concurrently, finance itself changed and became increasingly dominant in biopharma companies in terms of how they are governed and operated. This led to changes in corporate policies: as opposed to a "retain-and-invest" policy in non-financialized companies, biopharma firms have shifted to a financialized

"downsize and distribute" policy driven by maximizing shareholder value ideology to return capital to shareholders instead of re-investing in R&D and productivity.

The financialization of biopharma companies is characterized by (1) corporate governance, driven by an MSV ideology, as evidenced by increasing share buybacks and dividends, inequitable increases in drug pricing, and decreases in R&D productivity; (2) institutional control, largely dominated by venture capital (which is driven by "short-termism" and inpatient capital, and therefore at odds with drug innovation) and hedge funds; and (3) stock engineering, as evidenced by share price engineering.

In a review of the literature, there seem to be some key gaps that I hope to address in the next few sections. First, previous definitions of financialization seem narrow because they only focus on MSV ideology. Second, studies have inconsistent or limited definitions of innovation. I propose using a comprehensive measure of innovation with weighted patent counts, NMEs and new drug approvals, and innovativeness of drugs. Third, there have been few empirical analyses of the actual effect financialization has on *innovation.* Fourth, it is unclear what the full impact of venture capital on innovation in biopharma is. Finally, most of the analyses in the literature draw from companies that are listed on stock exchanges and do not often include private companies—mostly due to the lack of publicly available data.

Over the next few chapters, using a neo-Schumpeterian lens (to allow for the inherent entanglement between finance and innovation in biopharma), I aim to first define financialization and describe its characteristics in biopharma (Chapter 4), and then empirically evaluate the relationship between financialization and innovation in biopharma (Chapters 5 and 6). I also aim to incorporate private companies in my analyses by looking at databases such as PitchBook, which includes comprehensive, survey-based data on private companies. The goal of the subsequent chapters is to use a variety of empirical methods with both a micro and meso lens, supported by case studies, to look

at the effect of corporate strategies, institutional control, and other firm characteristics on innovation in biopharma.

Chapter 3: Research design and methods

My primary research aim is to ***define and characterize financialization in biopharma and study the effect of the current financial model in biopharma on innovation.*** This overarching question seeks to characterize and analyze complex relationships in biopharma with a focus on financialization and its effects on innovation. For my thesis, I aim to first define financialization and describe its characteristics in biopharma, and then empirically evaluate the relationship between innovation and innovation in biopharma. My research aims are as follows:

1. Aim 1: Define financialization in biopharma and how it relates to innovation
2. Aim 2: Characterize financialization patterns in biopharma over time
3. Aim 3: Empirically study relationships between financialization and innovation

3.1 Research aims, questions, and hypotheses

Aim 1: Define financialization in biopharma

There have been quite a few attempts at defining general financialization; however, there lacks a clear, consistent definition of financialization. Specific to biopharma, Lazonick's definition, focused on share buybacks (Lazonick 2009, Lazonick and Tulum 2011, Lazonick 2016), is the most widely used. However, none of these definitions relate to the context of innovation—and given the complexity of biopharma, and how innovation is at the center of the industry, these definitions lack a fundamental lens through which financialization is studied.

Using a neo-Schumpeterian theoretical lens, as laid out above, I plan to construct a definition of financialization in biopharma that will serve as the basis for Aims 2 and 3. By expanding previous lenses of financialization and looking

more broadly at innovation and finance systems that shape the biopharma sector, this definition will also be a key contribution to the literature.

Aim 2: Characterize financialization patterns in biopharma over time

A core focus of this aim is to characterize the flow of private and public capital in the biopharmaceutical industry, and determine if, and how, the biopharmaceutical industry has become more financialized over time. This will aim to characterize inflows of capital over the past ten years into private companies (through IPOs), as well as market capitalization of public companies, and examine share buybacks, profit, etc. This will look at corporate practices both in private and public biopharmaceutical companies, M&A activity, licenses, etc.

The goal is to characterize financialization in biopharma and describe these trends over time with a focus on the last ten years (i.e. 2011-2020).

Research question 1: In what ways has the biopharmaceutical industry become financialized?

Hypothesis 1: The biopharma industry is financialized by (1) a high degree of venture capital financing; (2) stock engineering practices both in private and public companies; (3) a high degree of M&A financing; (4) biopharma companies offer stock repurchases and dividends (absolute value); and (5) stock repurchases are significantly close to 1.0 or higher as a ratio of stock repurchases and dividends to R&D expenditures.

Research question 2: Has the biopharmaceutical industry become more or less financialized in the 2010s?

Hypothesis 2: The biopharmaceutical industry has become more financialized in the 2010s by investing less in R&D and more in financialized practices as measured by: (1) more venture capital financing; (2) more evidence of stock

engineering; (3) higher IPOs at higher valuations yet at earlier stages of clinical development; (4) more M&A activity at higher prices; (5) increased stock repurchases and dividends (absolute value); and (6) increased stock repurchases as a ratio of stock repurchases and dividends to R&D expenditures and revenue.

Aim 3: Study relationships between financialization (measured by share repurchases, and dividends) and innovation

Using an empirical approach, I have examined complex relationships in biopharma through measures of financialization and innovation. I created a dataset containing relevant measures of financialization, R&D, M&A, and innovation, including patent citations, drug approvals, NME approvals, and drug innovativeness. The analytical approach that I used is structural equation modeling (SEM), which allows for the study of complex relationships and can inform causal relationships. This allows the construction of latent variables (e.g. financialization or innovation) that are constructed from a number of measurements.

Additionally, I looked at research intensity and efficiency, and factors associated with higher research efficiency. I also looked at M&A patterns and whether M&A is associated with higher innovation, as M&A is long believed in the pharma industry to be essential to innovation.

Research question 3: What is the effect of financialization on innovation in biopharma?

Hypothesis 3: Higher financialization (i.e. more stock repurchases, dividends) leads to lower innovative outputs (i.e. patents, innovative drugs, and R&D productivity). Higher M&A activity also leads to lower innovative outputs, especially compared to investing in more R&D internally. Additionally, higher internal R&D spend leads to higher innovative outputs.

Research question 4: What are the factors associated with higher research efficiency?

Hypothesis 4: R&D efficiency remains low in the industry, and likely is associated with firm size and R&D intensity.

Research question 5: Is M&A associated with higher innovation?

Hypothesis 5: M&A is associated with higher innovation if measured by more drug approvals.

3.2. Methodology for empirical aims

Methods for Aim 2: Characterize financialization in biopharma

Using descriptive analyses, I characterized financialization patterns in biopharma over time. First, I took an aggregate meso-level view of these changes over time, looking at available data on all biopharma companies. These included the following: valuations of early-stage private biotech companies; alliances, mergers, and acquisitions; R&D expenditures; share repurchases; dividends; tax rates; venture capital expenditures; and IPOs. These were examined over time (with an emphasis on 2011-2021). Next, I collected firm-specific data for additional analyses. For example, I looked at the ratio of dividends and share repurchases to R&D expenditures to examine these trends over time for the major biopharma companies.

Private company data (e.g. early-stage private companies) were obtained from PitchBook. Other public company data (e.g. R&D spending, M&A activity, share repurchases, IPO amounts, etc.) were collected with S&P's Capital IQ tool. Only IPOs that raised ≥$50 million were included in the analysis. IPOs at the preclinical or clinical development stage were collected by SEC

filings. Data were visualized and analyzed with GraphPad Prism Software (GraphPad, San Diego, CA, USA).

Additionally, I supplemented the quantitative data with case studies, including a case study on Biogen, using SEC filings, and a review of news and analyst coverage available online.

Methods for Aim 3: Study relationships between financialization (measured by share repurchases, and dividends) and innovation

To examine empirical relationships between innovation and financialization in biopharma, I constructed a large, firm-level database that included data on the top 50 public biopharma companies (defined by 2020 revenue), in addition to all the firms they have acquired since 2009. I constructed panel data, which included multi-dimensional data involving measurements over time (2011 to 2021).

The primary analytical method was structural equation modelling (SEM, or structural econometric modelling). This has been utilized in the literature to study complex relationships, and a key payoff of a structural econometric model is that it allows for going beyond the conclusions of a more conventional empirical study to provide potentially causal relationships (Anderson and Gerbing 1988, Bollen 2011, Low and Meghir 2017). Importantly, SEM allows for the construction of latent variables that can be constructed through a composite of measurements (Cliff 1983). This allows for relationships between conceptual variables (such as innovation or financialization) to be studied (Rigdon 2016). Structural equation models identify mechanisms that determine outcomes, and—under the correct assumptions and conceptual construction of latent variables—can identify causal relationships between latent variables using path diagrams (Biddle and Marlin 1987, Bentler 1988, Mouchart and Orsi 2016). There are limitations of SEM, however, which I discuss in Chapter 6. For example, conclusions of causality should be limited, as causal determinations

are subject to a number of factors inherent to latent variable construction and structural equation modelling.

The SEM model includes innovation as the key dependent variables of interest, looking at weighted patent counts, NME approvals, and ASMR values for approved drugs. The key independent variables include financialization measures, such as executive compensation, share repurchases, and dividends. Other independent variables will include M&A activity as well as firm-level information such as geography, firm size, etc. Model fit was assessed by several tests, including the comparative fit index (CFI) and the root mean square error of approximation (RMSEA), which is related to residual in the model. Acceptable model fit is indicated by a CFI value of 0.90 or greater and an RMSEA value of 0.06 or less (Hu and Bentler 1998).

The top 50 biopharma companies (by 2021 revenue) were included in the analysis, in addition to all the companies they have acquired since 2011. The companies included in the analysis are listed in **Figure 4.**

Figure 4. Companies included in the analysis

AbbVie Inc. (NYSE:ABBV)	Gilead Sciences, Inc. (NasdaqGS:GILD)	Perrigo Company plc (NYSE:PRGO)
Amgen Inc. (NasdaqGS:AMGN)	Grifols, S.A. (BME:GRF)	Pfizer Inc. (NYSE:PFE)
Astellas Pharma Inc. (TSE:4503)	GSK plc (LSE:GSK)	Recordati Chimica e Farmaceutica BIT:REC)
AstraZeneca PLC (LSE:AZN)	Hikma Pharmaceuticals PLC (LSE:HIK)	Regeneron Pharmaceuticals, Inc. (NasdaqGS:REGN)
Bausch Health Companies Inc. (NYSE:BHC)	Horizon Therapeutics (NasdaqGS:HZNP)	Roche Holding AG (SWX:ROG)
Bayer Aktiengesellschaft (XTRA:BAYN)	Incyte Corporation (NasdaqGS:INCY)	Sanofi (ENXTPA:SAN)
Biogen Inc. (NasdaqGS:BIIB)	Ipsen S.A. (ENXTPA:IPN)	Santen Pharmaceutical Co., Ltd. (TSE:4536)
BioMarin Pharmaceutical Inc. (NasdaqGS:BMRN)	Jazz Pharmaceuticals plc (NasdaqGS:JAZZ)	Shionogi & Co., Ltd. (TSE:4507)
Bristol-Myers Squibb Company (NYSE:BMY)	Johnson & Johnson (NYSE:JNJ)	Swedish Orphan Biovitrum AB (publ) (OM:SOBI)
Chugai Pharmaceutical Co., Ltd. (TSE:4519)	Krka, d. d. (LJSE:KRKG)	Sumitomo Pharma Co., Ltd. (TSE:4506)
CSL Limited (ASX:CSL)	Kyowa Kirin Co., Ltd. (TSE:4151)	Taisho Pharmaceutical Holdings Co., (TSE:4581)
Daiichi Sankyo Company, Limited (TSE:4568)	H. Lundbeck A/S (CPSE:HLUN A)	Takeda Pharmaceutical Company (TSE:4502)
Eisai Co., Ltd. (TSE:4523)	Mallinckrodt plc (NYSEAM:MNK)	UCB SA (ENXTBR:UCB)
Eli Lilly and Company (NYSE:LLY)	Merck & Co., Inc. (NYSE:MRK)	United Therapeutics (NasdaqGS:UTHR)
Emergent BioSolutions Inc. (NYSE:EBS)	Novartis AG (SWX:NOVN)	Vertex Pharmaceuticals (NasdaqGS:VRTX)
Endo International plc (OTCPK:ENDP.Q)	Novo Nordisk A/S (CPSE:NOVO B)	Viatris Inc. (NasdaqGS:VTRS)
	Ono Pharmaceutical Co., Ltd. (TSE:4528)	
	Otsuka Holdings Co., Ltd. (TSE:4578)	

Company-level measures

A firm-level dataset was constructed using firm-level data from S&P Capital IQ, including revenues, share repurchases, dividends, R&D expenditures, firm size, and headquarter locations. This was then merged with product-level data available from the FDA, including new molecular entities (NMEs) and all drug approvals by each company from 2011 to 2021. Measures of innovation were included as well, including patent data to construct weighted patent citation data for each firm. Additional measures of innovation include NMEs, ASMR, and R&D ratios (NME approved: R&D).

Drug counts

A tangible innovative output in biopharma is an approved drug. The number of approved drugs has been commonly used as a simple measure of innovative outputs (Kaitin and DiMasi 2011). In a systematic review how "innovativeness" in drug development is defined, Kesselheim et al. found that using drug counts by tallying the yearly number of all new drugs is the most commonly used metric in the literature (Kesselheim, Wang et al. 2013). Many studies include the approval of new molecular entities (NMEs) or new chemical entities (NCEs), which are used synonymously as the primary determinant of innovation.

To create a drug count database, I used the FDA's database (https://www.fda.gov/drugs/development-approval-process-drugs/drug-approvals-and-databases) and sorted the drugs by sponsor. I used the FDA's definition of new molecular entity to include whether the approved drugs were NMEs or not NMEs. I included approved drugs that were developed by a company that was acquired by the 50 companies in the dataset (for example, all of Celgene's drugs were counted as Bristol Meyers Squibb's drug approvals).

Therapeutic value

Health technology assessment (HTA) and therapeutic value are important tools in assessing medicines' cost-effectiveness to inform reimbursement and pricing

(Kergall, Autin et al. 2021). One useful assessment is France's ASMR (Amélioration du service médical rendu) measurement. France's Transparency Commission (TC), part of the National Authority for Health (Haute Autorité de Santé), evaluates the added benefit of new drugs in relation to the relevant comparator (Le Pen 2018). France sets its reimbursement level for new medicines based on a five-point system that reflects the medicine's added value. The ASMR scale ranks each drug compared to existing treatment options:

- ASMR I: major improvement
- ASMR II: important improvement
- ASMR III: moderate improvement
- ASMR IV: minor improvement
- ASMR V: no improvement

Several studies have looked at ASMR values and other measures. One study found that ASMR is positively associated with the disease severity, the quality-adjusted life-year (QALY) gain provided by the drug, and the validation of the incremental cost-utility ratio in the Economic Opinion (Kergall, Autin et al. 2021). Another study also found associations between ASMR values and QALY for oncology drugs and was similar to technology appraisals from NICE in the UK (Drummond, de Pouvourville et al. 2014).

To create a drug therapeutic value database, I used ASMR data from France's HAS added to the drug count database I constructed using FDA approval data.

Patent data

Trajtenberg and Jaffe, beginning in the late 1990s, make a compelling case for the use of weighted citations from patent data as a measure of innovation and economic output. In various works they outline that weighted patent counts are more strongly associated with innovation. Patent counts weighted by citations (WPC) are better indicators of the value of innovations than simple patent counts (SPCs) (Trajtenberg 2002). Weighted patent counts have been used in

other industries as a measure of innovation and to characterize innovation systems (Henderson, Jaffe et al. 1998, Jaffe, Fogarty et al. 1998, Mowery, Sampat et al. 2002).

More highly cited patents give potential indicators of value, such as likelihood of commercializability (Shane 2001), perceived economic value (Harhoff, Narin et al. 1999, Jaffe, Trajtenberg et al. 2000), economic growth (Kogan, Papanikolaou et al. 2017), scientific quality (Poege, Harhoff et al. 2019), and research productivity (Lanjouw and Schankerman 2004). They have also been used to measure knowledge spillovers (Jaffe, Trajtenberg et al. 1993, Jaffe and Trajtenberg 1999).

In the context of biopharma, several studies have used patent citations as a measure of innovation. Although many patents in the biopharma industry do not result in new drugs (Harris 2002, Pisano 2006, Mazzucato and Tancioni 2008), patents represent the potential "innovativeness" of a firm. For example, Kesselheim and Avorn used patent citation data to assess the value of pharmaceutical innovation (Kesselheim and Avorn 2009). Another study by Sapsalis et al. studied biotech patents to measure innovation between universities and firms (Sapsalis, de la Potterie et al. 2006).

The weighted citation can be measured with the following equation, where *WPC* is the weighted patent citations, *t* is the year following the issuance date, *Ci* is the number of patent citations in a year, and n_t is the number of patents issued during year *t* (**Figure 5**).

Figure 5. Formula: weighted patent citations

$$WPC_t = \sum_{i=1}^{n_t} (1 + C_i)$$

Historically, the most common source of patent citation data has been the National Bureau of Economic Research (NBER). This data was originally created by Bronwyn H. Hall, Adam B. Jaffe, and Manuel Trajtenberg, and

published in 2001 (Hall, Jaffe et al. 2001) with later updates. A valuable resource, it provided the citation information for US patents from 1963 to 2006 and has recently been updated to 2013. The original complete dataset to 2006 consists of 3 million patents, and their citations, and is open for public research use (Sharma and Tripathi 2017). This resource has been used extensively in the literature when measuring innovation through weighted patent citations (Atanassov, Nanda et al. 2007, Nagaoka, Motohashi et al. 2010, Kogan, Papanikolaou et al. 2017, Entezarkheir and Moshiri 2019).

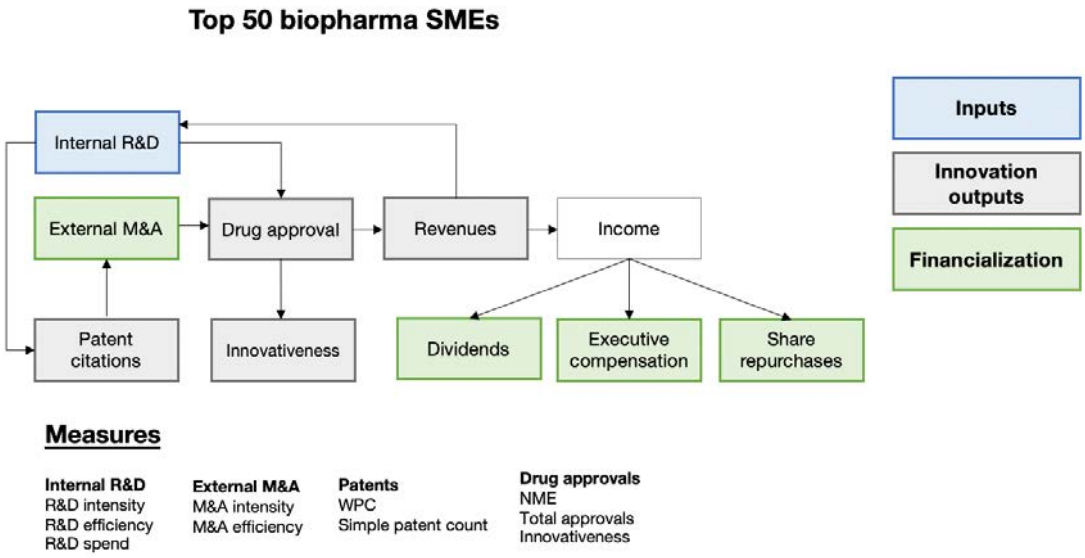
However, the NBER database for patent citations was not feasible for use in my data collection, since the sample has not been updated to include patents issued beyond 2013. Thus, I used another data source, the Wharton Research Data Services (WDRS) US Patents dataset. These data are directly parsed from the USPTO's XML files and covers the years 2011-2019. Although there were two years of data missing for my analyses, the WDRS was a superior choice compared to NBER's database.

To create the firm-level patent citation database for my sample of the top 50 biopharma firms, I used firm data from Compustat and linked it to the patent citation at WRDS using GVKEYs, the more "permanent" identifier used in Compustat (Lerner and Seru 2017). I made sure to include all GVKEYs and linked it to a single firm identifier, which was then associated with each patent. I extracted all patent identifiers based on the GVKEYs and included patent identifiers that were linked by M&A, which would include patents acquired by a firm by an acquisition. Then, I used the patent identifiers to extract forward and backward weighted patent counts, which I linked to my firm-level database.

Frameworks and variable relationships

A working framework outlining the variables underlying the analyses is presented in **Figure 6.** Inputs are in blue, while measures of financialization are in orange, and innovation outputs are shown in green.

Figure 6. Framework of variable relationships



NME: new molecular entity; M&A: merger & acquisition; R&D: research & development; WPC: weighted patent citations.

Bivariate analyses were used to examine the relationship between financialization (measured by aggregate share repurchases) and innovation (measured by aggregate drug approvals and NMEs). **Table 3** presents a summary of the variables of interest and outcomes.

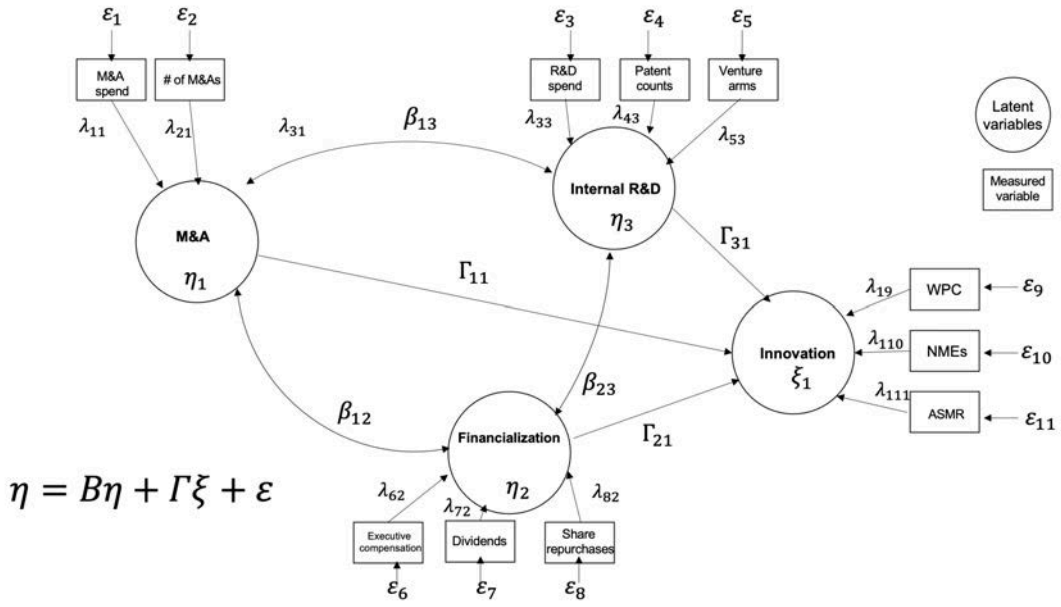
Table 2. Summary of variables and outcomes of interest in the SEM model

Variable	Description	Type of variable	Measures
Dependent variable	Innovation	Latent variable	- Drug approvals (number of FDA approvals) - NME approvals (number of NME approvals by the FDA) - Weighted patent counts - HTA (ASMR value)
Independent variables	Financialization	Latent variable	- Share repurchases ($ billion) - Dividends ($ billion) - M&A activity ($ billion in acquisitions) - Valuation premiums

	Internal R&D	Latent variable	- Simple patent counts - R&D expenditures ($ billion)
	Other	Measured variables	- Firm size
Primary outcome	Relationship between financialization and innovation	N/A	- Regression coefficients
Secondary outcomes	- Relationship between internal R&D spending and innovation - Relationship between internal R&D spending and M&A	N/A	- Regression coefficients

A working diagram of the SEM model is provided in **Figure 7**, where η_n represents latent variables, ξ represents the dependent variable (innovation), ε represents variance of the measured variables, Γ_{xy} represents regression coefficients between observed variables to the dependent variable, λ_{xy} represents regression coefficients between observed to latent variables, and β_{xy} represents regression coefficients between latent variables.

Figure 7. SEM model inputs and outputs



R&D: research & development; SPC: simple patent count; WPC: weighted patent counts.

A complete list of aims, research questions, and hypotheses are laid out in **Table 4.**

Table 4. Research aims, questions, and hypotheses.

Research aim	Research question	Hypotheses
Aim 1: Define financialization in biopharma and how it relates to innovation	--	--
Aim 2: Characterize financialization patterns in biopharma over time	1. In what ways has the biopharma industry become financialized?	1. The biopharma industry is financialized by: (1) a high degree of venture capital financing; (2) increasing number of low-quality IPOs; (3) stock engineering practices in both private and public companies; (4) companies offer stock repurchases and dividends (absolute value); and (5) stock repurchases are significantly closer to 1.0 or higher as a ratio of stock repurchases and dividends to R&D expenditures.
	2. Did the biopharma industry become more or less financialized in the 2010s?	2. The biopharma industry has become more financialized in the 2010s by lower R&D spend compared to more financialized practices as measured by: (1) more venture capital financing; (2) more IPOs at earlier stages of development (3) more evidence of stock engineering; (4) more M&A activity at higher prices; (5) increased stock repurchases and dividends (absolute value); and (6) increased stock repurchases as a ratio of stock repurchases and dividends to R&D expenditures and revenue.
Aim 3: Empirically study relationships between financialization and innovation	3. What is the effect of financialization on innovation in biopharma?	3. Higher financialization (i.e. more stock repurchases, dividends, valuations) leads to lower innovative outputs (i.e. patents, innovative drugs, and R&D productivity). Higher M&A activity also leads to lower innovative outputs. Additionally, higher internal R&D spend leads to higher innovative outputs.
	4. What factors are associated with higher research efficiency?	4. R&D efficiency remains low in the industry and is likely associated with firm size and R&D intensity.
	5. Is M&A associated with higher innovation?	5. M&A is associated with lower innovation measured by more drug approvals.

The results of Aims 1 and 2 are presented in Chapter 4, and the results of the empirical analyses of the top 50 biopharma firms are presented in Chapter 5.

Chapter 4: Defining and characterizing financialization in biopharma

There are few robust studies on financialization in biopharma, and a comprehensive definition of financialization in biopharma, especially one that relates to innovation, is lacking. The goal of this chapter is to define and characterize financialization through a neo-Schumpeterian lens in order to be able to study the effects of financialization on innovation in biopharma empirically.

4.1. Theoretical framework: a neo-Schumpeterian lens to study biopharma financialization and its effect on innovation

In Chapter 2 (Section 2.10), I presented my theoretical framework for defining and studying financialization in biopharma in relation to innovation. Briefly, given the goal of studying financialization relative to innovative outputs with analysis needed at the micro- or meso-level, I propose using a neo-Schumpeterian lens for studying financialization in biopharma, since innovative competition is the core principle underlying the neo-Schumpeterian approach (Hanusch and Pyka 2007).

As I described in Chapter 2, the biopharma industry is more characterized by Schumpeter Mark I firms in which entrepreneurs and new firms play a larger role in innovation (Schumpeter 1912, Schumpeter 1934, Nelson and Winter 1982, Malerba and Orsenigo 1996). These types of firms are characterized by creative destruction in which entrepreneurs and new firms play a key role in innovative activities (Malerba and Orsenigo 1996). After the 1980s, however, more biotechnology firms arose and were largely the source of innovation in biopharma (i.e. largely Schumpeter Mark II firms). The innovation ecosystem is now more diffuse, with most new drugs originating in biotech companies that are then acquired or licensed to larger pharma.

Most Schumpeterian and neo-Schumpeterian studies have focused on innovation and have not thoroughly incorporated the broad influence of finance on innovation (Jan, David et al. , Mazzucato 2015, Mazzucato and Semieniuk 2017)—especially from an empirical perspective. Therefore, I take a neo-Schumpeterian approach to defining financialization in biopharma and spend the following two chapters on empirical analyses looking at complex relationships between finance and innovation systems in biopharma.

4.2. Defining financialization in biopharma

There have been quite a few attempts at defining general financialization. However, there lacks a clear, consistent definition of financialization in biopharma.

Specific to biopharma, Lazonick's definition, focused on share buybacks, is the most widely used. However, none of these definitions relate to the context of innovation and, given the complexity of biopharma, where innovation is at the center of the industry, these definitions lack a fundamental lens through which financialization can be studied. The definition I offer for financialization in biopharma is:

> **Financialization in biopharma is the strategy of prioritizing financial accumulation over technical innovation, mediated by the influence of finance and shareholder-driven corporate governance, in order to benefit shareholders.**

This definition includes the lens of innovation, which is an important context for studying financialization in a technological-based industry. In **Table 5**, I contextualize and try to operationalize this definition based on parameters established by the literature review in Chapter 2.

Table 5. Operational definitions of financialization

Lens	Type	Description	Examples
Meso	Institutional control	Venture capital and hedge funds are key agents of control in a company, not management	- Increase in VC financing - Increase in early-stage IPOs to create quicker exits for VCs
Micro	Stock engineering practices	Share price manipulation or stock market speculation	- Increasing valuation of private companies - Releasing press releases to move the stock and raise capital at higher price
Micro	Corporate governance	Driven by a "maximizing shareholder value" ideology, management aims to govern company to maximize shareholder value	- Share repurchases - Dividends - Executive compensation - Lower R&D expenditures - M&A

Source: Original table

4.3. Institutional control

Venture capital

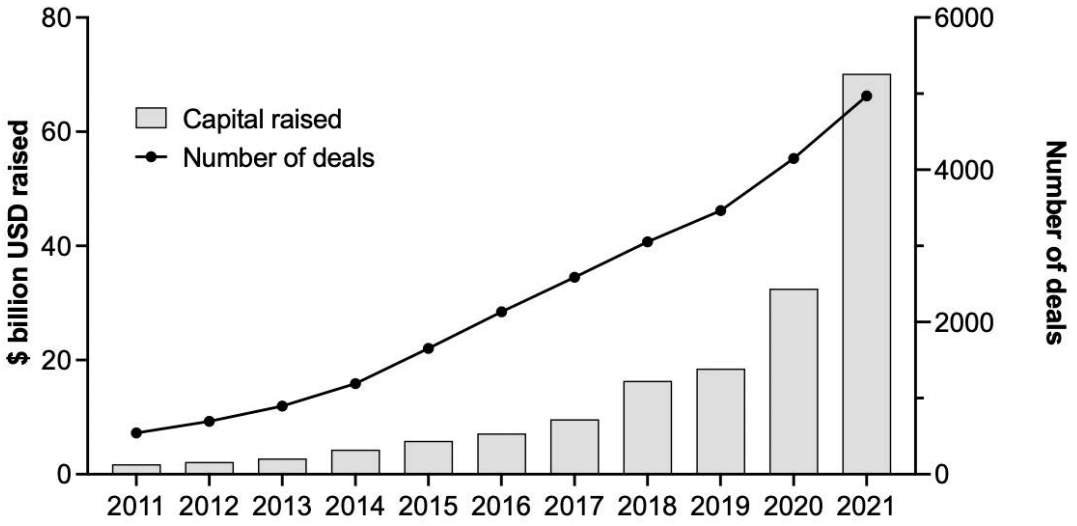
Although venture capital can be a good substitute for risk-averse banks (Mazzucato 2015), finance from venture capital is characterized by short-termism and driven by returns. Public finance (e.g. the National Institutes of Health or small business innovation research funding) shapes the direction of innovation in a purposeful manner, and even financing from larger pharmaceutical companies to smaller biotech companies drives the way biotech companies innovate.

Short-termism is defined as the excessive focus of corporate managers and shareholders on short-term results—usually short-term financial gains for a fund (Rappaport 2005, Dallas 2012). This is especially true in venture capital, which is driven by goals of returning ≥10x on the portfolio. This short-termism of venture capitalists (the major financiers of biotech companies) contrasts with the long-term nature of drug development (Andersson, Gleadle et al. 2010). Venture capital is a major source of financing for biotech companies early in the

drug development life cycle. Pisano shows that from 1978 through 2004, venture capital invested $38 billion (in 2004 dollars) in US biotech companies (Pisano 2006), or $51 billion adjusting for inflation.

From 2011 to 2021, there has been a nearly 40-fold increase in venture capital deployed in private biopharma companies, from $1.8 billion in 2011 to $70.2 billion in 2021, as shown in **Figure 8.** The number of deals has increased 8.2-fold, from 543 deals in 2011 to 4,969 deals in 2021.

Figure 8. Capital raised from VC financing in biopharma

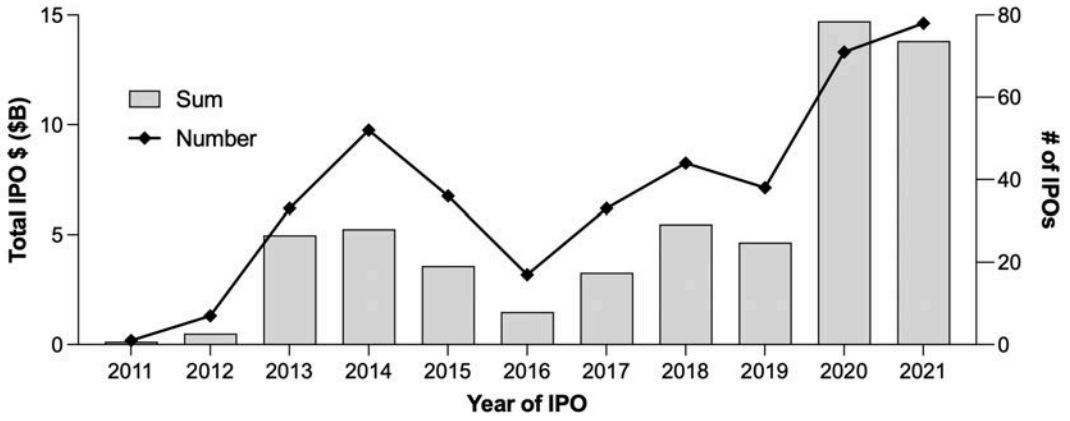


Source: original figure based on data from Pitchbook.

IPOs

One of the clear outcomes of a VC-dominated industry is the need for VCs to exit, and one of the most common forms of liquidity for VCs is through IPOs. The number of IPOs raising ≥$50 million skyrocketed during the pandemic, reaching 71 IPOs in 2020 and 78 in 2021, with $14.7 billion and $13.8 billion raised, respectively (**Figure 9**).

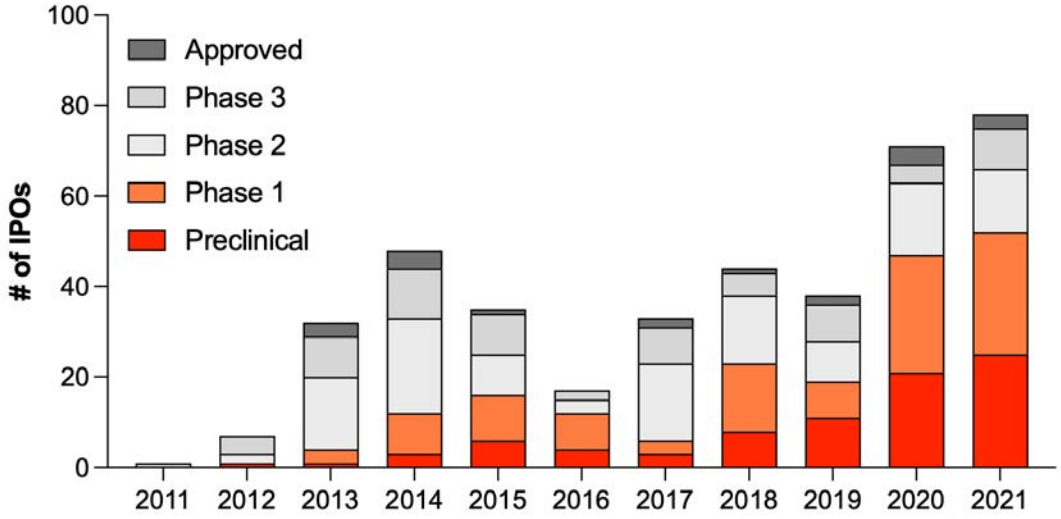
Figure 9. Capital raised from IPOs in biopharma



Source: original figure based on data from Pitchbook.

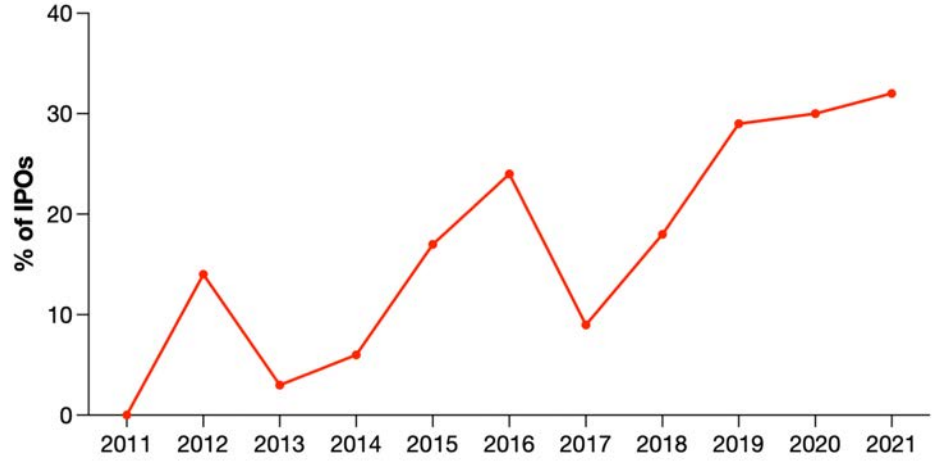
Importantly, there has been a clear trend of early-stage IPOs over time, where IPOs are trending earlier in clinical development stage, with more preclinical companies comprising the total IPOs over time compared to Phase 1 or later. Preclinical IPOs comprised nearly a third of IPOs in 2021. Companies in Phase 1 development or earlier comprised 67% of IPOs in 2021 vs. 46% or less between 2011-2015 (**Figure 10** and **Figure 11**).

Figure 10. IPOs by phase of development



Source: original figure based on data from SEC filings and Pitchbook.

Figure 11. Percentage of IPOs in preclinical development

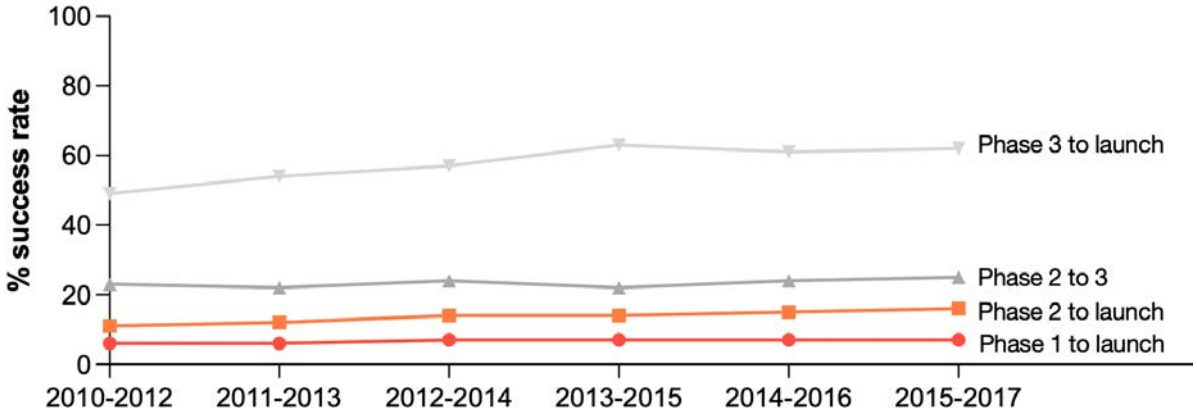


Source: original figure based on data from SEC filings and Pitchbook.

The fact that biopharma companies are launching IPOs at earlier stages is problematic—and a sign of financialization—due to the high risk involved in drug development in Phase 1 or earlier. *The rate of success for the pharma industry as a whole, for a drug from Phase 1 to launch, is around 7% and has*

not improved in the 2010s. Even the rate of success for a drug moving from Phase 2 clinical development to Phase 3 clinical development is low, at around 25% (Dowden and Munro 2019) (**Figure 12**).

Figure 12. Rates of success (%) by phase of clinical development



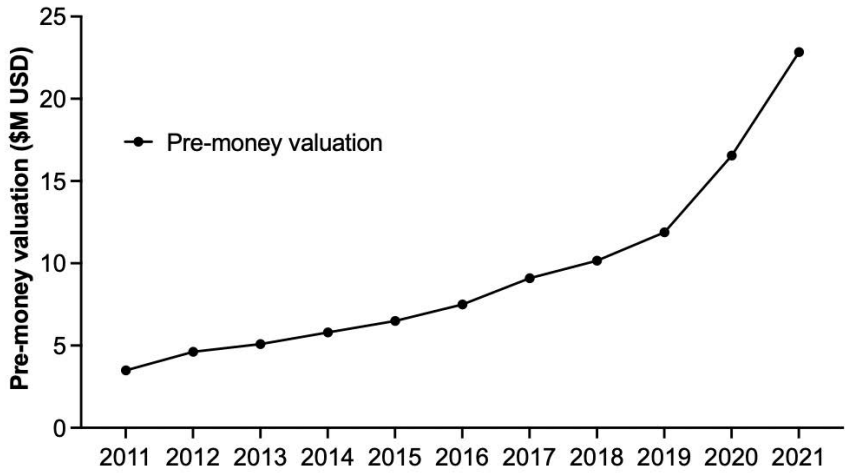
Source: Adapted from Dowden and Munro 2019

4.4. Stock engineering practices

Private companies

A form of financialization includes higher valuations of early-stage SME biotech companies, which I hypothesize also negatively impacts innovation. Pre-money valuations indicate the equity value of companies before raising capital. The median pre-money valuation of these companies has increased 5.5-fold, from $3.5 million to $22.8 million, respectively (**Figure 13**).

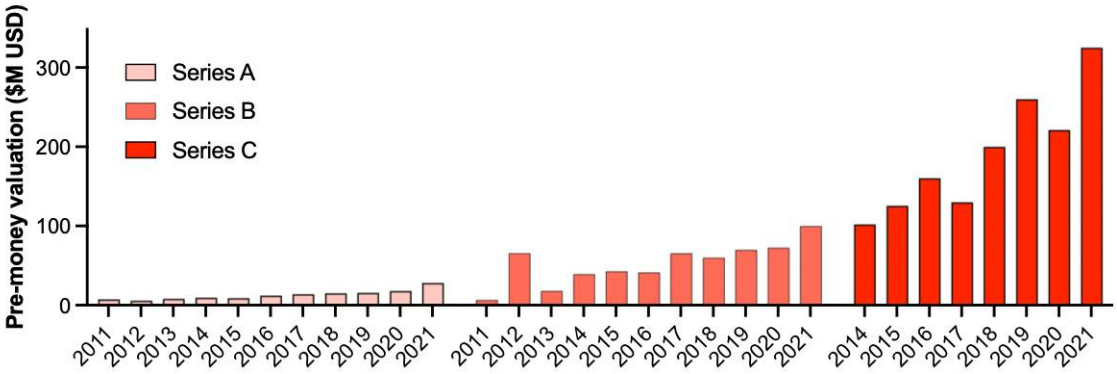
Figure 13. Pre-money valuations in VC-backed biopharma companies



Source: original figure based on data from Pitchbook.

The trends are most pronounced in earlier rises: median Series A valuations have increased from $7.5 million to $28 million, from 2011 to 2021, respectively, and median Series B valuations have increased from $6.5 million to $100 million, respectively (**Figure 14**).

Figure 14. Pre-money valuations of VC-backed biopharma companies by funding round



Source: original figure based on data from Pitchbook.

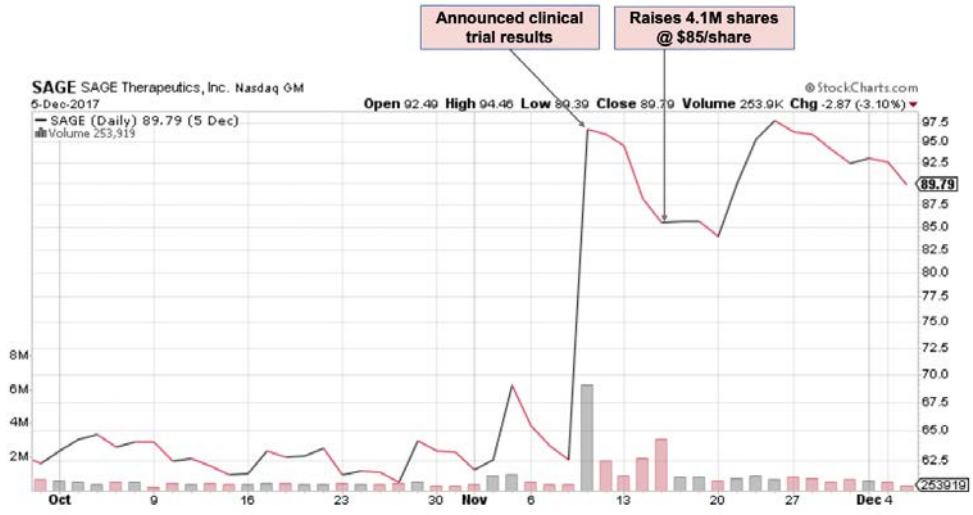
Public companies

One common practice that publicly traded biopharma companies often employ is leveraging news and signals to use the stock market to their advantage. This

practice occurs as follows: (1) a biopharma company, Company A, plans to issue a press release based on a clinical trial readout that it knows is positive; (2) Company A discusses under confidentiality with a bank that it intends to raise capital via a secondary offering on the public market; (3) Company A issues press release on the news; (4) Company A immediately raises capital at a higher share price, thus avoiding diluting its price per share.

One example of this (of countless) is Sage Therapeutics. Sage Therapeutics is developing therapeutics for central nervous system disorders. On November 9, 2017,[4] Sage announced a positive Phase 3 clinical trial. As a consequence, its share price rose from $62.50 to $96.00 a share in one day (38%). A few days later, on November, the company raised 529,411 shares at $85.00 share for approximately $345 million, as shown below (**Box 1**).

Box 1. Sage Therapeutics Case Study: stock manipulation



Source: original figure based on data from stockcharts.com.

This sort of practice is an example of financialization through an MSV ideology since the company decided to wait until its share increased to raise additional capital. This action avoided the need to dilute existing shareholders. As

[4] Sage Therapeutics press release. https://investor.sagerx.com/news-releases/news-release-details/sage-therapeutics-announces-brexanolone-achieves-primary

Hanusch and Pyka described, “short-term signals of potential technological breakthroughs are misinterpreted in the financial sphere of an economy and cause a positive feedback within expectation formation” (Hanusch and Pyka 2007).

4.5 Alliances, mergers, and acquisitions in biopharma

Biotech-pharma partnerships—also referred to as “R&D alliances” in the literature (Pisano 2006, Lazonick 2009, Lazonick 2010) —are an essential component to innovation in biopharma. Technology is usually developed by smaller biotech companies and then licensed to, or acquired by, larger pharma companies for late development and commercialization. These partnerships usually provide capital to the smaller biotech company for early drug development. The first major license agreement in biopharma occurred when Genentech licensed the use of insulin to a major pharmaceutical company, Eli Lilly. This agreement served as a template that would shape the evolution of the biopharma industry even today (Pisano 2006).

There are two different types of M&A: growth-oriented and consolidation-oriented (Anand and Singh 1997). Both characterize the biopharma industry—for example, the 2019 acquisition of Celgene by Bristol-Meyers Squibb (BMS) was consolidation-oriented, supposedly for efficiency improvements and growing market share. At the time of the acquisition, BMS said that the transaction would provide over $20 billion in “synergy value,”[5] including $2.5 billion in cost-cutting to “achieve efficiencies across the organization.”[6] Of the $20 billion in synergies, ~10% was from manufacturing, ~35% from R&D, and ~55% from selling, general and administrative (SG&A) expenses. This included leveraging BMS’ biologics capabilities for manufacturing, optimizing research and reducing overlapping resources, and cutting overlapping commercial

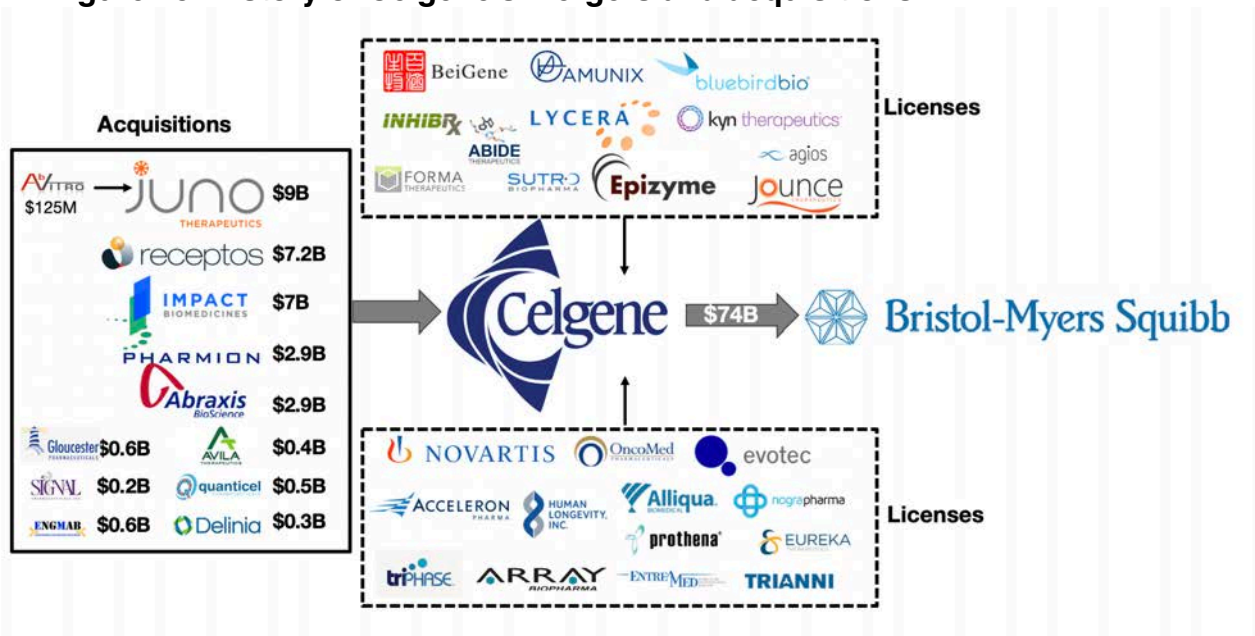
[5] Bristol-Myers Squibb Investor Presentation, March 2019, slide 17

[6] Bristol-Myers Squibb press release 1/3/2019: https://news.bms.com/news/corporate-financial/2019/Bristol-Myers-Squibb-to-Acquire-Celgene-to-Create-a-Premier-Innovative-Biopharma-Company/default.aspx

activities in oncology, immunology, and inflammation franchises. BMS also hinted that its intention with the acquisition was to increase its market share in various areas: in a press release, BMS said, “The combined company will be #1 in oncology, #1 in cardiovascular, and top 5 in immunology and inflammation.”[7]

Celgene was famous for making extensive R&D alliances, license agreements, and acquisitions. It made a complicated web of agreements and acquisitions with over $32 billion spent in acquisitions and over 25 major license agreements. **Figure 15** shows these relationships leading up to its acquisition by BMS.

Figure 15. History of Celgene's mergers and acquisitions



Source: original figure based on data from SEC filings

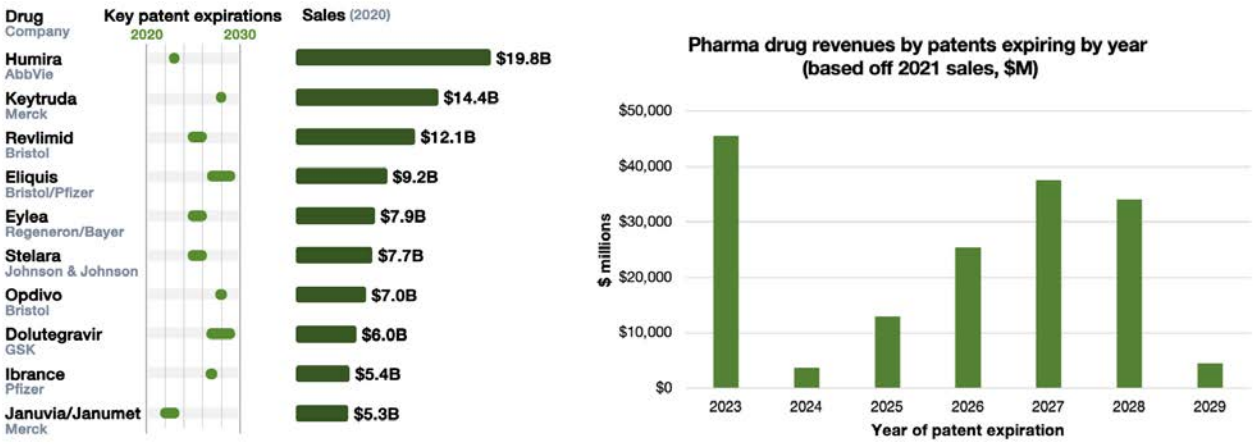
Importantly, large pharma companies have been faced with major patent expirations (called a “patent cliff”) from blockbuster drugs (e.g. Humira, Keytruda, and Revlimid, drugs that each have over $10 billion in annual revenues). Once these drugs go off patent, generics or biosimilars enter the

[7] Bristol-Myers Squibb press release 3/19/2019: https://news.bms.com/news/corporate-financial/2019/Bristol-Myers-Squibb-Files-Investor-Presentation-Highlighting-Significant-Benefits-of-Pending-Transaction-with-Celgene/default.aspx

market and lead to significantly reduced revenues (Song and Han 2016). The patent cliff phenomenon is nothing new, and pharma faced similar problems in the 2010s (Harrison 2011). However, during the 2020s, an unprecedented number of blockbuster drugs have lost or are due to lose patent protection, representing a total of **$155 billion** in drug sales at risk from 2023 to 2029 (**Figure 16**).

Pharma companies have deployed a number of tactics to address patent cliffs, including filing additional patents to extend the patent life around a drug, repositioning the drug to a new indication, or innovating internally (Kakkar 2015). However, recently, the most common practice has been to look externally by acquiring companies or new drugs.

Figure 16. Looming patent cliffs and revenues at risk in the 2020s



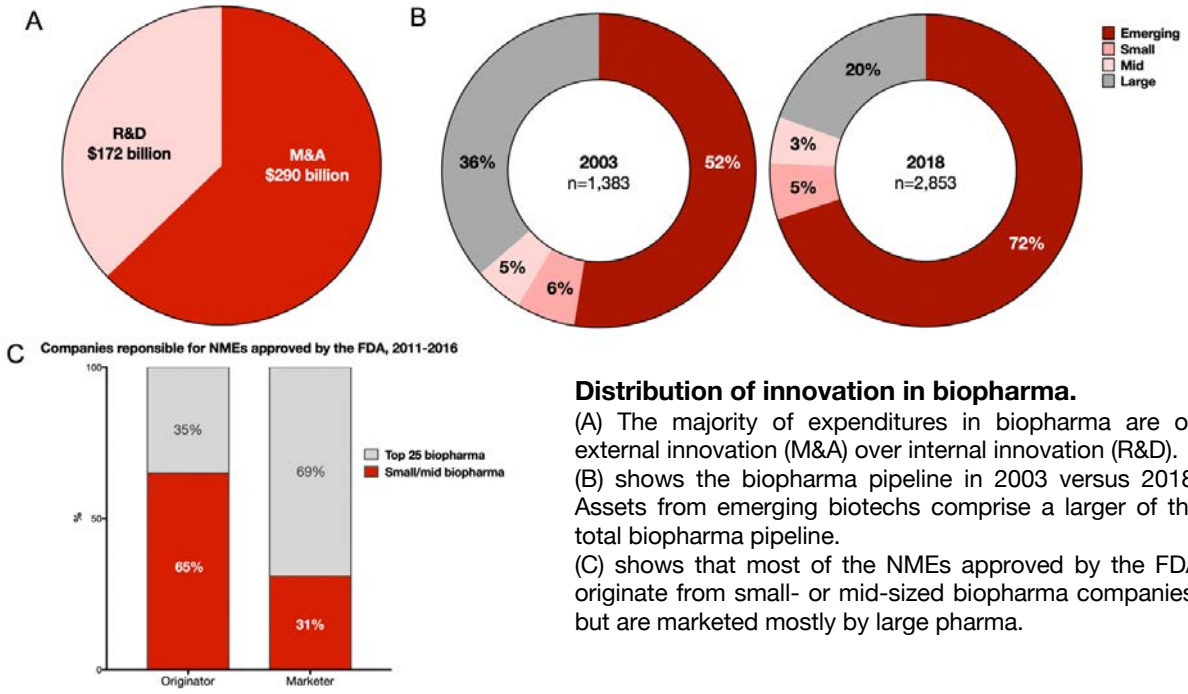
Indeed, biopharma spends relatively little capital on R&D compared to on external spending. In 2018, total capital on M&A in biopharma was $290 billion[8] compared to $172 billion on R&D costs.[9] Importantly, R&D costs usually include license fees—which would be considered external innovation instead of internal innovation. Upfront license fees were $32 billion in 2018—which is a fraction of total license fees paid.[10]

[8] Data from Pitchbook.
[9] IQVIA Pipeline Intelligence, April 2018; IQVIA Institute, March 2019.
[10] Data from Pitchbook.

Moreover, R&D expenditures are mostly spent on clinical development: in 2018, for example, $127 billion was spent on clinical development compared to only $48 billion on basic science, and a dismal $6-7 billion on translational efforts (Fernandez, Stein et al. 2012).

Finally, the majority of pharma's pipeline is from emerging biotech companies—and this distribution is changing significantly over time.[11] In 2003, for example, 52% of the biopharma pipeline was assigned to emerging biotech companies versus 36% to large pharma. In 2018, 72% of the biopharma pipeline was attributed to emerging biotech companies (**Figure 17, B**). Additionally, NMEs approved by the FDA originate from small- or mid-sized companies but are marketed, mostly by large pharma (**Figure 17, C**).

Figure 17. Distribution of innovation in biopharma



Distribution of innovation in biopharma.
(A) The majority of expenditures in biopharma are on external innovation (M&A) over internal innovation (R&D).
(B) shows the biopharma pipeline in 2003 versus 2018. Assets from emerging biotechs comprise a larger of the total biopharma pipeline.
(C) shows that most of the NMEs approved by the FDA originate from small- or mid-sized biopharma companies, but are marketed mostly by large pharma.

Source: original figure based on data from SEC filings and S&P Global.

This supports the work from Arora and Gamberdella characterizing the shift of innovative labor in the 1980s and 1990s; the shift is even more dramatic into

[11] IQVIA Pipeline Intelligence, April 2018; IQVIA Institute, March 2019.

the 2000s. Innovation was once concentrated and integrated in large pharma companies, then diffused into a network of innovators in smaller biotech companies (Arora and Gambardella 1990, Gambardella 1995). In the 1970s and early 1980s, almost all drug discoveries took place inside traditional pharma companies (Shepherd 2018). However, as shown above, this pattern has dramatically shifted in the last 20 years.

Significant M&A marked the start of 2019 with the mega acquisition of Celgene by Bristol-Meyers Squibb for $74 billion, announced on January 4th. A few days later, on January 8th, Takeda closed on the acquisition of Shire for $62 billion (Japan's biggest-ever foreign takeover and the eighth largest M&A event in biopharma history). Other noteworthy acquisitions in 2019 included Loxo Oncology for $8 billion (acquirer: Eli Lilly), Spark Therapeutics for $4.8 billion (acquirer: Roche), and Auris Health for $5.75 billion (acquirer: JnJ). A list of the top ten M&A events in biopharma are tallied below in **Table 6**.[12]

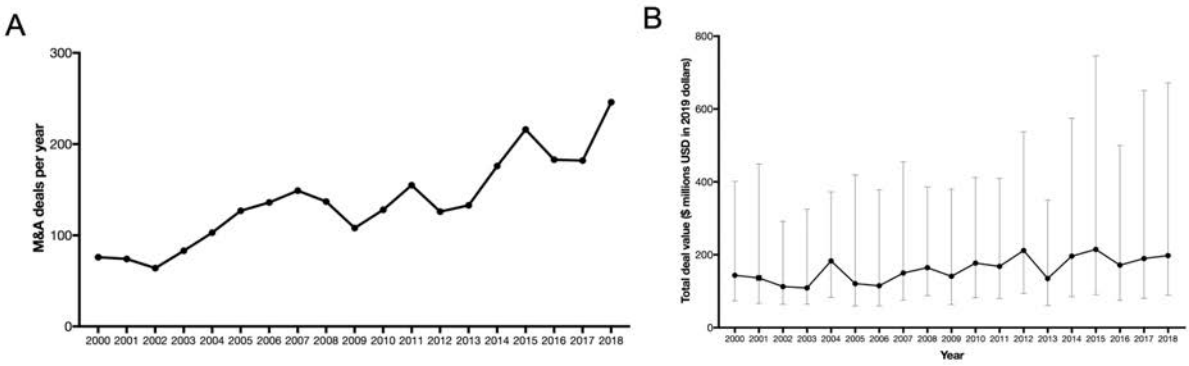
Table 6. Top M&A in biopharma

Rank	Year	Acquirer	Target	Transaction type	Amount ($B)	Amount ($B adjusted for inflation)
1	1999	Pfizer	Warner-Lambert	Acquisition	111.8	168
2	2000	Glaxo Wellcome	SmithKline Beecham	Merger	76	111
3	**2019**	**Bristol-Myers Squibb**	**Celgene**	**Acquisition**	**74**	**74**
4	2004	Sanofi	Aventis	Acquisition	73.5	86
5	2015	Actavis	Allergan	Acquisition	70.5	75
6	2009	Pfizer	Wyeth	Acquisition	68	79
7	2002	Pfizer	Pharmacia	Acquisition	64.3	90
8	**2018**	**Takeda**	**Shire**	**Acquisition**	**62**	**62**
9	2016	Bayer	Monsanto	Acquisition	54.5	57
10	2009	Merck	Schering-Plough	Acquisition	47.1	55

[12] Source: FirstWord Pharma; press releases.

An analysis of M&A since 2000 is presented in **Figure 18**. The number of M&A deals per year has more than doubled. However, interestingly, the total deal value (adjusting for inflation) has remained relatively stable.

Figure 18. M&A in biopharma

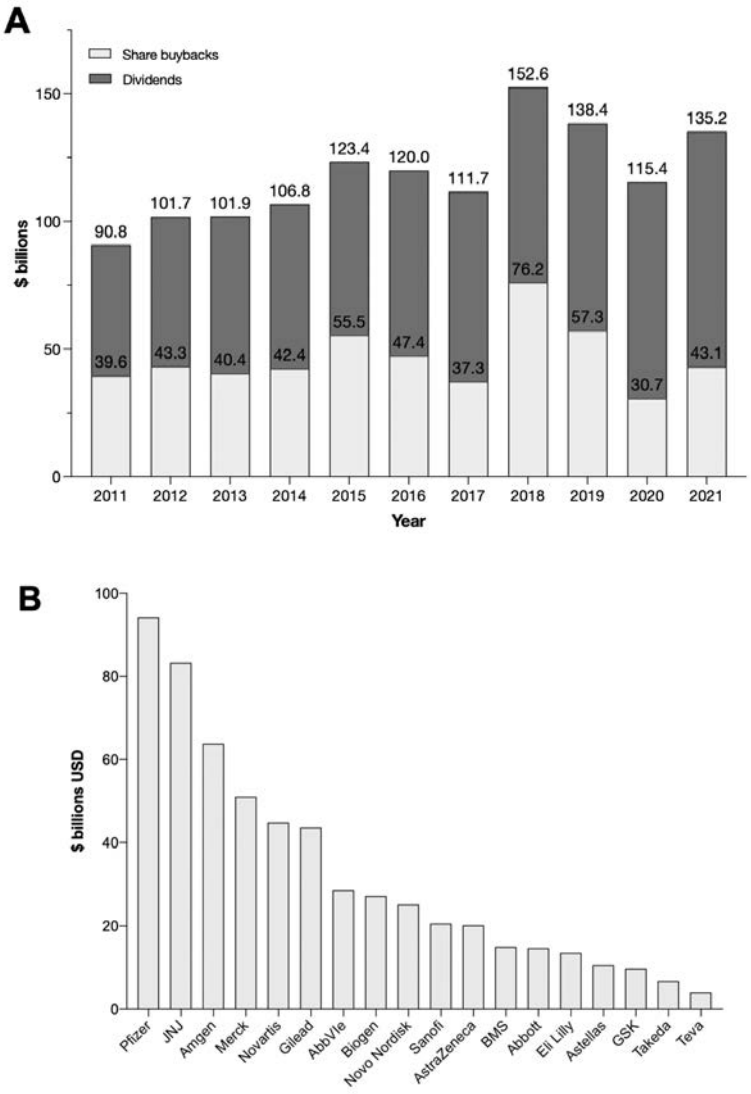


(A) The number of annual M&A deals in biopharma has risen more than two-fold since 2004.
(B) Shows the median total value (bars represent interquartile ranges).
Source: original figures based on data from SEC filings and S&P Global.

From 2011 to 2021 the top 20 biopharma companies spent $513 on share buybacks and $784 billion in dividends. In 2018 there was an estimated total of $78 billion in share buybacks among biopharma companies (**Figure 19, A**).[13] Johnson & Johnson, Pfizer, AbbVie, Merck, and Celgene were the most active in buying back shares (**Figure 19, B**). AbbVie alone spent $15 billion in share buybacks, the most of any biopharma company in 2018. Strikingly, AbbVie spent a mere $5.3 billion in R&D expenditures in 2018,[14] a ratio of almost 3:1 share buybacks to R&D expenditures. Of the biopharma companies that repurchased shares in 2018, the combined R&D expenditure was $43.2 billion.

[13] Data obtained from marketbeat.com
[14] SEC filings.

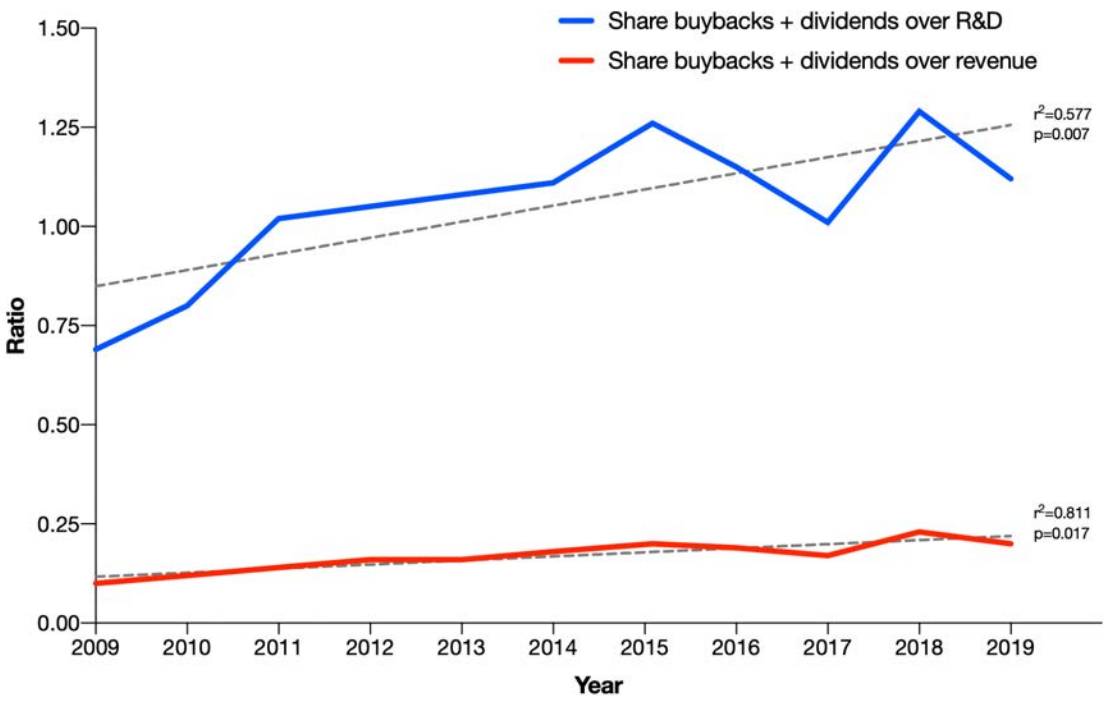
Figure 19. Share repurchases in biopharma



(A) shows share repurchases and dividends over time in the top 20 biopharma companies from 2011 to 2021.
(B) shows total repurchases by firm over that period.

Source: original figure based on data from SEC filings and S&P Global.

Figure 20. Share repurchases and dividends in biopharma as a ratio to R&D and revenue



Source: original figure based on data from SEC filings and S&P Global.

Not only are the raw amounts of cash used for dividends and share repurchases increasing over time, but their ratio to R&D or revenue are also significantly rising. From 2009 to 2019, the ratio of share buybacks and dividends to R&D increased from about 0.7 to 1.3 (r^2=0.577, p=0.007). Meanwhile, the ratio of share buybacks and dividends to revenue rose significantly, and showed a strong linear trend (r^2=0.811, p=0.017), although the linear trend was not as steep as the ratio to R&D (**Figure 20**).

This suggests that large biopharma companies are investing their cash into share repurchases and dividends to benefit shareholders instead of investing it into R&D. Instead of reinvesting cash flow into internal R&D or even to buy new assets, these companies are prioritizing shareholder value over innovation.

One egregious example of this and its direct impact on patients is Biogen. In 2021, Biogen's drug for Alzheimer's disease, Aduhelm (aducanumab), was controversially approved with an extremely muddled history. The drug originally failed both Phase 3 trials, but upon reanalysis, one of the trials (ENGAGE) met its primary endpoint. However, the drug's clinical efficacy was questioned, and there were significant safety concerns with up to half of patients experiencing brain swelling and 17% of patients showing brain bleeds (microhemorrhages).[15] *The FDA's advisory committee voted against approval*. However, the FDA ended up approving the drug against the committee's decision (a highly unusual practice). Biogen priced the dubious drug at a whopping $56,000 a year. Estimates later showed the drug would cost Medicare alone $12 billion (36% of its budget).[16] Later, it was discovered *Biogen had extensive contact and lobbying with the FDA ahead of their approval decision*.[17] Meanwhile, instead of spending capital for R&D and additional trials, *Biogen spent $18.7 billion in share buybacks from 2018 to 2021 and $28.8 billion from 2011 to 2021*.[18] Faced by pressure from Congress, patients, and other stakeholders, Biogen pulled Aduhelm from the market in January 2024. These practices indicate a massive problem where shareholders are benefiting at the expense of patients, and corporate greed caused Biogen to improperly push a drug through the approval process (**Box 2**).

[15] FDA label.

[16] The High Price of Aduhelm's Approval: An Investigation into FDA's Atypical Review Process and Biogen's Aggressive Launch Plans Prepared by the Staffs of the Committee on Oversight and Reform and Committee on Energy and Commerce (2022).

[17] *Ibid.*

[18] Own analysis from S&P Capital IQ data.

Box 2. Biogen case study: financialized practices directly hurt innovation for patients

Timeline of Aduhelum development and problems

2007

- Biogen licenses aducanumab from Neurimmune for $380M

2015

- Biogen begins 2 Phase 3 studies of aducanumab, EMERGE and ENGAGE

2019

- March 2019: interim analyses showed **futility** that both EMERGE and ENGAGE would **miss primary endpoints.**
- October 2019: **Results changed** to show EMERGE met primary endpoint while ENGAGE **failed**
- Safety was concerning: **17% had brain bleeds**

2020

- July: Biogen submitted BLA application to FDA
- November: FDA advisory committee voted **against** approval

2021

- June: FDA approved Aduhelm under accelerated approval pathway
- Biogen priced Aduhelm at **$56,000 a year**
- December: EMA and Japan **rejected Aduhelm**

Timeline of Biogen's dubious financial and business practices

$28.8 billion in share buybacks, 2011-2021

	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	TOTAL
Buybacks ($M)	498	985	400	887	5,000	1,000	1,365	4,353	5,888	6,678	1,800	$28,835

Inappropriate contact and lobbying at the FDA

- Biogen inappropriately collaborated on a joint meeting for a briefing document for the advisory committee
- Biogen had at least 115 meetings, calls, and email exchanges with FDA in 2019, a record at FDA for any product

Tax cuts

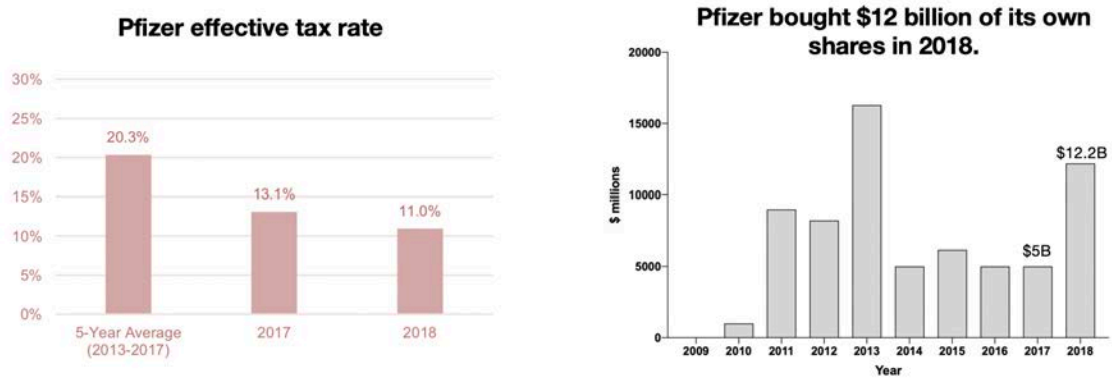
The Trump administration and Republican Congress in the US lowered corporate tax rates in 2017 under the Tax Cuts and Jobs Act (TCJA) with the claim that corporations would invest the savings, boost economic activity, and create jobs (Oxfam 2019). The TCJA has been very beneficial to pharma companies (and their shareholders). **Pfizer, for example, reported a $10.7 billion benefit in the fourth quarter of 2017 due to the tax cuts**.[19] The nonprofit group Oxfam published an analysis of pharma companies following the implementation of the TCJA, and found that the effective tax rate of major pharma companies dropped in 2018: the actual rate Pfizer paid in tax globally across all its operations dropped from 20% over the five-year average pre-TCJA down to 11%. Johnson & Johnson, and Abbott, also seem to have

[19] Pfizer 4Q18 earnings call

dropped to 16.7% and 14.2%, respectively— lower than their effective rates in both 2017 and their five-year average pre-TCJA (Oxfam 2019).

What did the biopharma companies do with the tax savings? Well, since these companies' main strategy is to maximize shareholder value, it is unlikely that any of the retained income was reinvested in R&D or jobs, as the proponents of TCJA argued. Indeed, share repurchases among major biopharma companies rose significantly from 2017 to 2018, up ~75% year over year, likely driven in part by tax savings in the US. Pfizer's corporate tax rates and share repurchases over time are shown in **Figure 21.**

Figure 21. Pfizer tax rates and share repurchases



Source: original figure based on data from SEC filings and S&P Global.

Interestingly, Pfizer—who reported a ~$10 billion benefit from the TCJA—repurchased $12 billion of its own shares in 2018. This is shown above, where Pfizer reported only an 11% tax rate compared to 20% in the prior years (data from Pfizer's public SEC filings).

4.7 Executive compensation

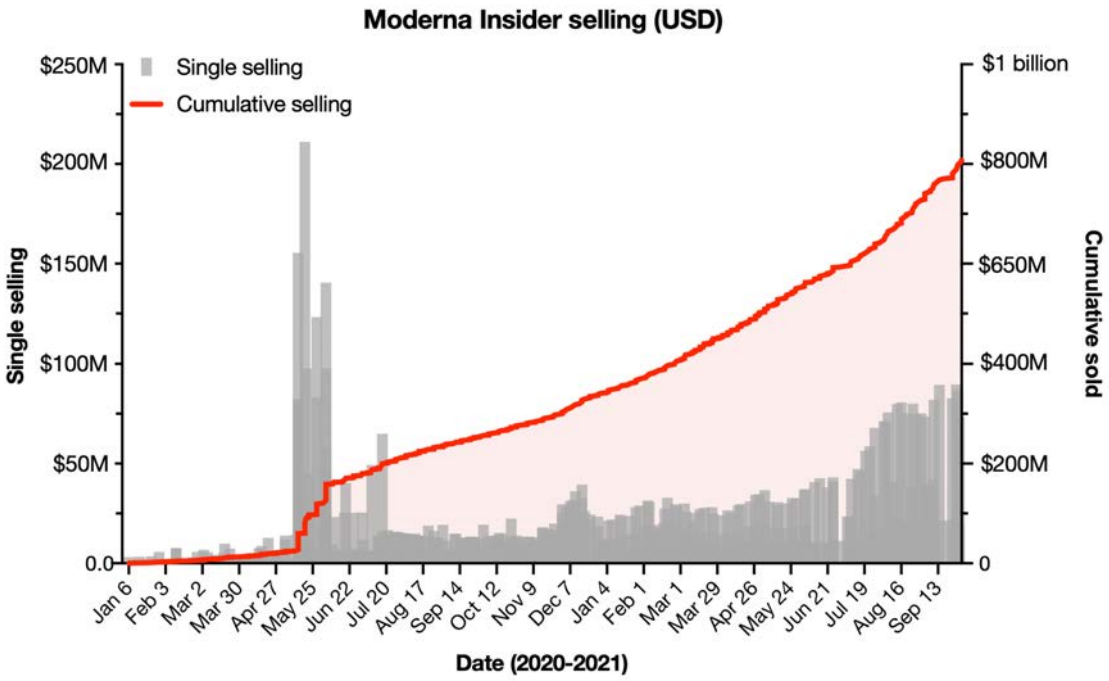
The COVID-19 pandemic has exacerbated financialization in biopharma and illustrates the need for regulation of biopharma companies to prevent them from prioritising shareholders over patients—especially after receiving significant public funding. For example, after receiving $483 million from the US government (BARDA) and $65 million in initial funding from DARPA to develop

a vaccine, Moderna's share prices rose ~650% from the beginning of the pandemic (Whitfill 2020).

Although Moderna provided a life-saving vaccine, its shareholders and executives have benefited through enormous profits based on Moderna's vaccine. For example, since January 2020, Moderna executives have pocketed over $800 million from selling shares.

The individual and cumulative insider selling of Moderna shares is highlighted in **Figure 22.** The individual sales include $290 million to Moderna's chief executive officer (CEO), $66 million to its chief financial officer (CFO), and $121 million to its chief medical officer (CMO). Moderna's CMO and CFO sold $30 million of stock following the company's May press release in 2020. The individual-level sales are represented in **Table 7**.

Figure 22. Moderna insider selling in 2020-21



Source: original figure based on data from SEC filings and S&P Global.

Table 7. Amount of Moderna shares sold by directors and executives, January 2020 to September 2021

Role	Total sold
Chief accounting officer	$ 9,866.00
Chief executive officer	$ 290,662,077.00
Chief financial officer	$ 66,934,360.00
Chief medical officer	$ 121,124,169.00
Director	$ 10,457,964.00
General counsel and secretary	$ 41,106,590.00
President	$ 157,211,476.00
Chief technical officer	$ 119,955,476.00
Total	$ 807,561,978.00

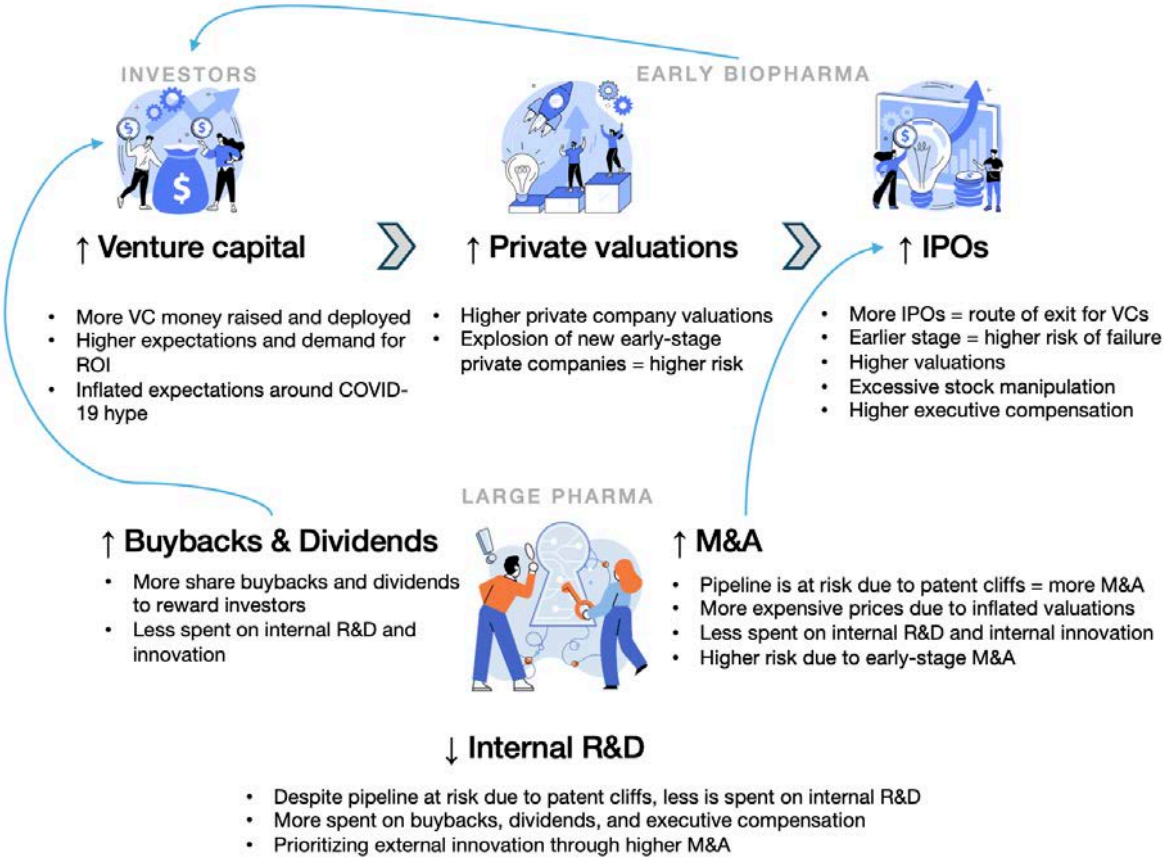
Source: SEC filings and S&P Global.

These sales are enormous compared to typical compensation and the normal pace of stock-based compensation. The reason why these insiders sold their shares is obvious: they doubt the long-term value of the company and instead are looking at short-term opportunities to profit from the company. Moving forward, we need more responsible reporting and transparency from all players in the war against COVID-19. Pharma companies need to avoid issuing press releases to pump up their stock; pharma executives with conflicts of interest shouldn't be heading the government's response for vaccine development; and there should be limits on the number of shares executives can sell after pumping up a stock with press releases. The public sector was critical to fixing the COVID-19 pandemic, but it needs to do a better job at shaping innovation responsibly and making sure biopharma companies don't misuse these funds, as they have done.

4.8. Summary

Financialization has been predominant in the biopharmaceutical industry, and this system and its effects are summarized in the graphical abstract of **Figure 23.**

Figure 23. The financialized biopharma ecosystem



In summary, the biopharma industry is heavily financialized, characterized by: (1) a high degree of venture capital financing, which has exploded in the last decade, and leads to higher numbers of IPOs at earlier stages (which leads to substantially higher risk for new investors) in order to return capital to VCs; (2) stock engineering practices in both private and public companies, including exploding valuations in the private market driven by VC investments; (3) higher M&A, driven by patent cliffs and pharma's need to replenish pipelines; (4)

increasing amounts of stock repurchases and dividends (absolute value) at the expense of innovation; and (5) stock repurchases are higher than 1.0 as a ratio of stock repurchases and dividends to internal R&D expenditures.

Nearly all these trends have increased between 2009 and 2019. More venture capital financing has flowed into biopharma, which has changed the landscape of the biopharma ecosystem, leading to drastic increases in private valuations and a substantial rise in IPOs after 2017. These IPOs have trended to much earlier stage companies, which adds substantial risk to the public market, while VCs capture returns by gaining liquidity to exit. A large portion (two-thirds in 2021) of the companies that IPO are at either preclinical or Phase 1 development, which adds substantial risk to the market, given the ultra-low rates of success of preclinical and Phase 1 drugs. Once companies are public, there is more evidence of stock engineering, where, for example, companies raise capital on positive news to minimize dilution.

Furthermore, large pharma has increased M&A spend over time due to looming patent expirations and pharma's need to refill the pipeline. Due to the inflated IPO and public markets, and companies at the relatively early stages of clinical development, acquisition prices have trended upwards over time, with capital flowing back to VCs, and pharma taking on the risk of development.

At the same time, pharma has increasingly spent more on share repurchases and dividends, both in absolute terms, and relative to internal R&D spend, which has led to lower internal R&D spend, and therefore higher rates of looking externally for innovation (i.e. more M&A). The stock repurchases are in some cases egregious—for example, Biogen, who spent enormous amounts on share repurchases, while exhibiting dangerous behavior to bring an ineffective drug to the market for Alzheimer's.

Additionally, COVID-19 has led to egregious practices in stock engineering and executive compensation after firms received large taxpayer-funded investments from multiple government agencies. In my paper with Professor Mazzucato on policy directions for ARPA-H, we offered several policy

suggestions (Whitfill and Mazzucato 2023) based on taxpayer-funded innovation and financialized pharma companies. Although there is little precedent for this, ARPA-H and other agencies could encourage or require pharma company profits to be reinvested into R&D once innovation has succeeded. In pursuit of a similar goal, the Clinton administration explored capping the federal tax deductions companies could take for executive pay (Bank, Cheffins et al. 2016). That strategy was rolled back, but ARPA-H might look for other ways to restrict egregious financialized practices.

There is also little regulation of IPOs and private companies with VCs enjoying free reign to increase valuations; IPO companies at super risky stages capturing returns at the expense of risk to the public markets; and pharma companies looking for M&A. In the future, there should be more scrutiny from regulatory agencies such as the Securities and Exchange Commission (SEC) on early-stage IPOs that add risk to public markets.

The next chapter of my thesis examines how these trends affect innovation in the biopharmaceutical industry.

Chapter 5. Empirical studies of finance and innovation systems in biopharma

To date, there have been few empirical analyses of the actual effect financialization has on *innovation* in biopharma. While many have described the problems of financialization in biopharma, such as prioritization of profits, drug price increases, rising executive compensation, stock price manipulation, inequitable profit distribution, profiting from taxpayer-funded innovation, and corporate greed during the pandemic (Lazonick and Tulum , Busfield 2020, Collington 2020, Keenan, Monteath et al. 2023, Roy 2023), these studies lack an examination of the *consequences* of some of these financialized business practices on innovation, beyond corporate greed and prioritizing profits over patients. The effect of financialization on innovation in biopharma firms remains unclear.

While some case studies (e.g. in Tulum, Andreoni, and Lazonick's recent book *From Financialisation to Innovation in UK Big Pharma*) have begun to look at bivariate associations between measures of financialization and innovation (Tulum, Andreoni et al. 2022), empirical studies linking the effect of financialization on innovation are lacking.

An additional gap in the literature when considering the effect of financialization is the approach to measuring innovation. For example, a 2022 study by Liu et al. measured innovation by a ratio of net increment of intangible assets to total assets, which inadequately captures pharmaceutical innovation such as the innovativeness of new medicines (Liu, Zhao et al. 2022).

The goal of this chapter is to address these major gaps in the literature with two primary objectives: (1) to measure innovation more comprehensively in biopharma firms and (2) to provide empirical analyses to show relationships between innovation and financial strategies in biopharma firms. The latter goal is achieved through a variety of approaches, including bivariate statistics, as well as more complex approaches such as multivariable regressions and

structural equation modeling to account for the complexities of the innovation ecosystem in biopharma. Using this approach allows an examination of the causality of financial strategies (e.g. R&D expenditures, M&A strategy, share buybacks, dividends, executive compensation) on innovation.

In this chapter, I also look at R&D efficiency trends in the biopharma industry, which has been a key area of concern in terms of the industry's productivity, and I consider factors that could explain those R&D efficiency trends.

5.1 Company characteristics included in the sample

Inclusion criteria included firms that are primarily biotech or pharmaceutical companies that are publicly traded on a major stock exchange. The firms must have been public since at least 2011. The top 50 biopharma firms by 2021 revenues were then included in the analysis.

Exclusion criteria included firms that are headquartered in China (due to lack of public information available), medical device firms (e.g. Abbott), or companies that rose to the top 50 biopharma firms only due to COVID-19 (i.e. Moderna).

The firms included in the data sample are presented in **Figure 24**, with baseline characteristics of these firms in **Table 8.**

Figure 24. Companies included in the data sample

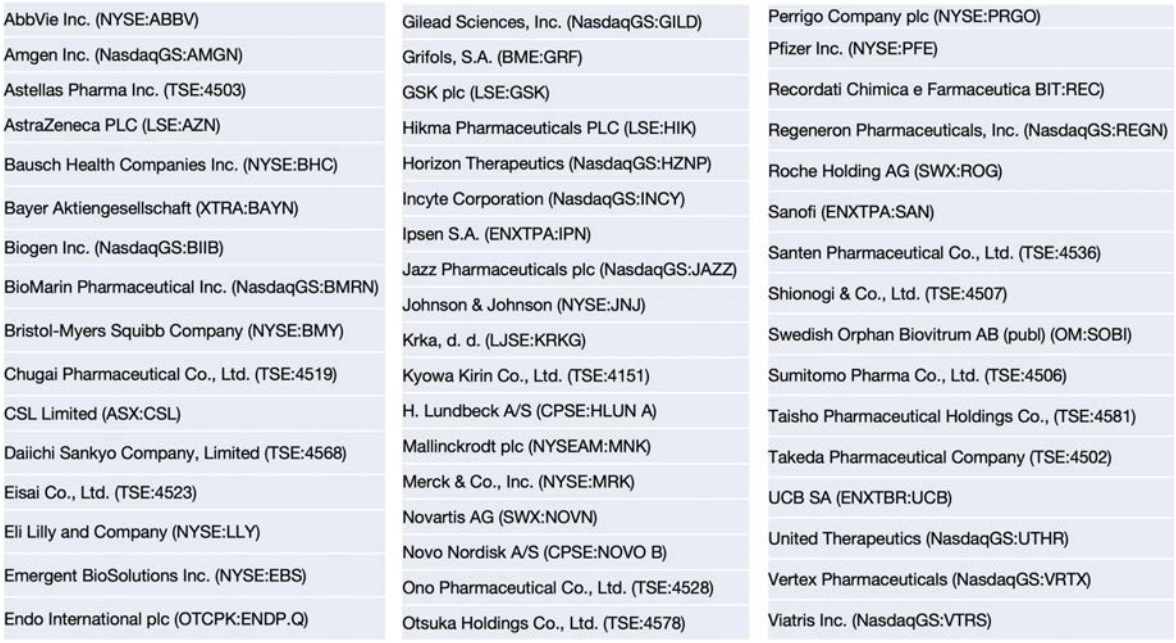


Table 8. Baseline information of firms included in the sample

Variable	N=50
Firm size (assets in 2021), mean $B USD (SD)	36.6 (49.1)
Firm age, years (SD)	88 (62.5)
Firm location	
APAC	13 (26%)
EU/UK	20 (40%)
US	17 (34%)

5.2 Revenues and R&D expenditures

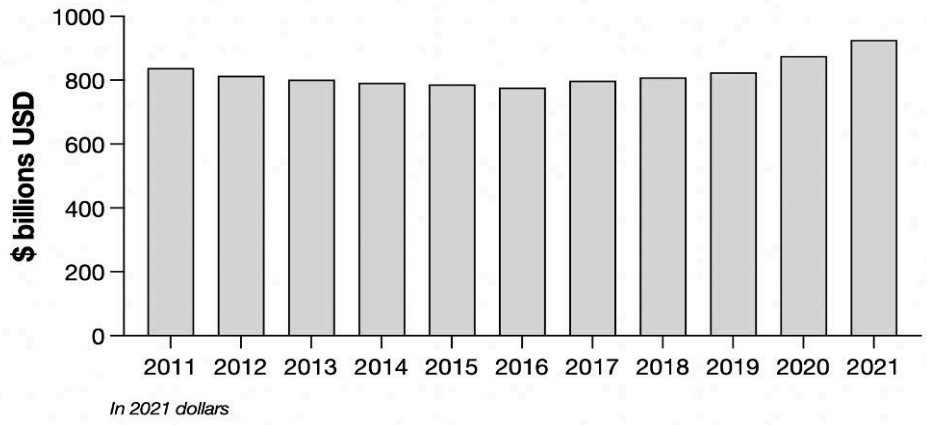
I first looked at revenues and R&D expenditures for the top 50 biopharma firms from 2011 to 2021 and calculated ratios of R&D expenditures to revenues to look for trends over time.

From 2011 to 2021, the 50 biopharma firms earned $9.05 trillion in revenues, adjusted for inflation. The top five companies with revenues were

JnJ, Roche, Pfizer, Novartis, and Bayer at $949 billion, $714 billion, $695 billion, $639 billion, and $601 billion in revenues, respectively.

The trends in revenues are presented in **Figure 25.** When adjusting for inflation, there was a slight decrease in revenues from 2011 to 2016, with an increasing trend from 2017 to 2021 and a notable increase in revenues from 2019 to 2021 (from $824.8 billion to $926.3 billion, an increase of 12.3%). The five firms with the largest percent increases from 2019-2021 were Horizon Pharma (130%), Regeneron (127%), Vertex (68%), BMS (64%), and Abbvie (56%).

Figure 25. Revenues by top 50 biopharma firms, 2011-2021

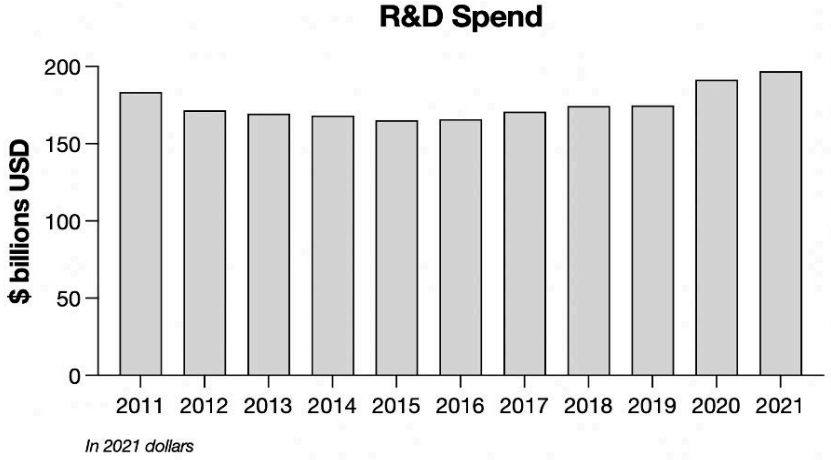


Source: original figure based on data from SEC filings and S&P Global.

The 50 biopharma firms spent $1.50 trillion in R&D expenditures from 2011 to 2021. The five firms with the highest spend during this period were Roche, JnJ, Novartis, Merck, and Pfizer at $135.8 billion, $123.6 billion, $111 billion, $108 billion, and $106 billion in R&D expenditures, respectively.

Trends in R&D expenditures are included in **Figure 26.** Interestingly, when adjusting for inflation, R&D spend for the 50 firms was flat between 2012 and 2018, with an increasing trend in R&D spend between 2018 and 2021 (from $137.8 billion to $160.0 billion, an increase of 16%).

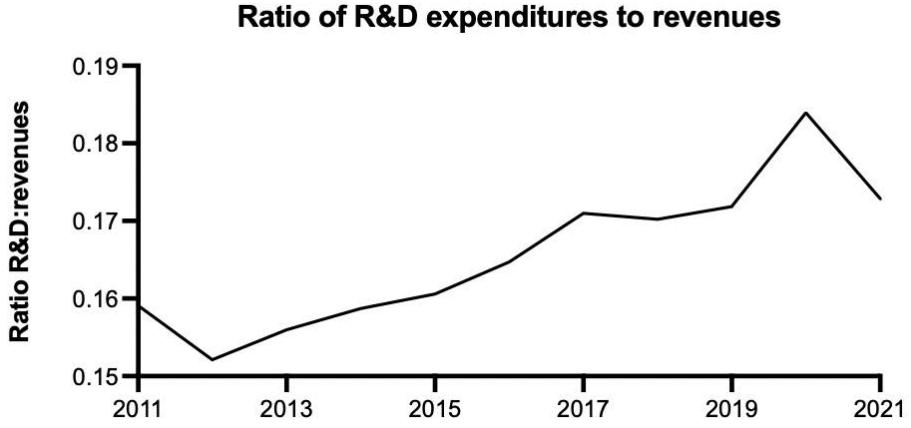
Figure 26. R&D expenditures by top 50 biopharma firms, 2011-2021



Source: original figure based on data from SEC filings and S&P Global.

When looking at the ratio of R&D expenditures to revenues of the top 50 firms over time, there has been an increase from 0.16 in 2011 to 0.17 in 2021, peaking in 2020 at 0.18 (likely due to R&D investments into COVID-19). These data are reflected in **Figure 27.**

Figure 27. Ratio of R&D expenditures to revenues over time, 2011-2021



Source: original figure based on data from SEC filings and S&P Global.

Baseline characteristics of each firm, including headquarters, ln(firm size), age, revenues, R&D expenditures, and ratio of R&D expenditures to revenues, are presented in **Table 9**.

Table 9. Baseline characteristics of biopharma firms by revenue, 2011-2021 (adjusted to 2021 dollars)

Firm	HQ	ln(firm size)	Age (years)	Revenues ($M USD)	R&D expenditures ($M USD)	Ratio: R&D to revenues
JnJ	USA	12.1	135	$949,074	$123,569	0.13
Roche	EU	11.5	125	$713,523	$135,771	0.19
Pfizer	USA	12.1	172	$695,247	$106,453	0.15
Novartis	EU	11.8	98	$638,900	$110,987	0.17
Bayer	EU	11.8	158	$600,933	$61,512	0.10
Merck	USA	11.6	130	$539,922	$107,991	0.20
Sanofi	EU	11.8	17	$531,999	$78,585	0.15
GSK	EU	11.6	21	$488,433	$71,376	0.15
AbbVie	USA	11.9	133	$356,003	$53,983	0.15
AstraZeneca	EU	10.2	22	$335,803	$67,205	0.20
BMS	USA	11.6	134	$296,739	$68,430	0.23
Eli Lilly	USA	10.8	145	$281,609	$67,383	0.24
Gilead	USA	11.1	34	$270,690	$41,209	0.15
Amgen	USA	9.9	41	$269,091	$49,054	0.18
Takeda	JP	11.7	240	$236,910	$50,598	0.21
Novo Nordisk	EU	10.3	98	$206,584	$27,123	0.13
Astellas	JP	9.9	16	$144,660	$25,622	0.18
Biogen	USA	10.1	43	$128,350	$26,403	0.21
Viatris	USA	9.3	60	$126,403	$6,912	0.05
Daiichi Sankyo	JP	9.3	122	$120,276	$24,821	0.21
CSL	AU	9.8	105	$82,879	$7,618	0.09
Otsuka	JP	8.3	100	$79,201	$17,379	0.22
Eisai	JP	8.5	80	$77,028	$16,362	0.21
Bausch	USA	10.3	168	$67,820	$3,860	0.06
Chugai	JP	9.5	96	$65,535	$10,385	0.16
Regeneron	USA	10.1	33	$63,127	$20,544	0.33
UCB	EU	9.7	93	$62,228	$16,353	0.26
Grifols	EU	10.0	81	$56,737	$3,068	0.05
Perrigo	EU	9.3	134	$53,469	$1,921	0.04
Sumitomo	JP	9.4	16	$50,506	$10,035	0.20
Kyowa Kirin	JP	9.0	26	$40,805	$5,966	0.15
Shionogi	JP	9.1	143	$37,553	$6,682	0.18
Taisho	JP	9.0	109	$34,613	$2,745	0.08
Vertex	USA	9.2	32	$33,823	$15,281	0.45
Mallinckrodt	EU	7.7	154	$33,182	$3,003	0.09
Lundbeck	EU	8.6	106	$32,267	$6,138	0.19
Ipsen	EU	8.6	92	$27,622	$4,124	0.15
Ono	JP	8.8	304	$24,383	$6,447	0.26
Hikma	EU	8.4	43	$21,759	$1,056	0.05
Santen	JP	8.2	131	$21,472	$2,428	0.11
Krka	EU	8.0	67	$19,186	$1,817	0.09
Jazz	EU	9.4	16	$18,650	$2,116	0.11
Endo	EU	7.9	24	$18,171	$1,863	0.10
Recordati	EU	8.1	95	$17,226	$1,450	0.08
United Therapeutics	USA	8.6	25	$17,066	$4,290	0.25
Incyte	USA	8.0	19	$15,668	$10,417	0.66
BioMarin	USA	8.7	24	$13,855	$7,576	0.55
Horizon	EU	7.9	16	$12,014	$953	0.08
SOBI	EU	8.6	82	$10,009	$1,340	0.13
Emergent	USA	7.1	23	$8,830	$1,842	0.21

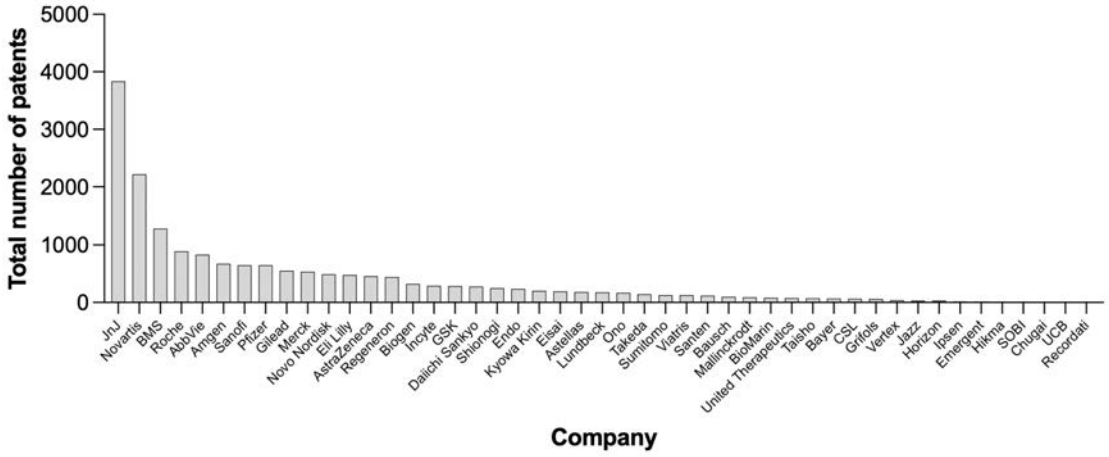
5.3 Measuring innovation

As described in Chapter 3, I used several variables to measure biopharma firms' innovation. These included weighted patent data (from 2011 to 2019, as described in Chapter 3), total new drug approvals by the FDA, new molecular entities approved by the FDA, as well as the innovativeness of drugs, measured by ASMR values.

5.3.1 Patents

First, I looked at total patent counts by firm from 2011 to 2019. Simple patent counts are often used as a measure of R&D output, but are less of a measure of innovation (Nagaoka, Motohashi et al. 2010). However, I present simple patent counts by firm in **Figure 28.** The five firms with the highest number of total patents published from 2011 to 2019 are JnJ, Novartis, BMS, Roche, and Abbvie (3,836, 2,218, 1,273, 890, and 830, respectively). Three firms (Krk, Otsuka, and Perrigo) were missing patent data from the WRDS and COMPUSTAT databases.

Figure 28. Simple patent count by firm

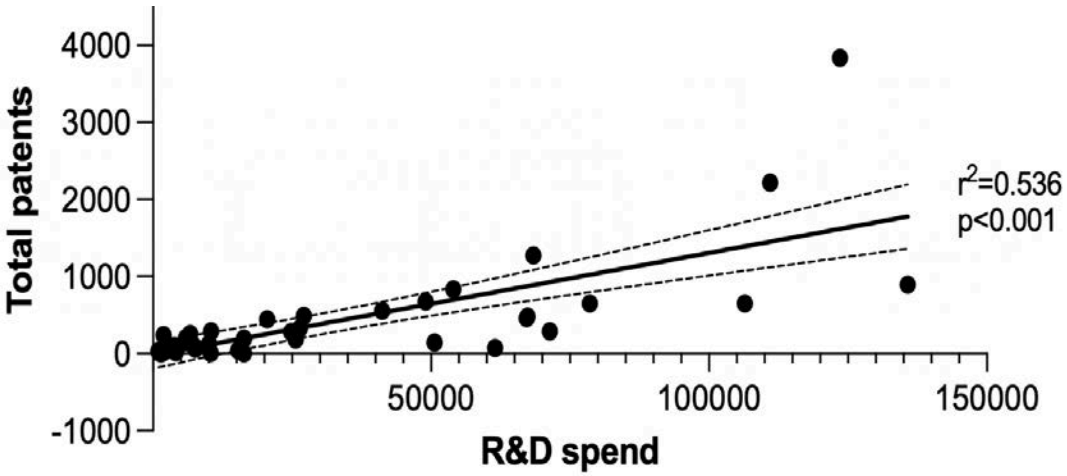


Source: original figure based on data from COMPUSTAT.

To illustrate how simple patent counts are a function of R&D output, I analyzed the relationship between R&D expenditures and total number of patents. There

was a linear relationship between the two variables (r^2=0.536, p<0.001), shown in **Figure 29.**

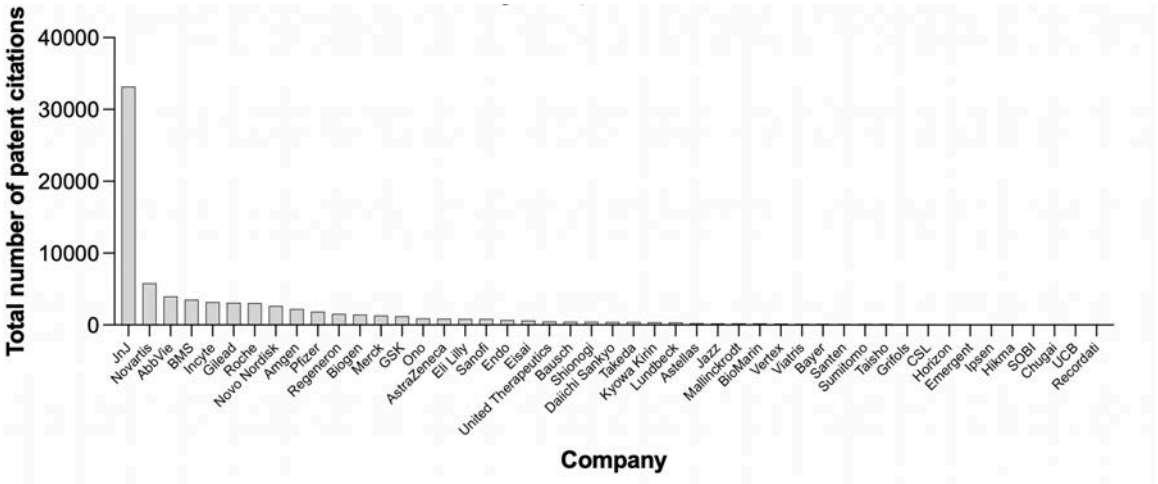
Figure 29. Simple patent count by R&D spend



Source: original figure based on data from SEC filings, S&P Global, and COMPUSTAT.

I then looked at the total number of patent citations by firm from 2011 to 2019. JnJ had by far the most patent citations, at 33,196, compared to the next highest firm, Novartis, at 5,815 patent citations. These are presented in **Figure 30.**

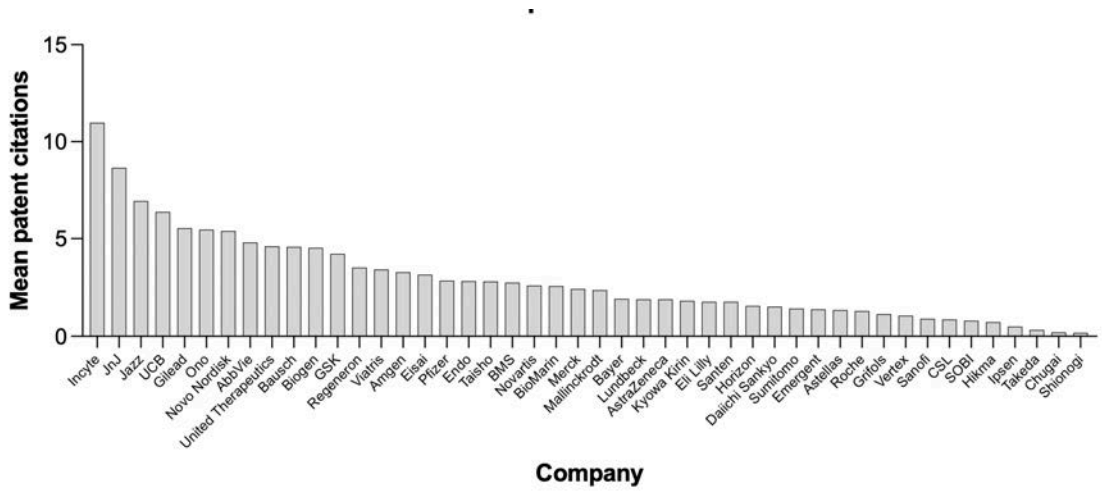
Figure 30. Total patent citations by firm



Source: original figure based on data from COMPUSTAT.

I then looked at the mean patent citations by firm, which is a measure of the total patent citations divided by the total number of patents for each firm. Interestingly, this turned up unusual suspects: smaller firms such as Incyte, Jazz Pharmaceuticals, UCB, and Gilead made the top five. The number of mean citations by firm is presented in **Figure 31**.

Figure 31. Mean weighted patent citations by firm



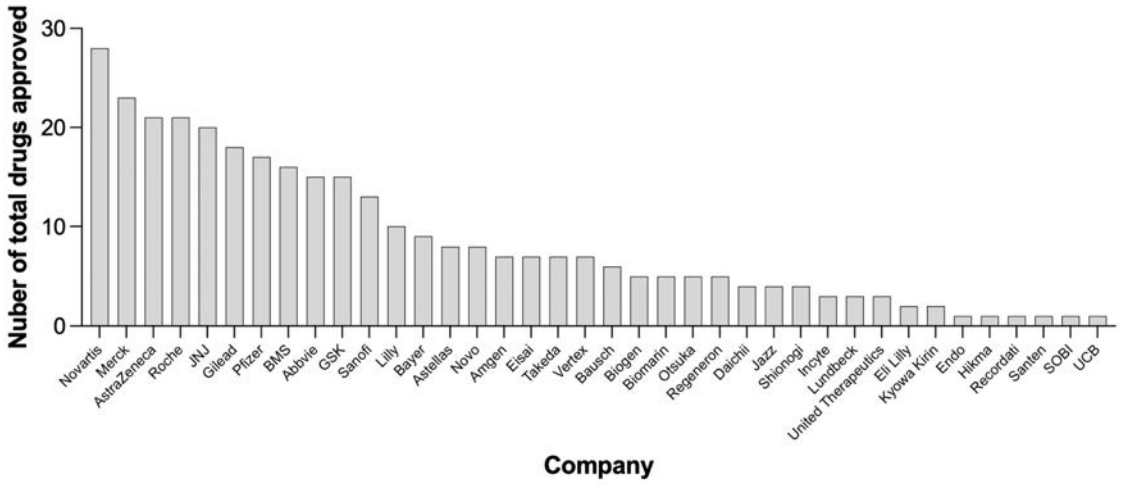
5.3.2 New drug approvals and their innovativeness

For another dimension of innovation, I looked at the biopharma firms' new drug approvals and new chemical/biological entities (NCE or NBE, respectively), approved in the US by the FDA, as well as their innovativeness, measured by France's HTA ASMR values.

There was a total of 330 drug approvals by the FDA from the top 50 biopharma firms from 2011 to 2021. Of these, 178 (54%) were classified as NCEs or NBEs.

First, looking at total number of drug approvals, the top five firms with the highest number from 2011 to 2021 were Novartis, Merck, AstraZeneca, Roche, and JnJ, with 28, 23, 21, 21, and 20 new drug approvals, respectively (**Figure 32**).

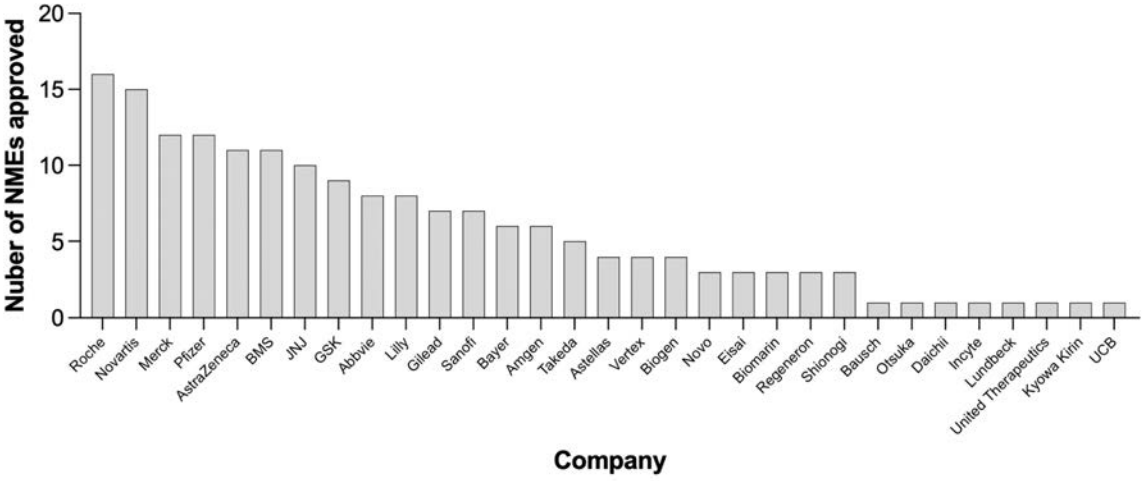
Figure 32. Total number of FDA drug approvals, 2011-2021, by firm



Source: original figure based on data from FDA.

Then, looking at the number of NMEs or NBEs, the top five firms with the highest number of NME or NBE approvals from 2011 to 2021 were Roche, Novartis, Merck, Pfizer, and AstraZeneca with 16, 15, 12, 12, and 11 approvals, respectively (**Figure 33**).

Figure 33. Total number of FDA NME or NBE approvals, 2011-2021, by firm

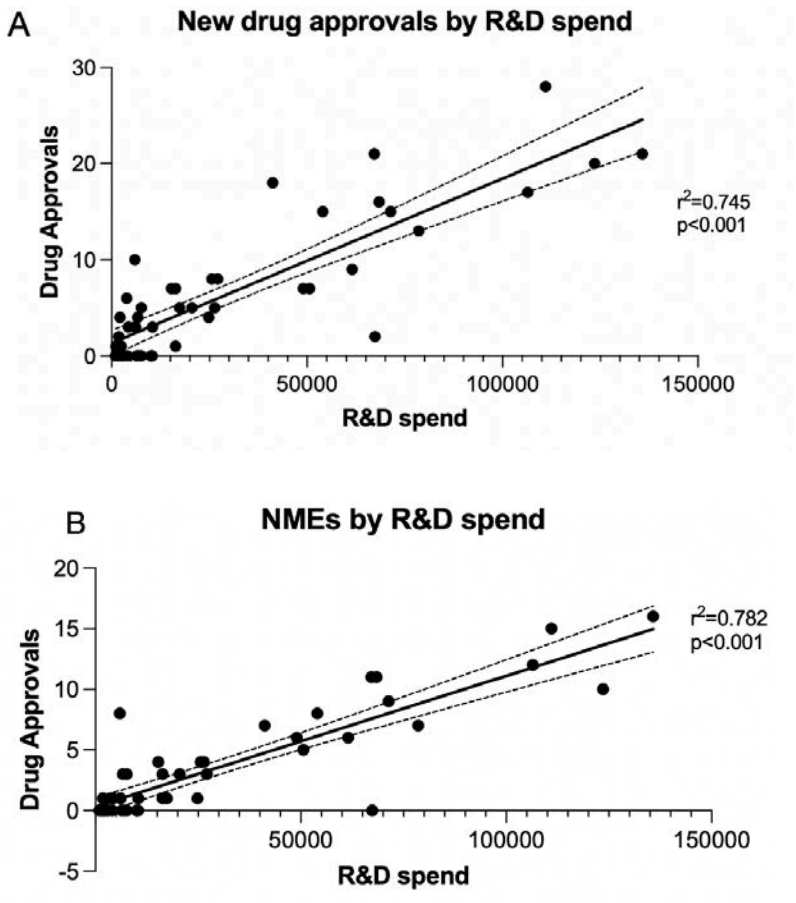


Source: original figure based on data from FDA.

5.3.3 New drug approvals by R&D expenditure

Next, I looked at new drug approvals, and NME or NBE approvals, by R&D expenditure. Unsurprisingly, a strong linear relationship emerged with more drug and NCE/NCE approvals associated with higher R&D expenditures (r^2 = 0.745, p<0.001 and r^2 = 0.782, p<0.001, respectively) (**Figures 34, A and 34 B,** respectively).

Figure 34. Total new drug approvals and NME/NBE approvals by R&D expenditures



Source: original figure based on data from FDA, SEC filings, and S&P Global.

5.3.4 Medical innovation over time

Next, I used the French National Authority for Health (Haute Autorité de Santé*)* evaluation of the added benefit of new drugs (Le Pen 2018) using the ASMR

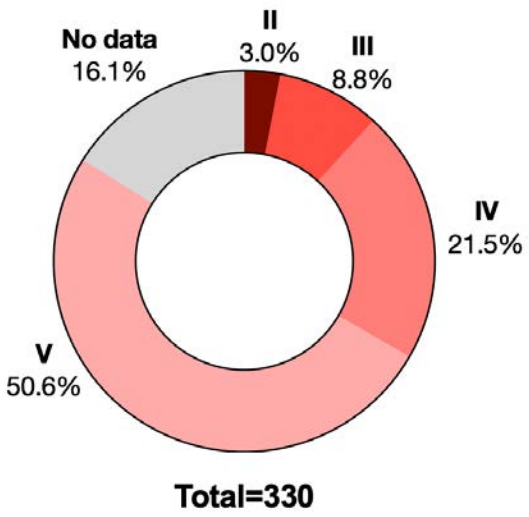
(amélioration du service médical rendu) scale. The ASMR scale ranks each drug compared to existing treatment options. There are five ranks:

- ASMR I: major improvement
- ASMR II: important improvement
- ASMR III: moderate improvement
- ASMR IV: minor improvement
- ASMR V: no improvement

Thus, the lower the ASMR value, the more innovative the drug is.

Of the 330 FDA drug approvals from 2011 to 2021 from the top 50 biopharma firms, data were available for 227 drugs. The majority (50.6%) were ASMR V, 22% were ASMR IV, 8.8% were ASMR III, and 3% were ASMR II. There were no drugs that received a ASMR value of I. (**Figure 35**)

Figure 35. ASMR values for drug approvals, 2011-2021

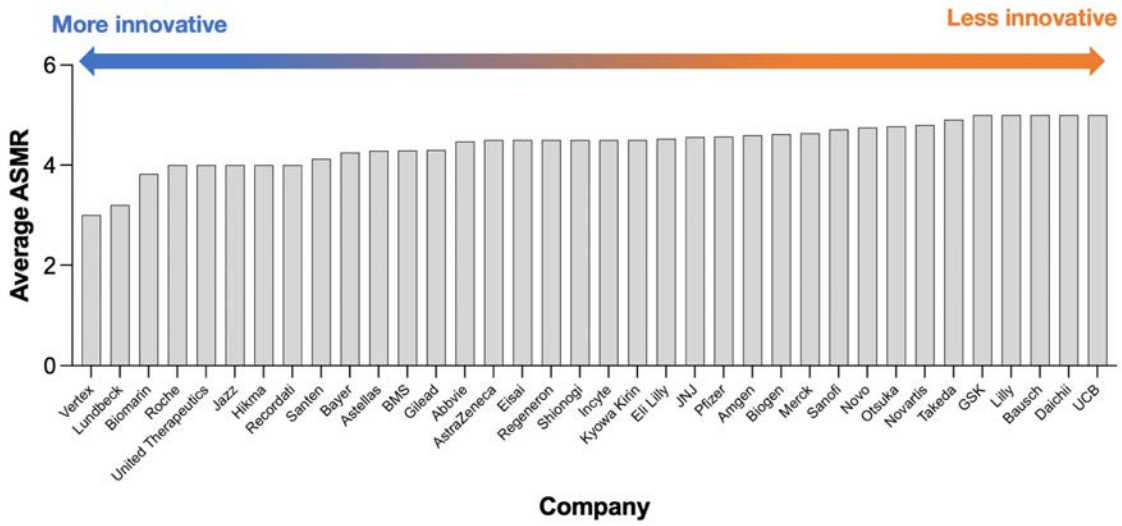


Source: original figure based on data from the French National Authority for Health and FDA.

Interestingly, looking at the mean ASMR values turned up unusual suspects in the top three firms with the most innovative drugs: Vertex, Lundbeck, and Biomarin, with mean ASM values of 3.0, 3.2, 3.8, respectively. Vertex and

Biomarin both focus on rare diseases, which may have driven the ASMR scores. The mean ASMR value of drugs by firm is presented in **Figure 36**. Innovation measures by firm are presented in **Table 10.**

Figure 36. Mean ASMR values by biopharma firm, 2011-2021



Source: original figure based on data from the French National Authority for Health and FDA.

Table 10. Innovation measures by biopharma firm

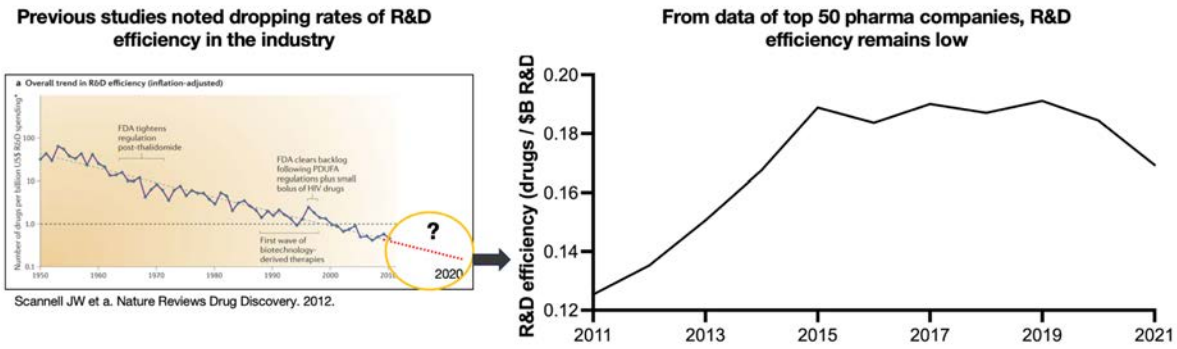
Company	Total patents	Patent citations	Mean patent citations	Drug Approvals	NME/NBEs	Mean ASMR
AbbVie	830	3988	4.80	15	8	4.30
Amgen	673	2229	3.31	7	6	4.57
Astellas	182	246	1.35	8	4	4.25
AstraZeneca	458	872	1.90	21	11	4.47
Bausch	99	453	4.58	6	1	5.00
Bayer	70	135	1.93	9	6	4.13
Biogen	321	1456	4.54	5	4	4.60
BioMarin	82	213	2.60	5	3	3.20
BMS	1273	3529	2.77	16	11	4.29
Chugai	5	1	0.20	0	0	
CSL	63	55	0.87	0	0	
Daiichi Sankyo	278	424	1.53	4	1	5.00
Eisai	194	616	3.18	7	3	4.50
Eli Lilly	478	854	1.79	2	0	4.50
Emergent	15	21	1.40	0	0	
Endo	237	674	2.84	1	0	
Gilead	554	3073	5.55	18	7	4.29
Grifols	62	71	1.15	0	0	
GSK	285	1202	4.22	15	9	4.91
Hikma	11	8	0.73	1	0	4.00
Horizon	30	47	1.57	0	0	
Incyte	289	3172	10.98	3	1	4.50
Ipsen	18	9	0.50	0	0	
Jazz	32	222	6.94	4	0	4.00
JnJ	3836	33196	8.65	20	10	4.53
Krka			0.00	2	1	4.50
Kyowa Kirin	203	372	1.83	10	8	5.00
Lundbeck	177	338	1.91	3	1	3.00
Mallinckrodt	91	217	2.38	0	0	
Merck	536	1310	2.44	23	12	4.62
Novartis	2218	5815	2.62	28	15	4.78
Novo Nordisk	489	2637	5.39	8	3	4.71
Ono	168	919	5.47	0	0	
Otsuka				5	1	4.75
Perrigo				0	0	
Pfizer	647	1854	2.87	17	12	4.56
Recordati	1	0	0.00	1	0	4.00
Regeneron	442	1565	3.54	5	3	4.50
Roche	890	3060	1.30	21	16	3.82
Sanofi	649	846	0.91	13	7	4.64
Santen	117	106	1.78	1	0	4.00
Shionogi	250	446	0.18	4	3	4.50
SOBI	11	2	0.81	1	0	5.00
Sumitomo	127	103	1.43	0	0	
Taisho	72	103	2.83	0	0	
Takeda	143	405	0.33	7	5	4.80
UCB	3	1	6.38	1	1	5.00
United Therapeutics	78	498	4.61	3	1	4.00
Vertex	41	189	1.06	7	4	3.00
Viatris	127	135	3.44	0	0	

5.4 R&D efficiency and R&D intensity

A key challenge in the biopharma industry is R&D productivity, defined as ratio of drug approvals to R&D expenditure. R&D productivity has been widely documented as declining in the industry (Schuhmacher, Hinder et al. 2023). A key 2012 study in *Nature Reviews Drug Discovery* by Scannell et al. noted a precipitous drop in R&D efficiency (defined as number of drugs per $1 billion USD of R&D spending) over the decades from 1950 to 2010 (Scannell, Blanckley et al. 2012), dropping below 1.0 around the year 2000.

I sought to look at R&D efficiency using the sample of the top biopharma firms from 2011 to 2021. The results showed that R&D efficiency among the top 50 biopharma firms was well below the 1 drug per $1 billion of R&D spend: from 2011 to 2015, there was a slight rise in R&D efficiency among my sample of biopharma firms (0.12 to 0.19, respectively). However, this dropped somewhat from its peak of 0.19 in 2019 to 0.17 In 2021 (Figure 37).

Figure 37. R&D efficiency from prior decades compared to top 50 biopharma firms, 2011-2021

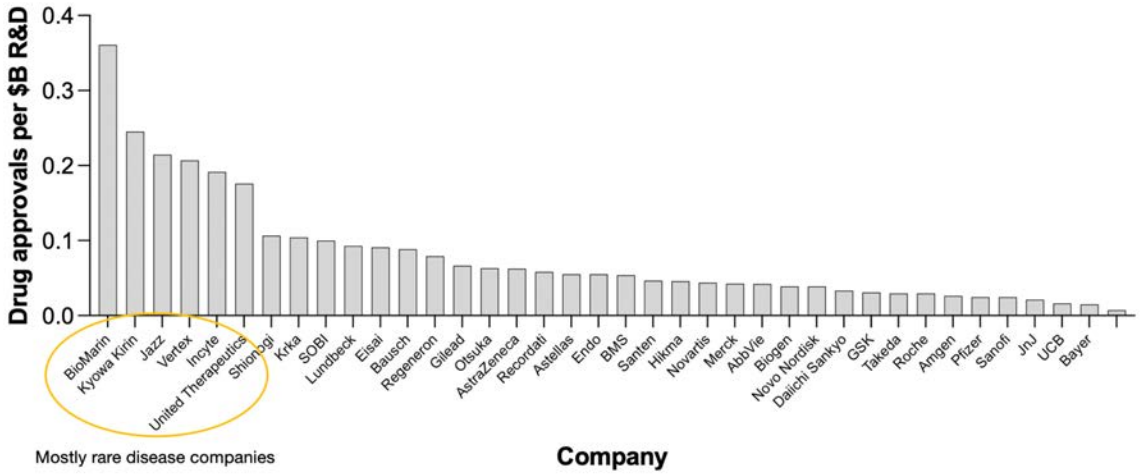


Source (right): original figure based on data from SEC filings and S&P Global.

I then looked at R&D efficiency by biopharma firm (**Figure 38**). This analysis revealed that the firms with the highest R&D efficiency tended to be smaller firms that often focus on rare diseases. The biopharma firms with the highest R&D efficiency included Biomarin (a firm focused primarily on rare diseases), followed by Kyowa Kirin, Jazz Pharmaceuticals, Vertex, Incyte, and United Therapeutics, with R&D efficiency values >0.1. Biomarin's R&D efficiency was

0.36 drug approvals per $1 billion of R&D spend. Interestingly, the largest companies by revenue had lower R&D efficiency (e.g. JnJ at 0.02, Pfizer at 0.02, Amgen at 0.03, and Roche at 0.03 drug approvals per $1 billion of R&D spend).

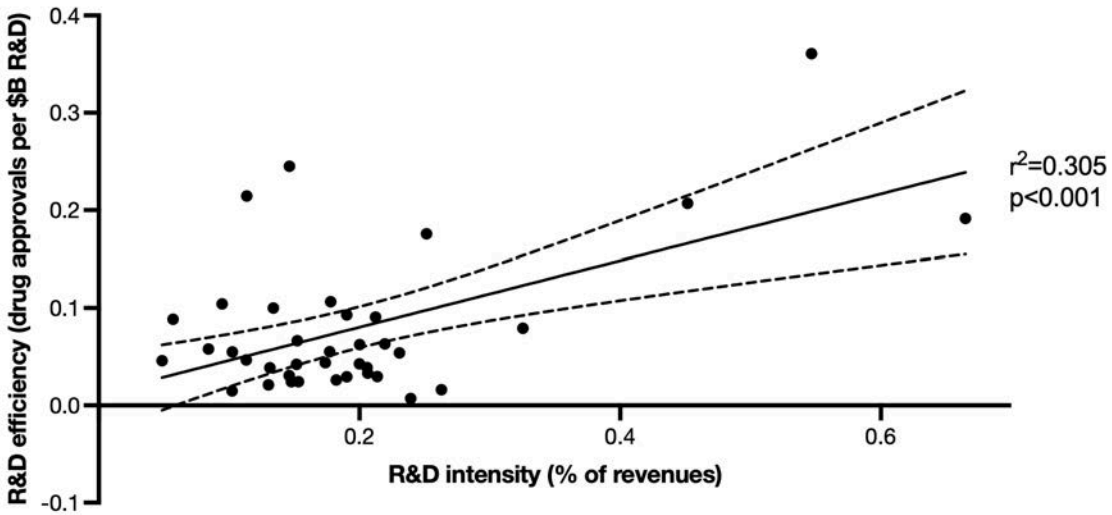
Figure 38. R&D efficiency by biopharma firm, 2011-2021



Source: original figure based on data from SEC filings and S&P Global.

I then looked at R&D efficiency by R&D intensity (defined as the ratio of R&D expenditures divided by revenues). There was a weak but significant linear trend of higher R&D intensity to higher R&D efficiency (r^2=0.305, $p<0.001$) (**Figure 39**).

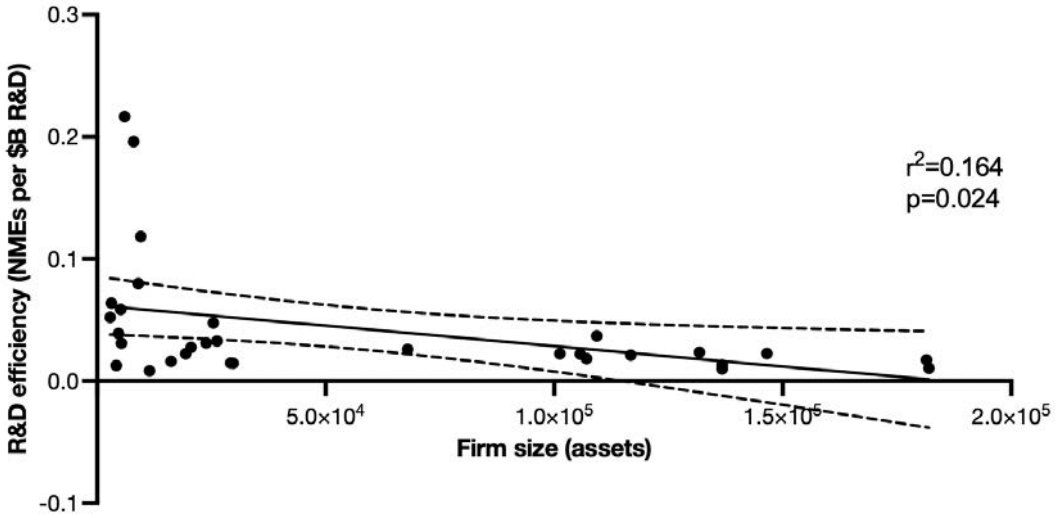
Figure 39. R&D efficiency by R&D intensity by firm, 2011-2021



Source: original figure based on data from SEC filings and S&P Global.

Additionally, I looked at R&D efficiency by firm size (measured by total assets in 2021) and found that there was an inverse linear relationship between firm size and R&D efficiency (**Figure 40**). The higher firm sizes were associated with lower R&D efficiency (r^2=0.164, p=0.024).

Figure 40. R&D efficiency by firm size, 2011-2021



Source: original figure based on data from SEC filings and S&P Global.

R&D efficiency and intensity for each biopharma firm are presented in **Table 11**.

Table 11. R&D efficiency and intensity

Firm	R&D efficiency (drug approval per $B R&D)	R&D intensity (R&D/ revenue)	R&D intensity (patents per $B R&D)	R&D intensity (patent citations per $B R&D)
BioMarin	0.361	0.55	10.82	28.11
Kyowa Kirin	0.245	0.15	34.03	62.36
Jazz	0.214	0.11	15.12	104.92
Vertex	0.207	0.45	2.68	12.37
Incyte	0.191	0.66	27.74	304.49
United Therapeutics	0.176	0.25	18.18	116.08
Shionogi	0.107	0.18	37.42	66.75
Krka	0.104	0.09		
SOBI	0.100	0.13	8.21	1.49
Lundbeck	0.093	0.19	28.84	55.07
Eisai	0.091	0.21	11.86	37.65
Bausch	0.088	0.06	25.65	117.36
Regeneron	0.079	0.33	21.51	76.18
Gilead	0.066	0.15	13.44	74.57
Otsuka	0.063	0.22		
AstraZeneca	0.063	0.20	6.81	12.98
Recordati	0.058	0.08	0.69	0.00
Astellas	0.055	0.18	7.10	9.60
Endo	0.055	0.10	127.18	361.69
BMS	0.054	0.23	18.60	51.57
Santen	0.047	0.11	48.19	43.66
Hikma	0.046	0.05	10.41	7.57
Novartis	0.044	0.17	19.98	52.39
Merck	0.043	0.20	4.96	12.13
AbbVie	0.042	0.15	15.38	73.87
Biogen	0.039	0.21	12.16	55.15
Novo Nordisk	0.039	0.13	18.03	97.22
Daiichi Sankyo	0.033	0.21	11.20	17.08
GSK	0.031	0.15	3.99	16.84
Takeda	0.030	0.21	2.83	8.00
Roche	0.029	0.19	6.56	22.54
Amgen	0.026	0.18	13.72	45.44
Pfizer	0.024	0.15	6.08	17.42
Sanofi	0.024	0.15	8.26	10.77
JnJ	0.021	0.13	31.04	268.64
UCB	0.016	0.26	0.18	0.06
Bayer	0.015	0.10	1.14	2.19
Eli Lilly	0.007	0.24	7.09	12.67
Chugai	0.000	0.16	0.48	0.10
CSL	0.000	0.09	8.27	7.22
Emergent	0.000	0.21	8.14	11.40
Grifols	0.000	0.05	20.21	23.15
Horizon	0.000	0.08	31.49	49.34
Ipsen	0.000	0.15	4.37	2.18
Mallinckrodt	0.000	0.09	30.30	72.26
Ono	0.000	0.26	26.06	142.55
Perrigo	0.000	0.04		
Sumitomo	0.000	0.20	12.66	10.26
Taisho	0.000	0.08	26.23	37.53
Viatris	0.000	0.05	18.37	19.53

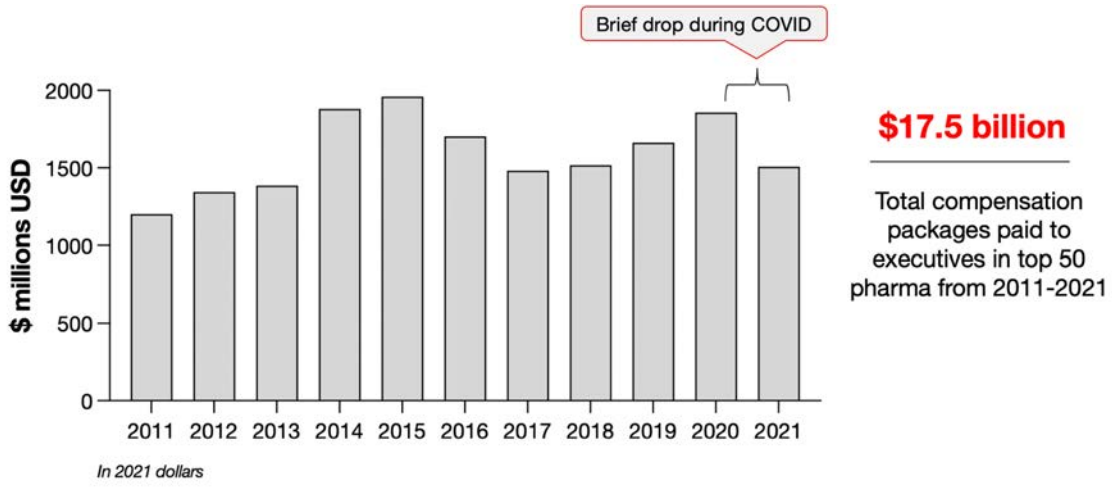
5.5 Trends in financialization

Next, I looked at various measures of financialization for the top 50 biopharma firms, including (1) executive compensation; (2) share buybacks; and (3) dividends from 2011 to 2021.

In total, **the top 50 biopharma firms spent $1.56 trillion across these measures from 2011 to 2021**. Meanwhile, the same firms spent $1.50 trillion in R&D expenditures during the same period, representing a ratio of 1.04 of financialized expenditures to R&D.

For executive compensation, the top 50 biopharma firms spent $17.5 billion in total compensation packages to executives (directors, executives, and officers). In 2021, this spend was $1.51 billion in executive compensation for 50 biopharma firms. There was a drop between 2020 and 2021, from $1.86 billion to $1.51 billion, respectively, possibility due to COVID-related dynamics. When adjusting for inflation, executive compensation peaked in 2015 at $1.96 billion (**Figure 41**).

Figure 41. Executive compensation across top 50 biopharma firms, 2011-2021

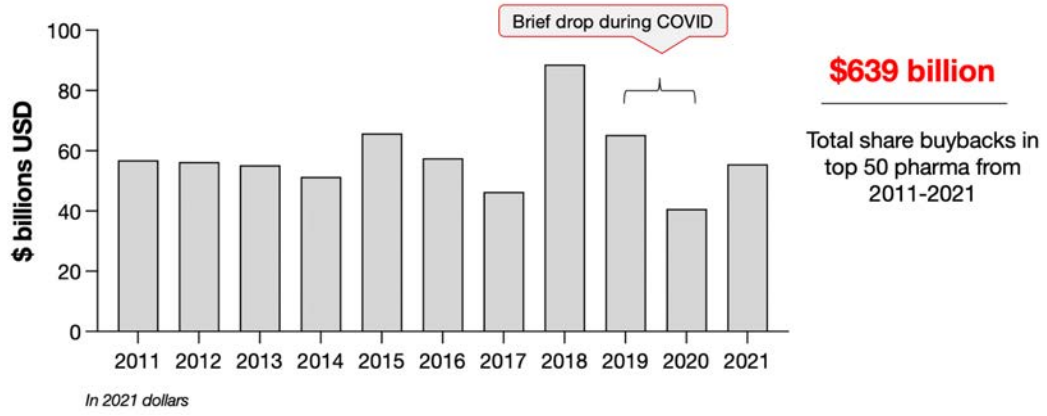


Source: original figure based on data from SEC filings and S&P Global.

I also looked at executive compensation (as a ratio of $1 million of executive compensation to $1 billion in revenues) and found several major outliers: Horizon Therapeutics at 48.2, United Therapeutics at 39.9, Endo Pharmaceuticals at 31.7, Regeneron at 27.7, Incyte at 25.9, Vertex at 22.8, Jazz Pharmaceuticals at 22.0, Emergent at 16.4, and Mallinckrodt at 11.2. The rest of the firms had values under 10 for $1 million of executive compensation to $1 billion in revenues.

Next, I looked at share buybacks across the top 50 biopharma firms. From 2011 to 2021, these firms spent $639 billion in share buybacks. There was not a strong trend; spend on share buybacks peaked in 2018 at $88.2 billion, then dropped in 2020 to the lowest levels of the decade at $40.7 billion, rebounding to $55.5 billion in 2021 (**Figure 42**).

Figure 42. Share buybacks across top 50 biopharma firms, 2011-2021

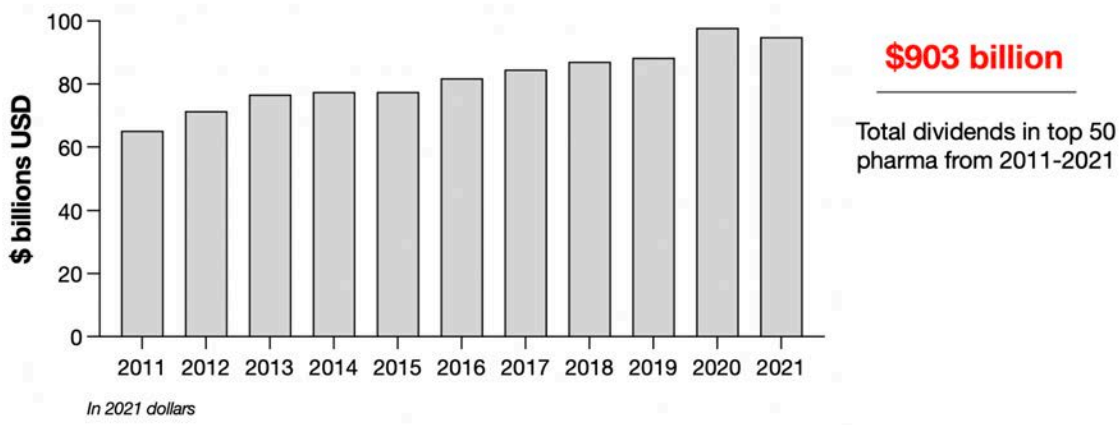


Source: original figure based on data from SEC filings and S&P Global.

The biopharma firms with the highest spend on buybacks were Pfizer, JnJ, Amgen, Merck, and Novartis at $88.4 billion, $75.9 billion, $64.3 billion, $53.4 billion, and $45.8 billion, respectively. As a ratio of share buybacks to revenues, the companies with the highest ratios were Biogen, Amgen, Regeneron, Gilead, and Novo Nordisk at 0.28, 0.27, 0.20, 0.18, and 0.17, respectively. Several

companies offered no share buybacks from 2011 to 2021, including Bayer, Eisai, Otsuka, and SOBI.

Figure 43. Total dividends across top 50 biopharma firms, 2011-2021



Source: original figure based on data from SEC filings and S&P Global.

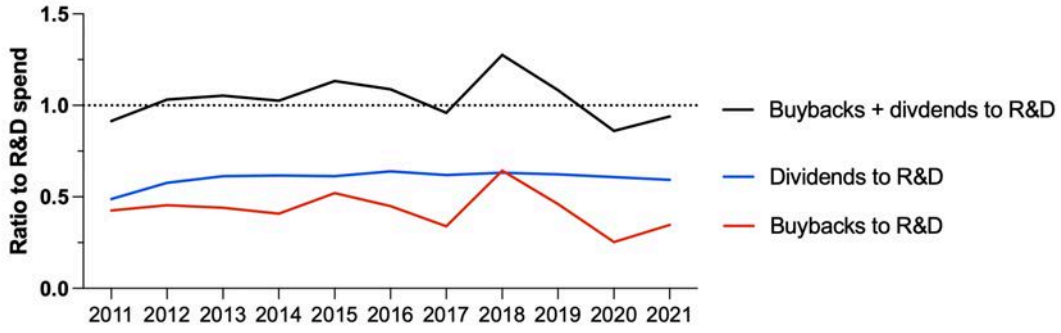
There was a strong association between geography and ratios of buybacks or dividends to revenues. The ratio of buybacks to revenue is 3.3-fold higher for firms based in the US vs. other countries (0.10 vs. 0.03, p<0.001) (**Table 12**).

Table 12. Share buybacks and dividends by geographical location

	Mean ratio (SD)		p-value
	US firms	Ex-US firms	
Ratio of share buybacks to revenue	0.10 (0.07)	0.03 (0.03)	<0.001
Ratio of dividends to revenues	0.05 (0.06)	0.06 (0.04)	0.704
Ratio of share buybacks and dividends to revenues	0.16 (0.10)	0.09 (0.06)	0.027

Looking at the ratio of share buybacks and dividends to R&D expenditures, the overall ratio of share buybacks and dividends over R&D expenditures for the top 50 biopharma companies was 1.04 from 2011 to 2021. The ratio hovered around 1.0 during this period, peaking at 1.28 in 2018 (**Figure 44**).

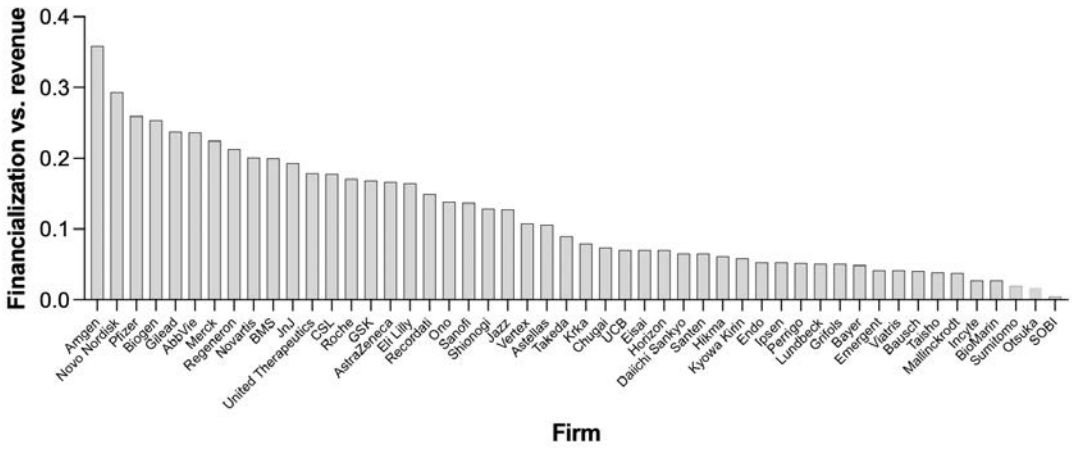
Figure 44. Ratios of share buybacks and dividends to R&D, 2011-2021



Source: original figure based on data from SEC filings and S&P Global.

I then looked at the most financialized firms, defined as a ratio of executive compensation + dividends + share buybacks over revenues. By this metric, the most financialized companies are Amgen, Novo Nordisk, Pfizer, Biogen, and Gilead with financialization ratios at 0.36, 0.29, 0.26, 0.25, and 0.24, respectively (**Figure 45**). Financialization measures by firm are presented in **Table 13**.

Figure 45. Financialization ratios by biopharma firm



Source: original figure based on data from SEC filings and S&P Global.

Table 13. Financialization measures by biopharma firm, 2011-2021

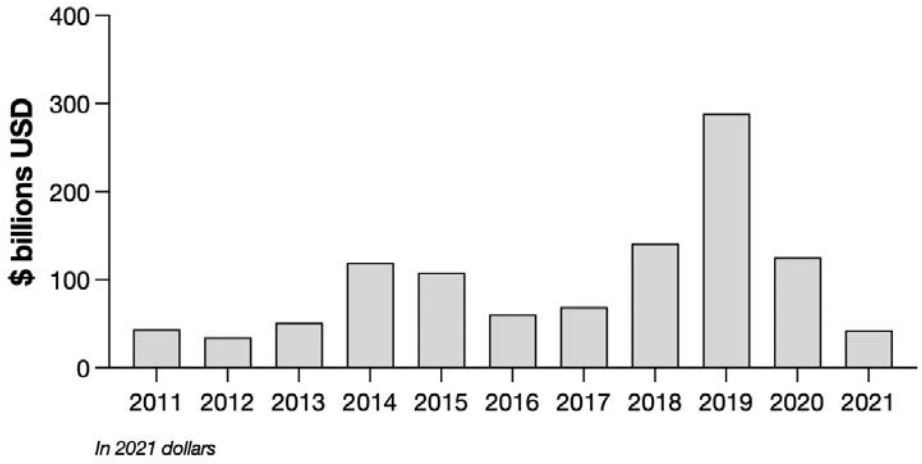
Company	Exec comp ($M)	Buybacks ($M)	Dividends ($M)	Sum ($M)	Financialization to revenues	Financialization to R&D
Amgen	$ 670	$ 64,262	$ 31,664	$ 96,596	0.36	1.97
Novo Nordisk	$ 238	$ 30,319	$ 30,099	$ 60,656	0.29	2.24
Pfizer	$ 440	$ 88,397	$ 91,957	$ 180,794	0.26	1.70
Biogen	$ 591	$ 32,053	$ -	$ 32,645	0.25	1.24
Gilead	$ 635	$ 43,705	$ 19,982	$ 64,322	0.24	1.56
AbbVie	$ 725	$ 34,653	$ 49,047	$ 84,426	0.24	1.56
Merck	$ 678	$ 53,391	$ 67,269	$ 121,338	0.22	1.12
Regeneron	$ 1,603	$ 11,853	$ -	$ 13,455	0.21	0.65
Novartis	$ 994	$ 45,831	$ 81,754	$ 128,579	0.20	1.16
BMS	$ 655	$ 24,177	$ 34,499	$ 59,331	0.20	0.87
JnJ	$ 685	$ 75,940	$ 106,783	$ 183,408	0.19	1.48
United Therapeutics	$ 603	$ 2,456	$ -	$ 3,059	0.18	0.71
CSL	$ 340	$ 6,573	$ 7,811	$ 14,723	0.18	1.93
Roche	$ 448	$ 31,961	$ 89,562	$ 121,971	0.17	0.90
GSK	$ 310	$ 13,348	$ 68,682	$ 82,339	0.17	1.15
AstraZeneca	$ 279	$ 10,647	$ 45,055	$ 55,981	0.17	0.83
Eli Lilly	$ 564	$ 16,920	$ 28,996	$ 46,480	0.17	0.69
Recordati	$ 55	$ 554	$ 1,968	$ 2,578	0.15	1.78
Ono	$ -	$ 862	$ 2,509	$ 3,371	0.14	0.52
Sanofi	$ 212	$ 20,020	$ 52,565	$ 72,797	0.14	0.93
Shionogi	$ 21	$ 2,400	$ 2,422	$ 4,842	0.13	0.72
Jazz	$ 370	$ 2,009	$ -	$ 2,379	0.13	1.12
Vertex	$ 705	$ 2,948	$ -	$ 3,653	0.11	0.24
Astellas	$ 71	$ 7,253	$ 8,060	$ 15,383	0.11	0.60
Takeda	$ 272	$ 901	$ 20,190	$ 21,363	0.09	0.42
Krka	$ 45	$ 229	$ 1,263	$ 1,538	0.08	0.85
Chugai	$ 67	$ 1	$ 4,798	$ 4,866	0.07	0.47
UCB	$ 86	$ 1,021	$ 3,267	$ 4,373	0.07	0.27
Eisai	$ 73	$ -	$ 5,339	$ 5,412	0.07	0.33
Horizon	$ 537	$ 307	$ -	$ 844	0.07	0.89
Daiichi Sankyo	$ 33	$ 2,454	$ 5,456	$ 7,943	0.07	0.32

Santen	$ 15	$ 439	$ 960	$ 1,414	0.07	0.58
Hikma	$ 125	$ 406	$ 824	$ 1,355	0.06	1.28
Kyowa Kirin	$ 27	$ 538	$ 1,855	$ 2,420	0.06	0.41
Endo	$ 506	$ 454	$ -	$ 960	0.05	0.52
Ipsen	$ 90	$ 270	$ 1,097	$ 1,457	0.05	0.35
Perrigo	$ 339	$ 1,436	$ 992	$ 2,767	0.05	1.44
Lundbeck	$ 83	$ 85	$ 1,463	$ 1,632	0.05	0.27
Grifols	$ 65	$ 540	$ 2,262	$ 2,867	0.05	0.93
Bayer	$ 364	$ -	$ 29,282	$ 29,646	0.05	0.48
Emergent	$ 170	$ 201	$ -	$ 372	0.04	0.20
Viatris	$ 757	$ 4,113	$ 399	$ 5,270	0.04	0.76
Bausch	$ 981	$ 1,786	$ -	$ 2,767	0.04	0.72
Taisho	$ 14	$ 467	$ 871	$ 1,352	0.04	0.49
Mallinckrodt	$ 325	$ 934	$ -	$ 1,259	0.04	0.42
Incyte	$ 372	$ 72	$ -	$ 444	0.03	0.04
BioMarin	$ 101	$ 290	$ -	$ 391	0.03	0.05
Sumitomo	$ 3	$ 0	$ 1,024	$ 1,027	0.02	0.10
Otsuka	$ 112	$ -	$ 1,264	$ 1,376	0.02	0.08
SOBI	$ 47	$ -	$ -	$ 47	0.00	0.03

5.6 M&A does not lead to more innovation

From 2011 to 2021, the top 50 biopharma firms spent $1.09 trillion in M&A (compared to $1.49 trillion in R&D during the same period). M&A spend in biopharma has been increasing over time, peaking in 2019 at $288 (due to BMS's $74 billion acquisition of Celgene) and decreasing from 2019 to 2021. The trends in M&A are presented in **Figure 46**.

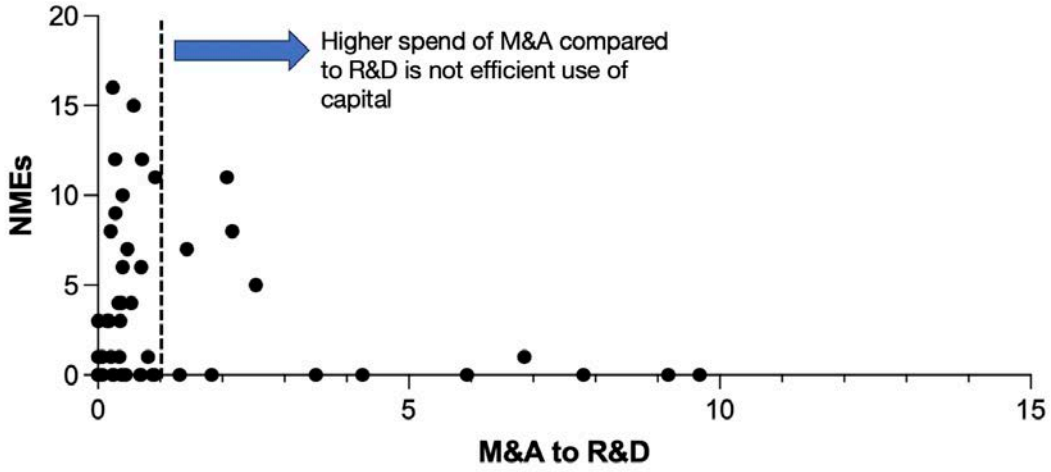
Figure 46. Total M&A spend among the top 50 pharma firms, 2011-2021



Source: original figure based on data from SEC filings and S&P Global.

I next looked at the relationship between M&A spend (compared to R&D spend) and found that higher spend of M&A compared to R&D did not lead to a higher number of NME approvals (**Figure 47**).

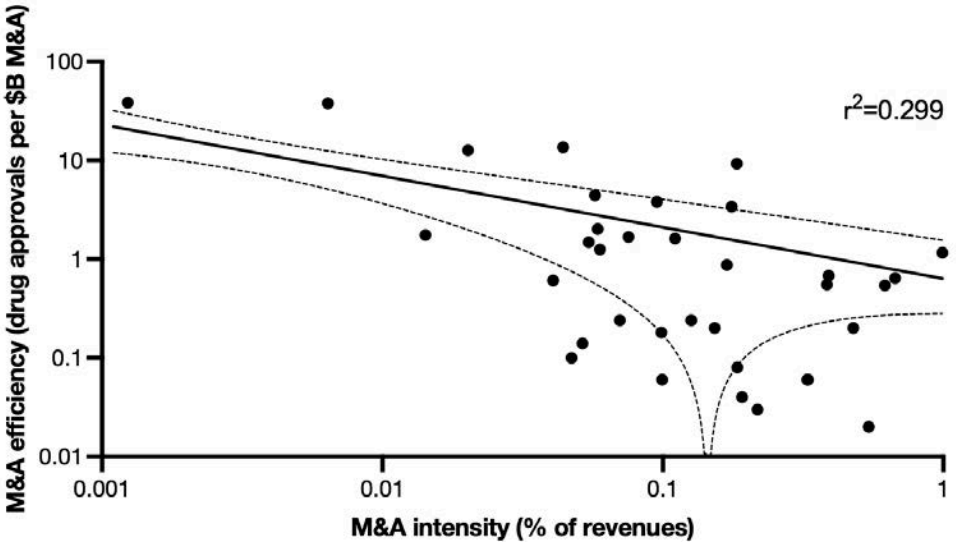
Figure 47. M&A ratio to R&D vs. NMEs



Source: original figure based on data from SEC filings, S&P Global, and FDA.

Additionally, I calculated M&A intensity (measured by M&A spend divided by revenues) and M&A efficiency (measured by drug approvals per $ billion of M&A spend) and compared the two (**Figure 48**). I found that there was a weak inverse logarithmic relationship between the two: the higher the M&A intensity, the lower the M&A efficiency (r^2=0.299, slope -0.520 [95% CI: -0.807, -0.327). M&A measures by firm are presented in **Table 14.**

Figure 48. M&A efficiency by M&A intensity



Source: original figure based on data from SEC filings, S&P Global, and FDA.

Table 14. M&A spend, intensity, and efficiency by firm, 2011-2021

Company	M&A number	M&A spend ($B)	M&A intensity (M&A/revenues)	M&A efficiency (new drug approvals per $B M&A)
AbbVie	3	$ 116.6	0.328	0.060
Amgen	14	$ 34.0	0.126	0.235
Astellas	13	$ 8.5	0.059	2.007
AstraZeneca	10	$ 61.9	0.184	0.081
Bausch	16	$ 26.5	0.390	0.680
Bayer	8	$ 24.4	0.041	0.614
Biogen	12	$ 14.2	0.111	1.621
BioMarin	3	$ 1.3	0.095	3.789
BMS	12	$ 141.7	0.477	0.198
Chugai	0	$ -	0.000	
CSL	1	$ 0.5	0.006	37.793
Daiichi Sankyo	3	$ 1.7	0.014	1.751
Eisai	1	$ 0.1	0.001	0.000
Eli Lilly	9	$ 16.8	0.060	1.251
Emergent	5	$ 1.6	0.184	9.257
Endo	6	$ 18.0	0.992	1.164
Gilead	11	$ 58.8	0.217	0.034
Grifols	9	$ 5.6	0.099	0.178
GSK	7	$ 20.0	0.041	0.000
Hikma	3	$ 1.0	0.044	13.565
Horizon	8	$ 7.4	0.619	0.538
Incyte	1	$ 0.3	0.020	12.648
Ipsen	4	$ 1.6	0.057	4.428
Jazz	6	$ 12.6	0.673	0.637
JnJ	7	$ 49.1	0.052	0.143
Krka	0	$ -	0.000	
Kyowa Kirin	3	$ 1.2	0.030	0.000
Lundbeck	4	$ 4.9	0.153	0.203
Mallinckrodt	9	$ 12.8	0.385	0.548
Merck	14	$ 29.8	0.055	0.000
Novartis	17	$ 63.5	0.099	0.063
Novo Nordisk	6	$ 9.8	0.047	0.102
Ono	0	$ -	0.000	
Otsuka	4	$ 6.0	0.076	1.672
Perrigo	9	$ 17.6	0.330	0.057
Pfizer	18	$ 75.5	0.109	0.000
Recordati	5	$ 1.0	0.058	0.000
Regeneron	1	$ 0.1	0.001	38.462
Roche	21	$ 32.6	0.046	0.000
Sanofi	11	$ 37.3	0.070	0.241
Santen	3	$ 1.1	0.050	0.000
Shionogi	3	$ 1.0	0.026	0.000
SOBI	2	$ 1.8	0.176	3.408
Sumitomo	4	$ 6.8	0.135	0.000
Taisho	5	$ 0.7	0.019	0.000
Takeda	14	$ 128.5	0.542	0.023
UCB	2	$ 3.4	0.054	1.475
United Therapeutics	1	$ 0.3	0.016	0.000
Vertex	5	$ 5.7	0.169	0.873
Viatris	7	$ 24.2	0.192	0.041

5.7 Structural equation modeling

The primary analysis of looking at causal relationships between M&A, R&D expenditures, and financialization on innovation was done with structural equation modeling (SEM). Structural equation models were used to explore relationships between key variables (financialization, M&A, and R&D spend) and innovation. These analyses revealed a significant relationship between internal R&D spend and innovation (standardized coefficient=0.876, p<0.001). The model is provided in **Figure 49** and the effects are shown in **Figure 50.**

Figure 49. SEM model

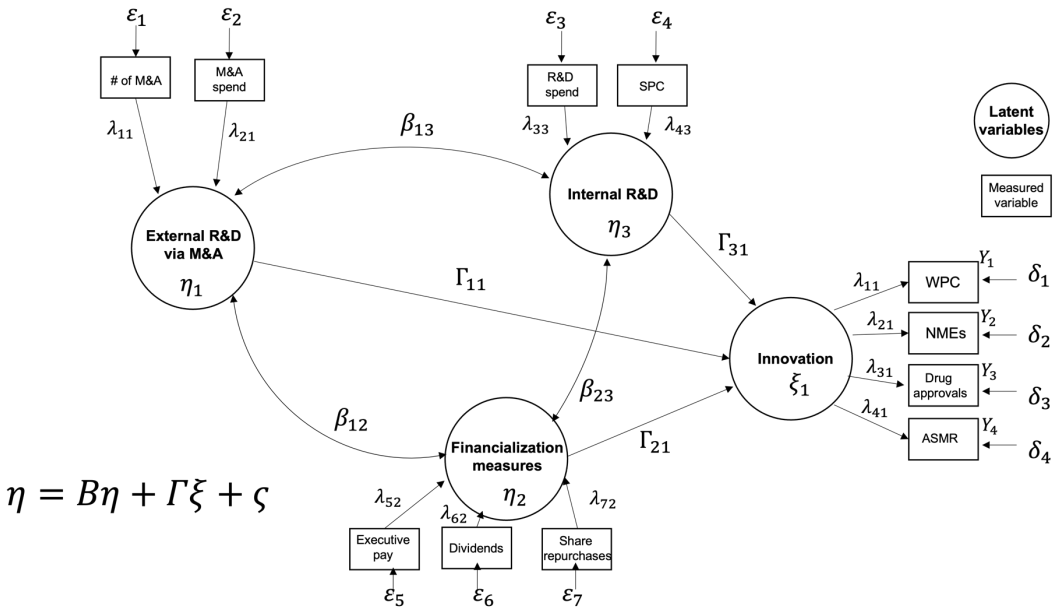


Figure 50. SEM model results

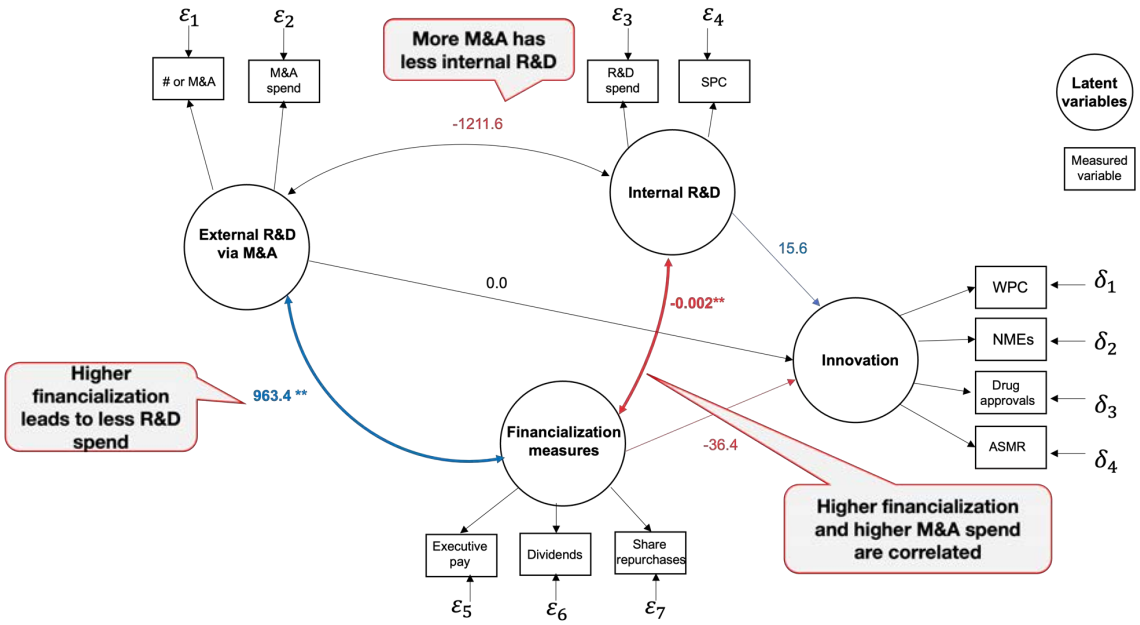


Table 15. Regression weights

Variables	Estimate	SE	p-value
Innovation ←internal R&D	13.66	73.93	0.853
Innovation ←financialization	-36.43	97.59	0.709
Innovation ← M&A	0.00	0.00	0.121
NMEs ← innovation	1.00	--	--
ASMR ← innovation	0.011	0.23	0.626
Total drug approvals ← innovation	1.60	0.13	**<0.001**
Mean patent citations ← innovation	-0.05	0.11	0.637
Dividends/revenue ←financialization	1.00	--	--
Share buybacks/revenue ←financialization	1.42	0.35	**<0.001**
Executive comp ←financialization	2,005.3	1,568.4	0.201
R&D/revenue ← internal R&D	1.00	--	--
Total patents ← internal R&D	-8,166.4	4,025.2	**0.042**
M&A spend ← M&A	1.00	--	--
M&A number ← M&A	0.00	0.00	**0.002**

Arrows indicate directional relationship

Table 16. Covariances

Variables	Estimate	SE	p-value
Financialization ↔ internal R&D	-0.002	0.001	**0.038**
Financialization ↔ M&A	963.4	377.6	**0.011**
M&A ↔ internal R&D	-1,211.6	682.9	0.076

Arrows indicate directional relationship

These analyses show several important outcomes. First, higher financialization leads to lower internal R&D spend (p=0.038). More financialized companies also spend more on M&A (p=0.011) and less on R&D (p=0.076). Additionally, there is a negative relationship between financialization and innovation, although this relationship is not statistically significant.

Taken together with bivariate analyses, M&A does not lead to higher innovation, and more financialized companies spend less on internal R&D, which is associated with lower innovative outputs, such as drug approvals and patent citations.

5.8 Summary and conclusions

In this chapter, I have provided analyses of the top 50 biopharma firms to examine the empirical relationship between financialization and innovation. This study took a sample of 50 of the largest biopharmaceutical firms to look at the relationship between measures of innovation and financialization. I characterized key trends in R&D, financialization, and innovation over time. The 50 biopharma firms earned $9.05 trillion in revenue and spent over $1.56 trillion in share buybacks and dividends from 2011 to 2021, which was 1.04 times higher than the R&D expenditures ($1.50 trillion) during the decade. Executives from the 50 firms received nearly $18 billion over the same time period.

The 50 biopharma firms received 330 drug approvals from the FDA from 2011 to 2021. Of these, 178 (54%) were classified as NCEs or NBEs. There were clear linear trends of higher R&D spend and a higher number of new drug approvals. The majority of these drugs were not innovative, receiving an ASMR value of V, which indicates “no improvement” over existing comparator drugs.

My analyses revealed that smaller, specialized firms (e.g. Vertex, Lundbeck, BioMarin) had more innovative medicines.

Analyses of R&D efficiency showed interesting results: higher R&D efficiency was associated with increased R&D intensity (R&D spend divided by revenues), smaller firm sizes (measured by assets), and specialized firms with a narrower, more focused pipeline. Additionally, contrary to beliefs held in the pharma industry, my analyses showed that M&A activity is not associated with higher innovation: higher ratios of M&A spend to R&D spend are associated with a lower rate of NMEs; higher M&A intensity (a measure of M&A spend over revenues) is significantly associated with lower M&A efficiency (the number of new approved drugs per $1 billion of M&A spend); M&A is not associated with higher innovation; and there was a strong trend that more M&A spend leads to lower internal R&D spend.

Contrary to my hypotheses, higher financialization did not *directly* lead to less innovation. However, more financialized companies spend less on internal R&D, showing that more investments in R&D instead of share buybacks, executive compensation, dividends, or M&A could lead to more innovation in biopharma. Additionally, higher M&A spend led to lower R&D spend. Taken together, my research suggests that financialized companies have lower R&D spend, which in turn is associated with lower innovation, particularly fewer new drug approvals.

Biopharma firms should spend less on dividends, share buybacks, executive compensation, and M&A, and should focus on the R&D spend and increased R&D intensity that could lead to higher innovation.

Chapter 6. Summary and conclusions

6.1. Summary

Due to the complexity of drug development, the biopharmaceutical sector is inherently a capital-intensive industry. The sector has increasingly experienced shareholder-driven corporate governance, or financialization. However, to date, the term “financialization” has been poorly defined in the biopharma industry and has been generally restricted to describing share buybacks and dividends. Furthermore, no studies have examined the relationship between financialization and innovation or productivity in biopharma companies.

In my review of the literature, it was clear that there is no consistent definition of financialization in biopharma. Lazonick focuses on measuring financialization by executive compensation, share buybacks, and dividends (Lazonick 2009, Lazonick and Tulum 2011, Lazonick 2016, Lazonick and Tulum 2024). However, none of the definitions of financialization directly relate to the context of innovation—and given the complexity of biopharma where innovation as at the center of the industry, these definitions lack a fundamental lens through which financialization can be studied.

Most Schumpeterian and neo-Schumpeterian studies have focused on innovation and have not thoroughly incorporated the broad influence of finance on innovation (Jan, David et al. , Mazzucato 2015, Mazzucato and Semieniuk 2017)—especially from an empirical perspective (Jan, David et al.). Unique to biopharma, the financial sectors have a technical orientation, and financial and technological knowledge are not always distinct from each other. Therefore, I took a neo-Schumpeterian approach to defining financialization in biopharma:

Financialization in biopharma is the strategy of prioritizing financial accumulation over technical innovation, mediated by the influence of finance and shareholder-driven corporate governance, in order to benefit shareholders.

Importantly, this definition includes the lens of innovation, which is a key context for studying financialization in a technological-based industry.

While many in the literature have described the problems of financialization in biopharma, such as drug price increases, inequitable access to medicines, excessive executive compensation, stock price manipulation, and profiting from taxpayer-funded innovation, as well as patents and rent-seeking, these studies lack a deep empirical examination of the *consequences* of some of these financialized business practices on innovation beyond corporate greed and prioritizing profits over patients. How financialization actually affects innovation (whether positively or negatively) has been under-studied.

While some case studies have examined bivariate associations between measures of financialization and innovation, empirical studies linking the empirical effect of financialization on innovation are lacking. An additional gap in the literature when considering the effect of financialization is the approach to measuring innovation.

To date, there have been few empirical analyses of the effect financialization has on *innovation.* Missing from the literature is an examination of the *consequences* of some of these financialized business practices.

In Chapter 4, I showed that financialization has been predominant in the biopharma industry over the last decade and became much more prevalent from 2011 to 2021. The industry is driven by high degree of venture capital financing, which has skyrocketed over the last decade, leading to a record number of IPOs that are increasingly earlier stage (and thus riskier). Stock engineering practices have been predominant in the industry in both private and public companies, including massively increasing private company valuations to inflate VC portfolios. Additionally, large pharma has increased its M&A activity due to its need to replenish pipelines from patent cliffs. Finally, as a whole, biopharma companies spend more on stock repurchases and dividends than they spend on R&D.

Nearly all these trends increased from 2009 to 2021: (1) more venture capital financing has flowed into biopharma; (2) there is more evidence of stock engineering, particularly in private companies where valuations have risen by an order of magnitude over the last decade; (3) there are higher IPOs at higher valuations yet at earlier stages of clinical development, which leads to risk taken on by the public markets, as well as pharma companies with an appetite for risky M&A to refill their pipelines; (4) there's more M&A activity at higher prices; (5) there's increased stock repurchases and dividends (absolute value); and (6) there are significant increases stock repurchases as a ratio of stock repurchases and dividends to R&D expenditures and revenue. Additionally, corporate government practice has taken advantage of lower corporate tax rates, resulting in profits rather than R&D funding. In 2017, the Tax Cuts and Jobs Act (TCJA) was passed with the claim that corporations would invest the savings and boost economic activity and create jobs. However, the TCJA has greatly benefitted to pharma companies (and their shareholders).

Additionally, I showed several examples where financialization is problematic to innovation. Celgene, for example, spent billions of dollars on share repurchases while developing an ineffective drug for Alzheimer's, which was harmful to patients. I also showed how the Covid-19 pandemic illustrates the need for regulation of biopharma companies to prevent them from prioritizing shareholders over patients (Whitfill 2020)—especially after receiving significant public funding. Moderna benefited heavily from the government-funded technology behind its Covid-19 vaccines with a massive valuation and extraordinary compensation packages totaling nearly a $1 billion even before its vaccine was approved.

In Chapter 5, I provided analyses of the top 50 biopharma firms to examine the empirical relationship between financialization and innovation. This study took a sample of 50 of the largest biopharmaceutical firms to look at the relationship between measures of innovation and financialization. I characterized key trends in R&D, financialization, and innovation over time. The

50 biopharma firms earned $9.05 trillion in revenue and spent over $1.56 trillion in share buybacks and dividends from 2011 to 2021, which was 1.04 times higher than the R&D expenditures ($1.50 trillion) during the decade. Executives from the 50 firms received nearly $18 billion over the same time period.

The 50 biopharma firms received 330 drug approvals from the FDA between 2011 and 2021. Of these, 178 (54%) were classified as NCEs or NBEs. There were clear linear trends of higher R&D spend and a higher number of new drug approvals. The majority of these drugs were not innovative, receiving an ASMR value of V, which indicates “no improvement” over existing comparator drugs. My analyses revealed that smaller, specialized firms (e.g. Vertex, Lundbeck, BioMarin) had more innovative medicines.

Analyses of R&D efficiency showed interesting results: higher R&D efficiency was associated with increased R&D intensity (R&D spend divided by revenues), smaller firm sizes (measured by assets), and specialized firms with a narrower, more focused pipeline. Additionally, contrary to beliefs held in the pharma industry, my analyses showed that M&A activity is not associated with higher innovation: higher ratios of M&A spend to R&D spend are associated with a lower rate of NMEs; higher M&A intensity (a measure of M&A spend over revenues) is significantly associated with lower M&A efficiency (the number of new approved drugs per $1 billion of M&A spend); M&A is not associated with higher innovation; and there is a strong trend that more M&A spend leads to lower internal R&D spend.

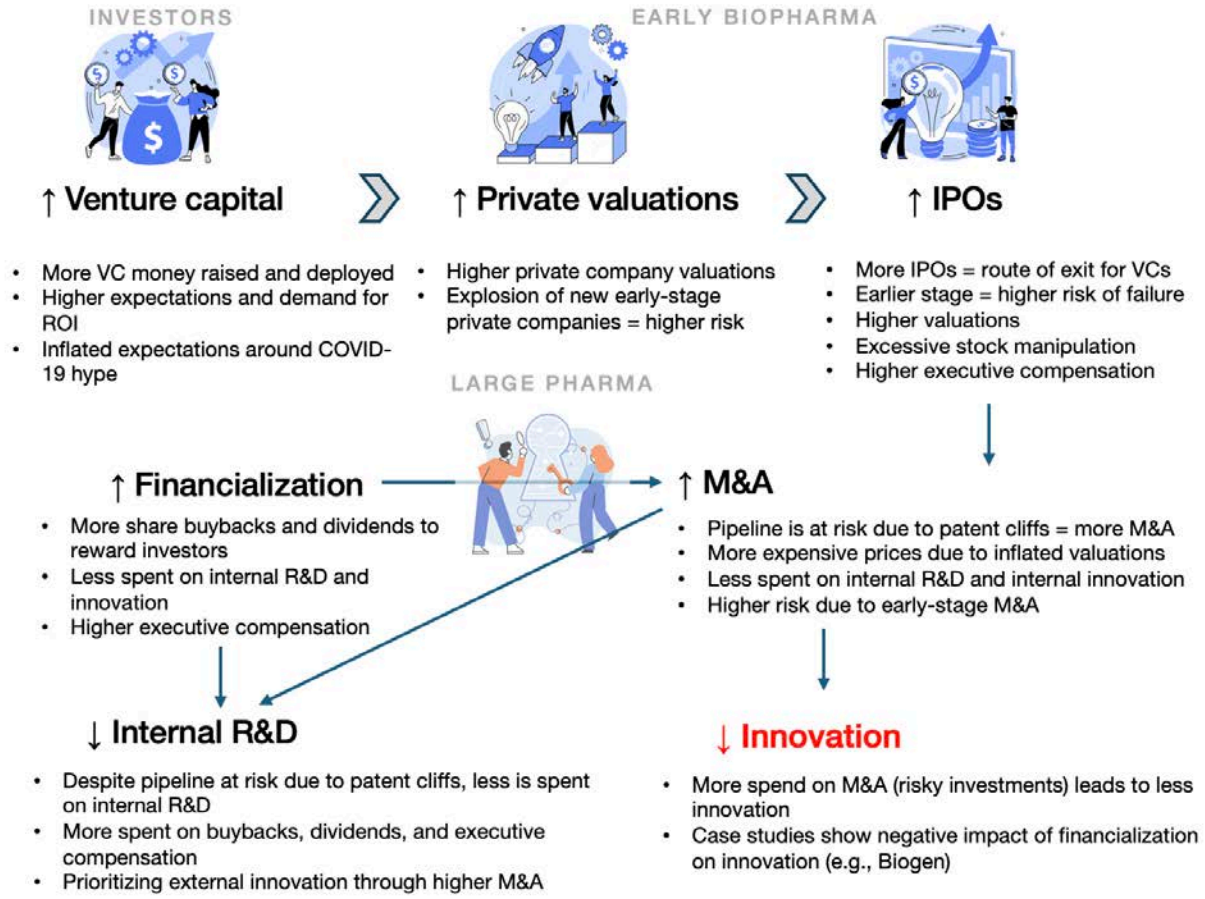
Contrary to my hypotheses, higher financialization did not directly lead to less innovation. However, the more financialized companies spent less on internal R&D, showing that more investments in R&D, instead of share buybacks, executive compensation, dividends, or M&A, could lead to more innovation in biopharma. Additionally, higher M&A spend led to lower R&D spend. Taken together, my research suggests that financialized companies have lower R&D spend, which in turn is associated with lower innovation, particularly fewer new drug approvals. Additionally, my case study in Chapter

4 demonstrated that Biogen's egregious business practices and share buybacks ultimately led to the approval of an unsafe and ineffective drug that was ultimately harmful to patients—while shareholders and executives pocketed massive profits.

Biopharma firms should spend less on dividends, share buybacks, executive compensation, and M&A, and should focus on R&D spend and increased R&D intensity, which could lead to higher innovation.

A summary of the findings of my thesis is presented in **Figure 51**. It shows the biopharma ecosystem and how investors can make profits even without drug approvals. Additionally, it highlights that higher financialization leads to less internal R&D and more M&A, **which in turn leads to lower innovation**. Profits from acquired companies then flow back to investors, who perpetuate the cycle of increasing private valuations and early IPOs, leading to riskier investments.

Figure 51. The financialized biopharma ecosystem and its impact on innovation



6.2. R&D efficiency is associated with smaller, concentrated firms with higher R&D intensity

It is widely known that R&D efficiency (e.g. the number of drug approvals per $1 billion of R&D input) in the biopharma industry has been declining, as noted by Scannell et al. in *Nature Reviews Drug Discovery* in 2012, which found that R&D efficiency has halved roughly every nine years since 1950, falling about 80-fold from 1950 to 2010 when adjusting for inflation (Scannell, Blanckley et al. 2012). Other studies have pointed to the "productivity crisis" in the biopharma industry (Pammolli, Magazzini et al. 2011), and suggested this decline may be due to the concentration of R&D in high-risk areas of clinical

development (Pammolli, Magazzini et al. 2011), evidenced by increasing R&D spend in the industry (Paul, Mytelka et al. 2010).

My studies offer new insights into biopharma R&D efficiency. There have been limitations in the literature, and many studies look at the industry as a whole, while others have flawed approaches, leading to misleading conclusions about productivity in the sector. For example, a study by Schumacher et al. published in 2021 showed “economies of scale” (i.e. firm size) lead to higher R&D efficiency (Schuhmacher, Wilisch et al. 2021). They argue that economies of scale, and thus greater R&D efficiency, can result from the lower cost of capital, greater portfolio diversity, better leveraging of R&D technologies, greater data ownership, and other factors. A key limitation of this study was the inclusion of only 14 of the largest pharmaceutical firms. Other studies have suggested an economies-of-scale effect in increasing R&D efficiency (Schuhmacher, Hinder et al. 2023). However, my studies of a much larger sample size of biopharma firms (n=50 vs. n=14 or n=16 in Schumacher’s studies) indicate a strong conflicting trend to the economies-of-scale concept, showing that smaller, specialized firms have higher R&D efficiency than larger pharma companies.

For example, BioMarin’s R&D efficiency is nearly 15-fold higher than that of Pfizer’s. BioMarin has a much smaller footprint than Pfizer (~3,000 employees vs. ~83,000) and has a much more focused pipeline and disease focus than Pfizer. BioMarin focuses on rare diseases CNS (central nervous system) diseases, whereas Pfizer is much more diversified. Another key factor is BioMarin has the highest R&D intensity (R&D spend divided by revenues) at 0.55, which is 3.7 times higher than Pfizer’s.

Another example is Vertex, which, like BioMarin, concentrates on rare diseases, where a focused approach has been successful in terms of drug approvals. A specialized R&D focus leading to higher R&D efficiency is supported by recent studies showing an increased focus on rare and orphan

indications may be associated with higher R&D efficiency (Pammolli, Righetto et al. 2020).

My studies indicate several factors that are significantly associated with higher R&D efficiency: increased R&D intensity (R&D spend divided by revenues); smaller firm sizes (measured by assets); and specialized firms with a narrower, more focused pipeline. My conclusions that smaller firms have better R&D efficiency conflicts with prior studies (Schuhmacher, Wilisch et al. 2021, Schuhmacher, Hinder et al. 2023), but by using a much larger sample size (roughly 3.2-fold more firms), I was perhaps able to better tease out the effect of firm size on R&D efficiency.

6.3. Mergers and acquisitions are not associated with higher innovation

It has been a long-established belief in the biopharma industry that M&A is essential for innovation (Ascher, Bansal et al. 2020, Khetan 2020). This argument (which is supported by several studies) is that M&A can gain new technologies and assets, economies of scale for consolidation, and portfolio realignment (Chang and Wei 2016). Another key reason for M&A is to fill pipelines due to pending patent cliffs and thus profit losses. Additionally, NME approvals are increasingly coming from smaller biopharma firms instead of large pharma; one analysis showed that 63% of all NMEs approved in 2018 came from smaller biopharma firms, meaning that innovation is diffuse in the industry and not concentrated in the larger pharmaceutical firms (Shepherd 2018).

My analyses show the top 50 biopharma firms spent $1.09 trillion on M&A from 2011 to 2021 (compared to $1.49 trillion on internal R&D), peaking in 2019 due to the BMS/Celgene acquisition.

The relationship between M&A and innovation is complex. While financialization has increased M&A incentives (such as cost reductions, outsourcing, monopolization of IPR) (Froud, Johal et al. 2006, Keenan,

Monteath et al. 2023), other motives may exist such as pipeline expansion or portfolio diversification. Keenan and Monteath analyzed M&A activity in the biopharma industry and posited a distinction in the motive behind M&A based on acquisition size: “higher deal values are more likely to reflect the underlying tenets of financialization based on shareholder value, market capitalisation and the concentration of corporate control and decision-making power as part of global production and financial networks” (Keenan, Monteath et al. 2023). Indeed, higher deal sizes are likely more indicative of financialized motives such as generating rent incomes from patents (Fernandez and Klinge 2020).

While limitations in my data prohibited sensitivity analyses to distinguish between M&A deal sizes, my studies contradict the traditionally held belief that M&A is critical to innovation in biopharma. I showed that higher ratios of M&A spend to R&D spend are associated with a lower rate of NMEs. Additionally, I showed that higher M&A intensity (a measure of M&A spend over revenues) is significantly associated with lower M&A efficiency (the number of new approved drugs per $1 billion of M&A spend). This trend was logarithmic. Finally, in my SEM model, I showed that M&A was not associated with higher innovation (measured by multiple variables, including patent citations, new drug approvals, NME approvals, and therapeutic value of drugs), and there was a strong trend that more M&A spend leads to lower internal R&D spend. Taken together with multiple types of analyses, I show evidence that contrasts with the industry’s belief that M&A is critical to innovation in biopharma.

These conclusions are supported by academic studies of M&A and innovation. For example, Monos in 2009 showed in a 60-year analysis that the cumulative number of NMEs was lower in companies that were heavily involved in M&A (i.e. Wyeth, Pfizer, BMS, and JnJ) (Munos 2009). Other studies have shown that higher M&A activity does not increase return on investment, profit margin, or research productivity (Demirbag, Ng et al. 2007, Ornaghi 2009). Another recent study confirms my conclusions about the impact on internal R&D spending, and empirically showed that R&D leads to decreases in filed

patents and there are not significant changes in the number of drug approvals compared to pre-M&A levels (Schutz 2023). Importantly, this study also found there were net drug price increases post-M&A (Schutz 2023). Other empirical studies support the findings that M&A leads to a decline in innovation measured by fewer patents and less R&D spending (Danzon, Epstein et al. 2007, Munos 2009, Ornaghi 2009, Comanor and Scherer 2013, Haucap, Rasch et al. 2019, Karim and Meder 2019).

These observations could be driven by several factors. First, many acquisitions are made to fill pipelines; many biopharma firms acquire firms that are in mid-clinical-stage development, and there is significant development risk that often leads to failure to lead to an approved drug. A recent study showed that overall success rates from Phase 2 to approval are just 15% as of 2018 (Dowden and Munro 2019). Additionally, a merger reduces innovative activities post-merger as firms usually consolidate and reduce redundancies (Ornaghi 2009), which likely leads to a reduction in new innovative focus while having a negative impact on patients, for example through drug price increases.

Indeed, a study by Hammoudeh et al. showed that less innovative pharma companies that acquire biopharma firms cut R&D and shift development from high-novelty products to cheaper, less-risky drugs (Hammoudeh and Nain 2024). Cunningham et al. showed that acquired drugs are less likely to be developed when they overlap with the acquirer's drug pipeline (Cunningham, Ederer et al. 2021), which suggests that some acquisitions (which the authors coin "killer acquisitions") may be done to kill new drug entrants to the market to maintain a monopoly with the acquirer's existing portfolio.

6.4. Venture capital and IPOs

My studies in Chapter 4 showed an explosion in venture capital funds deployed from 2011 to 2021; in private biopharma companies in the same period there

was a 40-fold increase in venture capital deployed**.** At the same time, the median pre-money valuation of these companies increased 5.5-fold. The trends are most pronounced in earlier rises: Series B valuations increased over 15-fold during the decade.

Venture capital is a major source of financing for biotech companies early in the drug development life cycle. Although venture capital can be a good substitute for risk-averse banks (Mazzucato 2015), finance from venture capital is characterized by short-termism and driven by returns. Venture capital is inherently focused on shareholders and short-term results—usually short-term financial gains for a fund (Rappaport 2005, Dallas 2012) with goals of returning ≥10x on the portfolio. This short-termism of venture capitalists (the major financier of biotech companies) contrasts with the long-term nature of drug development (Andersson, Gleadle et al. 2010). In fact, many VC funds want IPOs at earlier stages to have liquidity, so they can exit the company sooner.

Indeed, the VC explosion has simultaneously led to an explosion in the number of biopharma IPOs, and, over time, these IPOs have tended to be at a much earlier (i.e. riskier) stage of development. Two-thirds of the IPOs in 2021 were at Phase 1 clinical development or earlier (i.e. lacking human data). A 2021 study of biotech startups by Huayamares et al. found a similar percentage—65%—of IPOs in 2021 were preclinical or Phase 1 (Huayamares, Lokugamage et al. 2022).

These early-stage IPOs are widely problematic due to negative impacts on innovation for small biopharma firms, market volatility and market risk due to a high cost of capital for biopharma firms, and potential cuts in firms' pipelines. Additionally, innovation (as measured by patents) typically decreases when firms go public and public companies tend to focus on less risky indications vs. staying private.

6.5. Policy implications

Public finance (e.g. the National Institutes of Health or small business innovation research funding) shapes the direction of innovation in a purposeful manner. As Mazzucato and I laid out in our paper on policy directions for a new DARPA-like agency for health, ARPA-H, there are several opportunities to change the way health innovation is financed (Whitfill and Mazzucato 2023), one of which could be a venture capital arm within ARPA-H.

ARPA-H and other government agencies could explore novel investment mechanisms, borrowing from the venture capital model that has fueled innovation for decades. In the current system, agencies such as the NIH or National Science Foundation (NSF) fund only the earliest stages of innovation. Then private investors provide funds for promising but still-risky ventures and receive an ownership stake that might eventually be worth nothing—or yield many multiples of the original investment. The government could realize some of these returns by extending its funding further into the development pipeline in the form of grants to companies that convert to equity at some future event, such as when a product moves into clinical trials, is licensed to another company, or reaches the market.

There is precedent for a government-led venture model. For example, the Central Intelligence Agency's venture arm, In-Q-Tel, is a nonprofit venture fund that supports cutting-edge innovation for national security (Reinert 2012). In-Q-Tel even works with private equity firms and corporate venture groups to create an integrated, public-private investment ecosystem that enhances the likelihood of success (Roberts and Schmid 2022). Another example at the DoD is OnPoint Technologies, created in 2002 to invest in new power and energy solutions. Onpoint was initially funded with $62 million and grew its assets to nearly $150 million by 2009 (Mara 2011). Other government venture arms that took equity investments in companies include the Advanced Agricultural Research and Commercialization Corporation (AARCC), created in 1992 under the US Department of Agriculture to provide equity investments to startup firms,

and Red Planet Capital, created in 2006 in partnership with a $75 million investment from NASA (Webb, Guo et al. 2014).

At the state level, some states have adopted a publicly funded venture model. Connecticut has a quasi-public venture arm, Connecticut Innovations (with whom I have worked through my company, Azitra). This agency awards grants to companies that later convert into equity. The funds have helped spur innovation in the state while capturing returns for the public.

Given these precedents and the potential of mission-oriented government programs as a source of patient capital, there are untapped possibilities for turning government agencies (such as the nascent ARPA-H agency) into venture capital-like models, taking equity instead of giving grants, (Roberts and Schmid 2022) that would be more conducive to the long-term innovation that is required for drug development.

In addition to mission-oriented government agencies with a quasi-venture capital model, numerous policy implications arise from this work, including capital allocation and corporate strategies, a closer look at M&A by the Federal Trade Commission (FTC), more scrutiny by the SEC, and restrictions on executive compensation.

My findings suggest that M&A is harmful to innovation in the biopharma industry and leads to lower investments in R&D and more financialization. Additionally, higher M&A is associated with fewer drug approvals. A policy lever is already in play to regulate consolidation in biopharma through the FTC (Reed 2019, Albert, Director et al. 2024). In March 2021, the Multilateral Pharmaceutical Merger Task Force was formed by Chairwoman Rebecca Kelly Slaughter to consider how to address the concerns that pharmaceutical mergers and acquisitions raise (Vesterdorf, Fountoukakos et al. 2023). The Task Force culminated in a two-day workshop in July 2022 on FTC and M&A in pharma. Since then, the FTC has been vocal about using anti-trust actions to prevent M&A consolidation in the industry that could lead to higher drug

prices. This could be an important mechanism to curb anti-innovative M&A in biopharma.

Additionally, my studies have found that executive compensation is generally rising in the industry, with $17.5 billion in executive compensation in just 50 biopharma companies over a decade (mean $1.6 billion per year). I have also presented an egregious case study of executive compensation at Moderna, where executives profiteered significantly (~$1 billion) after receiving large taxpayer-funded investments from multiple government agencies. In my paper with Mazzucato on policy directions with ARPA-H, we offer several policy suggestions (Whitfill and Mazzucato 2023) based on taxpayer-funded innovation and financialized pharma companies. Although there is little precedent for this, ARPA-H and other agencies could encourage or require pharma company profits to be reinvested into R&D once innovation has succeeded. In pursuit of a similar goal, the Clinton administration explored capping the federal tax deductions companies could take for executive pay (Bank, Cheffins et al. 2016). That strategy was rolled back, but ARPA-H might look for other ways to restrict egregious financialized practices.

My studies also showed that companies have commenced IPOs at much earlier stages in the drug development cycle—the majority of which do not even have human data—with the high number of IPOs driven by the pandemic and excitement of investing in the industry when there were lofty expectations (Cameron and Morrison 2021). Investing in publicly traded biopharma companies is inherently risky, especially for investors without any scientific expertise. One study from 2015 found that from 1996 to 2015, 84% of the 335 firms that made IPOs were operating at a net loss in 2015 and collectively had a net loss of $69 billion (Williams and Spaulding 2018). Undoubtedly, this number has worsened with early-stage firms comprising the majority IPOs in recent years. The SEC could have more scrutiny on these early-stage IPOs by adding more guardrails to the types of investors in these IPOs or by banning the IPOs altogether. Additionally, the SEC could adopt the most stringent

policies (e.g. longer lockup periods) to prevent VCs from investing in companies just to IPO and make a quick return on investment for liquidity.

Finally, my findings suggest that large, financialized corporations spend less on internal R&D and more on M&A. My studies point to a negative, although statistically non-significant, impact of financialization on innovation. Additionally, my studies found that R&D efficiency is not equal throughout the industry; smaller biopharma firms and those with higher R&D intensities are associated with higher R&D efficiency. My findings suggest that policies that promote diffuse innovation (e.g. less consolidation), lower spend on financialization, and higher internal R&D spend would lead to higher innovation in the biopharma industry.

I acknowledge here and throughout this thesis (the majority of which was written before June 2024) that some of these policy suggestions are now thrown into question given the United States Supreme Court's decision in *Relentless, Inc. v. Department of Commerce* (2024) to overturn the Chevron doctrine in *Chevron USA, Inc. v. NRDC*, 467 US 837 (1984) that granted federal agencies the authority to interpret broad Congressional laws. The power of federal agencies was further weakened in the recent Supreme Court case *Loper Bright Enterprises v. Raimondo* (2024). Together, these cases have stripped authority to regulate industries from federal agencies, leaving scientific and other interpretations of broad laws to the courts. Now, the power of federal agencies, such as the FTC, SEC, ARPA-H, and FDA, may have limited authority to regulate the biopharma industry to enact some of the policy changes I suggest.

Nevertheless, it is possible that Congress could legislate for certain agencies to be given specific authorities and it could enact some of the policies mentioned above, which—in summary—include: (1) allowing federal agencies to use novel investment mechanisms into companies, including equity investments; (2) using the FTC to scrutinize M&A activity; (3) imposing limits on executive compensation, particularly for the recipients of federal funds; and (4)

using the SEC to more closely regulate early IPOs to prevent VCs from launching IPOs just to make quick liquid returns.

6.6. Key contributions to literature

Throughout this thesis, I have made a number of new, key contributions to the literature. Importantly, I have provided a concrete definition of financialization in the context of biopharma, using a neo-Schumpeterian approach to account for the fact that financial and technological knowledge are entangled in the biopharma industry (Jan, David et al. , Mazzucato 2015, Mazzucato and Semieniuk 2017).

Additionally, I provided an updated and expanded characterization of financialization in the biopharma industry over the past decade using two separate approaches—an industry-level analysis and a firm-level analysis, with added triangulation through examples. The industry-level analysis adds to the literature with data from private companies, which is often lacking in studies of financialization in biopharma.

I also used a complex modeling technique to examine empirical relationships between financialization and innovation in biopharma. I constructed a latent variable of innovation, using various key measures of innovation, such as patent citations, new drug approvals, new NME/NBE approvals, and—importantly—a healthcare technology assessment of the innovative value of each drug. The multiple measures, including a measure of the value of each drug, constituted a novel approach for measuring innovation. This builds on prior empirical studies that looked at financialization and innovation but had limited or confined measures of innovation (Orhangazi 2019, Tulum, Andreoni et al. 2022, Dosi, Marengo et al. 2023).

These studies also found that higher M&A does not lead to more innovation, contrary to long-held beliefs in the biopharma industry.

Finally, I added to the literature by using updated data and novel approaches to show R&D efficiency trends in the industry.

6.7. Limitations

There are a number of limitations to this study. The innovation and R&D ecosystems in the biopharmaceutical sector are very complex, with a very long lag between R&D investments and drug approvals. This inherently makes analyses difficult when linking R&D investments to drug approvals over a discrete period of time. However, by taking a decade of data and using structural equation modeling, trends and associations emerged.

This study also focused on the biopharma industry in the US, using patent and drug approval data specific to the US. For example, drug approvals in other countries were not included, which limits some of the conclusions to the context of the US only.

There were also limitations in the data itself—especially patent data. Patent data were obtained at the firm level, not by drug. Additionally, patent data were only available from 2011 to 2019 due to limitations in the WRDS database; thus, data were missing for two years and three biopharma firms. There were also limitations in using patent data for innovation analyses. Simple patent counts can be a metric of financialization itself, as large pharma companies with larger balance sheets file more patents (Arora, Belenzon et al. 2015). I tried to account for this by using patent counts as a measure of R&D, not innovation, and I used weighted patent citation data as a measure of innovation, as weighted patent citations may offer a proxy for the technological impact of the value of innovation in biopharma (Trajtenberg 2002, Mazzucato and Tancioni 2012). Another limitation of the patent data was the inability to link patents to other variables to determine breadth of innovativeness.

There were also limitations to the analyses of M&A. My analyses did not distinguish between the type of M&A (growth-oriented or consolidation-oriented) (Anand and Singh 1997), as the data were in aggregate and did not include firm-level information of the acquired targets. Additionally, there were limitations to the private company and venture capital data used in this study, as these were obtained from Pitchbook and are sometimes inaccurate.

Furthermore, there are limitations of SEM models. For example, construction of latent variables can be problematic and are subject to theoretical imputation as well as idiosyncrasies of the data (Anderson and Gerbing 1988, MacCallum, Browne et al. 2007, Grace and Bollen 2008, Sarstedt, Hair et al. 2016). Additionally, correlations between latent variables tend to be underestimated while correlations between observed measures with latent variables tend to be overestimated (Dijkstra 1983). Nevertheless, SEM overall offers advantages over simplistic regressions to observe relationships between concepts, i.e. latent variables.

SEM models aim to look at causality, causal relationships between latent variables derived from the model should not be assumed (Cliff 1983). This is due to bias and data limitations in constructing latent variables as well as the fact that composite measures operate as contributors to a construct rather than causing it (MacCallum, Browne et al. 2007, Bollen 2011, Sarstedt, Hair et al. 2016). Additionally, in the structural equation model, there was a small sample size due to a firm-level analysis. The low sample size was challenging for a strong model fit.

Future studies are needed with larger sample sizes to further examine the relationships between innovation and financialization in the biopharma industry.

6.8. Conclusions

Throughout this thesis, I provided a new definition of financialization specifically for the context of studying finance-driven innovation strategies in the biopharmaceutical industry. This began with a theoretical, neo-Schumpeterian approach and resulted in practical definitions, a characterization of financialization at the industry level in biopharma, as well as an empirical analysis of financialization and innovation in a sample of the 50 largest biopharma firms.

From an industry-level analysis, I found that, consistent with prior studies, financialization has been predominant in the biopharmaceutical industry and has rapidly worsened in recent years. There is an unprecedented degree of venture capital financing in the industry, which has led to more IPOs at earlier stages, as well as rising valuations in private companies. Pharma companies eager to refill pipelines due to looming patent cliffs have increased M&A spend. Finally, pharma companies spend more on share buybacks and dividends than they do on internal R&D.

From a firm-level empirical analysis of 50 of the largest biopharmaceutical firms which looked at the relationship between measures of innovation and financialization, there were trends of higher R&D spend and a higher number of new drug approvals. My analyses revealed that smaller, specialized firms (e.g. Vertex, Lundbeck, BioMarin) had more innovative medicines. Analyses of R&D efficiency showed interesting results: higher R&D efficiency was associated with increased R&D intensity, smaller firm sizes, and specialized firms with a narrower, more focused pipeline. Additionally, contrary to beliefs held in the pharma industry, my analyses showed that M&A activity is not associated with higher innovation: more M&A is associated with a lower rate of NMEs and lower M&A efficiency; M&A is not associated with higher innovation; and there is a strong trend that more M&A spend leads to lower internal R&D spend.

Contrary to my hypotheses and contrary to the assumptions of key pieces of literature on financialization, higher financialization did not directly lead to less innovation in this study. However, I found that higher financialization led to lower internal R&D investments, showing that more investments in R&D instead of share buybacks, executive compensation, dividends, or M&A could lead to more innovation in biopharma. Additionally, higher M&A spend led to lower R&D spend.

Taken together, these findings show that higher financialization leads to less internal R&D and more M&A, which then leads to lower innovation. Profits

from acquired companies flow back to investors, who perpetuate the cycle of increasing private valuations and early IPOs, leading to riskier investments.

Biopharma firms should spend less on dividends, share buybacks, executive compensation, and M&A, and should focus on the R&D spend and increased R&D intensity that could lead to higher innovation. It is critical that governments step in with mission-oriented finance, and regulations to curb excessive executive compensation, and larger M&A that would negatively impact innovation.

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