Financial Intermediation and the Funding of Biomedical Innovation: A Review *

Andrew W. Lo† and Richard T. Thakor‡

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Abstract

We review the literature on financial intermediation in the process by which new medical therapeutics are financed, developed, and delivered. We discuss the contributing factors that lead to a key finding in the literature—underinvestment in biomedical R&D—and focus on the role that banks and other intermediaries can play in financing biomedical R&D and potentially closing this funding gap. We conclude with a discussion of the role of financial intermediation in the delivery of healthcare to patients.

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† MIT Sloan School of Management, Laboratory for Financial Engineering (LFE), Computer Science and Artificial Intelligence Laboratory (CSAIL), and NBER.

‡ University of Minnesota – Carlson School of Management and MIT LFE.

1. Introduction

Healthcare development and delivery are essential for both the health and wellbeing of all economic agents and the functioning of the economy, as the recent COVID-19 pandemic has illustrated. The market capitalization of U.S. biotechnology (biotech) and pharmaceutical (pharma) firms—those firms directly responsible for developing new medical therapeutics—has been growing over time (Figure 1), as has the amount they invest in biomedical research and development (R&D). Aggregate healthcare spending has also been increasing over time both in absolute terms and as a percentage of U.S. GDP, and is predicted to reach $6.2 trillion for the U.S. by 2028.[1]

However, despite the increasing importance of healthcare therapeutics to the global economy, an emerging literature has documented significant underinvestment relative to the social optimum in the R&D necessary to create these therapies (see Lo and Thakor (2021) for a review). One reason for this underinvestment is a persistent R&D "funding gap" (e.g., Schumpeter (1942), Arrow (1962), Hall and Lerner (2010), Kerr and Nanda (2015), Nanda and Rhodes-Kropf (2016)). A variety of explanations have been put forth for why this funding gap is particularly severe for biomedical R&D, related to the financing frictions arising from the long duration, large capital requirements, and technical difficulty of drug development (Lo and Thakor (2021)). The consequences of

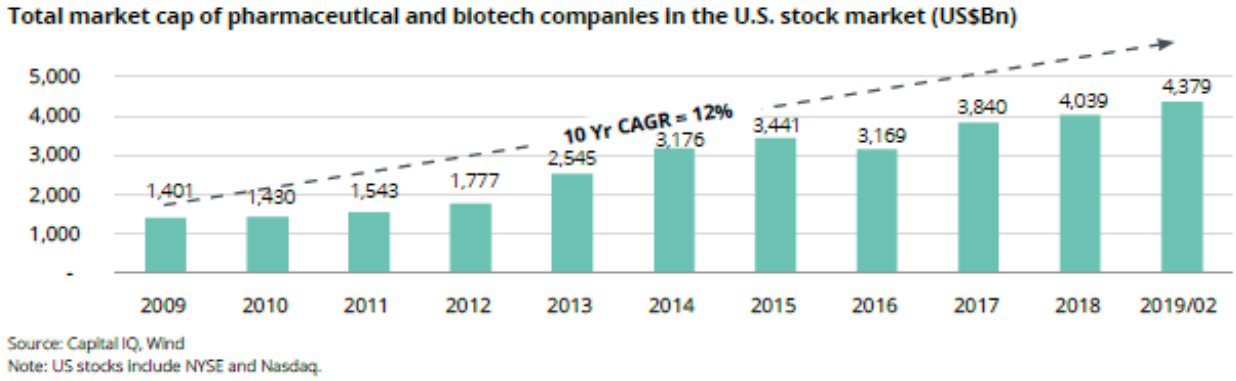
[1] https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NHE-Fact-Sheet

this gap are profound, eventually leading to lower R&D activities and fewer life-saving therapies for patients.

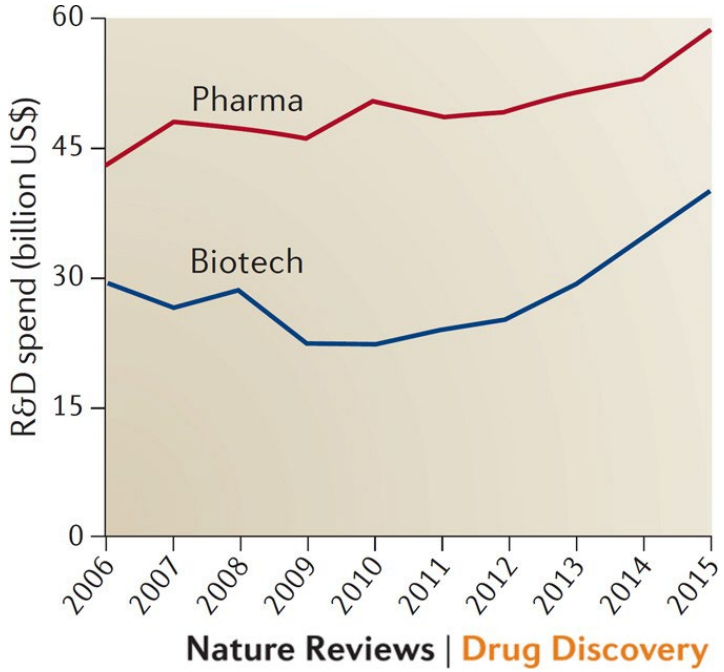
Figure 1: Biopharma R&D and Market Capitalizations

Panel A figure taken from Deloitte, Panel B figure taken from Mullard (2016).

Panel A: Biotech and Pharma Firm Market Capitalizations.



Panel B: Biotech and Pharma R&D Expenditures



What has received relatively less attention is the role that *financial intermediaries* play in biomedical funding. For example, banks—the center of the financial intermediation universe—are an important funding source for all types of firms. Other funding sources include intermediaries such as venture capital (VC) and private equity (PE) firms, who also exercise control over rights in the firms they finance. Moreover, a core economic function of many financial intermediaries is to facilitate the flow of funds from investors to firms by reducing frictions due to information asymmetries, pledgeability, and other contracting issues, thereby increasing aggregate investment (e.g., Boyd and Prescott (1986), Coval and Thakor (2005), Diamond (1984), Ramakrishnan and Thakor (1984), and Donaldson et al. (2018)).

These background facts raise the following questions: (1) How important are financial intermediaries in biomedical financing? (2) What role can intermediaries such as banks play in reducing the funding gap in medical innovation, and what are the impediments in doing so? (3) What regulatory and structural changes can be made to minimize these impediments? (4) What role can security design play? These questions also relate to the broader issue of whether and how finance benefits society (see Zingales (2015)).

In this review paper, we provide answers to these questions, with the goals of connecting financing issues to the role of banks and other financial intermediaries, and to identify and stimulate interest in research questions at the intersection of biomedical R&D and financial intermediation. We summarize the emerging literature on biomedical financing—with a specific focus on the drug development process (see our companion

paper, Lo and Thakor (2021), for a more detailed review of that process)—and discuss how financial intermediation research can help answer the four questions posed above. We also discuss the literature at the intersection of financial intermediation and healthcare delivery.

We begin by providing an overview of the institutional features of the drug development process and establishing the key link between financing and drug development. In the U.S., this process is heavily regulated by the Food and Drug Administration (FDA), which requires firms to demonstrate the safety and efficacy of their drugs through a multi-phase testing process that lasts about 8 years on average (DiMasi and Grabowski (2007)). The development process is very capital-intensive—with recent estimates of the cost to develop a single drug reaching over $2.5 billion (DiMasi et al. (2016))—and the chance of success is relatively low (Wong et al. (2019)). Furthermore, the drug development process requires specialized technical expertise to assess the prospects of a project. These features necessitate the external financing of biomedical R&D, thus linking it to financing supply, as has been more generally shown in the literature on financing R&D and innovation (e.g., Brown et al. (2009) and Nanda and Rhodes-Kropf (2016)).

However, we argue that the specific institutional features of the drug development process *amplify* financing frictions related to adverse selection, moral hazard, the non-pledgeability of knowledge assets, and asymmetric information regarding cash flow prospects. These frictions lead to reduced funding for potentially valuable R&D. We begin by presenting a simple conceptual framework that highlights the key frictions of

the drug development process and show how underinvestment in R&D occurs. The model highlights the opportunities for intermediaries to help reduce underinvestment in R&D.

With this foundation, we then explore the existing and potential role of intermediaries in financing biomedical R&D. We first provide stylized facts from which we can establish that a significant amount of current funding to biopharma firms comes from financial intermediaries in the form of VC funding and bank loans. We then provide a discussion of the relative benefits and costs of these intermediaries as funding sources. VC firms provide equity financing for firms that may not have the capacity for debt financing (due to minimal collateral), particularly innovative firms (Kortum and Lerner (2000)). However, VC contracts can be subject to hold-up problems and other frictions (e.g., Hellmann (1998), Kaplan and Strömberg (2004), Gompers and Lerner (2001)). Banks can potentially resolve some financing frictions through relationship loans in a way that does not significantly increase the risk exposure of lenders. Specifically, banks can bring to bear their special expertise in screening and monitoring, and can also resolve problems related to the non-pledgeability of certain assets in ways that markets cannot. As relationship lenders, banks can also attenuate moral hazard, diminish reliance on collateral, and help to protect the proprietary information about borrowers' R&D that they obtain as part of their relationships (e.g., Bhattacharya and Chiesa (1995), and Dang et. al (2017)). However, structural and regulatory impediments may hinder the ability of banks to perform these functions.

We then provide a normative discussion of how banks and other financial intermediaries—functioning in concert with the capital market—can exploit their unique capabilities to close the R&D funding gap. We discuss possible solutions, such as modifying risk weights in capital requirements for banks to reflect the fact that much of the intrinsic project-level risk in biomedical R&D is idiosyncratic (Jørring et. al (forthcoming)), thus potentially encouraging more lending. Another approach is to make structural changes that enable the government to provide "jump-start" assistance, akin to the creation of Fannie Mae and Freddie Mac that facilitated securitization in mortgage markets. We also discuss the possible role of security design innovations in facilitating banking and capital market solutions, and argue that such innovations can be a powerful force in helping banks and markets to close the R&D funding gap. Intermediaries can also play a significant role in fostering such innovations through their underwriting function. We review a small but emerging literature that proposes innovative security designs to cope more effectively with the frictions and risks that obstruct increased biomedical R&D funding. This represents a very promising area for future research, with a potentially high societal impact.

Finally, we also provide a discussion of the role of intermediaries in healthcare *delivery*—i.e., how an approved therapeutic is delivered to patients. Intermediaries play a key delivery role through the provision of healthcare insurance to patients, but they also play a critical role in funding healthcare *providers* such as hospitals, clinics, and nursing homes. We review a new literature that highlights the importance of financial intermediaries in the provision of healthcare to patients and shows how frictions related

to these intermediaries can affect quality of care. This opens several exciting new avenues for future research.

2. The Drug Development Process and Financing Frictions

To understand the role that financial intermediation plays in biomedicine, we must first provide a brief overview of the drug development process, and the frictions related to the process that impede financing for biomedical R&D.

2.1 Drug Development and Approval

Although the healthcare sector consists of many sub-industries, it is often helpful to differentiate between two broad categories of drug development firms: biotech and pharma firms. Biotech firms are typically smaller and younger, and derive their products from biological material, whereas pharma firms have traditionally derived their products from chemicals. This distinction is changing rapidly, thanks to scientific breakthroughs pioneered by biotechs which precipitate their acquisition by big pharma. As a result, a clean separation along the lines of the production process used is not always possible (e.g., Carlson (2016), Thakor et. al. (2017), and Lo and Thakor (2021)).

Nonetheless, distinguishing between biotech and pharma firms is important. For example, the risks for investors differ across these firms: pharma companies tend to have more approved drugs, and therefore more assets in place to manufacture them, whereas biotech companies tend to have more early-stage drugs in their development pipeline, exhibit lower profitability, and have fewer assets in place (e.g., Thakor et. al (2017)). We

will return to the issue of why this distinction is particularly important when we discuss the potential role of banks—for example, the greater likelihood that pharma firms have positive cash flows and assets that can be used as collateral for loans. In what follows, we will use the term "biopharma" to refer to both types of firms and distinguish between the two only when necessary.

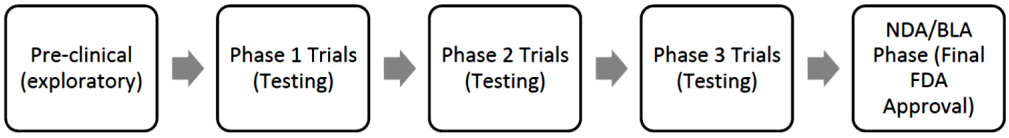
For any drug that is developed in the U.S., the approval of the FDA to demonstrate safety and efficacy is needed before the drug can be sold to consumers. The FDA approval process is depicted in panel A of Figure 2. It begins with an informal preclinical phase, which involves the discovery of new treatments and compounds, and laboratory tests to determine if the drug may cause harm to humans before actual testing. Following this process are three formal phases of clinical trials that consist of testing the drug on human subjects, with phase 1 having the smallest number of subjects and phase 3 the largest. After successfully completing the three clinical trial phases, the drug candidate must undergo a final FDA review (a new drug application (NDA) or biologic license application (BLA)).[2] If this review is successful, an approval for consumer use is issued. Even after the drug is marketed to consumers, the FDA engages in monitoring its performance to determine if any harmful effects of the drug are detected that did not surface in the clinical trials (sometimes known as "phase 4").

[2] Drugs that are derived from living organisms are referred to as "biological compounds" and undergo biologic license application (BLA) review, while drugs that are derived from chemical compounds go through new drug application (NDA) review. The review and approval process—as well as safety and efficacy requirements—are essentially the same. The difference is mainly legal—the Public Health Service (PHS) Act requires firms that manufacture biologics to hold an interstate commerce license for the product.

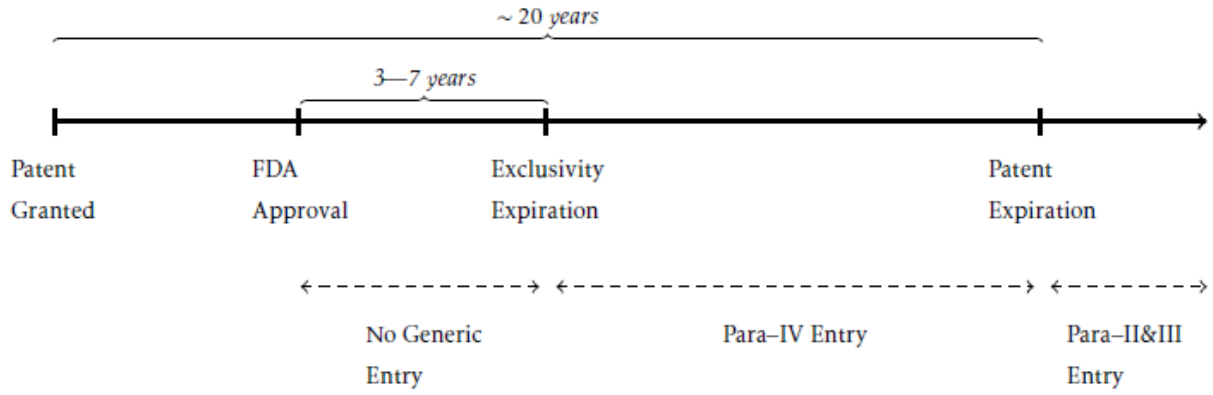
Figure 2: The Drug Development Process

Figures adapted from Li et al. (2021b).

Panel A: The Approval Process for Drugs



Panel B: Exclusivity and Patent Protection on Drugs



The drug development process typically takes many years. DiMasi and Grabowski (2007) point out that on average, the length of time from preclinical trials to FDA approval is almost 8 years. The process is also very costly. DiMasi et al. (2016) show that the cost of developing a drug from start to finish is almost $2.6 billion (in 2013 dollars). Furthermore, the risk of scientific failure is substantial. The estimated probability of FDA approval for a drug entering phase 1 clinical trials ranges from 6.9% to 19% (see Wong et al. (2019), Thomas et. al (2016), Hay et. al (2014), and DiMasi et al. (2010)). Table 1 provides the probabilities of ultimate success from each phase of the drug development process, as estimated by various studies.

Table 1: Clinical Development Success Rates

This table provides historical clinical development success rates, denoted by probability of success (POS), from the indicated phase of the development process to approval. Probabilities are calculated from phase to phase, and include all indications of a drug with the expection of DiMasi et al. (2010) which only includes lead indications. Data are from Wong, Siah, and Lo (2019).

	Wong, Siah, and Lo (2019)	Thomas et al. (2016)	Hay et al. (2014)	DiMasi et al. (2010)
Phase 1 to App	6.9%	9.6%	15.3%	19.0%
Phase 2 to App	28.8%	15.2%	23.1%	26.8%
Phase 3 to App	59.0%	49.6%	58.4%	59.5%
Number of Drugs	15,102	Unknown	4,736	1,316
Years	2000-2015	2006-2015	2003-2011	1993-2009
Number of Companies	5,764	1,103	835	50

However, for firms that succeed in obtaining FDA approval, the benefits are significant. One benefit is "marketing exclusivity," a period of typically 3 to 7 years during which the firm enjoys monopoly rents and no competing drug can enter the market. This benefit is in addition to the patent protection rights owned by the drug developer, typically a 20-year period from a patent's filing date (but the exclusivity period runs concurrently with the patent life and does not lengthen it). Marketing exclusivity is stronger than patent protection as it prevents any direct competitor (a generic version of the drug) from entering into the marketplace—after this exclusivity

period expires, generic drug manufacturers have the ability to enter into the marketplace by legally challenging the patents the drugs are based on—see Li et al. (2021b) for details.[3]

A second benefit is the generation of "knowledge capital." The scientific expertise gained from the drug development process can be reused on subsequent projects, which represents a *non-pledgeable* asset that has value, but cannot be easily used as part of a contract to obtain financing (see Krieger et al. (2022) for the theory and supporting evidence of this, which they refer to as "commercialization capital").[4] Moreover, to the extent that there are informational spillovers for other firms from the drug development activities of one firm, there will also be social welfare benefits that will not be internalized by the firm engaged in drug development.

2.2 Financial Frictions and the Need for External Financing

Not only is the cost of developing even a single drug high, evidence suggests that development costs have been increasing over time (Scannell et al. (2012)). These high development costs imply that biopharma companies need large amounts of external financing, especially since firms lacking FDA-approved products have a paucity of

[3] The specific length of the exclusivity period granted depends on the particular type of drug, and development incentives promoted by the FDA. For example, orphan drugs—drugs which target rare diseases—are granted the longest exclusivity of 7 years to incentivize developers to work in the area. Li et al. (2021b) show that the expiration of exclusivity implies, on average, a reduction in cash flows from sales of the drug due to increased competition. At the same time, firms make efforts to replace the drug with more commercially and scientifically "impactful" innovation when they have a diminished ability to make legal settlements with the competition.

[4] Some portion of knowledge capital can potentially be contracted upon—for example, through patents and non-compete agreements—but Krieger et al. (2022) provides examples of other forms of knowledge capital that cannot easily be contracted upon, including advertising and relationships with industry leaders (i.e., physicians), scientific knowledge for post-marketing research, and experience in the process of researching and manufacturing in specific therapeutic areas.

revenue (Thakor et. al (2017)). Biopharma companies rely heavily on external equity financing (e.g., Giambona et al. (2021) and Thakor and Lo (forthcoming)), in line with the more general documented link between equity markets and R&D investments by firms (e.g., Brown et al. (2009)). Even small biotech firms with assets only in the preclinical phase are often able to access public equity markets using IPOs (Aghamolla and Thakor, (2021)). More recently, special purpose acquisition companies (SPACs) offer another way for biotech firms to raise financing and tap public equity markets without the need to go through the formal IPO process. SPACs have been receptive to buying early-stage biotech firms—for example, in 2020 there were 33 biotech-focused SPACs that raised a total of $6.3 billion (DeFrancesco (2021))—and thus represent a potentially helpful addition to the mix of financing choices. Debt financing generally has weaker appeal for biotech firms due to their negative cash flows and the lack of tangible assets that can be used as collateral, although debt financing can be viable in some circumstances, as we discuss later.

While all firms accessing public equity markets must contend with external financing frictions, biopharma firms are confronted with an amplification of those frictions due to the institutional features of drug development. For example, asymmetric information, which leads to adverse selection costs (e.g., Myers and Majluf (1984)), can be exacerbated due to the combination of low probabilities of eventual success (i.e., FDA approval) and the highly technical and specialized nature of the drug development process. As evidence of this, Liu (2021) estimates a dynamic structural model using project-level data on biotech startups, and finds that information-induced financing

frictions leads to a firm value loss of approximately 24% and potentially higher, which is a large magnitude that is in line with the competitive landscape in this sector and the importance of information; we explore this point in more detail below.

These features of drug development can also lead to moral hazard that is difficult to detect and attenuate (e.g., Lo and Thakor (2021)). The fact that many of the assets generated by the drug development process are *not* pledgeable to financiers only compounds this problem. While non-pledgeability is also encountered in other contexts (e.g., Tirole (2006)), for biopharma firms this is a much bigger issue. To see why, consider Eli Lilly's acquisition of Hybritech in 1986. A major issue in the valuation of Hybritech was that its most valuable asset was its monoclonal antibody (MoAb) research to treat cancer, while its tangible diagnostic instrument assets represented a much smaller fraction of its overall value. Not only was it almost impossible for Hybritech to pledge its MoAb research assets to obtain debt financing, it was also challenging for Eli Lilly to determine exactly how much it was worth.

The need for external financing and the heavy reliance on equity also means that the prospects of biopharma firms will be tightly linked to the state of the economy and the overall market, since the pricing and availability of this form of financing is highly correlated with economic conditions—continuation financing for drug development is cheaper and easier to obtain in bull markets than in bear markets. Mace (2020) provides project-level evidence of this effect, showing that drug firms are more likely to discontinue projects during market downturns. Thus, market fluctuations can further amplify the financing frictions that biopharma firms face, especially for smaller biotech

firms. In line with these observations, even though the scientific risk of drug development is idiosyncratic (Jørring et. al (forthcoming)), biopharma firms still contain a substantial amount of systematic risk (e.g., Thakor et. al (2017)).

A standard approach to reducing informational gaps is through information disclosure to investors. However, for biopharma firms, this is problematic due to the "two-audience signaling problem"—any information disclosed to investors is also unavoidably disclosed to one's competitors (e.g., Kamien and Schwartz (1978), and Bhattacharya and Ritter (1983)). A number of empirical studies have demonstrated, using project-level data for drug development firms, that competitors respond strongly to any information that is disclosed about a firm (see Krieger (2021), Krieger et al. (2022), Aghamolla and Thakor (2022), Lewis and White (2021)).

2.3 Behavioral Considerations

As with other industries, the biopharma industry is not immune to the behavioral biases of its managers. A number of studies have documented various biases in which corporate overconfidence leads to overinvestment (Malmendier and Tate, 2005), investor sentiment causes temporary deviations from rational stock prices (Morck, Shleifer, and Vishny, 1990; Baker and Wurgler, 2007), and periods of economic prosperity induce greater risk taking (Thakor, 2015).

These biases—along with other well-documented behaviors such as loss aversion, anchoring, framing, herding, etc. (Lo, 2017, ch. 2)—are especially relevant given the outsized risks and rewards associated with therapeutics companies. In the face of these

high stakes and binary winner-take-all outcomes, it is not difficult to develop behavioral explanations for industry trends such as underinvestment in research (Budish, Roin, and Williams, 2015), reduced innovation among the biggest biopharma companies (Krieger, Li, and Papanikolaou, 2022), herding behavior among biopharma executives and investors around "hot" technologies or targets (Booth, 2012), and lack of use of more complex financial intermediation tools such as securitization and OTC derivative contracts.

For example, Baker and Wurgler (2007) point out that younger, smaller, more volatile, and high-growth companies are more sensitive to investor sentiment, and that limits to arbitrage imply that rational investors cannot undo the impact of sentiment investors. Thus, when investor sentiment is high, these firms tend to be overvalued and when investor sentiment is low, they tend to be undervalued. If the managers of these firms are rational, they will not overinvest when their firms are overvalued, but they may cut back on investment when they are undervalued.[5] This implies underinvestment on average across the investor sentiment cycle, and investment that is procyclical with the state of the stock market if investor sentiment is positively correlated with the level of the market. An another example, Thakor (2015) relies on the "availability heuristic" of Tversky and Kahneman (1973) to explain how investors can underestimate risk initially and be willing to provide funding, but may suddenly cut off funding when they learn the true risk in their investments. Managers, who are cognizant of this, may underinvest

[5] They may issue equity when overvalued, as in Baker and Wurgler (2002), but would have no reason to then use this funding for negative-NPV projects. See also Dittmar and Thakor (2007) for an alternative explanation based on disagreement.

initially in order to limit expected future losses from continuation funding being cut off, thereby displaying risk aversion as documented by Krieger, Li, and Papanikolaou (2022). Moreover, this funding continuation risk may also induce them to display short-termism in their R&D investments since the risk grows with the duration of the project, as documented by Budish, Roin, and Williams (2015).[6]

Although there can be little doubt that behavioral factors do play a role in biopharma corporate decisions, it is difficult to disentangle the impact of these factors from rational economic responses to the effects of scientific complexity, Knightian uncertainty, and ethical and fiduciary responsibilities to shareholders, patients, and other stakeholders.

One example is provided by Dr. Bruce Booth, a partner at Atlas Venture, one of the most successful biotech VCs in the industry. In commenting on the nearly 1,000 oncology projects in the industry's pipeline in 2012, Dr. Booth observed that over 20% of these projects were directed at the same eight biological targets (Booth, 2012). His explanation is decidedly behavioral:

> The real reason for this concentration…[is] fundamentally a reflection of our industry's collective risk avoidance, as well as a misperception of aggregate risk. Portfolio decision-making in large and small companies leads to an overwhelming bias towards precedented mechanisms as a means to reduce biologic risk. No head of discovery ever got fired for producing too many

[6] See Thakor (2021) for a theory of rational short-termism.

> Development Candidates, and the lowest risk way of doing that is through "fast follower" (and even slow "fast follower") incremental improvements. In the shot on goal mentality of R&D, more of these shots are better. Most R&D portfolio prioritizations punish novel target programs as low "confidence in mechanism", and therefore riskier than precedented targets. The math from these models is hard to challenge, having made some of those models in a prior life… In the end, all this leads to an industry pipeline—big and small companies alike—full of groupthink programs that follow the "hot" target trends like lemmings.

Included in Booth's behavioral arguments are also some rational explanations for industry concentration, including herding as a response to biological risk, capital allocation decisions that scale with conviction, and corporate incentives for focusing on higher Sharpe-ratio projects. As he acknowledges, the "math from these models is hard to challenge." The math he is referring to is, of course, mean-variance portfolio optimization with a concave utility function.

Although there are, indeed, behavioral aspects to the biopharma industry, Booth's insightful critique of his industry's challenges also highlights the potential for financial intermediation to address some of those challenges.

2.4 Real Options

As is well understood, R&D investment is equivalent to purchasing a real option (e.g. Schwartz (2004)), and a number of studies have explicitly modeled the biopharma R&D

process using real options (Myers, 2015). More generally, the real options literature can provide some insights into some of the observed patterns of biomedical R&D investment.

First, as Myers (2015) lays out, R&D for a drug candidate can be viewed as a series of real call options to continue investment, and conditional on success in a given phase the option is almost always worth exercising. He argues that this creates "R&D leverage," due to the obligation to pay for future R&D (i.e. to exercise the option in the future). This rationalizes the low reliance on debt by drug development firms, as R&D leverage pushes out financial leverage (see Myers and Shyam-Sunder (1996) and Myers and Howe (1997)). It also explains why investors demand higher rates of return from early-stage R&D compared to later-stage R&D—it is not due to higher risk, which is idiosyncratic and thus diversifiable, but rather because R&D leverage is higher at earlier stages. This argument is also consistent with the notion of continuation financing risk forging a link between these investments and the market, which we emphasize below.

Second, when a firm has the opportunity to make an irreversible investment with high future uncertainty, e.g.., like R&D, the option to delay the investment always has value, analogous to delaying the option to exercise a financial option. A number of studies have used real options models to explain delay and hysteresis in investment (e.g. Dixit (1989, 1991), McDonald and Siegel (1986)), and Pindyck (1988)). These earlier papers did not examine strategic interactions with competition. Smets (1991) develops a model in which the effects of R&D competition on the option to delay investment can be studied. The roles of option values and competition are additive in the model, so competition reduces the value of investment, but leaves unaffected the option value of delaying investment.

In a richer setting, Weeds (2002) introduces two forms of uncertainty in a model of R&D investment with competitive interactions: economic uncertainty over the future profitability of the project and technological uncertainty over the success of the R&D investment. Economic uncertainty generates option value and the incentive to delay, whereas technological uncertainty generates a first-mover advantage through the winner-takes-all nature of the patent system and thus potentially diminishes the incentive to delay. Despite this, Weeds (2002) shows the surprising result that competition among a small number of firms does *not* necessarily undermine the option to delay investment. Rather, it *increases* the value of delaying investment because the first mover has the fear of starting a patent race.

Thus, the insights of the real options literature can help to rationalize some facts related to drug development, such the low usage of debt, high costs of capital, and reduced investment relative to the social norm if delayed investments are not eventually made.[7] The specific institutional features of the drug development process discussed above may further exacerbate these effects, and when combined in a real options model may produce further insights.

3. A Simple Model of Biomedical R&D Financing

With these institutional features of the drug development process and the frictions that biopharma firms face as a backdrop, in this section we develop a simple model of a

[7] If there are completely unexpected technological shocks, for example, then R&D investment that could have yielded immediate societal benefits but is delayed may never be made because a better alternative arrives at a future date prior to the investment being made.

firm seeking external financing for staged R&D. In this model, the firm is able to raise financing with either debt or equity. We show that the frictions the firm faces compel it to rely on equity rather than debt, and one consequence is underinvestment in R&D relative to the social optimum. The model points to opportunities for intermediaries to reduce underinvestment in R&D, which will then serve as the basis for our discussion on potential solutions.

3.1 The Framework

Most R&D financing is multi-stage, with later investments predicated on the information revealed by the outcomes of earlier investments. Consequently, our stylized framework adopts this structure, and also features both moral hazard and asymmetric information as frictions that R&D-intensive firms must cope with.

Consider a model with three dates. At $t = 0$, the firm needs investment capital I to fund preclinical R&D and clinical trials. There are two types of firms, G and B, with a commonly-known prior probability $g \in (0,1)$ of G. Each firm privately knows its own type; outsiders share a common prior at $t = 0$. Both types of firms have the same probability of scientific success, but B is more prone to moral hazard at a future date than G, in a way that will be made precise shortly.

If the firm is successful in raising I at $t = 0$, the results of its preclinical process and clinical trials will privately reveal to the firm at $t = 1$ whether its drug development will be successful or not at $t = 2$. Success means a pledgeable pre-tax payoff of $X > 0$, and failure means a payoff of 0. Let x represent the project payoff at $t = 2$. Then the probability

distribution of x is $x = X$ with probability $p \in (0,1)$ and $x = 0$ with probability $1 - p$. We assume that drug development success ($x = X$) also generates a non-pledgeable knowledge asset worth $\Omega > 0$ to the firm and to society.[8]

Success at $t = 1$ is not sufficient to realize X at $t = 2$. The firm must also invest an additional ΔI in the drug development process and expend managerial effort $e \in \{0,1\}$ costing ke, with $k > 0$, after which it will obtain $x = X$ at $t = 2$. Absent ΔI or $e = 1$, the cash flow at $t = 2$ is 0 with probability 1. We assume that if external financing is raised, the manager always chooses $e = 1$, and if it is not raised, they always choose $e = 0$. Thus, we are not incorporating the lack of observability of e as an additional moral hazard in the model.[9]

We take as given the need for staged financing, which is common in medical R&D, so I is raised at $t = 0$ and ΔI is raised at $t = 1$. A simple way to endogenize it in the model would be to assume a dissipative cost associated with putting cash on the balance sheet that is not invested right away.[10] The firm can raise I and ΔI through either debt or equity. The corporate tax rate is $T \in (0,1)$, so the choice of debt versus equity will be affected by the value of the debt tax shield.

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[8] The assumption that the knowledge asset has value to society is meant to capture the idea that knowledge produced by biomedical R&D often involves drug discoveries and patient care solutions that are not only profitable to the firms investing in the R&D, but also socially beneficial. For example, the monoclonal antibodies research done in the 1980s to find a cure for cancer now has potential societal benefits in treating COVID-19.

[9] Effectively, this means we are assuming that external financiers can observe and contract on e. If financing is raised, they observe whether the firm is being run or not. We avoid adding this moral hazard, although it exists in the real world, because it is an unnecessary friction in our model. If we were to add it and assume that bank monitoring can resolve it more effectively than market financing (as in Holmstrom and Tirole (1997)), we would have another benefit to banks playing an expanded role in such financing.

[10] For example, there may be agency problems of free cash flow within the firm, as in Jensen (1986), that cause value dissipation with idle cash.

Outsiders (investors) do not see what the firm's manager sees at t = 1 regarding the outcome of the project at t = 2. These outsiders simply observe a signal $\phi \in \{0, X\}$ of x, where $\phi = X$ signals "success" and $\phi = 0$ signals "failure." The precision of ϕ is denoted by $\eta \in \{0,1\}$, where $\eta = 1$ means ϕ has perfect precision, and $\eta = 0$ means it is completely uninformative, i.e., for some fixed $x \in \{0, X\}$,

$$\Pr(\phi = X \mid x, \eta = 1) = 1 \tag{1}$$

$$\Pr(\phi = X \mid x, \eta = 0) = 0.5 \tag{2}$$

with $\Pr(\eta = 1) = r \in (0,1)$.

The likelihood, r, of an informative signal will be affected by a host of factors, including the amount of information the firm chooses to disclose (call it d), the technical complexity of the information (call it c), and the cost to investors of receiving and processing the information (call it ψ), which may depend both on the complexity of the information and the sophistication of investors.[11] We assume that:

$$\frac{\partial r}{\partial d} > 0, \quad \frac{\partial r}{\partial c} > 0, \quad \text{and} \quad \frac{\partial r}{\partial \psi} < 0 \tag{3}$$

Given this intuitively plausible specification, we can view r as the *expected* precision of ϕ.

There is also a macroeconomic state $m \in \{u, d\}$ that is realized at t = 1. The realization $m = u$ means the economy is "up" (a boom) and the realization $m = d$ means the economy is "down" (a recession). The common prior is $\Pr(m = u) = \mu \in (0,1)$.

[11] Sobel (2012) provides an analysis of information complexity with processing costs for senders and receivers of information as an alternative to cheap-talk models for explaining incomplete/coarse information communication. Boot and Thakor (2001) provide a model of information disclosure that features information complexity and processing costs.

All agents are risk-neutral, and the riskless rate of return is zero for simplicity. The market for external financing is competitive, so investors provide financing to earn an expected return equal to the riskless rate of zero. The manager of the *G* firm has no private benefit from running the firm, and seeks to maximize firm value. The manager of the *B* firm enjoys a state-contingent private benefit from operating the firm from $t = 1$ to $t = 2$.[12] This benefit, π, is enjoyed only when $m = d$, and we assume $\pi > k$, so the manager will find it privately optimal to raise financing and run the firm if possible to do so. The idea is that the agency costs of external financing are likely to be worse during a recession than a boom because there is a relative paucity of positive-NPV options for investment in a recession, making the pursuit of private-benefit projects more attractive. The random variables x and m are assumed to be mutually independent.

We assume that all debt repayment is tax deductible. Since the large R&D investments that R&D-intensive firms make are also tax deductible, debt is not the only source of tax shields in this setting.

The sequence of events at $t = 1$ is as follows (Figure 3). First, m is realized and commonly observed, and then the realizations of ϕ and η are commonly observed. After this, the firm decides whether to raise ΔI, possessing private information about the value of x that will be realized at $t = 2$.

[12] The assumption that only the manager of the *B* firm enjoys a private benefit from running the firm can be relaxed. All that is needed is that the manager of the *G* firm has a smaller private benefit than the manager of the *B* firm.

Figure 3: Summary of Sequence of Events

$t = 0$	$t = 1$	$t = 2$
• Firm seeks external financing of I during drug development. • Financing is raised from either debt or equity. • There are two types of firms: G and B. Each firm's manager knows their type privately. Others share common priors about the firm's type.	• The manager of each firm privately observes whether the drug development will succeed or fail at t =2. • Outsiders (investors) get a signal ϕ of the date-2 outcome, with precision η and expected precision r. • The firm needs continuation financing of ΔI to finish drug development. • Availability of funding depends on the realization of ϕ and a macroeconomic state m, which is either up (boom) or down (recession).	• Eventual payoff, x, of drug development is realized, where x is $X > 0$ with probability p and 0 with probability $1 - p$.

3.2 Key Features

The model has numerous features that deserve further explication.

Signal of Success/Failure: We assume that investors receive a noisy but informative signal ϕ of the firm's payoff. The reason for including this is to allow what investors learn to be influenced by what the firm does. The complexity of the firm's R&D activities as well as its disclosure policy will affect the precision of this signal, and hence the firm's cost of financing. Moreover, its disclosure policy may also affect its real cash flows, so the firm can make its decisions based on the impact on both x and its cost of financing. These

features are meant to capture the reality of the R&D-intensive firm's decisions about capital raising and information disclosure with the attendant negative spillover effects of two-audience signaling.

Additional ΔI investment: We assume that, at the interim date, the firm must raise additional financing to continue. This is an important feature of the model for two reasons. First, as indicated earlier, it represents the practical reality of staged financing by existing financial intermediaries in financing biomedical R&D. Second, it makes the availability and cost of financing dependent on both the firm's information disclosure policy as well as the realization of the macro state m. The dependence on the firm's disclosure policy introduces a tradeoff for the firm: by disclosing more, it may sacrifice more real cash flows due to competitive reactions, but it also improves the terms of continuation financing by providing investors more information. The dependence on m means that the macro state affects financing terms through the assumption that moral hazard is contingent on the macro state. This introduces the empirically documented systematic risk for an R&D-intensive firm whose R&D payoff risk is idiosyncratic in the absence of external financing frictions.[13]

Complexity of Information and its Processing: While not a critical element of the model, this feature allows for the complexity of the firm's R&D to influence the amount of information the firm will choose to disclose. Because biomedical R&D involves highly

[13] The result that R&D-intensive firms that engage in R&D that has largely idiosyncratic scientific risk can nonetheless end up with high systematic risk is also encountered in the real options literature discussed above. This effect can rationalize why such firms hold significant systematic risk, akin to a financial leverage effect.

technical processes and outcomes, information processing costs for investors may increase as the information they need to process about its R&D increases in complexity. Thus, in line with existing theories that link the complexity of information to information processing costs (e.g., Boot and Thakor (2001), and Sobel (2012)), this feature allows us to explore some interesting side effects of financial intermediation, but is not essential to model the underinvestment problem in R&D.

***Private Benefit* (π) *and Macro State* (m):** The private benefit, π, introduces moral hazard, an important friction that contributes to underinvestment in R&D. By making the private benefit contingent on the macro state, financing frictions become correlated with the general economy, thereby introducing systematic risk for the R&D firm through its external financing frictions, even when the scientific risk in R&D is idiosyncratic.

3.3 Analysis

We will analyze the model using backward induction starting with events at $t = 1$, the beginning of the second period.

Suppose investors observe ϕ and that $\eta = 1$. Since the signal to investors is perfect, they will agree to provide ΔI in financing only if $\phi = X$ and not if $\phi = 0$. Knowing this, the firm will seek financing only if it observes that $x = X$ and not if $x = 0$.

Let α_1 be the fraction of equity ownership that must be sold to raise ΔI. Then the competitive capital market financing condition yields

$$\alpha_1 = \frac{\Delta I}{\bar{X}(I + \Delta I, T)} \tag{4}$$

where $\bar{X}(I + \Delta I, T)$ is the after-tax total cash flow, defined as:

$$\bar{X}(I + \Delta I, T) \equiv X[1 - T] + T[I + \Delta I] \tag{5}$$

and $T[I + \Delta I]$ is the corporate tax shield that arises from the fact that the entire R&D investment of $I + \Delta I$ is a tax-deductible expense. Note that when $\eta = 1$, the macroeconomic state, *m*, is irrelevant, since financing is predicated only on the observed value of *x*.[14]

Next, suppose $\eta = 0$; in this case the realization of *m* matters. Suppose *m* = *u*. Then once again the firm (*G* or *B*) seeks financing only if *x* = *X* because, in the absence of any private benefit to running the firm, the manager does not want to raise financing to run the firm and expend a cost *k*. So, with *m* = *u*, investors *know* that the firm is seeking financing because its manager has observed *x* = *X*. Consequently, α_1 in this case is the same as that in (4).

Next, suppose $\eta = 0$ and *m* = *d*. In this case *G* seeks financing only if *x* = *X*, but *B* will seek financing regardless of *x*. Since investors know that $\eta = 0$, they will disregard ϕ—it has no information content. Let $\hat{\alpha}_1$ be the share of equity ownership that the firm must give to investors to raise ΔI. This share will depend on the posterior belief of investors about *x* when the firm seeks financing. Using Bayes' rule, we have

$$\Pr(x = 0 \mid \text{firm wants financing}, m = d, \eta = 0) = \frac{[1 - g][1 - p]}{p + [1 - g][1 - p]} \tag{6}$$

and

$$\Pr(x = X \mid \text{firm wants financing}, m = d, \eta = 0) = \frac{p}{p + [1 - g][1 - p]} \tag{7}$$

Suppose that we impose the following parametric restriction:

[14] Recall that *x* and *m* are independent of each other.

$$\left[\frac{p}{p+[1-g][1-p]}\right]\bar{X}(I+\Delta I,T)<\Delta I \tag{8}$$

Then it will be impossible for the firm to raise ΔI at $t = 1$ when $\eta = 0$ and $m = d$. Essentially, (8) will hold when p is sufficiently low, which corresponds to the low probabilities of success in drug development that we alluded to in the introduction. We have thus shown:

Proposition 1: *When $\eta = 1$, the firm seeks financing ΔI only when $x = X$ and always obtains it regardless of m. When $\eta = 0$ and $m = u$, the firm seeks financing only when $x = X$ and obtains it. When $\eta = 0$ and $m = d$, the firm is unable to raise financing regardless of x.*

Proof: Follows from the discussion preceding the proposition. ■

This proposition shows that even though the scientific risk in drug development is purely idiosyncratic—x is uncorrelated with m—the risk of investing in the firm at $t = 0$ is systematic. This is because the payoff to these investors depends on the probability of continuation financing at $t = 1$, which in turn depends on m. Thus, this proposition provides a way to reconcile the findings in Jørring et. al (forthcoming) and Thakor et. al (2017). The result that R&D-intensive firms have high systematic risk despite the scientific risk in drug development being largely idiosyncratic may seem surprising. However, when one considers the impact of continuation financing risk that is positively correlated with the market, this result becomes intuitive. Of course, as pointed out earlier, the "conversion" of idiosyncratic scientific risk into systematic risk of firms investing in R&D can also be explained based on behavioral aspects. It can also be explained through a real-options lens; as discussed above, the Myers (2015) "R&D leverage" argument can

rationalize why biopharma R&D firms have significant systematic risk, akin to a financial leverage effect.

Also note that Proposition 1 highlights an underinvestment in R&D at $t = 1$ that is caused by informational frictions. When $\eta = 0$ and $m = d$, even firms that privately know that the drug will be successful ($x = X$) are unable to raise financing for it. This not only causes a loss of the pledgeable cash flow, X, but also the knowledge asset, Ω, which reduces social welfare.[15] The probability of encountering this friction is the joint probability of an uninformative signal ($1 - r$) and a down market ($1 - m$), i.e., $[1 - r][1 - m]$. Given the assumed properties of r, this probability can be reduced by increasing disclosure. But the firm faces a tradeoff there in that increasing disclosure may reduce X due to the two-audience signaling problem.

We now turn to what happens at $t = 0$. The firm raises I at $t = 0$ by selling to investors an ownership fraction α_0, where α_0 is determined by the equilibrium pricing condition:

$$\alpha_0\{\Pr(\eta = 1)\Pr(x = X) + \Pr(\eta = 0)[\Pr(m = u)\Pr(x = X)]\}\bar{X}(I + \Delta I, T) = I. \tag{9}$$

Assuming that

$$\{rp + [1 - r]\mu p\}\bar{X}(I + \Delta I, T) > I\,, \tag{10}$$

we can solve for α_0 from (9) as:

$$\alpha_0 = \frac{I}{[rp + [1 - r]\mu p]\bar{X}(I + \Delta I, T)}\,. \tag{11}$$

[15] Implicit in this is the assumption that the knowledge asset created by the firm's R&D may accrue generally to society in addition to its firm-specific benefits. An example is the mRNA COVID-19 vaccines. Given this technology, many firms not involved in the vaccines' development are now developing mRNA-based drugs to treat other diseases.

We also need to ensure that the manager of the *G* firm is willing to raise financing at t = 0.[16] This requires the following parameter restrictions that we will assume hold:

$$\{rp + [1 - r]\mu p\}\{[1 - \alpha_0 - \alpha_1]\bar{X}(I + \Delta I, T) + \Omega - k\} > 0 \tag{12}$$

where α_0 and α_1 are expressed in terms of the exogenous parameters in (11) and (4), respectively.

Note that (12) also guarantees that (10) is satisfied, and that the manager of the *G* firm will be willing to raise financing at t = 1 when $x = X$. Thus, we have shown:

Proposition 2: *The firm will raise financing I for drug development at t = 0, and the cost of this external financing is decreasing in the likelihood of success in drug development (p) and in the expected precision (r) of the signal, ϕ, that investors receive about the drug development outcome.*

Proof: Much of the proof follows from the discussion preceding the proposition. For the remainder, note that using (11) and (12), we know that

$$\frac{\partial \alpha_0}{\partial p} < 0 \tag{13}$$

and

$$\frac{\partial \alpha_0}{\partial r} = \frac{-I\bar{X}(I + \Delta I, T)[1 - \mu]p}{\{[rp + [1 - r]\mu p]\bar{X}(I + \Delta I, T)\}^2} < 0\,. \tag{14}$$

■

Given this result, it is clear that the firm can reduce its cost of financing by increasing disclosure, *d*, that increases *r*. But if we make *X* a function of *d* (the two-

[16] If the participation constraint on the *G* firm is satisfied, so will the participation constraint of the *B* firm.

audience signaling problem), so that $\frac{\partial \bar{X}(I+\Delta I,T,d)}{\partial d} < 0$, then the firm will face a tradeoff that may lead to an interior value of d.

Finally, we turn to debt financing. If the firm borrows at both $t = 0$ and $t = 1$, then it can deduct its debt repayment and realize a tax shield. Let Λ_D be the agency cost of debt.[17] The debt repayment for borrowing ΔI at $t = 1$ will be ΔI since the only states in which the firm is able to borrow are those in which debt is riskless. That is, if D_R^t represents the repayment obligation on debt issued at date t, then $D_R^1 = \Delta I$. Our preceding analysis also makes clear that the debt issued at $t = 0$ will be risky. Thus, $D_R^0 > I$. The terminal after-tax cash flow of the firm at $t = 2$ when $x = X$ will be:

$$X - [X - D_R^0 - D_R^1]T = X[1 - T] + [D_R^0 + D_R^1]T \, . \tag{15}$$

The *incremental* tax shield generated by debt relative to equity, being realized at $t = 2$, is

$$\{[D_R^0 + D_R^1] - [I + \Delta I]\}T = [D_R^0 - I]T \, . \tag{16}$$

Thus, the availability of a tax shield from expensing R&D makes the tax shield advantage of debt financing relative to equity financing smaller for R&D-intensive firms than other firms.

Assuming that continuation debt financing at $t = 1$ will also be available only in the states in which equity financing is available, we see that the *expected* incremental tax shield of debt relative to equity will be

$$\{rp + [1 - r]\mu p\}[D_R^0 - I]T \, . \tag{17}$$

[17] We do not explicitly model it here for simplicity; however, risk-shifting has been modeled extensively in the literature, and there are a variety of ways in the which the model could be altered to generate risk-shifting moral hazard with debt.

Since

$$D_R^0 = \frac{I}{rp + [1-r]up} \tag{18}$$

we can write (17) as:

$$I[1 - rp - [1-r]\mu p]T\,. \tag{19}$$

When the agency cost of debt, Λ_D, exceeds the incremental value of the debt tax shield, the firm will prefer equity. This analysis thus shows that market-based debt financing for debt tax shield benefits will be far less attractive for R&D-intensive firms than other firms, so firms investing in large amount of R&D are likely to prefer equity.

3.4 Summary

The analysis in the previous section highlights the following potential roles that banks and other financial intermediaries can play in financing biomedical innovation:

(1) Providing debt financing with a sufficiently small agency cost of debt (i.e., reducing Λ_D) to make it optimal for the firm to prefer a bank loan over equity financing.

(2) Protecting the confidentiality of the borrower's drug development information to allow r to be raised without lowering X, thereby reducing adverse selection costs.

(3) Providing continuation financing with a higher probability to reduce the likelihood of the borrower losing X and Ω.

In the next section, we discuss each of these possibilities in the context of the financial intermediation literature.

4. Intermediation and Financing Biomedical R&D

We begin by providing stylized evidence regarding the existing amount of funding of biomedical R&D that is provided by intermediaries, in particular VC funds and banks. We then provide a discussion of the relative benefits and costs of intermediary funding, beginning with a brief discussion of VC funding based on the existing literature, and then focusing on bank financing using the theoretical framework of the previous section as a springboard, i.e., we discuss how banks can help reduce underinvestment in R&D via the three channels discussed at the end of the previous section.

4.1 Intermediary Funding of Biomedical R&D

The stylized model of Section 3 highlighted how underinvestment can arise in drug development and proposed several ways that intermediaries can help attenuate this problem. In this section we review the existing evidence for the extent and nature of intermediary financing in biomedical R&D.

Venture Capital

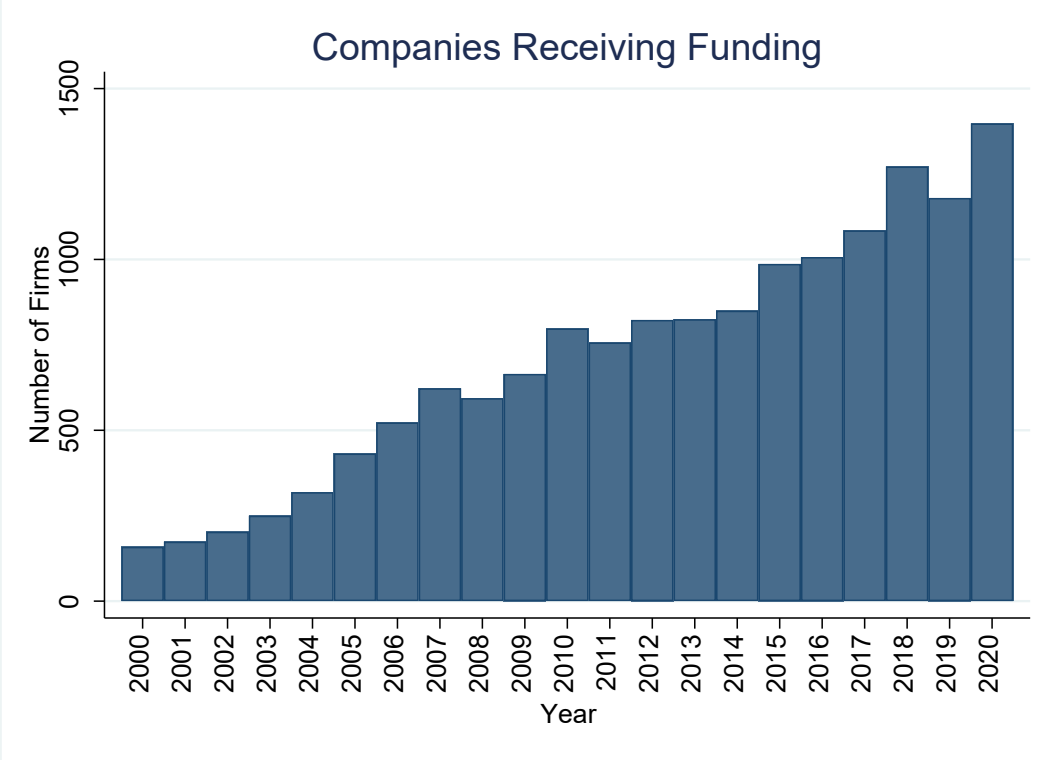
Perhaps the most common source of intermediary funding in the biotech industry comes from VC firms in the form of equity financing. A growing literature has established that VC firms are important funding sources for investment in firms that foster innovation (e.g., Kortum and Lerner (2000)). VC funding is particularly important for earlier-stage biotech firms that may not be able to gain access to broader public financing markets. For example, Liu (2021) provides theory and evidence that VC funding can help to dampen informational frictions that biotech startups face in financial markets. *Figure 4*

provides evidence on biopharma VC funding deals over time, and shows that VC funding has become increasingly prevalent in drug development over time, underscoring their importance in the biomedical ecosystem.

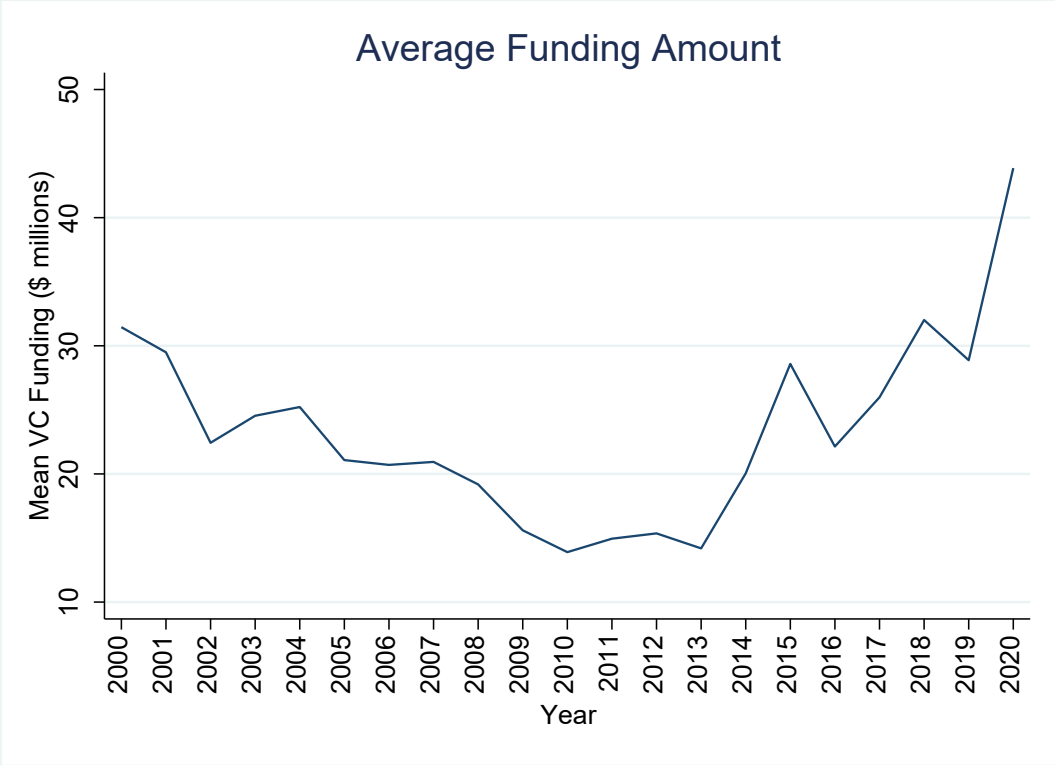
Figure 4: Biopharma VC Financing Deals

Data come from the Preqin database and consist of all funding rounds to firms with a primary industry classification of Pharmaceuticals or Biotechnology. Panel A provides the number of companies in the database that have a VC funding deal in each year. Panel B shows the mean amount of funding (conditional on obtaining VC funding) that a firm in each year obtains from VC firms. Panel C shows the aggregate amount of VC funding received by firms in each year. All dollar amounts are in real (2020) $ millions.

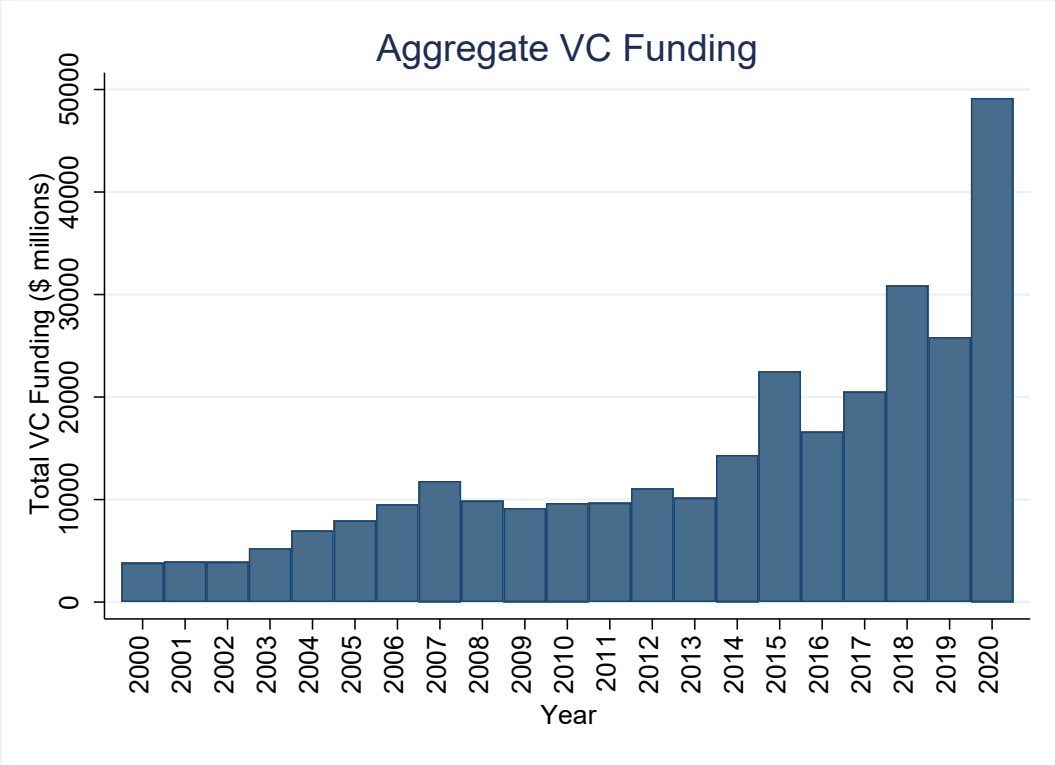
Panel A: Number of Biopharma Companies Receiving VC Funding



Panel B: Average Amount of VC per Funding Round for Biopharma Firms



Panel C: Aggregate Amount of VC Funding for Biopharma Firms



However, VC funding comes with a number of potential disadvantages. As the VC literature has long argued, VC contracts can be subject to hold-up problems and other frictions (e.g., Hellmann (1998), Kaplan and Strömberg (2004), Gompers and Lerner (2001)). This may be exacerbated by the fact that VC funding rounds are typically small relative to the average development cost of a drug (Aghamolla and Thakor (forthcoming)), in addition to the large degree of risk and uncertainty inherent in drug investments. Another example of potential frictions introduced by VC firms is provided by Li et al. (2021a), who show that ownership stakes by venture capitalists across biopharma firms can lead to VCs terminating some drug projects to reduce competition

among firms within its portfolios. The consequences of VC funding for drug development remains a fruitful area for additional research.

Bank Loans

As mentioned in Section 3, banks are another type of financial intermediary that may play a key role in funding drug development, through the provision of debt financing. However, a widely held point of view is that intangibles-heavy firms such as biotech companies do not commonly use debt financing. The previous discussions have highlighted potential impediments to the use of debt financing in biotech, such as risk-shifting moral hazard and the lack of tangible pledgeable assets to use as collateral in secured borrowing.[18] Moreover, because the marginal value of debt tax shields is relatively low due to the tax shield generated by the R&D investment itself, biotech firms would naturally use less debt than other firms.[19] Any other costs associated with debt—i.e. agency costs, financial distress, etc.—will further reduce the usage of debt.

However, *Figure 5* provides time-series evidence of the use of syndicated bank loans to biopharma firms, and demonstrates a substantial amount of bank debt usage: the average loan amount has exceeded $1 billion, and the total aggregate yearly loans has exceeded $150 billion in many of the past few years. However, *Figure 5* also shows that the vast majority of the borrowing is done by pharmaceutical, not biotech, companies,

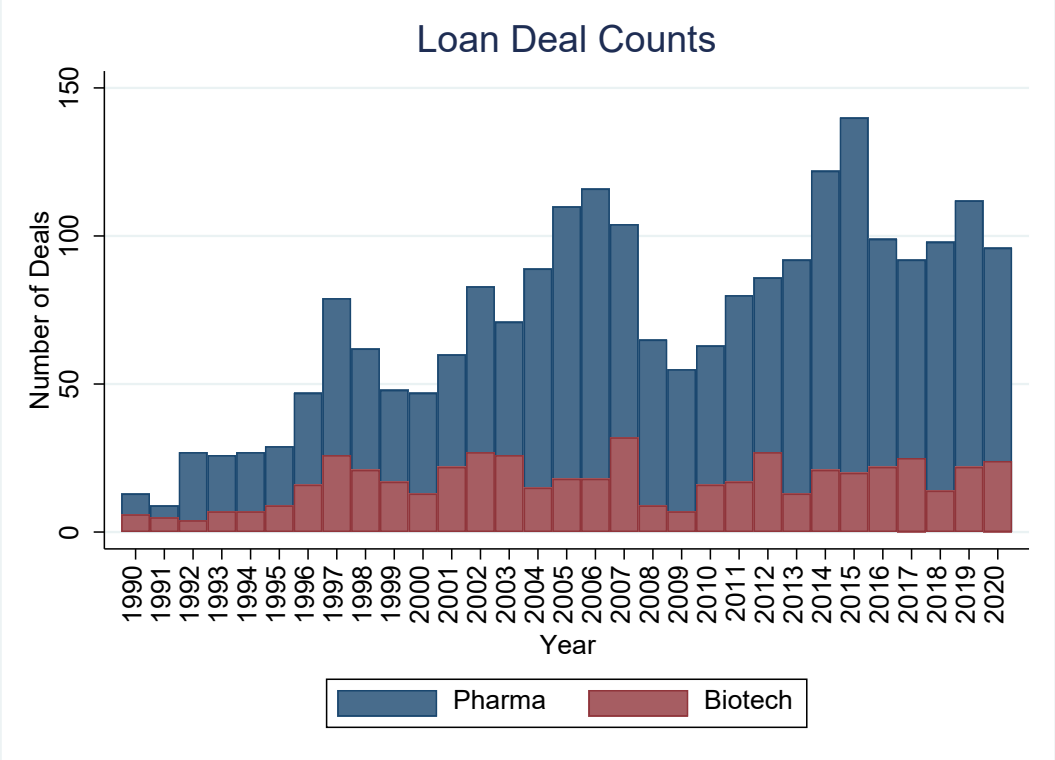
[18] The lack of tangible assets that can be used as collateral may be exacerbated due to the risk of their operations (e.g., Rampini and Viswanathan (2010)). See also Myers and Howe (1997) for a real options-based model in which the large investment costs inherent in drug development push out financial leverage capacity.

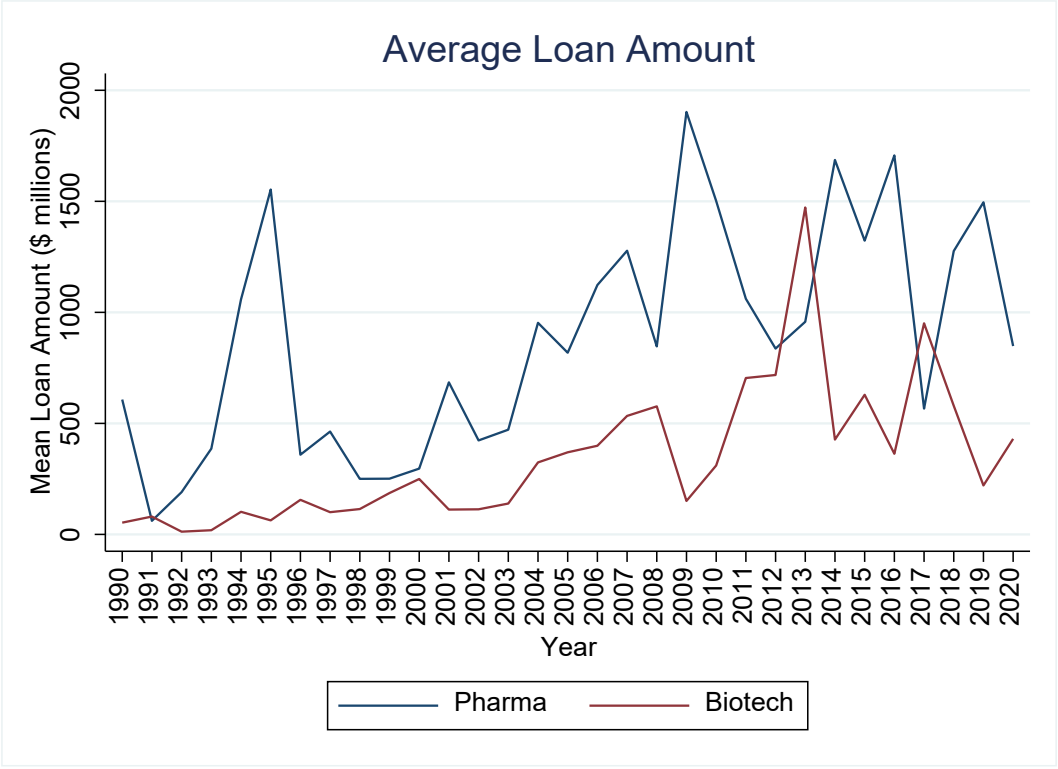
[19] In practice, the marginal benefit of the debt tax shield even for other firms seems to be low. Survey evidence (i.e. Graham and Harvey (2001)) has shown that managers view the debt tax shield to not be of first-order importance in terms of their capital structure decisions.

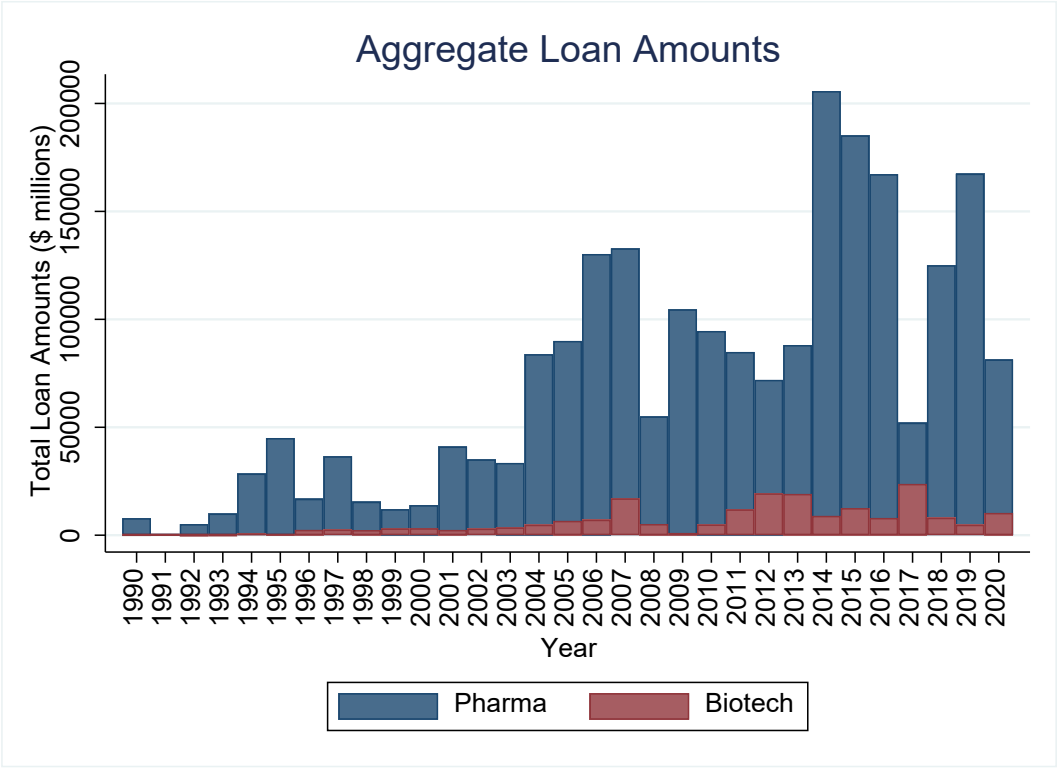
presumably because most biotech companies have negative cash flows and cannot support debt as easily whereas pharma companies are often profitable and can service significant amounts of debt through earnings and cash reserves. Deshpande and Nagendra (2017) and Mann (2018) also observe that biopharma companies can sometimes use patents as collateral, enabling them to take on debt.

Figure 5: Biopharma Bank Loan Financing Deals

Data consist of new syndicated loan deals from the Dealscan database, for pharma and biotech firms. Pharma and biotech firms are identified by SIC and NAICS codes following Thakor et al. (2017). All dollar amounts in real (2020) $ millions.







4.2 How Banks Can Facilitate Drug Development

Broadly speaking, the evidence shows that biopharma firms do utilize substantial debt. We now discuss the benefits that biopharma firms can reap from bank financing, and the potential roles that banks can play in further support of drug development.

Reducing the Agency Costs of Debt

The previous discussion has stressed the potential impediments to biopharma debt financing, such as risk-shifting moral hazard and the lack of tangible pledgeable assets to use as collateral in secured borrowing. These two are related, of course, since lenders use collateral as a way to reduce both adverse selection and moral hazard.[20] Banks may be able to overcome these impediments due to their unique capabilities.

Banks are experts in screening and reducing ex ante adverse selection. This role of financial intermediaries in general, and banks in particular, has been highlighted in numerous papers (e.g., Coval and Thakor (2005), Millon and Thakor (1985), and Ramakrishnan and Thakor (1984)). Reduced adverse selection can make debt financing cheaper for creditworthy firms, and a lower cost of debt can directly reduce risk-shifting moral hazard even without bank monitoring.

In addition, banks can also monitor their borrowers. Such monitoring has been viewed as an important function of banks in numerous studies (e.g., Diamond (1984), Holmstrom and Tirole (1997), Mehran and Thakor (2011), and Rajan and Winton (1995)). For example, bank monitoring in the Holmstrom and Tirole (1997) model has the effect

[20] See Besanko and Thakor (1987a,b), Chan and Thakor (1987), Boot and Thakor (1994), and Rajan and Winton (1995).

of limiting the borrower's ability to invest in a private benefit project to the bank's detriment, and thereby expands the borrower's debt capacity not only directly through bank borrowing, but also through other sources. That is, assured by the effect of the bank's monitoring, other lenders—including capital market investors—provide more debt financing. Rajan and Winton (1995) develop a theory in which collateral incentivizes the bank to monitor borrowers.

A third channel through which banks can reduce moral hazard as well as the reliance on collateral to do so is via *relationship banking*, which relies on long-term relationships (e.g., Rajan (1992), Boot (2000), and Boot and Thakor (2000)). While Rajan (1992) underscores the "dark side" of relationship lending—the lender's ability to "hold up" the borrower, due to the lender's access to proprietary information about the borrower generated during the relationship—Boot and Thakor (2000) focus on the way in which banks can add value to their borrowers through relationship lending. See Boot (2000) for a review. Recent empirical evidence illuminates the way in which relationship lending benefits the bank's borrowers. Banerjee, Gambacorta, and Selte (2021) document that, following Lehman's default, Italian banks offered more favorable continuation lending terms to firms with which they had stronger relationships.[21] Norden, Mesquita, and Wang (2021) find that the Covid-19 pandemic had a significantly negative impact on local credit, but Berger et. al (2022) document that while relationship borrowers received worse contract terms than others in the early stage of the pandemic, they received much

[21] This is consistent with the theory in Bolton et. al (2016) in which banks may insulate relationship borrowers from crises by offering relatively light loan terms during the crisis, but relatively tough terms during normal times.

better treatment during the subsequent recovery. They also report evidence of cross-sectional subsidization among relationship borrowers.

Of particular interest in the drug development context is the theoretical analysis in Boot and Thakor (1994), which shows that with optimal long-term (relational) contracting, a bank starts out providing secured loans to the borrower, but once the borrower establishes a good track record of repayment, the bank switches to unsecured lending at a low interest rate without triggering moral hazard. This result highlights two important aspects of relationship lending. First, banks can resolve moral hazard through optimal long-term contracting in the context of a lending relationship without having to rely on explicit (and directly intrusive) monitoring. Second, this contracting helps to reduce reliance on collateral—the borrower only needs to post it in the early stages of the relationship. Thus, the benefits of the relationship grow over time, consistent with the evidence in Lopez-Espinosa et al. (2017). This relationship may permit a biopharma firm to take on a loan when it otherwise may not have been able to do so. For example, a young biotech firm may be able to use its patents as collateral (e.g., Deshpande and Nagendra (2017) and Mann (2018)) in the early stages of its relationship with the bank,[22] and then enter into a long-term contract with the bank that aligns with the typically long development cycle of the drug.

One might ask: if banks can do this, why can't other lenders? While other lenders may be able to do so, there are two special characteristics about banks that give them a

[22] Collateral can help attenuate both moral hazard and private information problems that may be acute with such firms. See, for example, Chan and Thakor (1987).

comparative advantage in facilitating long-term relationships. First, they finance themselves with (insured) deposits, which represent a "stickier" and hence more stable source of funding than market-based financing, facilitating the bank's ability to make long-term lending commitments (see, for example, Song and Thakor (2007) and Kashyap et al. (2002)). Second, there is empirical evidence that banks are more efficient users of collateral in loan contracts than non-bank lenders. Cerqueiro et al. (2020) use Swedish data to document when collateral rights are redistributed *away* from banks to other creditors, the amount and maturity of corporate debt shrink, while investment and growth slows down.

Thus, there are numerous ways in which greater involvement by banks in funding biopharma firms can decrease moral hazard and increase the use of bank debt in these firms.

Protecting Proprietary Information

The result that greater information disclosure can lower the firm's cost of external financing has been well-established both empirically and theoretically. For example, Klein et al. (2021) provide recent evidence that transparency is valuable for investors in securitization in that it reduces agency problems. However, as discussed earlier, biopharma firms face a two-audience signaling problem. Bhattacharya and Ritter (1983) pointed out that any information disclosure to investors is also conveyed to the firm's

competitors, who can act as free riders on that information for their own drug development decisions.[23]

A number of recent studies have used project-level drug development data to provide evidence of these informational effects, establishing that a firm's competitors learn from the firm's development outcomes. Krieger (2021) shows how news about a firm's trial failures can alter the investments of a firm's competitors when they obtain such information. Krieger et al. (2022) show a similar effect via safety warnings on approved marketed products; when a firm experiences a negative shock to an existing product, it affects the R&D investment decisions of competitors in the same therapeutic area. Such effects have also been demonstrated through the mandated disclosure of clinical trial outcomes. Aghamolla and Thakor (forthcoming) examine how disclosure requirements affect the propensity of private firms to undertake an IPO, and the subsequent effect on clinical trial decisions. Using the Food and Drug Administration Amendments Act (FDAAA) of 2007 as an exogenous shock to disclosure requirements, following which all biopharma firms were mandated to publicly post clinical trial registrations and summary results for phase 2 and later trials, Aghamolla and Thakor (forthcoming) show that private biopharma firms were significantly more likely to tap public equity markets following the increase in disclosure requirements. This is consistent with a decline in the marginal cost of disclosure through IPOs, since firms already had to disclose more information. They also show that disclosure-induced IPOs

[23] See also Kamien and Schwartz (1978), Bhattacharya and Chiesa (1995), and Gertner et al. (1988).

lead to a change in clinical trial decisions—biopharma firms reduced the size of their drug portfolios, shifting to safer investment sources via acquisitions. Hsu et al. (2021) also use the FDAAA as a shock to disclosure requirements and show that peer firms learn from the disclosed information through increased trial suspensions.

The effect of information disclosure is exacerbated by the fact that R&D competition (before a drug is approved) and product market competition (after a drug's exclusivity period has expired) are both intense for biopharma firms. A variety of studies have used project-level clinical trial data to demonstrate competitive effects in the industry. See, for example, Branstetter et al. (2014, 2016), Aghamolla and Thakor (2022), Garfinkel and Hammoudeh (2021), Li et al. (2021b), and Thakor and Lo (2022).

Given the chilling effect of information disclosure on biopharma firms, banks have the potential to help. Bhattacharya and Chiesa (1995) and Yosha (1995) have developed models in which borrowers sometimes prefer to use banks rather than the capital market even though capital market financing is cheaper. The reason is that instead of having to abide by the information disclosure rules of the market and publicly disclose valuable proprietary information, these firms can simply reveal the information privately to their banks, and trust these banks to not reveal it to the firm's competitors.[24] Thus, biopharma firms can "have their cake and eat it too" by enjoying the benefits of disclosure—disclosing the relevant information to the bank helps lower the cost of financing—but in

[24] Dang et al. (2017) provide a different explanation for banks to be "secret keepers," based on the idea that *not* revealing interim information about asset values can improve intergenerational risk sharing among depositors.

such a way that the firm does not lower its cash flows by revealing the information to its competitors.

Providing Continuation Financing

An important strand of the banking literature focuses on the role of loan commitments—agreements by a bank to lend a firm a specified sum of money—and highlights how they can help reduce moral hazard. For example, Boot et al. (1987) develop a model in which the bank provides a sufficient subsidy on the loan interest rate itself that it eliminates (effort-aversion) moral hazard on the part of the borrower. To make up for the expected loss in lending, the bank charges an up-front commitment fee to the borrower. This fee is a sunk cost by the time the borrower takes a loan under the commitment, and thus has no impact on the provision of effort by the borrower. Thus, Boot et al. (1987) provide a microfoundation for the use of loan commitments. Kashyap et al. (2002) explain why most loan commitments are made by *banks*. Their explanation is that keeping on-balance-sheet liquidity is costly, but a deposit-funded bank has to maintain a minimum amount to meet deposit withdrawals. Thus, it is economical for such a bank to also make loan commitments, since these require the bank to keep liquidity as well to satisfy takedowns under commitments.

Subsequent loan commitment studies have focused on the idea that bank loan commitments can provide insurance against future credit rationing (Thakor (2005)). This suggests that borrowers with loan commitments as well as those with long-term relationships should be better positioned to obtain continuation financing from banks

than from other sources. Supporting empirical evidence is provided by Banerjee et al. (2021).[25]

In the context of our model, this means that biopharma firms engaged in borrowing from relationship banks through loan commitments can anticipate a higher probability of being able to obtain continuation financing at $t = 1$, and thus a lower likelihood of losing X and Ω. The ability of the bank to obtain proprietary information about the borrower after making the loan commitment can also be valuable, since it can enable the bank to invoke the Material Adverse Change (MAC) clause if it suspects that a B borrower is attempting to take down the commitment when $m = d$ and the firm has observed $x = 0$. This can further improve the terms of the loan commitment contract and enhance the probability of the firm obtaining continuation financing at $t = 1$. Boot et al. (1993) provide a theory of bank loan commitments in which the commitment attenuates borrower moral hazard but has an escape clause for the bank like the MAC clause.

Thus, bank financing via loan commitments can help to mitigate an important risk faced by biopharma firms, the inability to secure financing to continue clinical trials to bring a drug to fruition. While the risk of limited future funding has been argued for innovation investments in general (e.g., Nanda and Rhodes-Kropf (2016)), this risk is particularly pressing for drug development firms due to the structure of clinical trials. For example, if a biopharma firm pauses clinical trials in the middle of a phase of testing due to lack of funding, any results that it has garnered from the incomplete trial may be

[25] Bord et al. (2021) provide evidence that when bank lending drops (say, due to negative capital shocks), the net effect on the supply of credit to small firms is negative, and that this has real effects.

rendered invalid by the FDA. Myers and Howe (1997) coined the term "R&D leverage" to refer to the need for biopharma firms to secure continuation financing for future investments in clinical trials for a drug in order to bring it to approval. This R&D leverage effect is further amplified by the fact that investments are risky and costly. In line with this insight, although the medical risk of drug development is idiosyncratic (see Jørring et. al (forthcoming) for empirical evidence), biopharma firms—especially biotech firms—have high degrees of systematic risk. For example, over various samples, Myers and Shyam-Sunder (1996), Myers and Howe (1997), DiMasi et al. (2003), and Thakor et. al (2017) show that biopharma firms have high betas, which is consistent with their need for continuation financing and thus dependence on financial markets. Mace (2020) uses project-level data to show that drug projects are more likely to be discontinued during market downturns.

The incremental value that bank financing can provide is likely to be higher for biotech firms than pharma firms for two reasons. First, biotech firms are smaller and more opaque. Thus, the role of banks as screening specialists and monitors is more valuable for these firms. Second, pharma firms have more well-developed product pipelines and higher profitability (e.g., Thakor et. al (2017)), so they have greater access to non-bank sources of finance.

In summary, the long-term outlook for greater bank involvement in providing drug development funding remains an intriguing question that bears further research.

4.3 Impediments to Bank Financing

Despite the advantages highlighted in the previous sections about the advantages that banks can bring in financing drug development, there are several potential impediments.

Bank Regulation

One such impediment comes from regulation. Banks are subject to risk-based capital requirements, and some are also subject to regulatory stress tests. Thus, banks with riskier assets need to keep more equity capital (e.g., Ahnert et al. (2021)). Stress tests may also result in some banks being required to keep more liquid assets on their books.[26] Banks view equity capital as significantly more costly than deposits, and are thus averse to keeping more of it on their books.[27]

One implication of this aversion is that when banks are required by regulators to increase their capital ratios, they may react by reducing lending rather than raising more equity. For example, Doerr (2021) provides evidence that regulatory stress tests—after which banks are inclined to improve their capital adequacy ratios—result in reduced lending, particularly to riskier businesses (e.g., Acharya et. al (2018), Cortes et. al (2020), Doerr (2021)). Aghamolla et. al (2021) provide evidence of these effects in a healthcare context via hospitals. Additional research is needed to show the extent to which these effects impact the drug development process.

[26] There is an ongoing debate on whether such liquidity requirements are welfare enhancing. Many papers have argued that they are not, e.g., Kahn and Wagner (2021), and Thakor (2014, 2018).
[27] See Thakor (2014) for an extensive discussion of this issue. This reluctance exists despite the benefits of capital during crises (see, for example, Berger and Bouwman (2013)).

As indicated earlier, investments in biopharma firms, especially in early-stage biotech firms, seem very risky to financiers. So whether it is stress tests or the risk-weighting of bank assets that are used to determine capital requirements, there are non-trivial challenges to a greater flow of credit from banks into these firms. However, the scientific risk in drug development R&D is largely idiosyncratic (see Jørring et. al (forthcoming)). Thus, if a bank could make loans to a large number of biopharma firms and is willing to provide loan commitments that assure these firms of access to continuation financing even in economic downturns—thereby reducing financing-driven systematic risk—much of the bank's risk would be diversifiable.

Achieving this diversification is likely to be easier for larger banks because they have the capital to write many more loans to biopharma firms than smaller banks. But even for the largest banks, a change in the regulatory approach for assessing the riskiness of loans to biopharma companies will be needed. For example, the risk weights on these loans will need to be lower as the bank's lending to this sector becomes more diversified, i.e., as it makes more loans to biopharma firms. Usually, regulators would view this as greater *concentration risk*, but the idiosyncratic nature of the scientific risk in biopharma R&D turns this reasoning on its head.

Stress tests may be a solution. Bank examiners would need to be educated on the idiosyncratic nature of the risk in biopharma R&D, and take this into account in their bank examination reports. This would also require consistency across regulators when

assessing bank risk.[28] This need could be met by the emergence of biomedical analytics companies that have the expertise to assess such risks, much like the debt rating agencies that emerged organically to meet the risk assessment needs of both borrowers and lenders in corporate debt markets.

Risk Attitudes of Banks and Investors

The risk attitudes of bank CEOs and the relative lack of familiarity of bank investors with biomedical assets—especially those holding bank equity and subordinated debt—may also play a role in inhibiting greater bank funding of biopharma. The fact that drug development R&D is highly risky from a scientific perspective, and also requires substantial technical expertise to understand, may contribute to this challenge.

Goel and Thakor (2008) develop a model that shows overconfident managers are more likely than rational managers to become CEOs when an (implicit) intrafirm tournament among managers determines who rises to the top. Hagendorff et al. (2021) provide evidence that the personal attributes of bank CEOs affect bank risk taking. Thus, if bank CEOs are somewhat unfamiliar with the nature of the risks involved with investing in biopharma firms (due to the technical nature of these investments), they may shy away from it due to high perceived risk.[29]

[28] Agarwal et al. (2014) document that bank regulators implement identical rules inconsistently due in part to differences in incentives and that this can adversely affect the effectiveness of regulation.
[29] For example, hedge funds that seek to invest in the biopharma sector often hire chemistry PhDs to better understand the prospects of the drug candidates developed by the firms they are investing in.

Similarly, bank investors may also be unfamiliar with the risks, which may cause them to disagree with the bank's decision to invest more in this sector. The bank's CEO may be sensitive to this potential disagreement over strategy with major investors, since there is evidence that it may increase the likelihood of the CEO being replaced.[30]

Thus, impediments to greater bank lending to biopharma firms are not limited to regulators. Solutions for overcoming these impediments must also address these factors. We turn to this issue in the next section.

5. Potential Solutions

Any solution to the problems of bank lending to biopharma firms must address the issue of how the risk perceived by banks as well as their regulators can be reduced, as the preceding discussion highlights. There are two fundamental risk reduction approaches that we consider here. The first involves security design, and the other is regulatory assistance.

5.1 Security Design

Jørring et al. (forthcoming) propose the idea of "FDA Hedges," insurance contracts that pay off upon the failure of individual drug projects during the FDA approval process, not unlike a credit default swap. Jørring et al. (forthcoming) develop a theoretical model to highlight the informational frictions that allow these contracts to reduce underinvestment in R&D and enhance welfare. They also provide evidence that these

[30] Huang et al. (2020) provide empirical evidence that manager-shareholder disagreement can lead to a higher probability of the CEO being fired, even controlling for firm performance.

contracts have little systematic risk, so if they are freely traded on exchanges, investors would not demand a systematic risk premium, making their pricing attractive to a wide spectrum of investors. They also provide a discussion of the feasibility of introducing these contracts. If biopharma firms were to purchase FDA hedges, an important source of risk in the drug development process would be eliminated. Consequently, banks would also perceive less risk in lending to these firms. Alternatively, banks could serve as *intermediaries* in the issuance of such contracts to investors. Along similar lines, Thakor and Lo (2021) take a mechanism design approach to derive the optimal set of securities to fund biopharma R&D and reduce underinvestment. This solution is similar in spirit to FDA hedges; Thakor and Lo (2021) show how financial intermediaries such as banks can serve an important coordination role between biopharma firms and investors.

A variety of other financial innovations have been proposed in the context of biopharma to reduce underinvestment in which banks can play a role; see Lo and Thakor (2021) and Lo (2021) for surveys. Fernandez et al. (2012) first proposed the idea of a "megafund" which pools together a number of different biomedical projects into a single financial vehicle. The idea relies on basic portfolio theory and the notion of diversification, that some of the individual risks associated with drug projects will cancel each other out, reducing the overall risk of the fund. This in turn will provide a more attractive risk/return profile to investors, thus allowing additional funds to flow to the investments. Such a vehicle can also engage in securitization, which creates a role for banks as underwriters.

The megafund concept has been extended and refined in several ways, including: the incorporation of government guarantees (Fagnan et al., 2013); the use of dynamic leverage as a function of the clinical phases of portfolio assets (Montazerhodjat, Frishkopf, and Lo, 2016); applications to disease-specific portfolios of drug targets such as pediatric cancer (Das et al., 2018), ovarian cancer (Chaudhuri et al., 2019), brain cancer (Siah et al., 2021a), rare diseases (Fagnan et al., 2014, 2015; Kim and Lo, 2016; Das, Huang, and Lo, 2019), and vaccines (Vu et al. 2022); correlated portfolio constituents (Lo and Siah, 2021); collaboration with patient advocacy groups (Kim and Lo, 2019) and venture philanthropists (Alvarez and Lo, 2022); and the estimation of probabilities of success of clinical trial outcomes, which serve as key inputs to the securitization and portfolio management process (Wong, Siah, and Lo, 2019a,b; Lo, Siah, and Wong, 2020; Siah, et al. 2019, 2020, 2021b).

5.2 Regulatory Assistance

Such innovations in security design can be complemented by government assistance. For example, in the 1930s, home mortgage lending was considered very risky, and the perception among investors and policy makers was that depository institutions were lending too little for home buying. The ultimate solution was the introduction of mortgage securitization and the establishment of Fannie Mae to facilitate the securitization of home mortgages. This opened the spigot for the flow of bank (and S&L) credit into home mortgages. Similar examples exist in other sectors. For example, the

Farm Credit System (FCS) was set up to facilitate the flow of credit into farming because it was perceived that traditional banking would underinvest in this sector.[31]

Something similar could be put into place for the biopharma sector, with government potentially solving a coordination problem among banks. For example, Thakor and Lo (2021) note that the government could serve as an intermediary in mechanism design between investors and biopharma firms. Alternatively, the government could create an agency that acquires biopharma loans, then securitizes them, allowing banks to buy securitized claims against a large and diversified pool of biopharma loans. Each bank could avail itself of diversification far beyond what it could do on its own, and take maximum advantage of the idiosyncratic nature of R&D risks in drug development.

5.3 Practical Considerations

Given the rather obvious benefits of applying the tools of financial intermediation of Sections 5.1–5.2 to biomedical assets, a natural question is: why these tools have not already been applied more widely? There are several possible answers to this question.

The most facile explanation is, of course, behavioral: the industry has not traditionally financed its operations through these channels, hence cultural inertia has prevented biopharma companies from pursuing such funding sources. As with many

[31] Bergman et al. (2020) examine how farmers react to liquidity shocks when they face financial constraints. The FCS was introduced in response to the difficulties faced by farmers due to these constraints induced by the farm debt crisis of the 1980s.

behavioral arguments, this is not entirely satisfying—even if true—because cultural inertia should give way to new practices that yield significant financial gains.

Another possibility is the fact that the biopharma industry does recognize the value of these ideas, but neither the demand for nor the supply of sophisticated forms of financial intermediation has reached a sufficient level to warrant widespread adoption in the industry until now. It is easy to forget that the complete sequencing of the human genome—a central pillar of biomedical innovation and the basis of today's most innovative therapeutics—was achieved in 2003, less than two decades ago. Since then, the number of biotech startups has exploded and the impact on therapeutic development has been transformational, as underscored by the trends depicted in *Figures 1* and *4*. Given the rapid pace of biomedical innovation during that time, the need for financial intermediation has grown considerably.

Another factor is the lack of reliable quantitative models for measuring the risk exposures of biomedical assets and the corresponding financial risks contained in structured products based on such assets. For example, one of the key drivers of the growth in mortgage-backed securities in the 1990s was the development of mortgage prepayment models and the application of Gaussian copula models to estimate default probabilities of these instruments (Salmon, 2009). Such models have only recently been developed (see Section 5.1) and, as with any novel technology, will take some time before it becomes accepted and widely used.

However, there are signs that both the biopharma and financial industries are poised to apply these quantitative models to securitizing biomedical assets in the near

future. The benefits of a portfolio approach to drug development have now been demonstrated by two biotech companies—BridgeBio Pharma and Roivant Sciences—and both companies have made use of private debt issues to move their drug development programs forward. These examples, and the need for alternate sources of funding, have become particularly compelling in the wake of the biotech crash of 2021 and the capital flight out of the sector. As we write this review, the financial industry—including investment banks, rating agencies, and other intermediaries—is preparing to take on this funding challenge.

6. Intermediaries and Healthcare Delivery

Our discussion thus far has focused on the role of intermediaries in the healthcare *development* process, i.e., the R&D of new drugs and therapies by biopharma firms. However, at the other end of the healthcare spectrum is healthcare *delivery*, the provision of healthcare to patients by doctors, hospitals, and clinics. Financial intermediaries such as health insurance companies already play an important role in giving patients access to healthcare, and an emerging literature has sought to document how these intermediaries and healthcare delivery interact.

6.1 Patients and Health Insurance

Patients in the U.S. face medical costs that are lumpy, large, and often unexpected, and thus need to insure against these risks (see Gruber (2022) for a review). While health insurance markets are heavily regulated in the U.S. and other countries, insurance

companies exercise discretion over the features of the insurance products offered to consumers, including deductibles and the extent of coverage. [32] Since insurers also need financing, this opens the possibility that the financial characteristics of insurance companies influence the products they offer to patients, thus influencing patient health. For example, a negative financial shock to an insurance company may result in higher premiums for certain consumers, causing them to switch to plans with less comprehensive coverage and negatively impacting health outcomes. Evidence of the link between the financial incentives of insurance companies and consumer health remains an open research question with potentially important consequences.

6.2 Buying Cures vs. Renting Health

One other aspect of medical cost that involves financial intermediation is the affordability of transformative but expensive one-time treatments such as gene and cellular therapies. One example is the Novartis drug Zolgensma, a gene therapy—a one-time cure that provide a lifetime of health—that commands a $2.1 million price tag. Wong et al. (2021) estimate that, between January 2020 and December 2034, total cumulative spending on these therapies could be as high as $306 billion. The only way the healthcare system can afford such costs is via financial intermediation. In particular, Montazerhodjat, Weinstock, and Lo (2016) propose the creation of "drug mortgages," which are amortized payment plans allowing health insurers to spread payments over a

[32] Several studies have also shown that the cost of this insurance has important financial implications for households. For example, Gallagher, Gopalan, and Grinstein-Weiss (2019) show that subsidized healthcare eligibility (via Medicaid) reduces the home payment delinquency rate as a result of lower out-of-pocket medical expenditures.

period of years. These drug mortgages can then be pooled and securitized in much the same way that home mortgages are treated, bringing much larger amounts of capital into this sector to fund these life-saving therapies.

6.3 Healthcare Provision, Banks and Private Equity

Healthcare *providers*—doctors, hospitals, clinics, etc.—also interact with financial intermediaries in a variety of ways, with important consequences for health outcomes.[33] Banks are an important financial intermediary that provide funding to healthcare providers—for example, Aghamolla et. al (2021) show that 93% of hospitals in their sample use leverage, and bank loans comprise roughly 34% of total hospital assets. However, Aghamolla et. al (2021) show that, given the reliance on bank loans by hospitals, negative credit supply shocks can be transmitted through banks and have deleterious effects. More specifically, Aghamolla et. al (2021) show that after the relationship banks of hospitals experience regulatory stress tests, they increase the cost of credit that hospitals—which are risky borrowers—face. In response, hospitals try to cover the increased credit expense by increasing the number of patients they admit, but this increase in revenues comes at the expense of quality of care as measured by several subjective and objective measures (e.g., patient satisfaction, readmission rates, mortality). These results show that banks play a critical role in funding healthcare providers, and that financial-sector shocks can easily spill over into the health sector. In a developing market context, Cramer (2022) provides evidence that an Indian regulatory reform that

[33] Recent papers have shown how hospitals respond to shocks to their financial investments, resulting in shifts in treatment; see Adelino et al. (2015), Adelino, Lewellen, and McCartney (forthcoming).

expanded banking access to previously unbanked areas subsequently led to better health outcomes, due to households gaining access to health insurance through banks and providers gaining access to credit. Additional research is needed to refine our understanding of the dependencies between banks and healthcare providers.[34]

Another type of financial intermediary that interacts with healthcare providers is a PE firm. In recent years, PE acquisitions of healthcare providers have increased, and it is unknown whether this trend is beneficial for or harmful to the health of patients served by these providers. While PE firm ownership may improve the financial health of providers, it may come at the expense of quality of care. A number of recent studies in both the healthcare and finance literatures have attempted to explore the effects of PE acquisition on hospitals (see, e.g., Bruch et al. (2020b), Offodile et. al (2021), Gao et al. (2021), and Liu (2021)). Overall, these studies conclude that an acquisition by a PE firm results in higher revenue and operating profit, but *not* at the expense of quality of care—in fact, there is some evidence of an *improvement* in care quality. The endogeneity of the decision of a PE firm to target a hospital may contribute to the lack of conclusive evidence regarding the effects on care quality. Some studies have made progress in controlling for this potential bias; for example, Liu (2021) exploits changes to state-level regulation as

[34] Recent studies have also provided evidence of the effect of population health on banking outcomes, opening the possibility of the reverse direction of causality. For example, Doerr, Kabas, and Ongena (2022) provide evidence that as populations age, banks experience increased deposit inflows due to the propensity of seniors to save, resulting in greater credit supply but a relaxation of lending standards. Li and Ye (2022) show that worsening population health—instrumented through the propagation of the opioid epidemic—results in reduced deposit growth and credit.

shocks to PE firm entry to establish causality. More research using additional empirical strategies are needed to fully establish the effects of PE ownership on hospitals.

The impact of PE ownership has also been explored in the context of other healthcare providers. Bruch et. al (2020a) provide evidence of a growing number of acquisitions of women's health clinics by PE firms. Gupta et. al (2021) examine PE investments in nursing homes and employ a variety of empirical strategies to deal with endogeneity concerns. They find that PE firm ownership leads to a significant *decline* in patient health—mortality increases and other measures of patient wellbeing decline. They attribute this effect to decreases in staffing and a shift in operational expenditures away from patient care. One reason for the difference in documented patient outcomes after PE acquisition between hospitals and nursing homes may be due to the type of insurer involved (Liu (2021)). Nursing homes primarily serve Medicare patients, which may necessitate greater cost cutting by PE firms to boost revenues. In contrast, PE firms are able to boost revenues in hospitals by renegotiating prices with private insurers (Liu (2021)).

These examples clearly highlight the fact that the relationship between financial intermediaries and healthcare provision is an area ripe for future research.

7. Conclusion

The intersection of biomedical financing and financial intermediation is an area with enormous social welfare ramifications as well as fascinating open research questions. Intermediaries such as VC/PE firms and banks currently play an important

role in funding drug development and healthcare delivery, and may in the future play an increasing role in helping biopharma firms reduce underinvestment in medical R&D. However, there are regulatory and structural impediments that will need to be overcome for this to happen. We have provided a discussion of some of these impediments, with some initial—and somewhat speculative—thoughts on potential solutions for overcoming them. Our hope is to have lowered the cost and increased the reward for our colleagues to contribute to this growing literature.

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